Anatomy and Physiology of Domestic Animals

6 Bones and skeletal system

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Bones

Introduction

Osteology is the study of bones. The skeleton provides the basic scaffolding for the body. The skeletal system includes the bones, and the cartilage, ligaments, and connective tissues that hold everything together.

Markings on Bones Skeleton **Skeletal Cartilage** Skeleton Classification Axial Skeleton The Skull The Vertebral Column Appendicular Skeleton Thoracic Limb Pelvic Limb Avian Skeleton loints Types of Joints Synovial Joints Specific Joints Intervertebral Articulations Thoracic Limb Pelvis Pelvic Limb

Classification of bones

The human skeleton contains 206 major bones whereas the number of bones in different animals varies. The bones can be classified into five categories including long bones, short bones, flat bones, irregular bones, and sesamoid bones (Fig. 6.1).

• Long bones. These are bones that are longer than they are wide. Some of the bones of the limbs are

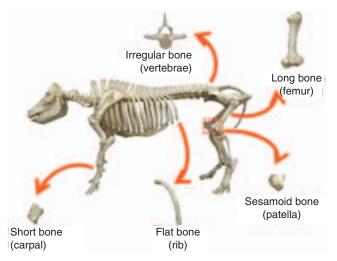


Fig. 6.1. Types of bones. Examples of the various types of bones as found in the pig skeleton.

long bones. Long bones are characterized by an elongated shaft and somewhat enlarged extremities that bear articular surfaces. Examples of long bones include the humerus, radius, femur, tibia, metacarpals, and metatarsals.

- Short bones. Short bones are generally cubeshaped, and examples include the carpal and tarsal bones.
- Flat bones. Flat bones, as the name implies, are thin and flattened. They include two plates of compact bone separated by cancellous or spongy bone. Examples include the sternum, ribs, scapula, and certain skull bones.
- Irregular bones. These are complex and irregularly shaped bones. Examples include the vertebrae and certain facial bones.
- Sesamoid bones. Sesamoid bones are small bones embedded in a tendon and resemble the shape of a sesame seed. Examples include the patella, and proximal and distal sesamoid bones of the digits.

Bone structure

Gross anatomy

Each bone consists of compact bone and cancellous bone. Compact bone, also called dense or cortical bone, is a term describing solid-looking bone. Compact bone is found on the surface of bones forming a protective outer coating; cancellous bone is found on the interior.

Cancellous bone, also called spongy bone, consists of a network of pieces of bone called trabeculae or spicules, interspersed with spaces filled with red or yellow bone marrow. Spongy bone predominates in short, flat, and irregular bones, as well as in the epiphyses of long bones. It is also found as a narrow lining of the medullary cavity of the diaphysis of long bones. The epiphyses consist mostly of cancellous bone with a thin outer coat of compact bone.

In developing long bones, the shaft is called the diaphysis and each extremity is called an epiphysis (pl. = epiphyses) (Fig. 6.2). The epiphysis consists mostly of cancellous bone with a thin outer coat of compact bone. It is generally enlarged relative to the diaphysis. The metaphysis is the joining point of the diaphysis and epiphysis. Between the diaphysis and epiphysis of growing bones is a flat plate of hyaline cartilage called the epiphyseal plate. After growth is complete, the plate is replaced by the epiphyseal line. The medullary cavity (medulla, "innermost part") is the space in the diaphysis containing bone marrow. At the joint surface on the bone is an articular surface consisting of a smooth layer of hyaline cartilage that covers the epiphysis where one bone forms a joint with another bone.

The fibrous covering surrounding that part of the bone not covered with articular cartilage is called the periosteum. It consists of dense irregular connective tissue. Its innermost layer consists of an osteogenic layer containing osteoblasts (bone germinators) that make new bone, and osteoclasts that break down bone. The periosteum contains nerve fibers, lymphatic vessels, and blood vessels that supply the bone. The periosteum is attached to the underlying bone by Sharpey's fibers extending from the fibrous layer into the bone matrix. There is a high density of Sharpey's fibers where tendons and ligaments attach to the periosteum.

The internal surfaces of the bone are covered with the endosteum. The endosteum lines the medullary cavity in long bones and covers the trabeculae of spongy bone.

Short, irregular and flat bones vary in the proportion of compact and cancellous (Fig. 6.3). Furthermore, these bones also do not have a shaft or epiphyses. They contain bone marrow between their trabeculae, but there is no bone marrow cavity. The internal spongy layer in flat bones is called the diploë (folded).

Microscopic anatomy of bone

There are four major cell types found in bone (Fig. 6.4). Osteocytes are the mature cells within bone that account for most of the population of bone cells. They are found within a lacuna (see next section, "Compact Bone"). Osteoblasts are cells that secrete the extracellular matrix on bone. They secrete collagen and ground

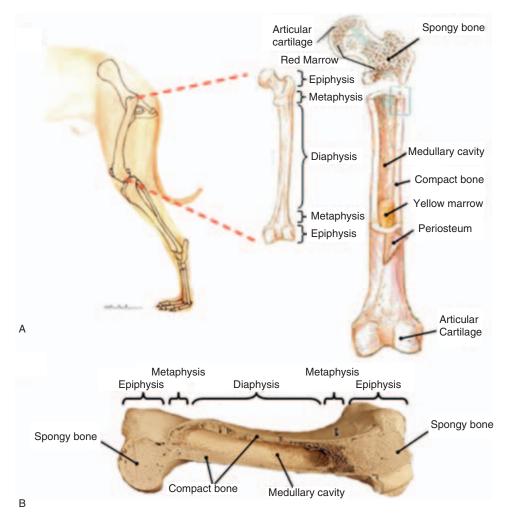


Fig. 6.2. Anatomy of long bones. A) Using the femur as an example of a long bone, the epiphysis is the enlarged area at either end of the bone while the diaphysis is the long shaft in the middle portion of the bone. The metaphysis is the joining point between the epiphysis and diaphysis. The periosteum is the fibrous covering around the outside of the bone not covered with articular cartilage. The endosteum is the fibrous and cellular tissue lining the medullary cavity of the bone. B) Cross section of an equine humerus showing exterior and interior anatomy.

substance that makes up unmineralized bone, called osteoid. Once these cells get embedded within the matrix, they become osteocytes. Osteoclasts are cells involved in resorption of bone, and are therefore present in areas where bone is being removed. Osteoclasts are giant multinucleated cells. Bone also contains a small number of mesenchymal cells known as osteoprogenitor cells. These are stem cells that can produce osteoblasts, and are therefore important in fracture repair. They are located in the inner, cellular layer of the periosteum, the endosteum that lines the marrow cavity, and the lining of vascular passageways in the matrix.

Compact bone

Although compact bone appears solid to the unaided eye, microscopically it contains considerable detail.

The structural unit of compact bone is the osteon, or Haversian system (Fig. 6.5). Each osteon appears as a cylindrical unit consisting of 3–20 concentric lamellae of bone matrix surrounding the central osteonal canal (Haversian canal, or central canal) that runs parallel to the long axis of the bone. The lamellae are like paper towels wrapped around a cardboard roll (i.e., osteonal canal). The osteonal canal contains the vascular and nerve supply of the osteon. The osteonal canals run parallel to the long axis of the bone, and they carry small arteries and veins.

A second group of canals, called perforating or Volkmann's, or lateral, canals, run at right angles to the long axis of the bone. These canals connect the blood vessel and nerve supply of the periosteum with that in the osteonal canal. These canals are lined with endosteum.

During bone formation, osteoblasts secrete the bone matrix. However, osteoblasts maintain contact with

one another via connections containing gap junctions. As the matrix hardens, the osteoblasts become trapped within it, thus forming the lacunae and canaliculi. The osteoblasts become osteocytes, or mature bone cells.

Osteocytes, the spider-shaped mature bone cells, are found in lacunae, the small cavities at the junctions of the lamellae. Only one osteocyte is found per lacunae,

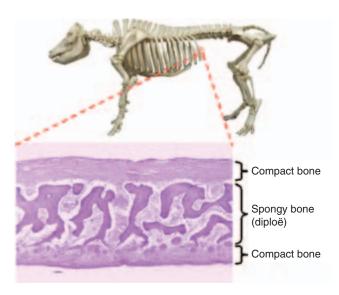


Fig. 6.3. Internal anatomy of flat bone. Flat bones consist of an outer layer of compact bone that sandwiches an inner layer of spongy, or trabecular, bone (diploë).

and these cells cannot divide. Numerous processes extend from each osteocyte into little tunnels running through the mineralized matrix called canaliculi, which connect adjacent lacunae. Therefore, there is a continuous network of canaliculi and lacunae containing osteocytes and their processes running throughout the mineralized bone. Canaliculi are important because they provide a route by which processes from one osteocyte can contact those of adjacent osteocytes. Therefore, via the canalicular system, all osteocytes are potentially in communication with one another. They pass information, nutrients, and/or wastes from one place to another.

Osteocytes can synthesize or absorb bone matrix. If the osteocyte dies, bone matrix resorption occurs due to osteoclast activity, which is later followed by repair or remodeling by osteoblast activity.

While mature compact bone has a lamellar structure in which the fibers run parallel, immature bone, also called woven bone, has a nonlamellar structure. Woven bone is put down rapidly during growth or repair, and its fibers are aligned at random resulting in lower strength. Woven bone is generally replaced by lamellar bone as growth continues.

Cancellous or spongy bone

Unlike compact bone, spongy bone does not contain osteons. As mentioned earlier, it consists of an irregular lattice network of bone called trabeculae. Red bone

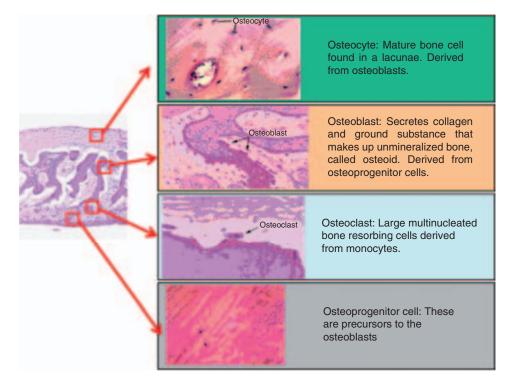


Fig. 6.4. Bone cells. The four types of bone cells, and their locations, are shown.

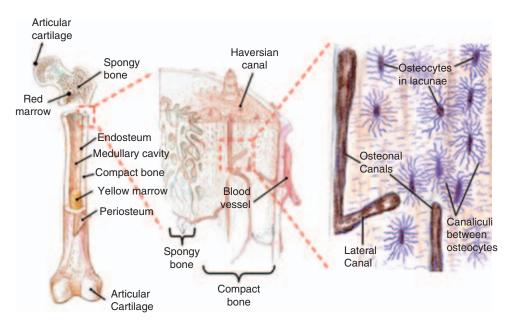


Fig. 6.5. Microscopic structure of compact bone. These figures represent longitudinal sections of the bone shown in increasing magnification from left to right. The osteon, or Haversian system, consists of a central osteonal canal surrounded by concentric lamellae of bone matrix. These canals are all interconnected by lateral canals that run horizontal, or at right angles, to the osteonal canals. Osteocytes, or mature bone cells, are found in cavities called lacunae that lie between the lamellar layers. The osteocytes have processes that project into canaliculi, which are narrow canals interconnecting the lacunae. The osteocytes pick up nutrients and oxygen from the blood and pass it via the canalicular system. (Figure modified from Marieb, 2003.)

marrow can be found in the space between the trabeculae. Osteocytes are found in lacunae within the trabeculae, and canaliculi radiate from the lacunae.

Chemical composition of bone

Bone consists of both organic and inorganic components. The major inorganic component is calcium phosphate, $Ca_3(PO_4)_2$, accounting for two-thirds of the weight of bone. Calcium phosphate interacts with calcium hydroxide, $Ca(OH)_2$, to form hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$. As the crystals of hydroxyapatite form, they also incorporate other inorganic materials including calcium carbonate, sodium, magnesium, and fluoride.

The remaining organic portion of the bone is made up of cells (osteoblasts, osteocytes, and osteoclasts) and osteoid, which includes collagen fibers and ground substance (proteoglycans and glycoproteins). The osteoid is secreted by osteoblasts.

Hematopoietic tissue in bones

Red bone marrow, which is hematopoietic (i.e., blood forming), is found in the spongy bone of long bones and the diploë of flat bones. Red bone marrow consists of mature and immature red blood cells, white blood cells, and stem cells that produce them. In newborns, the medullary cavities of spongy bones contain red bone marrow. In adult long bones, the medullary cavities of spongy bone become large fat-filled medullary cavities containing yellow bone marrow and extending into the epiphysis. Yellow marrow functions in fat storage, and contains mostly fat cells. Therefore, blood cell production in adult long bones is restricted to the head of the femur and humerus. However, if an animal is anemic, the yellow marrow can revert to red marrow to supplement red blood cell production. In contrast, the spongy bone found in flat bones, such as those in the hips, remains hematopoietic and therefore a good source when needing to sample bone marrow.

The osteonal and lateral canals are also the way in which blood cells formed in the marrow enter circulation. The sinuses of the bone marrow connect with the venous vessels running through these channels, and newly formed blood cells are released into them. From there they can leave the confines of the bone and enter the general circulation.

Bone development

Osteogenesis, or ossification, is the process of bone formation. Calcification, the process of calcium salt deposition, occurs during ossification. While calcification is

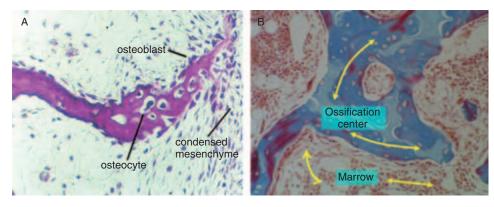


Fig. 6.6. Intramembranous ossification. A) Mesenchymal cells within the mesenchyme migrate and condense in specific areas forming a membrane that will become ossified. This condensed mesenchyme becomes more vascularized, and the cells become larger and rounded. The cells differentiate into osteoblasts secreting collagen and proteoglycans (osteoid). As the matrix becomes more dense and calcified, the osteoblasts become osteocytes contained within canaliculi. Some of the surrounding cells become osteoprogenitor cells. As osteoprogenitor cells come into apposition with the initial bone spicules, they become osteoblasts and continue appositional growth. B) Ossification begins in a relatively confined region called the ossification center.

associated with bone formation, it can occur in other tissues.

There are two general classes of bone formation. Intramembranous ossification occurs when bone develops from a fibrous membrane. The flat bones of the skull and face, the mandible, and the clavicle if present, are formed by this method. Intramembranous ossification can also result in the formation of bones in abnormal locations such as testes or whites of the eyes. Such bones are called heterotopic bones (*hetero* = different; *topos* = place). If cartilage serves as the precursor for the bone, formation is called endochondral ossification. Because of remodeling that occurs later, the initial bone laid down by either method is eventually replaced.

Intramembranous ossification

Early in embryonic development, elongate mesenchymal cells migrate and aggregate in specific regions of the body. Remember, mesenchyme is tissue from which all connective tissue develops. As these cells condense, they form the membrane from which the bone will develop (Fig. 6.6). This presumptive bone site becomes more vascularized with time, and the mesenchymal cells enlarge and become rounder. As the mesenchymal cells change from eosinophilic (i.e., stained with eosin dyes) to basophilic (affinity for basic dyes), they differentiate into osteoblasts. These cells secrete the collagen and proteoglycans (osteoid) of the bone matrix. As the osteoid is deposited, the osteoblasts become increasingly separated from one another, although they remain connected by thin cytoplasmic processes.

The site where the matrix begins to calcify is called the ossification center. Eventually, as the matrix becomes calcified, the osteoblasts become osteocytes. The osteocytes are contained in canaliculi. Some of the surrounding primitive cells in the membrane proliferate and give rise to osteoprogenitor cells. These cells come in opposition to the spicules, and become osteoblasts, thus adding more matrix. This results in appositional growth in which the spicules (areas of calcification extending from the ossification center) enlarge and become joined into a trabecular network having the shape of bone.

Endochondral ossification

Endochondral ossification begins similar to intramembranous ossification, with mesenchymal cells migrating and aggregating (Fig. 6.7). However, these cells now become chondroblasts, instead of osteoblasts, and begin making a cartilage matrix. Once made, the cartilage matrix grows by both interstitial and appositional growth. Interstitial growth is responsible for most of the increase in length of the bone, whereas the increase in width is produced by new chondrocytes that differentiate from the chondrogenic layer of the perichondrium surrounding the cartilage mass.

Bone formation begins when perichondrial cells in the midregion give rise to osteoblasts rather than chondrocytes. At this point, the connective tissue surrounding the middle of the cartilage changes from perichondrium to periosteum. A thin layer of bone begins forming around the cartilage model. This bone can be called either periosteal bone because of its location, or endochondral bone because of its method of

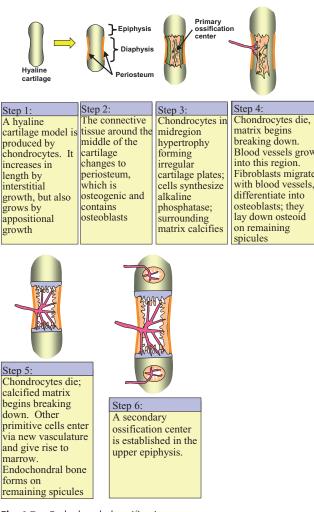


Fig. 6.7. Endochondral ossification.

development. This periosteal bone is sometimes termed the bony collar.

As the chondrocytes in the midregion become hypertrophic, the matrix becomes compressed. These cells begin to synthesize alkaline phosphatase, and the surrounding matrix begins to calcify. As the chondrocytes die, the matrix breaks down and the neighboring lacunae become interconnected. At the same time, blood vessels begin to enter this diaphyseal area vascularizing the developing cavity.

Cells from the periosteum migrate inward with the blood vessels and become osteoprogenitor cells. Other cells also enter to give rise to the marrow. The breakdown of the matrix leaves spicules that become lined with osteoprogenitor cells that then differentiate into osteoblasts. Osteoblasts then begin to produce the osteoid on the spicule framework. Bone formed in this manner is called endochondral bone, and this region becomes the primary ossification center. As the cartilage is resorbed (i.e., broken down), the bone deposited on the calcified spicules becomes spongy bone.

Eventually, a secondary ossification center develops in each epiphysis. Bone develops in these regions similarly to that in the primary ossification center. As the secondary ossification develops, the only cartilage remaining is that at the ends of the bones, and a transverse region known as the epiphyseal plate separating the diaphyseal and epiphyseal cavities.

As the cavity in the diaphyseal marrow enlarges, there is a distinct zonation that develops in the cartilage at either end of the diaphysis (Fig. 6.8). The following five regions develop beginning most distal from the diaphysis:

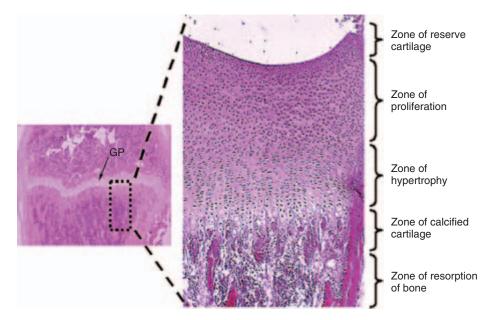


Fig. 6.8. Epiphyseal plate. The area between the diaphysis and epiphysis is the growth plate (GP), and it is characterized by distinct zonation as shown in this longitudinal section.

- 1. Zone of reserve cartilage. This region contains no cellular proliferation or matrix production. It contains small, scattered chondrocytes.
- 2. Zone of proliferation. The cartilage cells are dividing and organized in distinct columns in this area. The cells are larger than in the reserve zone, and are producing matrix.
- 3. Zone of hypertrophy. The cartilage cells are large with a clear cytoplasm containing glycogen in this region. The matrix is found in columns between the cells.
- 4. Zone of calcified cartilage. This area contains enlarged cells that are degenerating. The matrix is calcified.
- 5. Zone of resorption: Nearest the diaphysis, the cartilage in this region is in direct contact with connective tissue in the marrow cavity.

Bone growth, remodeling, and repair

Bone growth

As the bone grows, there is constant internal and external remodeling in the epiphyseal plate. While the epiphyseal plate remains constant in size, new cartilage is produced in the zone of proliferation while a similar amount of cartilage is resorbed in the zone of resorption due to the action of osteocytes. The resorbed cartilage is replaced by spongy bone produced by osteoblasts found between the zone of resorption and the diaphysis. As the cells in the proliferative region divide, an increase in length of the bone occurs as the epiphysis is moved away from the diaphysis.

The width of bone is increased by appositional growth of bone that occurs between the cortical lamellae and the periosteum as bone resorption occurs on the endosteal surface of the outermost region of the bone. As bones elongate, they are constantly remodeling, which involves resorption of bone in some areas concomitant with deposition in other areas.

Eventually, new cartilage production ceases. The cartilage that is present in the epiphyseal plate is converted to bone until no more cartilage exists. This is termed epiphyseal closure, and growth of the bone is complete. The only remaining cartilage is at the articular (i.e., regions where bones form joints) surfaces on the bone. The epiphyseal plate now becomes the epiphyseal line.

The major hormone controlling bone growth in young animals is growth hormone that is released from the anterior pituitary. Excessive secretion of growth hormone can cause gigantism, whereas hyposecretion can cause dwarfism. Thyroid hormones also play an important role in bone development. The action of these hormones is discussed in Chapter 12.

Bone remodeling and repair

While bone may appear to be dormant after animals reach adulthood, this is not true. In fact, bone remains very active, and is constantly being broken down (resorbed) and replaced in response to various physical or hormonal changes. This constant breakdown by osteoclasts and formation by osteoblasts is termed remodeling, and occurs at both the periosteal and endosteal surfaces.

The breakdown of bone by osteoclasts is called bone resorption. Osteoclasts bind tightly to either the endosteum or periosteum forming a leakproof seal. The osteoclasts release lysosomal enzymes and acids into this sealed region, which then digests the collagen fibers and organic matrix while the acid digests the minerals. The digested components are engulfed by the osteoclasts by endocytosis, packaged into vesicles, translocated across the osteoclast by the process of transcytosis, and released by exocytosis into the interstitial space where the material is absorbed into the capillaries. The canal that is formed establishes the future Haversian system. Eventually, the osteoclasts are replaced by osteoblasts that rebuild the bone.

Hormonal control

The control of bone homeostasis is poorly understood. Since bones are a major calcium storage site, calcium homeostasis plays a major role in bone mineralization (Fig. 6.9). The two hormones involved in calcium homeostasis are parathyroid hormone (PTH), produced by the parathyroid glands, and calcitonin, from the parafollicular cells (C cells) of the thyroid gland). PTH is released in response to low plasma ionic calcium levels, while calcitonin is released when plasma ionic calcium levels rise.

If resorption predominates, bones get weak such as in osteoporosis. If deposition predominates, bone spurs can develop. Estrogens are known to reduce bone resorption whereas parathyroid hormone promotes bone resorption. The decrease in estrogen level associated with menopause is linked with a weakening of the bones.

Repair of fractures

Fractures can be classified several ways:

- Bone end alignment. If the bone ends remained aligned following a fracture, it is called a nondisplaced fracture. Displaced fractures occur when the bone ends are out of alignment.
- Degree of break. If the break is all the way through the bone, it is termed a complete fracture; if not all the way through, it is an incomplete break.

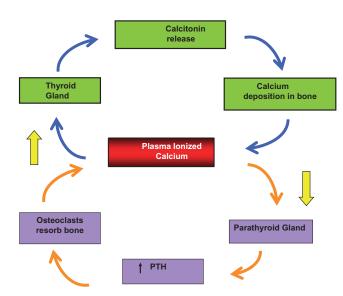


Fig. 6.9. Hormonal control of plasma ionic calcium concentration. An increase in plasma ionic calcium concentration results in the release of calcitonin from the thyroid gland. Calcitonin stimulates calcium deposition in bone. In contrast, a decrease in plasma ionic calcium concentration stimulates the release of parathyroid hormone (PTH) from the parathyroid glands, which promotes osteoclast activity resulting in an increase in plasma ionic calcium levels.

- Orientation of the break. If the break is parallel to the long axis, it is a linear fracture; if it is perpendicular to the long axis, it is a transverse fracture.
- Skin penetration. If bone protrudes through the skin, it is an open, or compound, fracture. A nonprotruding break is called a closed, or simple fracture.

The repair process for a fractured bone involves four steps (Fig. 6.10):

- 1. Hematoma formation. As a result of a fracture, the blood vessels tear causing the formation of a hematoma, a mass of clotted blood, at the fracture site. Bone cells begin to die and the site shows the classic signs of inflammation, i.e., pain, swelling, redness, and loss of function.
- 2. Fibrocartilaginous callus formation. Capillaries grow into the hematoma from which phagocytic cells invade and remove the debris. Fibroblasts and osteoblasts migrate into the fractured area from the periosteum and endosteum. The fibroblasts form collagen fibers, which serve to span the space in the break, thus connecting the two ends. As the fibroblasts differentiate into chondroblasts, they secrete cartilage matrix. Finally, osteoblasts close to the capillaries begin forming spongy bone; those found further away, secrete a bulging cartilaginous matrix. This entire mass,

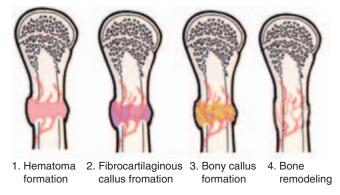


Fig. 6.10. Steps in fracture repair.

called a fibrocartilaginous callus, spans the fractured area.

- 3. Bony callus formation. Bone trabeculae begin to appear as a result of the actions of the osteoblasts converting the fibrocartilaginous callus into a bony callus made of spongy (or woven) bone. Bony callus formation continues until the two ends of the bone are firmly attached.
- 4. Bone remodeling. Remodeling begins during bony callus formation and continues until the bony callus is remodeled. The excess material is removed from both the periosteal and endosteal area, and compact bone is formed along the shaft.

Response to mechanical stress

Although bone deposition occurs in response to a bone injury, it can also occur when additional strength is needed. This can occur in response to new physical pressures placed on the bone as would occur if the bone is bearing weight at a different angle. Wolff's law states that a bone grows or remodels in response to forces placed on the bone. Such forces include weight bearing on the bone or muscles pulling on the bone. Since such forces are generally off-center, they tend to bend the bone. In response, the compact bone thickens on one side while thinning on the other side through the remodeling process. Spongy bone forms in the middle since mechanical forces acting on the bone sum to zero in this region (Fig. 6.11).

Nutrients necessary for bone deposition

Bone deposition requires vitamin C for collagen synthesis, vitamin D for calcium absorption in the gut, and vitamin A for bone deposition and removal, in addition to calcium, phosphorus, magnesium, and manganese.

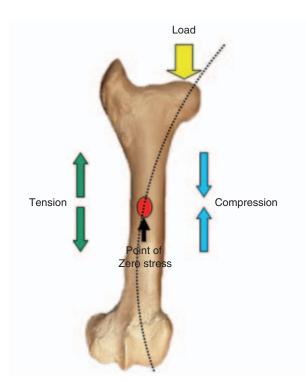


Fig. 6.11. Mechanical stress on bone. Using the femur as an example, the bone is acted upon by the load of the body weight. This load is transmitted through the bone as indicated by the dashed arc. This causes compression on one side of the bone while stretching the other side. These two forces sum to zero in the middle of the bone, creating the point of zero stress.

Homeostatic imbalances of bone

Osteomalacia and rickets

Osteomalacia is a condition in which the bones are insufficiently mineralized. Rickets is a name for the same condition when it is present in prepubertal animals. While osteoid is produced, calcium salts are not deposited; thus the bones remain soft. This is caused by inadequate calcium or vitamin D in the diet. Vitamin D is necessary for intestinal absorption of Ca^{2+} . When blood calcium levels decrease due to inadequate intestinal absorption, parathyroid hormone maintains plasma Ca^{2+} by stimulating the release of Ca^{2+} from the bone.

Parturient paresis (milk fever)

As dairy cattle begin milk production, the first milk produced (called colostrum) contains high concentrations of Ca^{2+} . Colostrum requires approximately 3 g of calcium per hour to produce. When the cow cannot mobilize this amount of calcium, she can develop milk

fever within 72 hrs following parturition. Symptoms include loss of appetite, followed by muscle weakness, decreased body temperature, labored breathing, and paralysis of hind legs. If left untreated, the cow can collapse into a coma and die.

To prevent milk fever, cows should be given sufficient vitamin D in the diet prior to parturition. If milk fever develops, cows are given an oral bolus of calcium carbonate.

Egg-laying fatigue in birds

Similar to milk fever in cows, high-producing egglaying hens can develop weak and brittle bones. A hen must deposit as much as 8–10% of her total calcium into the eggshell each day. Since the eggshell is deposited during the night, the hen must draw upon the calcium reserves located in a specialized type of bone called medullary bone. Under the influence of estrogens and androgens secreted from the developing follicles, medullary bone is produced in hens 2 weeks prior to commencement of egg laying. As blood calcium levels decrease during eggshell formation, the hen releases parathyroid hormone, which mobilizes bone calcium. If there are insufficient stores of calcium in the bones, the bones become weaker as they become demineralized.

Bones and skeleton

Markings on bones

The surface of bone is seldom smooth. Instead, it contains various depressions, bumps, and ridges that serve as sites where muscles and tendons originate or attach, and blood vessels and nerves travel. These various markings are shown in Table 6.1 and Figure 6.12. Learning them is helpful when studying the origins and insertions of muscles.

Skeleton

The skeleton includes all the bones of the body. These bones, and their articulations, have been altered during evolution to accommodate various functions. Therefore, the skeleton is an excellent example of the complementary nature of form and function. The skeletons of various species are shown in Figure 6.13. Since most of the remainder of the chapter is concerned with mammals, a brief discussion of features unique to avian species will be included at the end of the section on the skeleton.

Table 6.1. Bone markings.

Term	Description	Example
Projections Whe Crest	ere Muscles and Ligaments Attach Narrow ridge of bone; usually prominent	lliac crest
Epicondyle	Raised area on or above a condyle	Lateral epicondyle of the humerus
Fossa	Shallow depression, often serving as an articular surface	Olecranon and radial fossae of the humerus
Line	Narrow ridge of bone; less prominent than a crest	Gluteal line on wing of ilium
Process	Generally any bony prominence; sometimes used to name specific prominences	Crest, spine, trochanter, tubercle, tuberosity, etc.; olecranon process
Ramus	Armlike bar of bone	Ramus of the mandible
Spine	Sharp, slender, often pointed projection	Spine of the scapula
Tuberosity	Large rounded projection	Deltoid tuberosity of the humerus
Trochanter	Very large, blunt, irregular-shaped process; found only on the femur	Trochanter of the femur
Tubercle	Small rounded projection or process	Greater tubercle of the humerus
Projections Tha Condyle	t Help Form Joints Rounded articular projection	Occipital condyle of the skull
Cotyloid	A deep articular depression	Acetabulum of the hip joint
Facet	Smooth, nearly flat articular surface	Superior costal facet of the vertebrae
Head	Bony expansion carried on a narrow neck	Head of the femur
Trochlea	A pulley-shaped, articular structure	Trochlea of the femur
Depressions and Fissure	d Openings Allowing Blood Vessels and Nerves to Pass Narrow, slitlike opening	Palatine fissure
Foramen	Round or oval opening through a bone	Foramen magnum
Fovea	A shallow, nonarticular depression	Fovea capitis on the head of the femur
Incisure	A notch-shaped depression at the edge of a bone	Semilunar notch of the ulna
Meatus	Canal-like passageway	External auditory meatus
Sinus	Cavity within a bone, filled with air and lined with mucous membrane	Nasal sinuses
Sulcus	Furrowlike groove	Brachial groove of the humerus

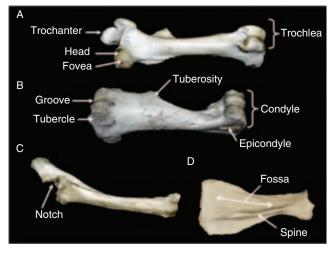


Fig. 6.12. Marking on bones. Various bovine bones are shown, including the femur (A), humerus (B), radius-ulna (C), and scapula (D), which are labeled to illustrate bone markings.

Functions of the skeletal system

The skeleton has five primary functions:

- 1. Support. The skeletal system provides the structure to which the bones attach, as well as the structural support for the entire body.
- 2. Storage of minerals and lipids. The bones provide a major storage for various minerals, particularly calcium. In addition, the bones contain a substantial amount of lipid.
- 3. Blood cell production. The bone marrow is a site of formation for all types of blood cells.
- 4. Protection. The vital organs of the body are protected by the skeletal system. The ribs surround the visceral organs, whereas the central nervous system is encased within the skull and spinal cord.
- 5. Leverage. Many of the joints of the body act as levers therefore assisting with movement.

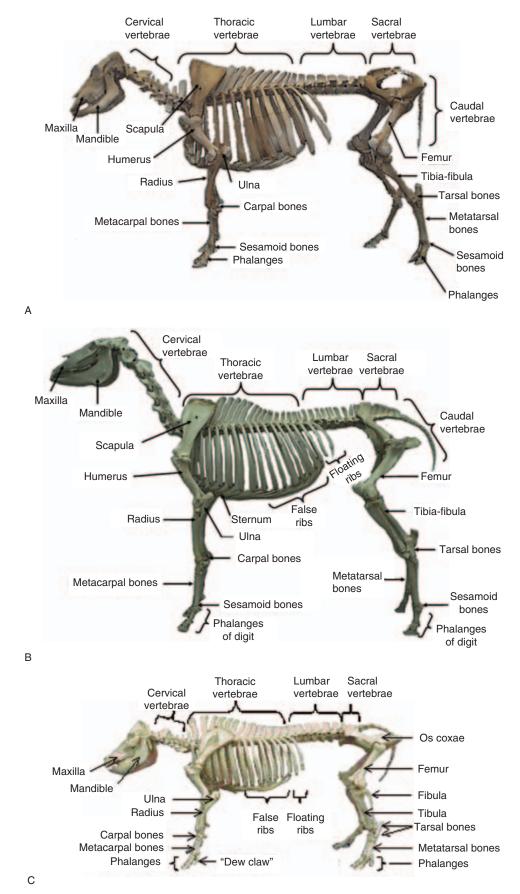
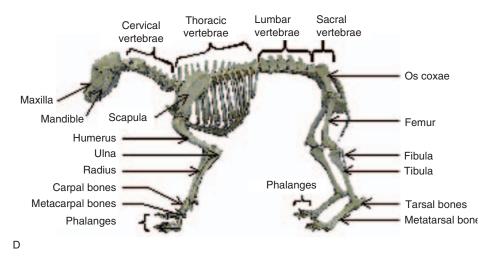
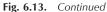


Fig. 6.13. Skeletons. A) Cow. B) Horse. C) Pig. D) Dog.





Skeletal cartilage

Types of cartilage

The skeleton begins as cartilage and fibrous membranes, but then is replaced with ossified tissue as the animal develops through gestation. Cartilage contains no nerves or blood vessels and is surrounded by a layer of dense irregular connective tissue called the perichondrium. Blood vessels found within the perichondrium provide nutrients for the chondrocytes within the cartilage.

There are three types of cartilage found in the skeleton. Hyaline cartilage is the most abundant and provides support and flexibility for the skeleton. The matrix contains only fine collagen fibers. Hyaline cartilage is found 1) on articular surfaces, 2) within costal cartilage connecting the ribs to the sternum, 3) in the respiratory cartilages forming the skeleton of the larynx and reinforcing passageways of the respiratory system, and 4) in nasal cartilages supporting the external nose.

Elastic cartilage contains more elastic fibers than hyaline cartilage. It, therefore, is better able to withstand bending. It is found in only two places in the skeleton: 1) the external ear, and 2) the epiglottis, which is the flap of tissue that covers the opening of the larynx during swallowing.

Fibrocartilage is highly compressible, possessing great tensile strength. It contains approximately parallel rows of chondrocytes with intervening thick collagen fibers. It is found in the menisci within the knee and intervertebral discs.

Growth of cartilage

Cartilage can continue to grow by two processes. Appositional growth occurs when new cartilage forms

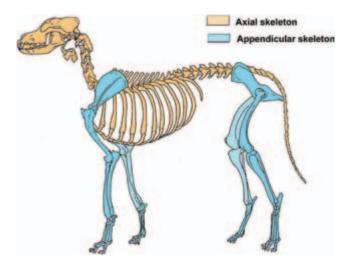


Fig. 6.14. Axial and appendicular skeleton. As shown with this dog skeleton. The axial skeleton includes the bones and cartilage protecting the soft structures in the head, neck, and trunk, and consists of the skull, hyoid apparatus, vertebral column, and thorax. The appendicular skeleton includes the limbs and bones connecting the limbs to the axial skeleton.

on the surface of preexisting cartilage. Interstitial growth occurs from inside of the cartilage mass in which lacunae-bound chondrocytes inside the cartilage divide and secrete new matrix, thereby expanding the cartilage from within.

Skeleton classification

The skeleton is divided into the appendicular skeleton and the axial skeleton (Fig. 6.14). The axial skeleton includes the skull, hyoid apparatus, vertebral column, ribs, and sternum. The appendicular skeleton includes the bones of the limbs and limb girdles. The thoracic limb or pectoral limb includes the scapula, humerus, radius, ulna, carpal bones, metacarpal bones, phalanges, and their sesamoid bones. The thoracic girdle or shoulder girdle includes the two scapulae, and the clavicle in man, which holds the shoulder laterally, but which is only vestigial in domestic animals.

Axial skeleton

The skull

The skull is a very complex structure made mostly of flat bones. Except for the mandible that is attached via a movable joint, the bones of the skull are connected by interlocking joints called sutures. The suture joints are characterized by a saw-toothed or serrated appearance that keeps the bones attached, but allows the cranium to expand and contract while remaining intact.

Suture lines are visible between the bones of the skull (Fig. 6.15). The internasal suture is between the two nasal bones while the frontonasal suture separates the frontal bones from the nasal bones. The frontoparietal suture separates the frontal bones from the parietal bones. The nasomaxillary suture separates the nasal bones from the maxillary bones.

The skull contains both cranial and facial bones (Table 6.2). The cranium includes those bones that sur-

round the brain. The cranium consists of the cranial vault, also called the calvaria, forming the superior, lateral, and posterior aspects of the skull, and the cranial base or floor that forms the inferior aspect of the cranium. The cranial base is divided by bony ridges into three distinct fossae: the anterior, middle, and posterior cranial fossa. The cranial bones form the cranial cavity that houses the brain, and also provide the site for attachment of head and neck muscles.

The skull contains approximately 85 named openings, including foramina, canals, fissures, and orbits. These provide passageways for the spinal cord, blood vessels, and the 12 cranial nerves to enter and leave the brain.

Cranium

The roof of the cranium is formed by the paired frontal and parietal bones (Fig. 6.16). The caudal aspect of the skull is formed by the unpaired occipital bone. The floor of the cranium is formed by the unpaired sphenoid bone. Finally, the rostral wall of the cranium is formed by the ethmoid bone.

The facial bones include those bones enclosing the nasal and oral cavities. These bones form the structure of the face; contain cavities for special senses, including sight, taste, and smell; provide openings for air and food; secure teeth; and provide attachment sites

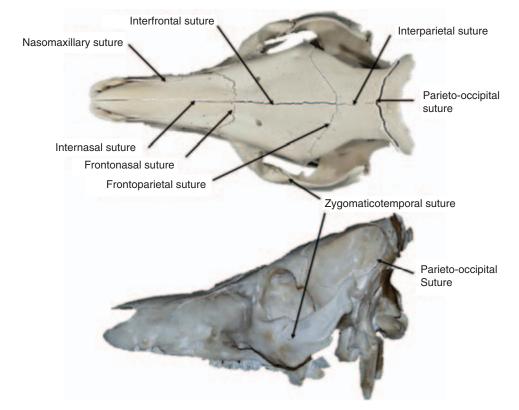


Fig. 6.15. Suture lines of the skull. These lines are shown on top and side view of skull of a pig.

Table 6.2.Bones of the skull.

Term	Description	Major Markings
Cranial Bones (Number)		
Frontal (2)	The rostral portion of the roof of the cranial cavity in most domestic species; in the ox, it forms the entire roof of the cranial cavity	Supraorbital foramina—allows the supraorbital arterie and nerves to pass
Parietal (2)	Along with frontal, forms the roof of the cranial cavity in most domestic animals except ox	
Occipital (1)	Forms caudal aspect of the cranial cavity, as well as the skull	 Foramen magnum—allows spinal cord to enter the vertebral canal Hypoglossal canal—passageway for hypoglossal nerv (XII) Occipital condyles—articulate with the atlas (first cervical vertebra) External occipital protuberance—site of muscle attachments; site of attachment of ligamentum nuchae in horse and ruminants
Temporal (2)	Forms caudolateral wall of the cranial cavity	 Zygomatic process—forms part of zygomatic arch, which forms bulge in cheek Mandibular fossa—articulation site for mandibular condyle External auditory meatus—canal leading from externater to the eardrum Styloid process—attachment site for hyoid bone and some neck muscles Mastoid process—attachment site for some neck and tongue muscles Stylomastoid foramen—passageway for facial nerve (VII) Jugular foramen—passageway for internal jugular veir and cranial nerves IX, X, and XI Internal acoustic meatus—passageway for cranial nerves VII and VIII Carotid canal—passageway for internal carotid artery
Sphenoid (1)	Unpaired bone forming floor of cranial cavity; it has several parts, including the body, greater wings, lesser wings, and pterygoid processes	 Sella turcica—helps form cavity for pituitary Optic canals—passageway for optic nerve (II) and ophthalmic arteries Superior orbital fissures—passageway for cranial nerves III, IV, VI, part of V, and ophthalmic vein Foramen rotundum—passageway for mandibular division of cranial nerve V Foramen ovale—passageway for cranial nerve V Foramen spinosum—passageway for middle meningeal artery
Ethmoid (1)	Unpaired bone forming rostral wall of cranial cavity; forms part of the nasal septum, caudal wall of nasal cavity, and part of medial wall of the orbit	Crista galli—attachment for the falx cerebri portion of dura mater Cribriform plate—passageway for the olfactory nerves (I) Dorsal and middle nasal conchae—forms part of lateral walls of nasal cavity
Facial Bones (Number) Mandible (1)	The lower jaw	Coronoid processes—insertion site of temporalis muscles Mandibular condyles—articulate with the temporal bones forming the temporomandibular joint in the jaw Mandibular symphysis—medial fusion site of mandibular bones Alveoli—sockets for teeth Mandibular foramina—passageway for alveolar nerve Mental foramina—passageway for blood vessels and

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Table 6.2. Continued

Term	Description	Major Markings
Maxilla (2)	Forms the upper jaw, and parts of the hard palate, orbits, and nasal cavity	 Alveoli—sockets for teeth Zygomatic processes—forms caudal part of zygomatic arches Palatine processes—forms much of the bony hard palate Incisive—passageway for blood vessels and nerves going through hard palate (fused palatine processes) Orbital fissures—passageway for maxillary branch of cranial nerve V, the zygomatic nerve and blood vessels Infraorbital foramen—passageway of infraorbital nerve to skin of face
Zygomatic (2)	Cranial portion of zygomatic arch; forms part of cheek and orbit	Temporal process—forms cranial part of zygomatic arch
Nasal (2)	Along with cranial portion of frontal bone, forms osseous roof of nasal cavity	
Lacrimal (2)	Forms medial surface of orbit	Lacrimal fossa—houses the lacrimal sac
Palatine (2)	Forms part of hard palate along with maxillary and incisive bones	
Vomer (1)	Unpaired bone forming part of osseous nasal septum	
Ventral nasal concha (2)	A fragile scroll of bone that increases nasal surface area	
Pterygoid (2)	Small bones in caudal part of nasopharynx	
Incisive or premaxillary (1)	Holds upper incisors	

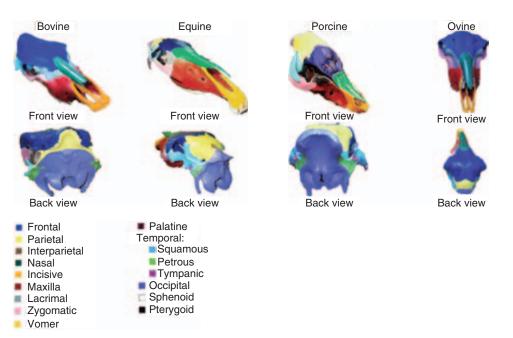


Fig. 6.16. Skulls of various species. The skulls of different species showing main bones.

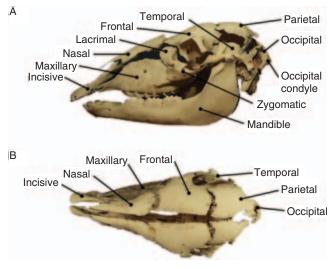


Fig. 6.17. Exploded equine skull. The various bones of the equine skull have been separated, showing side (A) and top (B) view.

for facial muscles. The facial region is divided into the oral, nasal, and orbital regions.

The oral region includes the incisive, maxillary, and palatine bones, as well as the mandible surrounding the oral cavity. The nasal region includes the nasal, maxillary, palatine, and incisive bones surrounding the nasal cavity. The orbital region includes the bony socket holding the eye, formed by portions of the frontal, lacrimal, palatine, sphenoid, and zygomatic bones. The zygomatic arch, which forms the ventral wall of the orbit, consists of the zygomatic bone and the zygomatic process of the temporal bones. An exploded view of the equine skull is shown in Figure 6.17.

Species differences

Unique to the horse and cat, the interparietal bone is found between the two parietal bones. In other species, this bone is present in the fetus, but fuses with surrounding bones during gestation. In the ox, the frontal bone forms the entire roof of the cranium, whereas the parietal bones help form the roof in other species.

In the dog, there are three types of skulls based on the proportions of the facial bones and cranial cavity (Fig. 6.18).

- 1. Mesaticephalic. Average conformation. Example, Siberian husky.
- 2. Dolichephalic. Has an elongated facial component. Example, collie.
- 3. Brachiocephalic. Has a shorter facial component. Example, bulldog.

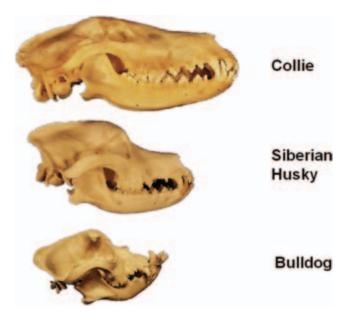


Fig. 6.18. Examples of dog skulls. The three general types of dog skulls are represented. The collie, Siberian husky, and bulldog represent the dolichephalic, mesaticephalic, and brachiocephalic types of skulls, respectively. Note the relatively long facial component on the collie and the short facial component on the bulldog.

The vertebral column

The vertebral column, also called the spine, protects the spinal cord, supports the head and serves as an attachment site for muscles affecting body movements. It consists of irregular bones connected by slightly movable joints.

The vertebrae (sing. = vertebra) are the irregularly shaped bones making up the spinal column. They are grouped into the cervical (neck), thoracic (back), lumbar (loin), sacral (croup), and caudal (tail) vertebrae. Each is named by the first letter of the group followed by the number within the group, e.g., C1, T3, L5, S3, and Ca20. The number of vertebrae by species is shown in Table 6.3.

Typical vertebrae are shown in Figure 6.19. The common features of a vertebra include the body, vertebral arch, vertebral foramen, and processes. The body is the thick, spool-shaped ventral portion of the vertebra. It is convex at the cranial end and concave at the caudal end, allowing articulation with the adjacent vertebrae. The vertebral arch is the dorsal portion of the vertebra consisting of two upright pedicles that form the wall of the vertebral foramen. Two half- (or hemi-) laminae project from the pedicles, and, meeting in the midline to complete the lamina, form the roof of the vertebral connects to form the vertebral canal.

Species	Cervical	Thoracic	Lumbar	Sacral	Caudal
Carnivore	C7	T13	L7	S3	Ca20–24
Pig	C7	T11–15	L6-7	S4	Ca20-23
Horse	C7	T18	L6	S5	Ca15-21
Ox	C7	T13	L6	S5	Ca18-20
Sheep	C7	T13	L6-7	S4	Ca16-18
Chicken	C7	T7	L14 (lumbarsacral)		

Table 6.3. Number of vertebrae.

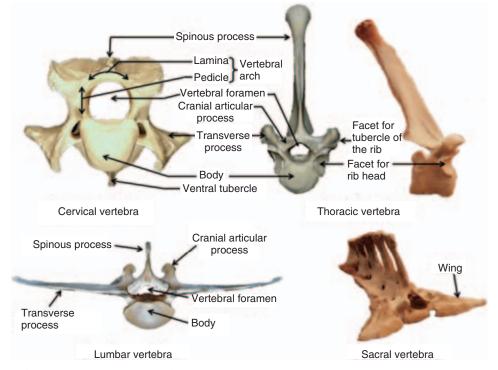


Fig. 6.19. Examples of various vertebrae. Examples of cervical, thoracic, lumbar, and sacral vertebrae are shown. Note that the cervical vertebrae have a reduced spinous process. Thoracic vertebrae have an exaggerated spinous process, and lumbar vertebrae have an exaggerated transverse process. Sacral vertebrae are generally fused, with the processes also tending to fuse.

There are seven processes coming from each vertebra. These include a midsaggital dorsal projection called the spinous process, two lateral extensions called the transverse processes, and four articular processes. The articular processes include two cranial and two caudal articular processes.

The first and second cervical vertebrae are called the atlas and axis, respectively (Fig. 6.20). The atlas supports the head, hence its name. It articulates with the occipital condyles (see Fig 6.17) forming the atlanto-occipital joint, which allows the head to make a "yes" motion, i.e., flexion and extension. The atlas is unique in that it lacks a body or a spinal process. The axis contains a large ridgelike spinous process and the dens, a peglike cranial process forming a pivot articulation with the atlas, and allowing a "no" motion. The thoracic vertebrae have articular facets for each pair of ribs to which they attach. The anticlinal vertebra is the one with the most upright-oriented dorsal process. Cranial to this vertebra, the dorsal processes are inclined cranially while those caudal to this vertebra are inclined caudally. This is an important landmark when reading radiographs.

Lumbar vertebrae are characterized by their large size and long, flatlike transverse processes. These vertebrae also lack costal facets since ribs do not articulate with them.

The sacral vertebrae fuse to form the sacrum. The wings of the sacrum (Fig. 6.19) articulate with the ilium forming the sacroiliac joint. This is the one site of connection between the axial skeleton and pelvic limb. Each sacral vertebra has dorsal and ventral foramina allowing the passage of spinal nerves.

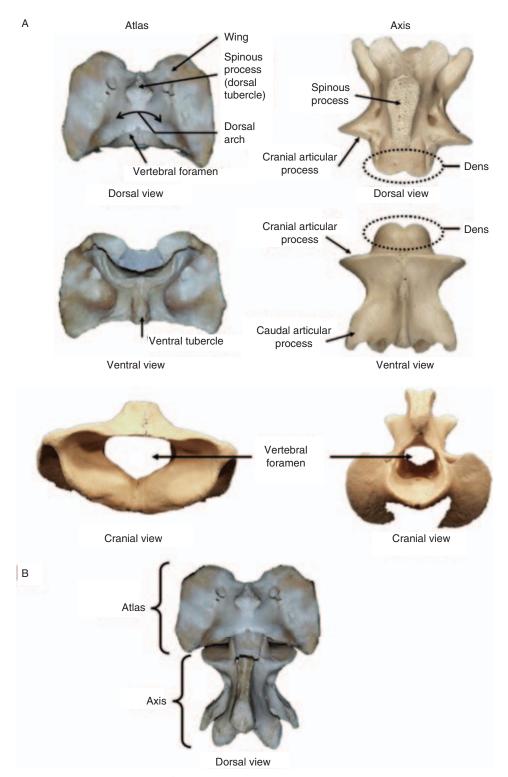


Fig. 6.20. Atlas and axis. The atlas and axis are the first and second cervical vertebrae, respectively. A) The dorsal, ventral and cranial views of the atlas and axis of a cow. B) The articulation between the atlas and axis.

Thorax

The thorax is the bony cavity formed by the sternum, ribs, costal cartilages, and bodies of the thoracic vertebrae (Fig. 6.21). The sternum, or breastbone, is com-

posed of the unpaired bones (sternebrae) forming the floor of the thorax. The number of sternebrae is eight in carnivores; six in pigs, horses, and humans; and seven in ruminants. The manubrium is the enlarged first sternebra while the xiphoid process is the last

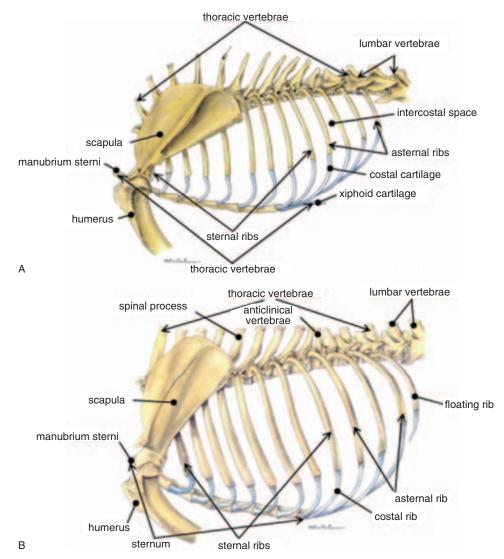


Fig. 6.21. Thorax of different species. A) Lateral aspect of cat. B) Lateral aspect of dog. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

sternebra capped by the xiphoid cartilage. The thoracic inlet is a region formed by the last cervical vertebra, the first pair of ribs, and the sternum.

The ribs consist of long, curved bones that form the lateral wall of the thorax. The ribs can be grouped as follows:

- 1. True ribs. They articulate directly to the sternum via their costal cartilage.
- 2. False ribs. They include all ribs that are not true ribs. Their costal cartilages merge to form the costal arch, which indirectly joins them to the sternum in all domestic species except the dog. Costal cartilage consists of hyaline cartilage.
- 3. Floating ribs. They include the last false ribs in the dog and man. There is one pair in dogs and two pairs in man. They end in costal cartilage that does not join to the sternum or the costal arch.

As shown in Figure 6.22, each rib consists of a head and a tubercle. The head articulates with the caudal and cranial costal fovea of adjacent thoracic vertebrae in the intervertebral disc found in between. The tubercle of the rib articulates with the transverse process of the same numbered vertebra. Between each rib is the intercostal space.

Appendicular skeleton

Thoracic limb

While humans have the clavicle to keep the shoulder in a lateral position, domestic animals lack this bone since their thoracic limb is maintained under their body. The top of the thoracic limb begins at the scapula.

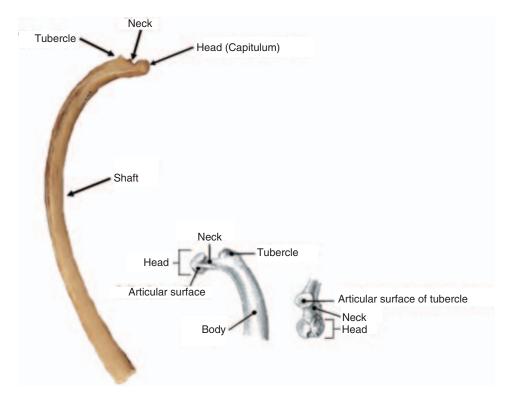


Fig. 6.22. Typical rib. A picture of a rib is shown. (The inserted rib drawing is from Constantinescu and Constantinescu, 2004.)

This is a flat, triangular bone in the shoulder (Fig. 6.23). The two scapulae constitute the thoracic girdle.

The lateral surface of the scapula contains the spine of the scapula that ends in the acromion, the expanded distal end of the spine of the scapula. The acromion is absent in the horse and pig. The area cranial to the spine is the supraspinous fossa; the area caudal to it is the infraspinous fossa. The medial surface of the scapula is called the subscapular fossa. On the dorsal border of the scapula is the scapular cartilage. The cavity in which the humerus articulates is the glenoid cavity. The supraglenoid tubercle, located near the cranial aspect of the glenoid cavity, is the site of attachment of the biceps brachii muscle. The coracoid process (Greek for "crowlike") is a small process on the medial side of the supraglenoid tubercle where the coracobrachialis muscle attaches. Found only in cats, the suprahamate process is a caudal projection from the acromion.

The humerus, sometimes called the brachial bone, is the largest bone in the thoracic limb (Fig. 6.24). It articulates proximally with the scapula in the glenoid cavity forming the shoulder joint, and distally with the radius and ulna forming the elbow joint.

The head of the humerus is a rounded process articulating with the glenoid cavity. The greater (lateral, major) tubercle is the large process craniolateral to the head, and can be palpated as the point of the shoulder. The lesser (medial, minor) tubercle is located on the medial side of the head. The bicipital, or intertubercular, groove is a sulcus between the greater and lesser tubercles through which the tendon of the biceps brachii muscle passes. The body of the humerus connects the two epiphyses of the bone. The deltoid tuberosity, to which the deltoid muscles attach, is the largest tuberosity on the bone. The distal end of the bone is called the humeral condyle and includes the humeral capitulum and humeral trochlea that are the two articulating surfaces, two fossae (three in cats), and the medial and lateral epicondyles. The olecranon fossa is a groove on the caudal surface of the distal end of the humerus in which the olecranon process of the ulna rests. The radial fossa, opposite the olecranon fossa, receives the proximal end of the radius while the elbow is flexed. The dog, and sometimes the pig, also has a supratrochlear foramen, which is a hole between the olecranon and radial fossa through which nothing passes.

The radius is the main weight-bearing bone of the forearm (Fig. 6.25). It articulates with the humerus and ulna in the elbow, and with the carpal bones and ulna at the distal end forming the antebrachiocarpal joint. The head of the radius articulates with the capitulum of the humerus, as well as the ulna. The styloid process is on the distal end of the radius.

The ulna functions mainly as a site for muscle attachments and formation of the elbow. It articulates proximately with the humerus and radius, and dis-

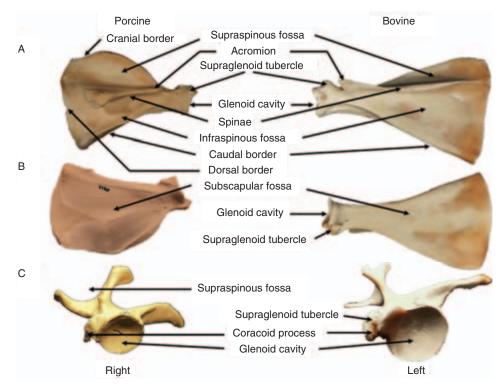


Fig. 6.23. Scapula of porcine and bovine. The lateral (A), medial (B), and caudal (C) views of the porcine and bovine scapula.

tally with the radius and carpal bones. The proximal end of the ulna is called the olecranon process, the point of the elbow, where the extensor muscles of the elbow attach. The trochlear notch is where the humerus articulates with the ulna. The distal end of the ulna also ends in the styloid process.

The radius and ulna fuse in the horse and ruminants. Because they are fused, these animals cannot supinate; therefore, the hand (mannus) is committed to permanent pronation. In contrast, these bones are not fused in carnivores; therefore, these animals can at least partially supinate their hands (paws).

Premature closing of the growth plates in the radius or ulna can cause deviations in these bones resulting in valgus or vargus deviations. Valgus is a lateral deviation distal to a joint; vargus is a medial deviation distal to a joint. For example, carpus valgus or carpus vargus are lateral and medial deviations distal to the carpus. Carpal valgus, a lateral deviation of the joints distal to the carpus, is also called "knock-knee"; carpal vargus, a medial deviation of the bones distal to the carpus, is called "bowlegged."

The distal portion of the thoracic limb is technically the manus (hand), commonly called the forepaw in carnivores (Fig. 6.26). It consists of the carpus, metacarpus, and digits, the latter with their individual phalanges, and their associated sesamoid bones.

The carpus, the wrist of man, consists of two transverse rows of carpal bones. The number of carpal bones varies between species. The pig and horse have eight carpal bones, although the first carpal bone in the distal row is sometimes missing in the horse. Dogs and cats have seven carpal bones due to the fusion of two carpal bones. Ruminants have six carpal bones since the first carpal bone is missing, the second and third are fused.

The metacarpal (MC) bones are located between the carpus and digits. In general, they are numbered I–V from medial to lateral. Species differ in the number of metacarpal bones due to absence or fusion of these bones. For example, the pig has four metacarpal bones since the MC I is missing, and the III and IV metacarpals are the weight-bearing bones; the II and V are reduced in size. Sesamoid bones (i.e., proximal and distal sesamoid bones) are associated with each weight-bearing metacarpal.

The horse has three metacarpals, with MC I and V missing. The II and IV metacarpals are commonly called splint bones because they are greatly reduced in size. The distal end of the splint bones is called the buttons of the splints. The III metacarpal is called the cannon bone.

Carnivores have five metacarpals, but MC I is reduced in size and bears no weight. It is part of the dewclaw, a digit that is not weight-bearing. Ruminants have two metacarpal bones since the MC I and II are missing and MC III and IV are fused into the so-called large metacarpal bone.

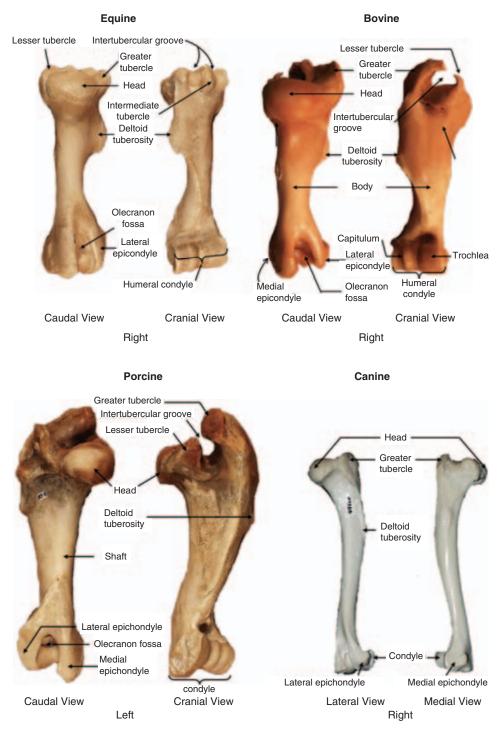


Fig. 6.24. Humerus of various species. The parts of the equine, bovine, porcine, and canine humerus.

The digits correspond with the fingers and toes of man. In general, there are five digits numbered from medial to lateral. However, the number varies by species. Digits generally consist of three phalanges, sesamoid bones, tendons, ligaments, vessels, nerves, and skin. The three phalanges are named the proximal phalanx, middle phalanx, and distal phalanx. In carnivores, there are four main weight-bearing digits. The dewclaw consists of digit I and MC I. The first digit is reduced in size, and has only two phalanges and one proximal sesamoid bone. Horses have one digit per limb that corresponds with the MC III metacarpal bone; pigs have four digits, with the first missing.

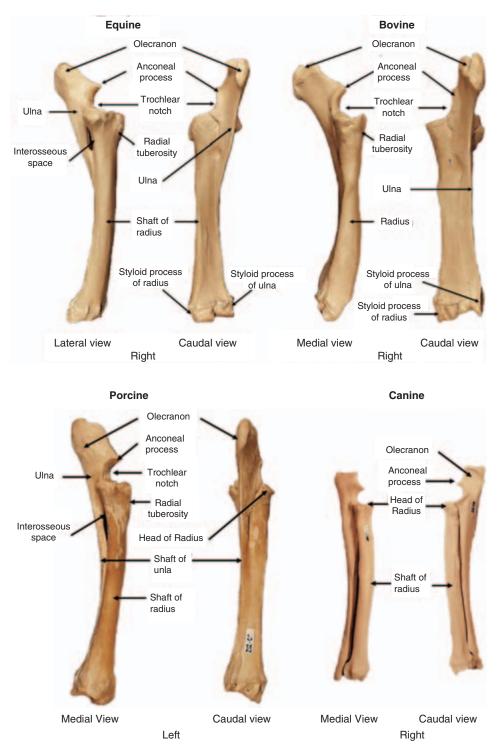


Fig. 6.25. Radius and ulna. The radius and ulna of various species.

Pelvic limb

The pelvic girdle, or bony pelvis, consists of the two hip bones (ossa coxarum), sacrum, and the first few caudal vertebrae (Fig. 6.27). It encases the pelvic cavity. The hip bone (os coxae) consists of the fused ilium, ischium, pubic, and acetabular bones. The acetabular bone is found in the center of the acetabulum, where it has fused with the other bones. The two hip bones are fused at the pelvic symphysis. This fusion includes the two pubic and two ischial bones.

The ilium is the largest and most cranial of the os coxae, consisting of a wing and body. It forms the cranial part of the acetabulum and articulates with the

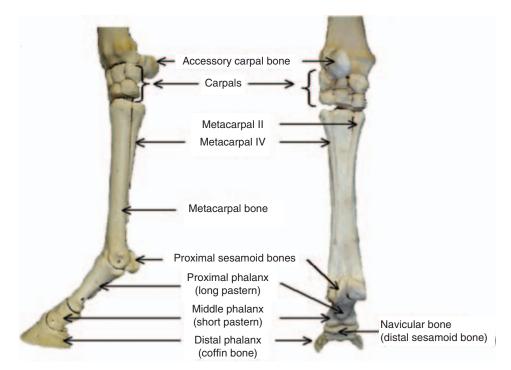


Fig. 6.26. Lower leg, including the mannus, of the horse.

sacrum at the sacroiliac joint. The tuber coxae are the prominences of the lateral wings, sometimes called the "hook" in the ox. The tuber sacrale is the medial process of the wing next to the sacrum. The ischium is the caudal-most portion of the os coxae forming the horizontal portion of the obturator foramen, the large opening in the floor of the ox coxae. The ischiatic tuberosity ("pin bone" in the ox) is the caudal part of the ischium, and is referred to as the "sit bones" in man. The pubis forms the cranioventral part of the os coxae. It consists of a central body and two branches.

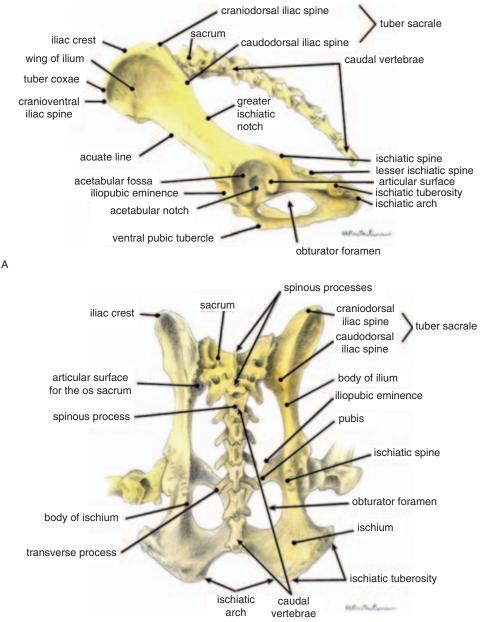
The acetabulum is the site where the head of the femur articulates. It is formed by the fusion of the ilium, ischium, pubic, and acetabular bones.

The femur, or thigh bone, articulates proximately with the hip bone forming the hip joint, and distally with the tibia forming the stifle joint (Fig. 6.28). Proximally, the head of the femur articulates with the acetabulum. There is a small depression, the fovea, in the head of the femur that allows for passage of the round ligament of the femur. The head of the femur is joined to the body of the femur by the neck. The greater trochanter is the large prominence found lateral to the head of the femur; the lesser trochanter is the smaller prominence found distal to the head on the medial side. Also found on the lateral side, distal to the greater trochanter, is the third trochanter, which is absent in dogs and ruminants. Note that trochanters are unique to the femur. The medial and lateral condyles are the two large prominences found at the distal end of the femur, and articulate with the tibia. Also on the distal end of the femur is the patellar surface, a groove bordered by two ridges that articulates with the patella. The patella, or kneecap, is the largest sesamoid bone.

The tibia and fibula are located between the femur and metatarsal bones (Fig. 6.29). The tibia, or shin bone, is located medially, and is the major weightbearing bone of the two bones. Located at the proximal end of the tibia are the medial and lateral condyles, separated by the intercondylar eminence. The condyles articulate with the corresponding condyles of the femur. The fibula is located more laterally and bears little weight. Distally, the fibula articulates with the tibia and the fibular tarsal bone. The distal fibula in the cow is represented by the separate malleolar bone.

The tarsus, or hock, consists of the three rows of bones between the tibia/fibula and metatarsal region (Fig. 6.30). Carnivores and pigs have seven tarsal bones, ruminants have five tarsal bones since four of them fuse, and horses have six.

The largest bone of the tarsus is the talus, or tibial tarsal bone. It is located on the dorsomedial side, and articulates with the tibia, or tibia and fibula in the dog, via its trochlea. The calcaneus is the second bone on the proximal row, just lateral to the talus. The calcanean tuberosity is a large process of the fibular tarsal bone acting as a lever for the common calcanean tendon, and is commonly called the point of the hock.



В

Fig. 6.27. Dog, pelvic girdle. A) Lateral view. B) Dorsal view. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

Metatarsal bones and digits are located distal of the tarsus. In the horse and pig, they follow the same pattern as the thoracic limb. In carnivores, the first metatarsal bone is more reduced than in the front limb, and the digit is often absent. In ruminants, the first and fifth metatarsal bone is absent, and the second is reduced to a tiny element.

Avian skeleton

The skeleton of birds has been adapted for flight (Fig. 6.31). This has resulted in many significant

differences compared to mammals. The neck consists of varying numbers of cervical vertebrae, with the joint between the vertebrae being synovial. The atlas articulates with a single occipital condyle, thus allowing great mobility. The extensive mobility in the atlanto-occipital joint and the neck allows the beak to be used in many motions.

The last cervical vertebra and first three thoracic vertebrae form the notarium. This fused structure, along with the synsacrum, provides rigidity to the spine in order to help with flight. The synsacrum consists of fused thoracic, lumbar, sacral, and caudal vertebrae. The synsacrum is also fused to the ilium. The

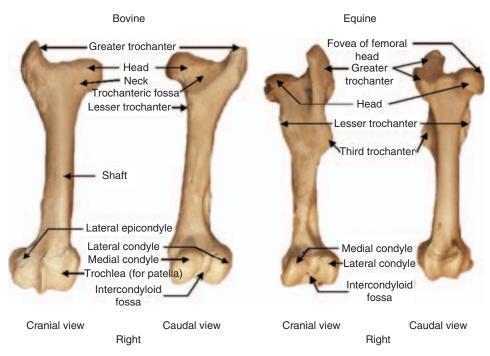


Fig. 6.28. Femur of bovine and equine.

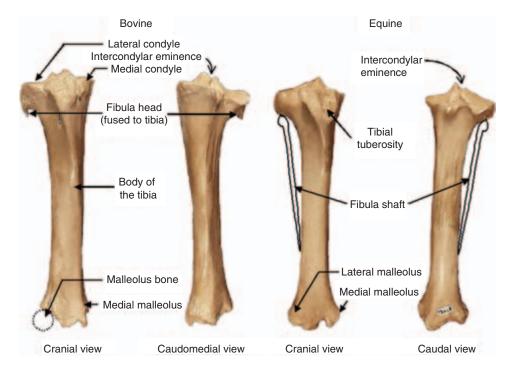


Fig. 6.29. Tibia and fibula of various species. The fibula for the equine was drawn to show where these bones would be if they were present on these specimens.

chicken has six free caudal vertebrae allowing flexibility of the tail. The caudal end of the spinal column, called the pygostyle, consists of four to six fused caudal vertebrae, and provides the site of attachment of some of the tail feathers. The pectoral girdle has evolved for flight. It consists of the scapula, coracoid bone, and clavicle (wishbone). The latter two bones are either missing or rudimentary in most mammals. The coracoid serves as a brace to essentially immobilize the shoulder joint from the

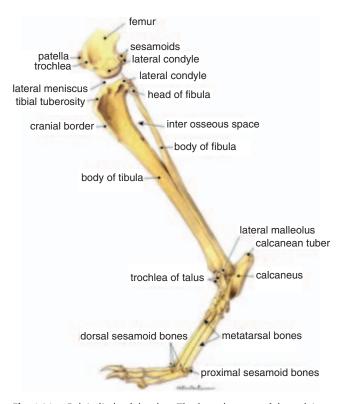


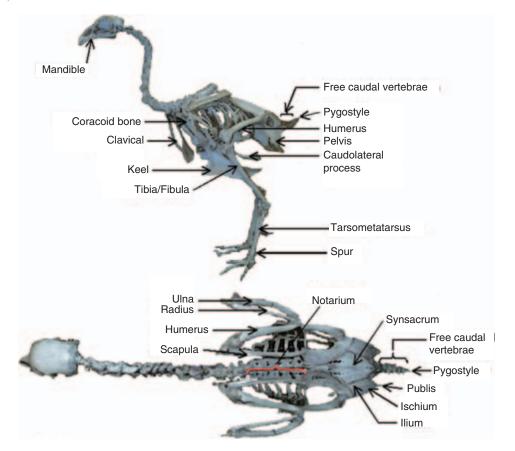
Fig. 6.30. Pelvic limb of the dog. The lateral aspect of the pelvic limb of the dog. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

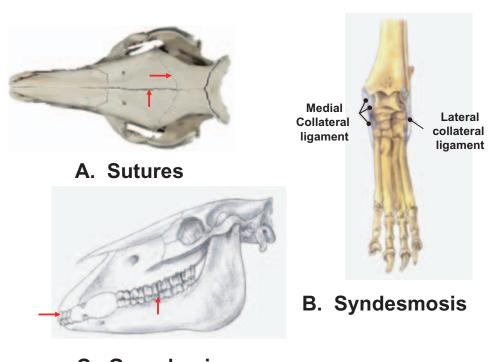
sternum. The sternum has ligamentous attachments directly to the ribs to further brace the shoulder from the sternum. Thus, the shoulder is not pulled toward the sternum as the pectoralis muscles pull the wings downward during flight.

The ulna is larger than the radius and the two are separated by a relatively large space; together they form a unit with a slight mediolateral convex configuration. The increased distance between these two bones adds strength that resists bending of these two bones during flight. The distal row of carpal bones fuses with the metacarpus forming the carpometacarpus. The carpometacarpus articulates with the radial and ulnar carpal bones at the wrist. Finally, there are three digits, including the alular digit having two phalanges, the major digit with two phalanges, and a minor digit with one phalanx.

The avian pelvic girdle consists of a partly fused ilium, ischium, and pubis. The ilium is joined to the synsacral portion of the vertebral column. The pelvic girdle has no pubis symphysis.

There are two articulations between the femur and the pelvis. The head of the femur articulates with the acetabulum formed by the pelvis similar to that in mammals. In addition, the femoral trochanter articulates with the antitrochanter of the ilium. The tarsal





C. Gomphosis

Fig. 6.32. Fibrous joints. Examples of fibrous joints include the following: A) Sutures as found between the bones in the skull. B) Syndesmosis joints in which ligaments connect the bones. C) Gomphosis joints exemplified by the teeth located in alveolar sockets.

bones are fused with other bones, giving the tibiotarsus and tarsometatarsus. Four digits are present and an accessory structure, the metatarsal spur, develops in males.

Laying hens have a special type of bone, called medullary bone, which allows hens to store calcium necessary for eggshell production. Medullary bone is found in bones possessing a good blood supply. It is absent in the humerus, metatarsus, and toes, with small amounts found in the skull and cervical vertebrae and larger amounts found in the femur and tibia. Found only when the birds are producing eggs, medullary bone grows from the inner endosteal surface of the shaft of long bones forming interlacing spicules that fill the marrow space.

Eggshell formation occurs largely at night, a time when laying hens are not eating and therefore are not absorbing dietary calcium. During the time of eggshell deposition, osteoclasts surround the trabeculae and actively reabsorb this bone in order to supply the calcium necessary for eggshell formation, which lasts approximately 20 hours. During the last 15 hours of eggshell formation, the shell gland of the hen secretes calcium at the rate of 100–150 mg/hr, a rate that would deplete blood calcium in 8–18 min. Thus, medullary bone provides an essential source of blood calcium necessary for shell deposition. The deposition of medullary bone is induced by estrogen.

Joints

Types of joints

Arthrology is the study of joints. Joints are vital to allow for the movement of the skeleton. Joints can be classified several ways including 1) the number of articulating bones, 2) structural classification, and 3) functional classification:

- 1. Number of articulating bones. A simple joint has two articulating joints, whereas a compound joint has more than two articulating bones.
- 2. Structural classification. Joints can be classified by the medium holding the joint together (Table 6.4):
 - a. Fibrous joint has fibrous tissue between bones allowing little or no movement, and has no joint capsule (Fig. 6.32). These joints usually ossify later. There are three types of fibrous joints: sutures, syndesmoses, and gomphoses.
 - b. Cartilaginous joints are held together by fibrocartilage, hyaline cartilage, or both (Fig. 6.33). These joints have slight movement, and like fibrous joints, they lack a joint capsule. There are two types of cartilaginous joints: synchondroses and symphyses. The best examples of

Structural Class	Characteristics	Туре	Mobility	Example
Fibrous	Ends of bones united by fibrous tissue	1. Sutures	Immobile (synarthrosis)	Bones of the cranium
		2. Syndesmosis	Slightly mobile (amphiarthrosis) and immobile	Distal tibiofibular joint
		3. Gomphosis	Immobile	The only example is the articulation of a tooth with its socket
Cartilaginous	Ends of bones united by cartilage	1. Synchondrosis (hyaline cartilage)	Immobile	Epiphyseal plates
		2. Symphysis (fibrocartilage)	Slightly movable	Pubic symphysis
Synovial	Ends of bones covered with articular cartilage, and a joint cavity enclosed with a joint capsule	1. Ball-and-socket	Freely movable	Coxofemoral (hip) joint and glenohumeral (shoulder) joint
		2. Pivot	Rounded end of one bone projected into sleeve or ring on another bone; freely movable but allows only uniaxial rotation	Between atlas and dens of axis; Proximal radioulnar joint in animals where pronation and supination possible
		3. Ellipsoidal	Both articulating surfaces are oval. Freely movable allowing flexion, extension, abduction, adduction, and circumduction	Radiocarpal joints
		4. Saddle	Each articulating surface has both concave and convex areas, resembling a saddle; freely movable	Carpometacarpal joint of thumb in man
		5. Plane (or gliding)	Articulating surfaces essentially flat; freely movable, but only slipping or gliding motions	Intercarpal and intertarsal joints; articulating surfaces of vertebral processes
		6. Hinge	Cylindrical projection of one bone fits into troughlike depression of other bone; freely movable but restricted to flexion and extension	Knee, elbow and interphalangeal joints.

Table 6.4. Structural classification of joints

synchondroses are the epiphyseal plates in long bones, which eventually close, and the joint between the first rib and the manubrium. An example of a symphysis is the pubic symphysis.

- c. Synovial joints have a joint cavity bounded by the articular surfaces joined by a synovial joint capsule, and are freely movable. The structure and types of synovial joints are discussed below.
- 3. The functional classification of joints indicates the degree of mobility in the joint:
 - a. Synarthrotic. Movements in these joints are absent or extremely limited. Examples of these joints include the sutures in the cranium.
 - b. Amphiarthrotic. There is slight movement in these joints. Examples include the intervertebral joints of sternoclavicular joints.
 - c. Diarthrotic. Also called synovial joints, these joints have considerable movement. They

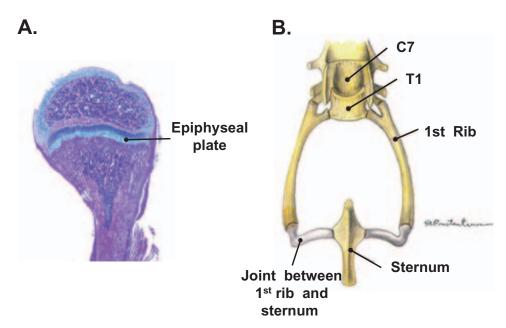


Fig. 6.33. Cartilaginous joints. A) The epiphyseal plate located in a growing long bone. B) The sternoclostal joint located between the 1st rib and sternum.

allow for one-, two-, or three-dimensional movement, and contain articular cartilage and synovial membranes. Many such joints also contain bursae sacs. Examples include shoulder, knee, wrist, and elbow.

Synovial joints

Anatomy of synovial joints

The synovial joint is a complicated joint, involving many parts. It is movable, and consists of a joint cavity, articular cartilage, and joint capsule with an inner synovial membrane, and an outer fibrous layer (Fig. 6.34). The fibrous layer attaches to the periosteum on or near the articular cartilage. The synovial membrane is highly vascular, well innervated, and produces synovial fluid. Synovial fluid is viscous and acts to lubricate the joint, provide nutrients, and remove waste from the hyaline articular cartilage.

The articular cartilage is a translucent, bluish-tinged cartilage, usually hyaline, that covers the articulating surfaces of the bone. The joint cavity is unique to synovial joints and contains a trace amount of synovial fluid. Outside the fibrous layer of the joint capsule may be ligaments that hold together the bones of the joints. The ligaments consist of bands of white fibrous connective tissue holding the joints together.

The meniscus or articular menisci is fibrocartilage that partially or completely divides a joint cavity. Menisci are found only in the stifle and temporomandibular joints. They serve to make the joint more stable by improving the fit between two articulating bones.

A bursa is a saclike structure between different tissues that acts as a ball bearing reducing the friction between the bones. The bursa is a flattened sac lined with a synovial membrane and containing a small amount of synovial fluid. While technically not part of the synovial joint, bursae are associated with such joints where ligaments, muscles, skin, tendons, or bones rub together. A bunion is an enlarged bursa at the base of the big toe in humans.

A tendon synovial sheath wraps completely around a tendon. It acts similar to a bursa, reducing friction between the tendons and bones.

Classification of synovial joints

The types of synovial joints can be classified as follows:

- 1. Ball-and-socket. Also called a spheroid or triaxial, this joint allows all movements, thus allowing the greatest range of motion. Examples include the iliofemoral (hip) joint and glenohumeral (shoulder) joint.
- 2. Hinge. Also called a ginglymus or monaxial joint, movement is limited to flexion and extension. Examples include the knee, elbow, and interphalangeal joints.
- 3. Pivot. Also called a trochoid or monaxial joint, it allows movement limited to rotation. Examples include the atlantoaxial or proximal radioulnar joint.

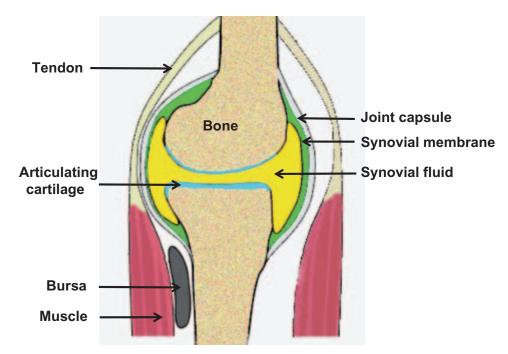


Fig. 6.34. General structure of a synovial joint. Modified from http://www.arthritis.ca/images/user/%7B9078931D-CA9E-4682-B65C-70F8782D168D%7D.gif

- 4. Ellipsoidal or condyloid. Also called a condyloid or biaxial joint, it is essentially a reduced balland-socket joint. Allows all angular motions, including flexion, extension, abduction, and adduction, but not rotation. Examples include the radiocarpal joints.
- 5. Saddle. Also known as sellar or biaxial, allows all movements except rotation. An example includes the carpometacarpal joint of thumb.
- 6. Plane. Also called an arthrodia, gliding, or biaxial joint, allows gliding in flexion, extension, abduction, and adduction. Such joints are present in intercarpal and intertarsal joints.

Movements of synovial joints

Synovial joints can make various types of movements and display different ranges of motion. The range of motion of synovial joints varies from nonaxial movement, which includes slipping motions only; to uniaxial movement involving motion in one plane; to biaxial movement, (movement in two planes); and to multiaxial movement involving movement in three planes.

There are three general types of movements possible in synovial joints: rotation, gliding, and angular. These are listed in Table 6.5.

In addition, there are special movements unique to synovial joints. The manus (hand) can undergo supination, palm-up position, and pronation, palm-down or back position. Supination involves the lateral rotation of the radius; pronation involves the medial rotation of the radius relative to the ulna. During pronation, the distal end of the radius crosses over the ulna so that the bones form an "X."

Inversion and eversion are terms describing the movement of the foot. During inversion, the sole of the foot turns medially; during eversion, the sole faces laterally.

Protraction and retraction involve nonangular anterior or posterior movement along a transverse plane. When the mandible is pushed outward from the jaw, this is protraction; pulling the mandible back is called retraction.

Elevation and depression are terms used to describe shoulders or jaw movement. When the shoulders are moved dorsally, it is called elevation; lowering the shoulders is called depression. The mandible is elevated or depressed during chewing.

Specific joints

Intervertebral articulations

The intervertebral articulations consist of cartilaginous and synovial joints. The cartilaginous joints are formed by the intervertebral discs joining the bodies of the vertebrae. The synovial joints are formed by

Movement	Description	Example
Rotation Rotation	Turning a bone around its own long axis	Femur can rotate away from median plane (lateral rotation) or toward median plane (medial rotation)
Nonangular Movements Gliding	One flat or nearly flat bone surface slips over another similar surface	Intercarpal and intertarsal joint movements
Angular Movements Flexion	Decreasing the angle of the joint	The elbow joint (humerus-radius/ulna)
Extension	Increasing the angle of the joint	The elbow joint (humerus-radius/ulna)
Dorsal and ventral flexion	Bending the spinal column dorsally or ventrally	The spine
Abduction	Moving a part away from the median plane	The shoulder joint (humerus-glenoid fossa)
Adduction	Moving a part toward the median plane	The shoulder joint (humerus-glenoid fossa)
Circumduction	Movement that traces a cone shape, thus combining flexion, abduction, extension, and adduction	Movement of a limb in a circular motion with the shoulder or hip remaining essentially stationary
Rotation	Movement around the long axis of a part	Radio-ulnar joint
Universal	All of the above movement	The shoulder joint

caudal and cranial articular processes of the adjacent vertebrae.

The first two joints within the vertebral column are atypical. The first, the atlanto-occipital joint, is a modified hinge type of synovial joint between the occipital condyles and the cranial articular surfaces of the atlas (i.e., first vertebral vertebra). This joint has a spacious joint capsule, and is specialized to allow a "yes" motion. The atlanto-axial joint is a pivot type of synovial joint. It is between the dens of the axis and the cranial articulation surfaces on the atlas.

Costovertebral joints

There are two types of articulations between the ribs and the vertebral column. The head of each rib forms a ball-and-socket type of synovial joint, with the causal and ostal facets of adjacent vertebrae. The tubercle of each rib forms a plane type of synovial joint with the transverse process of the corresponding rib.

Sternocostal joints

There is a pivot type of synovial joint between the first eight costal cartilages and the sternum. Each joint has a joint capsule and ligaments.

Costochondral joints

There is a fibrous joint between the ribs and costal cartilage. These have no synovial cavities or joint capsule.

Box 6.1 Rupture of an intervertebral disc

The rupture or degeneration of a disc between the vertebrae allows the pulpy nucleus to bulge or leak out of the disc. This usually occurs dorsally, or dorsolaterally. This can result in pressure being placed on the spinal cord or spinal nerves. It most commonly occurs at the thoracolumbar junction or neck region.

Thoracic limb

Shoulder joint

Also called the glenohumeral or scapulohumeral joint, the shoulder joint is a ball-and-socket type of synovial joint. The head of the humerus articulates with the glenoid cavity of the scapula. It contains a loose joint capsule with no true collateral ligaments. Instead, the muscles crossing the joint provide the support to minimize shoulder luxation (i.e., separation). Functionally, this is a freely movable joint (Fig. 6.35).

The intertubercular, or bicipital, sulcus is a groove between the greater and lesser tubercles. This site holds the biceps brachii tendon. There is a synovial sheath around this tendon as it passes through the intertubercular groove in carnivores, pigs, and sheep. In horses, oxen, and goats, there is an intertubercular bursa found between the intertubercular groove and the bicipital tendon. The transverse humeral ligament attaches between the greater and lesser tubercles

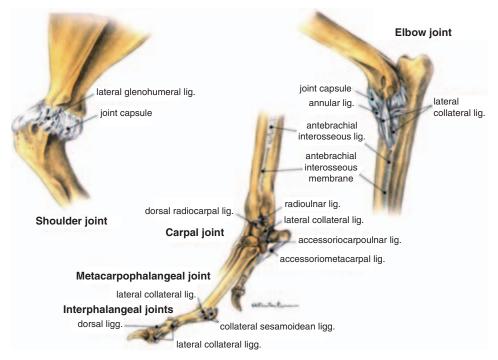


Fig. 6.35. Joints of the thoracic limb. The lateral aspect of the thoracic limb of the dog. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

holding the biceps tendon in the intertubercular groove.

Elbow joint

The humeroradioulnar articulation is a hinged type of synovial joint allowing flexion and extension. It is a compound joint since it consists of three bones. There is a joint capsule encasing all three bones.

The humeral condyle consisting of the capitulum and trochlea articulates with the head of the radius, and the anconeal process of the ulna fits into the olecranon fossa of the humerus. The medial and lateral collateral ligaments located on the sides of the joint restrict the movement to flexion and extension.

In horses and ruminants the proximal and distal joint between the radius and ulna is fused. In carnivores, these joints are not fused. This allows some rotation of the radius and, hence, some degree of supination of the forepaw, as well as return to pronation.

Carpal joint

The carpal joint consists of three main joints including the antebrachiocarpal, middle carpal, and carpometacarpal joint. The carpal joint is a hinged type of synovial joint. The antebrachiocarpal joint consists of an articulation between the distal radius and ulna and the proximal row of carpal bones. The distal row of carpal bones articulate with the metacarpal bones constituting the carpometacarpal joint. The middle carpal joint is between the two rows of carpal bones. There are plane joints between individual carpal bones.

Pelvis

Pelvic symphysis

This is a slightly movable fibrocartilaginous joint between the hip bones (os coxae). The front portion of this joint is formed by the pubic symphysis between the two pubic bones; the caudal portion is formed by the ischial symphysis between the two ischial bones.

Sacroiliac joint

The sacroiliac joint is a relatively immobile joint between the wings of the sacrum and the ilium. It is a combination of a cartilaginous and synovial joint. Fibrocartilage unites the ilium with the wing of the sacrum.

The sacrotuberous ligament connects the sacrum and first caudal vertebrae with the ischiatic tuberosity. This ligament stabilizes the caudad end of the sacrum between the os coxae. It is absent in cats.

Hip joint

Also called the coxal or coxofemoral articulation, this is a ball-and-socket synovial joint between the head of

the femur and the acetabulum of the hip bone. It is a freely movable (diarthrodial) joint allowing universal movement (i.e., flexion, extension, abduction, adduction, lateral rotation, and circumduction). It has no collateral ligaments; instead, its stability depends on the ligament of the head of the femur, a strong joint capsule, and a large muscle mass surrounding it. The ligament of the head of the femur connects from the acetabular cavity to the notch on the fovea capitis, a notch on the head of the femur. Found only in horses, the accessory ligament of the head of the femur extends from the prepubic tendon through the acetabular notch under the transverse acetabular ligament to the fovea capitis of the head of the femur. This ligament makes it harder for the horse to kick to the side, i.e., cow kick, although it doesn't totally prevent it.

Box 6.2 Hip dysplasia

Hip dysplasia involves a malformed hip joint resulting in a progressive degenerative disease. This disease has a high incidence in some breeds of dogs. Diagnosed radiographically, the condition causes pain. Treatments include cutting the pectineous muscle, removing the neck and head of the femur (head and neck osteotomy), or remodeling the acetabulum by cutting the hip bones and repositioning them.

Pelvic limb

Knee (stifle joint)

The knee, also known as the stifle joint, is a compound joint involving the femur, patella, and tibia. It is a hinge type of synovial joint allowing flexion and extension with little rotation (Fig. 6.36).

The joint between the patella and femur is called the femoropatellar joint, and contains a large joint capsule. The patellar ligament runs between the patella and the tibial tuberosity. Remember that the patella is a sesamoid bone, meaning that it is found within a tendon. Carnivores, pigs, and small ruminants have one patellar ligament; horses and oxen have three, including the lateral, middle, and medial.

The femorotibial joint is the articulation between the femur condyles and the tibia, and has an interposed menisci. These menisci include the medial and lateral menisci that sit between the tibial and femoral condyles.

The medial collateral ligament fuses with the joint capsule and medial meniscus and stabilizes the medial side of the stifle. The lateral collateral ligaments connect the lateral epicondyle and head of the fibula. It is separated from the lateral meniscus by the tendon of the popliteus muscle.

The cranial cruciate ligament originates on the caudolateral femur and inserts cranially on the tibia. It

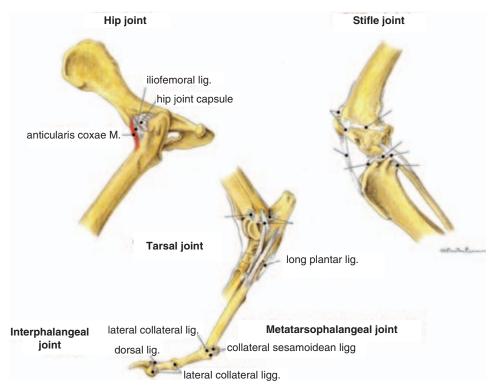


Fig. 6.36. Joints of the pelvic limb. The lateral aspect of the pelvic limb of the dog. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

prevents cranial movement of the tibia relative to the femur. The caudal cruciate ligament arises from the craniomedial distal femur and inserts on the tibia. It prevents caudal movement of the tibia relative to the femur.

Tarsus

The tarsus, or hock, is a compound hinge type of synovial joint. It allows only flexion and extension. The tibiotarsal portion of the tarsus is the most movable joint, and is an articulation between the proximal row of tarsal bones (i.e., the talus and calcaneus), and the fibula and tibia. The cochlea of the tibia receives the trochlear ridges of the talus. The proximal intertarsal joint is the articulation between the proximal row of tarsal bones and the central and fourth tarsal bones. The distal intertarsal joint includes the articulation between the central tarsal and tarsal bones I, II, and III.

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13 Cardiovascular system

Contents

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The cardiovascular system (*cardio* = heart; *vascular* = blood vessels) consists of three components: blood, the heart, and blood vessels. Blood is essential for transporting nutrients and wastes, thermoregulation, immunity, and acid-base balance. The heart and blood vessels help deliver the blood throughout the body.

Functions and composition of blood

Functions of blood

The study of blood, blood-forming tissues, and blood disorders is called hematology. Since animals consist of multiple layers of cells, they cannot rely on simple

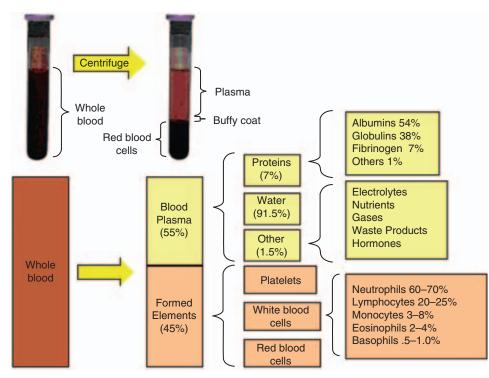


Fig. 13.1. Blood components. Centrifugation of whole blood containing an anticoagulant results in the separation of red blood cells, a buffy coat containing white blood cells and platelets, and plasma.

diffusion to deliver nutrients and remove wastes. Instead, the blood is necessary for these functions. Blood is a connective tissue consisting of materials suspended in a nonliving liquid matrix called plasma. Blood has three main functions: transportation, regulation, and protection.

Transportation

Blood transports O_2 and CO_2 between the lungs and the tissues. In addition, blood transports absorbed nutrients from the gastrointestinal tract to the liver and other cells; hormones from endocrine glands to target cells; waste products from cells to excretory sites including the liver, kidneys, and skin; and heat throughout the body.

Regulation

Blood serves a major role in maintaining homeostasis. Blood helps regulate pH via buffers, body temperature by either carrying excess heat to the skin for dissipation or by vasoconstricting to conserve heat, and osmotic pressure by maintaining blood protein and electrolyte levels.

Protection

Blood plays many roles in immunity. Some blood cells are phagocytic; others produce antibodies. Blood proteins such as complement and interferons are important in immunity. In addition, blood helps maintain homeostasis by clotting to prevent blood loss.

Physical characteristics of blood

Blood is denser and thicker than water. It contains both cellular and liquid components. The cells (formed elements) and cell fragments are suspended in plasma. Although fibers typically seen in connective tissue are not present, during the clotting process, dissolved proteins combine to form fibrous strands.

When centrifuged, the components of the blood will separate into three distinct compartments (Fig. 13.1). The formed elements move toward the bottom of the tube; the plasma appears near the top. Packed at the bottom of a centrifuged tube will be the erythrocytes, or red blood cells. Sitting on top of this layer will be a thin, whitish layer called the buffy coat. This layer contains leukocytes, or white blood cells, and platelets, which are cell fragments. The top layer is the plasma. The percentage of a blood sample that is erythrocytes is called the hematocrit. An abnormally high hematocrit is called polycythemia, which is an indication that there are too many erythrocytes per milliliter of blood. Such blood can carry elevated amounts of oxygen, but it has a greater viscosity, making it harder for the heart to pump such blood. Polycythemia can also be an indication of dehydration since decreased fluid volume will also result in an increased number of erythrocytes per ml of blood. Conversely, a low hematocrit reading indicates anemia, meaning that there are not enough erythrocytes, and thus a low level of hemoglobin, in the blood. This can result in an increased cardiac output as the animal attempts to deliver adequate oxygen to the tissues.

In dogs and horses, the spleen stores erythrocytes. In fact, horses can store up to 50% of the erythrocytes in the spleen. Therefore, when the animals exercise, the spleen can inject erythrocytes into the circulation, increasing the hematocrit by nearly 25% percent.

Box 13.1 Blood doping

In sports, the term *doping* was first used to describe the illegal drugging of racehorses at the beginning of the 20th century. Today, the term *blood doping* includes the transfer of autologous or homologous erythrocytes and the use of synthetic erythropoeitin (EPO) to increase the number of red blood cells. Synthetic EPO was developed as a treatment for anemia resulting from cancer therapy. Injecting EPO under the skin can increase the hematocrit, thus increasing the oxygen-carrying capacity of the blood. Recently, it was discovered that horses have been doped using drugs designed for Alzheimer's and Parkinson's disease, which increase blood flow to the brain, thus restoring function.

In race horses, using a "milkshake" was a popular practice for enhancing performance. The practice is thought to have begun in Australia in Standardbreds. A milkshake consisted of several ounces of sodium bicarbonate dissolved in a gallon of water. Sometimes confectionery sugar, electrolytes, or nutritional substances including creatine were added. The thought was that giving a milkshake 4–8 hours prior to a race would enhance performance.

Plasma

Consisting of over 90% water, plasma also contains nutrients, gases, hormones, waste products, electrolytes, and proteins. The nutrients include various components absorbed from the gastrointestinal tract or produced in the liver, including glucose, amino acids, and lipids. Oxygen and CO_2 are transported in the blood as are hormones produced in endocrine glands. Plasma proteins are the most abundant plasma solute. They can function as carriers for other nutrients such as transferrin that carries iron, act in immunity (immunoglobulins), and help in blood clotting (fibrinogen). The liver synthesizes most plasma proteins.

Formed elements in mammals

Formed elements of blood include erythrocytes (red blood cells, RBCs), leukocytes (white blood cells, WBCs) and platelets. RBCs and WBCs are whole cells, whereas platelets are cell fragments. There is only one type of RBC, but there are five types of WBC, including neutrophils, lymphocytes, monocytes, eosinophils, and basophils (Table 13.1). WBCs are grouped into either granulocytes or agranulocytes, depending on whether they contain obvious membrane-bound cytoplasmic granules. Granulocytes include neutrophils, eosinophils, and basophils. Agranulocytes include lymphocytes and monocytes. The number of various blood cells within the blood is shown in Table 13.2.

Types of blood cells in mammals

Erythrocytes

Erythrocytes, or red blood cells, are approximately 7–8 μ m in diameter. They are shaped like biconcave discs, thus increasing their surface area to volume ratio. They are flexible, and able to deform in order to move through capillaries. Erythrocytes in mammalian species lack a nucleus and organelles. Avian red blood cells, however, are nucleated. Certain glycolipids found on the plasma membrane of RBCs account for the various blood groups. Since RBCs lack organelles, they are unable to reproduce. They must produce ATP anaerobically because they lack mitochondria.

Erythrocytes are filled with hemoglobin (Fig. 13.2). Hemoglobin is a specialized protein that functions in oxygen transport. Each hemoglobin molecule consists of four polypeptide chains (two alpha and two beta), each of which contains a nonprotein heme portion. An iron ion (Fe²⁺) is bound in the center of each heme molecule, and can reversibly bind with one oxygen molecule.

Although most carbon dioxide is transported in the plasma as bicarbonate, about 13% is transported bound to hemoglobin as carbaminohemoglobin. In addition, hemoglobin binds nitric oxide (NO), a gas formed by endothelial cells, which functions as a neurotransmitter that causes vasodilation. As hemoglobin delivers oxygen, it can simultaneously release NO,

Table 13.1.	Summary of formed elements in blood.	
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Cell Type		Picture	Description	Cells/mm ³	Life Span	Function
Erythrocytes			Biconcave, anucleated discs; 3–7 μm in diameter, depending on species	4–6 million	100–120 days	Transport oxygen and carbon dioxide
Leukocytes						
Granulocytes	Neutrophils	63	Multilobed nucleus; small granules; 10–12 μm in diameter	3,000–7,000	6 hr-few days	Phagocytize bacteria and some fungi
	Eosinophils	60	Bilobed nucleus; red granules; 10–14 μm in diameter	100–400	8–12 days	Kill parasitic worms; destroy IgE-antigen complexes, inactivate histamine from allergic reactions
	Basophils	0	U- or S-shaped nucleus; 8–10 μm in diameter	20–50	Few hours to few days	Release histamine and other inflammatory mediators; contain heparin
Agranulocytes						
	Lymphocytes	0	5–17 μm in diameter	1,500–3,000	Hours to years	Involved in cell- mediated and humoral immunity
	Monocytes	0	14–24 μm in diameter	100–700	Months	Phagocytosis; develop into macrophages after leaving capillaries
Platelets			Granule- containing cytoplasmic fragments; 2–4 µm in diameter	150,000–400,000	5–10 days	Seal torn blood vessels

Species	Erythrocytes	Total WBC	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils
Dog	6–8 million	6,000–17,000	3,000–11,500	1,000–5,000	0–1,200	100–1,200	0-100
Cat	6–8 million	5,500-19,500	2,500-12,500	2,700-6,700	0-800	0-1,500	0-100
Horse	7–12 million	5,500-12,500	2,700-6,700	1,500-5,500	0-800	0-900	0-200
Cow	6–8 million	4,000-12,000	600-4,000	2,500-7,000	0-800	0-2,400	0-200
Sheep	10–13 million	4,000-12,000	700-6,000	2,000-9,000	0-800	0-1,000	0-300
Pig	6–8 million	11,000–22,000	3,200–10,000	4,500–13,000	200-2,000	100-2,000	0–400

Table 13.2. Blood cell numbers (cells/µl).*

* Values from Swenson and Reece (1993) and Thrall et al. (2004).

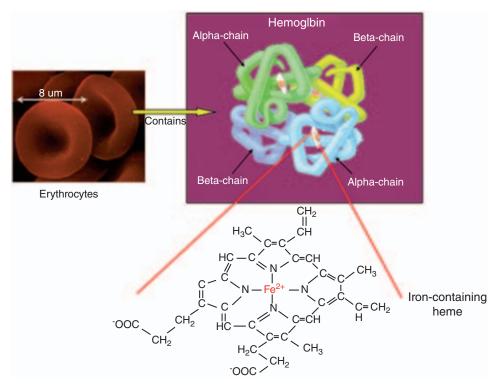


Fig. 13.2. Erythrocytes and hemoglobin structure. Erythrocytes (red blood cells) contain hemoglobin. Hemoglobin consists of four polypeptide chains, 2 alpha and 2 beta, each having a iron-containing heme molecule attached.

which dilates the capillaries allowing more blood, and therefore more oxygen, to be delivered.

Erythrocyte life cycle

Erythrocytes live about 120 days (Fig. 13.3). They get damaged as they squeeze through capillaries, and since they lack a nucleus and other organelles, they are unable to replace damaged structures. Damaged erythrocytes are removed from circulation by fixed phagocytic macrophages in the spleen, bone marrow, and liver. Once destroyed, the following steps occur:

- 1. The globin and heme portions are separated.
- 2. Globin is hydrolyzed into its component amino acids, which are then used for synthesis of other proteins.
- 3. The iron (Fe²⁺) removed from the heme binds to the plasma protein transferrin and is transported through the bloodstream to muscle fibers, liver cells, and macrophages in the spleen where it is stored attached to ferritin. Since Fe²⁺ and Fe³⁺ can damage molecules in the body, they are transported and stored bound to transferrin and ferritin.
- 4. When mobilized, the Fe^{3+} -transferrin complex transports iron to bone marrow where erythrocyte precursor cells internalize it via receptor-mediated endocytosis and use it to synthesize hemoglobin. Vitamin B₁₂ is needed for hemoglobin synthesis.
- 5. The non-iron portion of heme is converted to biliverdin, a green pigment, and then to bilirubin, a yellow-orange pigment.

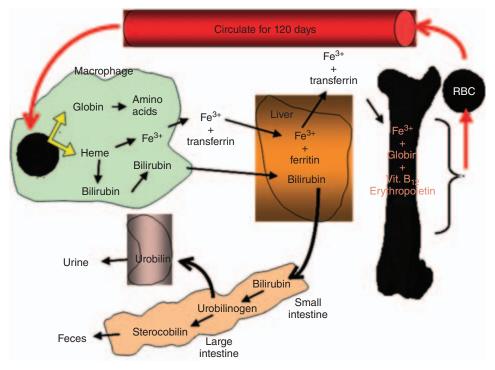


Fig. 13.3. Erythrocyte life cycle. Erythropoietin stimulates the production of new erythrocytes in red bone marrow. The erythrocytes circulate in the blood and have a life span of about 120 days. When worn out, they are phagocytized by macrophages in the spleen, liver, or red bone marrow. The iron in the heme molecule is recycled while the remainder of the heme molecule is metabolized and excreted.

- 6. Bilirubin is transported to the liver where it is secreted by liver cells into the bile.
- 7. Bile is released into the small intestine. In the large intestine, bilirubin is converted by bacteria into urobilinogen, which is converted to stercobilin, a brown pigment giving feces their characteristic color.
- 8. A small fraction of the urobilinogen is reabsorbed in the large intestine and converted to urobilin, a yellow pigment, which is excreted in the urine.

Leukocytes

Leukocytes, also called white blood cells, are the only blood cells that are truly complete cells containing nuclei and organelles. They do not contain hemoglobin. They generally account for only 1% of the blood volume, but they are an important component of the immune system.

They possess properties that allow them to carry out immune functions. WBCs leave the circulatory system by a process called emigration. Emigration involves several steps:

1. Near the site of inflammation, the endothelial cells lining the capillaries display cell adhesion molecules called selectins on their surface. Neutrophils have other cell adhesion molecules called integrins on their surface that recognize selectins. This causes the WBCs to line up along the inner surface of the capillaries near the inflamed site, a process called margination.

- 2. WBCs can move out of the capillaries through a process called diapedesis.
- 3. After leaving the bloodstream, they migrate via amoeboid action following a chemical signal produced by damaged tissue, a process called positive chemotaxis.
- 4. Neutrophils and macrophages become phagocytized and then ingest bacteria and dispose of dead matter.

Granulocytes

Neutrophils

Neutrophils account for 50–70% of WBCs. Twice as large as erythrocytes, their cytoplasm stains a pale lilac with very small granules. The granules stain with both basic and acid dyes. Some granules are considered lysosomes containing hydrolytic enzymes, and others contain antibiotic-like proteins called defensins. Since the nuclei consists of 3–6 lobes, these cells are often called polymorphonuclear leukocytes.

Attracted to sites of inflammation via chemotaxis, neutrophils are the first cells to be attracted by chemotaxis to leave the bloodstream. After leaving the capillaries, they are attracted to bacteria and some fungi. Neutrophils phagocytize these foreign cells and then undergo a process called a respiratory burst. Oxygen is converted to free radicals such as bleach (hypochlorite, OCl⁻), superoxide anion (O_2^-), or hydrogen peroxide. The defensin-containing granules merge with the phagosomes, and the defensins act like peptide "spears" producing holes in the walls of the phagocytized cells. The neutrophils then die.

Eosinophils

Eosinophils account for 2–4% of all leukocytes. They contain large, uniform-sized granules that stain redorange with acidic dyes. The granules do not obscure the nucleus, which often appears to have two or three lobes connected by strands. The granules contain digestive enzymes, but they lack enzymes that specifically digest bacteria.

Eosinophils function against parasitic worms that are too large to phagocytize. Such worms are often ingested or invade through the skin and move to the intestinal or respiratory mucosa. Eosinophils surround such worms and release digestive enzymes onto the parasitic surface.

Basophils

Accounting for only 0.5–1.0% of leukocytes, these are the rarest WBCs. Slightly smaller than neutrophils, they contain histamine-filled granules that stain purplish-black in the presence of basic dyes. The nucleus stains dark purple, and is U- or S-shaped. When bound to immunoglobulin E, these cells release histamine. Histamine is an antiinflammatory chemical that causes vasodilation and attracts other WBCs to the site.

Agranulocytes

Lymphocytes

Accounting for 25% of the WBCs, these cells contain a large, dark-purple–staining nucleus. The nucleus is typically spherical, slightly indented, and is surrounded by pale-blue cytoplasm. Lymphocytes are classified as either large (10–14 μ m) or small (6–9 μ m). The functional significance of the difference in size is unclear.

Monocytes

Monocytes are $12-20 \,\mu\text{m}$ in diameter and account for 3-8% of leukocytes. They contain a kidney- or horseshoe-shaped nucleus. They contain very small blue-gray-staining granules that are lysosomes. After leaving the bloodstream, monocytes become macrophages. Some become fixed macrophages, such as alveolar macrophages located in the lungs and Kupffer cells located in the liver. Others become wandering macrophages that move throughout the body and collect at sites of infection and inflammation.

Platelets

Platelets, which are fragments of cells, consist of plasma membranes containing numerous vesicles but not nucleus. When there is a tear in a blood vessel, platelets coalesce at the site and form a platelet plug. Chemicals released from their granules aid in blood clotting.

Box 13.2 Complete blood count (CBC)

If an animal is ill, often a blood sample will be taken in order to conduct a complete blood count (CBC), or hemogram. A CBC includes a hematocrit; descriptions of any abnormalities in blood cell shapes, size, color, or appearance; an assessment of blood hemoglobin; and a count of white blood cells. An increase in white blood cell count indicates an infection whereas a decreased count may indicate weakness from a long illness. A decrease in lymphocyte numbers is observed at the beginning of an infection or following the use of steroid medications. An increase in the number of lymphocytes can indicate prolonged illness or leukemia. When total neutrophil numbers are increased, it is usually a sign of a bacterial infection or some form of extreme stress. The quantities increase in the blood when the animal is suffering from an infection with parasites or has allergies. If a dog or cat experiences extreme or prolonged stress, eosinophil numbers decrease. If the platelet numbers are decreased, it may indicate that the animal has either used up a large quantity of the available cells in clot formation or that their number may be low and the animal is at great risk if bleeding.

Formation of blood cells

The formation of new blood cells is called hemopoiesis, or hematopoiesis. Prior to birth, hemopoiesis begins in the yolk sac and later occurs in the liver, spleen, thymus, and lymph nodes of the fetus. After birth, it occurs in red bone marrow, which is found between the trabeculae of spongy bone. This is found predominately in the axial skeleton, pectoral and pelvic girdles, and proximal epiphyses of the humerus and femur.

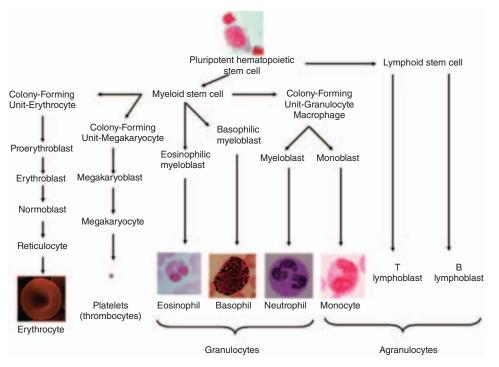


Fig. 13.4. Formation of blood-formed elements. Blood cells are produced from pluripotent hematopoietic stem cells. (Modified from Tortora and Grabowski, 2003.)

Within the red bone marrow are pluripotent stem cells. These can proliferate, or differentiate, into different blood cells, macrophages, reticular cells, mast cells, and adipoctyes. Macrophages are part of the innate immune system. Reticular cells form reticular fibers that serve as part of the matrix supporting red bone marrow cells (Fig. 13.4).

Pluripotent stem cells produce two other stem cells: myeloid stem cells and lymphoid stem cells. Myeloid stem cells differentiate within the red bone marrow to produce erythrocytes, platelets, monocytes, neutrophils, eosinophils, and basophils. In contrast, lymphoid stem cells begin in the red bone marrow but finish differentiating in lymphatic tissue forming lymphocytes. In addition, lymphocytes produce numerous cytokines, small glycoproteins that act as signals to modify other cells.

Myeloid cells produce progenitor cells. These cells are restricted, meaning that they are committed to becoming selected blood cells and cannot reverse to become stem cells. As shown in Figure 13.2, some of these progenitor cells become colony-forming units. Colony-forming units give rise to precursor cells, indicated by names ending in *-blast*.

Erythrocyte formation

Erythropoiesis is the production of erythrocytes in the red bone marrow. Hematopoietic stem cells divide to produce myeloid stem cells, which transform into proerythroblasts (Fig. 13.4). Proerythroblasts give rise to erythroblasts, which synthesize hemoglobin, and then are transformed to normoblasts. When the normoblast contains about 34% hemoglobin, it ejects most of its organelles, becoming a reticulocyte, the precursor of an erythrocyte. The process of hematopoietic stem cell to reticulocyte takes about 3–5 days. Reticulocytes are released into the bloodstream where, within 2 days, they release their ribosomes and become erythrocytes.

Erythropoietin (EPO), a glycoprotein produced mostly in the kidney, stimulates erythropoiesis. Although there is generally a small amount of EPO circulating in the bloodstream, hypoxia causes the kidney to produce EPO. Hypoxia can be caused by a reduced number of erythrocytes, reduced availability of oxygen such as might occur at increased altitudes, or increased tissue demand for oxygen. In contrast, excess erythrocytes or oxygen in the bloodstream reduces EPO synthesis.

Leukocyte formation

Hematopoietic stem cells produce lymphoid stem cells, which produce T and B lymphocytes. Leukopoiesis is the production of white blood cells. It is stimulated by various cytokines, generally produced by macrophages and T lymphocytes. Cytokines are glycoproteins, and they include interleukins and colonystimulating factors. An abnormally low level of white blood cells is termed leukopenia, which can be caused by radiation, shock, or chemotherapeutic agents.

Platelet formation

Platelet formation is stimulated by the hormone thrombopoietin (TPO). Thrombopoietin causes myeloid stem cells to develop into megakaryocyte-colony forming cells, which then become megakaryoblasts. Megakaryoblasts are large cells that later splinter into 2,000 to 3,000 fragments. Each fragment has a cell membrane and is called a platelet, or thrombocyte.

Formed elements and blood cells in birds

Although most of the formed elements in birds are similar to those in mammals, there are some notable differences. Formed elements of blood in birds include erythrocytes, leukocytes, and thrombocytes, the avian equivalent of platelets. Like mammals, the avian leukocytes are divided into granulocytes and agranulocytes. Avian granulocytes include eosinophils, basophils, and heterophils (equivalent to mammalian neutrophils). Avian agranulocytes include lymphocytes and monocytes. The number of various blood cells within the blood is shown in Table 13.2.

Thrombocytes

Thrombocytes are found in birds, reptiles, amphibians, and fish. Unlike platelets, they are nucleated. Thrombocytes are smaller than erythrocytes, and in good preparations, a small eosinophilic vacuole appears as an orange dot located at one end of the nucleus. Whereas mammalian platelets are derived from megakaryocytes, such precursors are lacking in birds. There remains some debate as to whether avian thrombocytes arise from antecedent mononucleated cells or multinucleated cells. Avian thrombocytes have a similar function to mammalian platelets.

Heterophils

Heterophils function similarly to mammalian neutrophils. In some avian species they are the most common peripheral leukocyte. They are typically round, with colorless cytoplasm and many eosinophilic, rodshaped to spherical granules. The granules may partially obscure the nucleus, which usually has two or three lobes and coarsely aggregated, purple chromatin. Often in blood smears the heterophil sometimes has a distinct ruby-colored central granule since the rod-shaped granules are dissolved, leaving the central one only.

Box 13.3 Heterophil/lymphocyte ratio in birds

While in many animals increased plasma corticosteroids are used as an indication of stress, it was shown that the blood ratio of heterophils (H) to lymphocytes (L) is also a good measure of stress. It was noted that when corticosterone is added to the feed of chickens, the number of blood lymphocytes increased while the number of heterophils decreased. The ratio of H/L is now commonly used as an indicator of prolonged stress in birds. Increased plasma corticosterone levels are an indication of acute stress in birds whereas H/L rations are a better indicator of long-term stress. One will not observe a change in H/L ration until approximately 12 hours after exposure to stress.

Hemostasis

Hemostasis is a series of responses that stop bleeding. As blood vessels are damaged or torn, hemostasis quickly controls the bleeding. The hemostasis response is rapid, localized, and well controlled so as not to spread throughout the body. Hemostasis entails three mechanisms: 1) vascular spasms, 2) platelet plug formation, and 3) blood clotting (coagulation). If bleeding is not stopped for any reason, an animal will hemorrhage and lose blood.

Box 13.4 Aspirin and gastric bleeding

In some conditions, such as arthritis, aspirin may be prescribed to treat dogs and cats. Aspirin belongs to a class of drugs called nonsteroidal antiinflammatory drugs (NSAIDs). Dogs are particularly sensitive to the gastrointestinal effects of NSAIDs, which include pain, bleeding (i.e., gastric hemorrhaging), and ulceration. Coated aspirin may help with the gastrointestinal effects. Aspirin can be given with food, 1–2 times a day.

Since cats cannot break down this drug as quickly as dogs, they are more sensitive to aspirin than dogs. Thus, time between doses is generally increased with cats. Cats are typically dosed at intervals of 48–72 hours.

Acetaminophen and ibuprofen are generally not recommended for dogs. These drugs can be fatal to cats.

Vascular spasm

When blood vessels become injured, the vessels constrict. This vascular spasm is triggered by injury to the vascular smooth muscle, chemicals released from endothelial cells and platelets, and reflexes involving local pain receptors.

Platelet plug formation

Platelets contain a large number of chemicals, including clotting factors, ADP, ATP, Ca²⁺, serotonin, enzymes that produce thromboxane A2, fibrin-stabilizing factor, and platelet-derived growth factor (PDGF). They also contain lysosomes and mitochondria. Fibrin-stabilizing factor helps strengthen blood clots. PDGF is involved in proliferation of vascular endothelial cells, vascular smooth muscle fibers, and fibroblasts, all of which help repair damaged vessels.

A platelet plug forms as follows:

- 1. Platelet adhesion. Platelets adhere to the collagen fibers of the connective tissue exposed in a damaged vessel wall.
- 2. Platelet release reaction. Adhesion to the vessel wall causes the platelets to become activated. They extend processes that allow them to contact and interact with adjacent platelets. They also liberate their vesicular contents in a process called the platelet release reaction. ADP and thromboxane A help activate neighboring platelets. Serotonin and thromboxane A cause vasoconstriction by causing the vascular smooth muscle to contract, thus decreasing blood flow.
- 3. Platelet aggregation. Released ADP makes adjacent platelets sticky, causing more and more platelets to adhere at the injured site.
- 4. Platelet plug. As more platelets adhere, a platelet plug forms.

Blood clotting

When blood clots, it forms a straw-colored liquid called serum and a gellike mass called a clot. The clot consists of insoluble protein fibers called fibrin that trap other formed elements of the blood.

Clotting, or coagulation, involves a series of chemical reactions resulting in fibrin thread formation. Clotting factors include calcium ions, inactive enzymes produced in the liver and released into the circulatory system, and chemicals released from platelets and damaged tissue. Clotting factors are generally named by Roman numerals indicating the order of their discovery, not their order in the clotting process.

The formation of a clot in an unbroken blood vessel is called a thrombosis, with the clot being called a thrombus. The movement through the blood of a clot, air bubble, fat from a broken bone, or debris is called

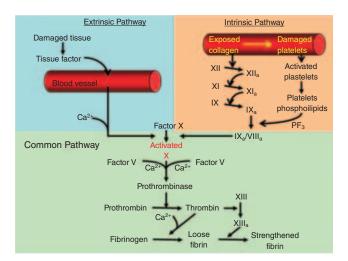


Fig. 13.5. Blood-clotting cascade. Both the extrinsic and intrinsic pathways result in formation of Activated Factor X that then combines with Factor V to form the active enzyme prothrombinase.

an embolus. These often lodge in the lungs producing a pulmonary embolism.

Clotting consists of three stages (Fig. 13.5): 1) two pathways, called the intrinsic and extrinsic pathways, leading to the production of prothrombinase, 2) conversion of prothrombin to thrombin, catalyzed by prothrombinase, and 3) thrombin catalyzing the conversion of fibrinogen into insoluble fibrin.

Extrinsic pathway

The extrinsic pathway is quicker and has fewer steps than the intrinsic pathway. Damaged tissue releases a tissue protein called tissue factor (TF), or thromboplastin, that initiates the formation of prothrombinase. Since TF comes from outside the blood, this pathway is called the extrinsic pathway. In the presence of Ca^{2+} , TF initiates a series of reactions resulting in the formation of factor X. Factor X then combines with factor V to form the active enzyme prothrombinase.

Intrinsic pathway

In the intrinsic pathway, all the factors necessary for blood clotting are present in (i.e., an intrinsic part of) the blood. The intrinsic pathway relies on the production of PF_3 , a phospholipid associated with the external surface of aggregated platelets. Like the extrinsic pathway, the intrinsic pathway results in the production of factor X.

Common pathway

Both the intrinsic and extrinsic pathways use a common pathway after the activation of factor X. Pro-

thrombin is converted to thrombin by prothrombinase. Thrombin then catalyzes the conversion of fibrinogen to fibrin. Activated factor XIII catalyzes the polymerization of cross-linked fibrin.

Role of vitamin K

Although vitamin K is not directly involved in clot formation, it is needed for the synthesis of four clotting factors by hepatocytes. These include factors II (prothrombin), VII, IX, and X. Vitamin K is normally synthesized by bacteria found in the large intestine and is absorbed through the intestinal wall along with other lipids.

Clot retraction and repair

Beginning about 30–60 minutes after clot formation, the clot becomes more stable through a process called clot retraction. Platelets contain actin and myosin, and these contractile proteins begin to contract, similar to muscle contraction. This platelet contraction pulls on surrounding fibrin strands, thus squeezing serum from the clot and pulling the ruptured edges of the vessel closer together. The platelets release factor XIII that helps strengthen the fibrin clot. Simultaneously, PDGF released by degranulating platelets stimulates smooth muscle and fibroblasts to divide and repair the damaged site. The fibroblasts form a connective tissue sheath over the injured area. Vascular endothelial growth factor then causes the endothelial cells to multiply and restore the blood vessel lining.

Fibrinolysis

A clot is not permanent. Following healing, the clot is removed by a process of fibrinolysis. The major clotbusting enzyme is plasmin, which is produced when the blood protein plasminogen is activated by tissue plasminogen activator secreted by endothelial cells. Plasminogen can also be activated by activated factor XII and thrombin released during the clotting process. Plasmin digests the fibrin threads and inactivates fibrinogen, prothrombin, and factors V, VIII, and XII.

Factors limiting clot growth and formation

Since blood clotting involves a positive feedback system, there must be systems in place to localize clot formation. Clots are prevented from spreading by 1) rapid removal of clotting factors, and 2) inhibition of activated clotting factors. Fibrin absorbs thrombin into the clot, thus limiting its site of action. Thrombin that escapes into circulation is inactivated by antithrombin III, an anticoagulant produced in the liver. Endothelial cells and WBCs produce prostacyclin, a prostaglandin that opposes the action of thromboxane A2. Prostacyclin inhibits platelet adhesion.

Heparin, produced by mast cells and basophils, is an anticoagulant that combines with antithrombin increasing its effectiveness. Protein C, also produced in the liver, inactivates factors V and VIII and enhances the activity of plasminogen activators.

Thrombolytic agents

Thrombolytic agents are chemicals injected to dissolve blood clots. Streptokinase, produced by streptococcal bacteria was one of the first commercial thrombolytic agents. More recently, a genetically engineered version of tissue plasminogen activator has been used.

Aspirin can inhibit vasoconstriction and platelet aggregation. It does so by blocking the synthesis of thromboxane A2.

Blood groups and crossmatching

Blood groups

On the surface of erythrocytes are various glycoproteins and glycolipids that act as antigens. Because of these isoantigens or agglutinogens, blood is categorized into various blood groups, each of which can have various blood types. In humans, the most common blood groups are the ABO blood group and the Rh blood groups, whereas animals have a variety of different blood groups.

Cattle have 11 major blood groups systems including A, B, C, F, J, L, M, R, S, T, and Z. The B group has over 60 different antigens. The J antigen is not a true antigen, but instead is a lipid found in body fluids that adheres to erythrocytes.

The antigen groups or blood types in dogs are known as the DEA system. They include DEAs 1.1, 1.2, and 3–8. DEAs 1.1 and 1.2 account for 60% of the canine population. Dogs having DEA 1.1 or 1.2 are considered A-positive; other dogs are considered Anegative. A-negative dogs do not have antibodies against A-positive blood.

Cats have three AB blood groups. Type A is most common, accounting for 95% of short- and longhair domestic cats. Type B is less frequent, and Type AB is rare. Cats with type-A blood have antibodies against A isoantigens whereas type-B cats have alloantibodies (i.e., antibodies found against antigens in some members of the same species) against B isoantigens.

There are seven blood groups in sheep including A, B, C, D, M, R, and X. The B group is highly polymorphic, and the R system is similar to the J system in cattle.

Five blood groups have been identified in goats: A, B, C, M, and J, with J being similar to that of cattle.

Crossmatching

Crossmatching is a procedure to determine whether donor blood is compatible with the recipient's blood. There are two types of crossmatches. In major crossmatching, the donor erythrocytes are compared to the recipient serum to determine whether either acquired or naturally occurring antibodies are present in the recipient serum against the donor erythrocytes. Minor crossmatching compares donor serum to recipient erythrocytes, checking for preformed antibodies in donor serum that could hemolyze recipient red cells. Minor crossmatching is less important since the donor serum is markedly diluted after transfusion, decreasing the risk of a significant reaction.

The heart

Anatomy of the heart

Location and exterior landmarks

The heart is an inverted cone-shaped structure located in the mediastinum, a mass of tissue occupying the medial region of the thoracic cavity extending from the sternum to the vertebral column, and between the lungs. The apex, or "pointed" end of the heart is directed caudoventrally; the base, or top of the heart, is directed dorsocranially.

The cranial and caudal sides of the heart can be located by other structures. The auricles point left, with the pulmonary trunk located between the two auricles. The aortic arch projects caudally.

The coronary groove partially encircles the heart except at the conus and indicates the separation of the atria and ventricles. The conus is the expanded outflow of the right ventricle into the pulmonary trunk. The interventricular grooves indicate the divisions between the two ventricles. The two auricles are visible on the left side of the heart, with the pulmonary trunk between them.

Pericardium

The membrane surrounding the heart is the pericardium. It consists of the fibrous pericardium and serous pericardium. The fibrous pericardium is a tough, inelastic, dense irregular connective tissue sac with one end attaching to the diaphragm and the other open end fusing with the connective tissue surrounding the blood vessels entering and leaving the heart. The fibrous pericardium anchors the heart within the mediastinum and prevents overfilling of the heart. Inside the fibrous pericardium is the serous pericardium, consisting of a parietal and visceral layer. The parietal layer lines the internal surface of the fibrous pericardium; the visceral layer, also called the epicardium, is an integral part of the heart wall.

Inflammation of the pericardium is called pericarditis. This results in decreased production of serous fluid, and a roughened serous membrane. As a result, the beating heart can be heard with a stethoscope rubbing against the serous layer (pericardial friction rub). In severe cases, inflammation leads to excess fluid production, which compresses the heart and decreases its pumping ability.

Layers of the heart

The heart wall consists of three layers: epicardium, myocardium, and endocardium. The epicardium is the outermost layer, and it is the visceral layer of the pericardium. It consists of a thin, transparent layer of mesothelium and connective tissue. The middle layer, or myocardium, is cardiac muscle and makes up the bulk of the heart. The innermost endocardium is a thin layer of connective tissue providing a smooth lining for the chambers of the heart and valves. The endocardium is continuous with the endothelial lining of the large blood vessels attached to the heart.

Cardiac muscle is also called involuntary, striated muscle. Like skeletal muscle, it contains actin and myosin that is organized into sarcomeres.

Fibrous skeleton of the heart

The heart also contains dense connective tissue surrounding the valves, forming a fibrous skeleton (Fig. 13.6). In addition to forming a point of attachment for the valves, the fibrous skeleton serves to eclectically insulate the atria from the ventricles.

Box 13.5 Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a disease characterized by dilation or enlargement of the heart chambers resulting in an abnormally large heart. This disease eventually results in heart failure, since the damaged heart muscle is too weak to efficiently pump blood to the rest of the body. DCM is very common in dogs, representing the most common reason for congestive heart failure (CHF). The left ventricle is most always involved. Since the myocardium cannot work effectively to pump blood out of the heart, subsequent backup of blood into the left atrium and ultimately into the lungs occurs commonly. This backup of blood into the lungs results in pulmonary edema and is a sign of congestive heart failure.

The treatment of dogs with dilated cardiomyopathy varies with the severity of heart failure and specific organ damage. Treatment may include oxygen administration, fluid therapy, and administration of drugs that improve breathing (bronchodilators) and drugs that modify heart function, such as control of the arrhythmias. If low doses of anti-arrhythmic drugs are effective, the heart can often be stabilized. Serious ventricular arrhythmias that can only be controlled by high doses of antiarrhythmic drugs have a poorer prognosis.

Heart chambers and vessels

The heart has four chambers. Two atria located superiorly, receive blood and pump it to the ventricles. Two ventricles located posteriorly pump the blood away from the heart (Fig. 13.6). The atria are separated by the interatrial septum; the ventricles are separated by the interventricular septum. There is an oval depression on the interatrial septum called the fossa ovalis (Fig. 13.7), a remnant of the foramen ovale, which is an opening between the atria in the fetus that closes shortly before birth.

Atria

The atria are the receiving chambers of the heart. Protruding from the atria are the auricles, which increase the atrial volume. The auricles are lined with pectinate muscles making them appear as if they were raked with a comb. The atria are relatively small and thinwalled, since they need to pump blood only to the ventricles.

Blood enters the right atrium from three veins: 1) the superior vena cava returns blood from the body regions in front of the diaphragm, 2) the inferior vena

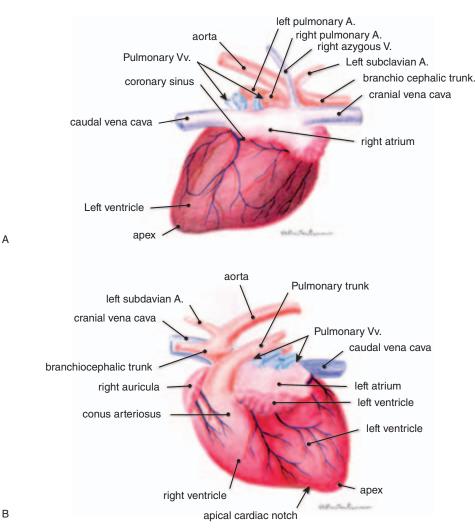


Fig. 13.6. External structure of the heart. A) Atrial side of the cat heart. B) Auricular side of the cat heart. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

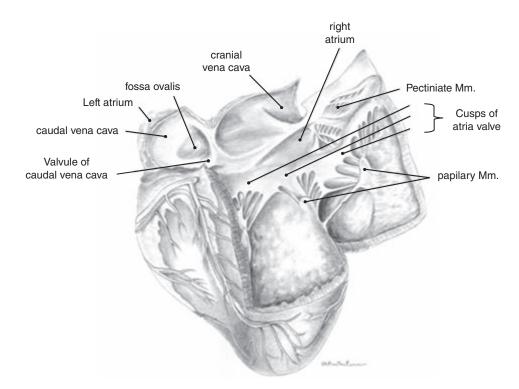


Fig. 13.7. Internal structure of the heart. The right side of the heart of a large ruminant is opened. (Reprinted from Constantinescu and Constantinescu, 2004. Used by permission of the publisher.)

cava returns blood from areas posterior of the diaphragm, and 3) the coronary sinus collects blood draining the myocardium (Fig. 13.6). Blood passes from the right atrium into the right ventricle through the tricuspid valve, so named because it consists of three leaflets or cusps.

Blood enters the left atrium via four pulmonary veins. Blood passes from the left atrium to the left ventricle via the bicuspid, or mitral, valve, named because it has two cusps.

Ventricles

The ventricles form the bulk of the heart. The right ventricle wall is thinner than the left since it has to pump blood only through the lungs via the pulmonary trunk. The left ventricle pumps blood to the body via the aorta, the largest artery in the body.

Blood leaves the right ventricle via the pulmonary valve. The left ventricle forms the apex of the heart. Blood leaves the left ventricle via the aortic valve. During fetal development when there is no pulmonary respiration, there is a temporary blood vessel called the ductus arteriosus that shunts blood from the pulmonary trunk into the aorta. This vessel closes shortly after birth, leaving a remnant called the ligamentum arteriosum. Inside the ventricles are muscle bundles called the papillary muscles, which serve as attachments for the chordae tendineae, tendinous cords attaching to the atrioventricular valves. The papillary muscles and chordae tendineae assist in valve function.

Box 13.6 Feline dilated cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a heart (cardio-) muscle disease (myopathy) in which the muscular walls of the left ventricle thickens (hypertrophy). The left ventricular walls may hypertrophy secondarily to other diseases such as systemic hypertension, or the hypertrophy can be a primary disease in itself.

HCM is diagnosed when thickening of the left ventricular walls is not caused by another disease. As HCM progresses, it can alter the heart structure and impair its functioning in several ways, including the following: 1) Ventricular chamber size may be reduced, thus limiting its ability to fill with blood; 2) Ventricular wall stiffness usually increases, which impairs the ability of the ventricle to relax, preventing it from filling efficiently; 3) There may be an increase in ventricular pressure during relaxation (diastole), causing blood to back up into the vessels of the lungs and subsequent congestive heart failure, which includes pulmonary edema and/or pleural effusion (seepage of vascular fluid into the lungs and/or pleural spaces).

Because the left ventricle is unable to fill adequately, less blood is pumped out to the body with each heartbeat. If the blood supply to other vital organs is inadequate, heart rate may increase as the body attempts to compensate. A decrease in blood flow to the kidneys can result in an increased release of rennin, which increases blood volume, increasing the pressures on the left side of the heart and contributing to congestive heart failure.

Pathways of blood through the heart

The heart acts as two pumps, side by side. The pulmonary circuit carries blood to and from the lungs and the systemic circuit transports blood throughout the remainder of the body (Fig. 13.8).

The right side of the heart receives deoxygenated blood from the body. This blood passes into the right atrium, through the tricuspid valve, and into the right ventricle. It is then pumped to the lungs via the pulmonary trunk. In contrast to other major arteries and veins in the body, the pulmonary artery carries oxygenpoor blood while the pulmonary vein carries oxygenrich blood.

The left side of the heart receives freshly oxygenated blood arriving from the lungs via the pulmonary vein. The blood passes from the left atrium to the left ventricle via the bicuspid valve. Blood is then pumped from the left ventricle into the aorta, passing through the aortic valve.

Heart valve operation

Atrioventricular valves

The atrioventricular (AV) valves lie between the atrium and ventricles. When open, the cusps of the valves push into the ventricles, allowing blood to flow from the atrium to the ventricles. While the AV valves are open, the papillary muscles and chordae tendineae are relaxed. When the ventricles contract, pressure in the ventricles increases and pushes blood back toward the atria. This blood pushes the cusps of the valves back toward the atria, closing the valves. Simultaneously, the papillary muscles contract, pulling on the chordae tendineae. The chordae tendineae prevent the cusps of the AV valves from everting into the atria. Damage to the AV valves or chordae

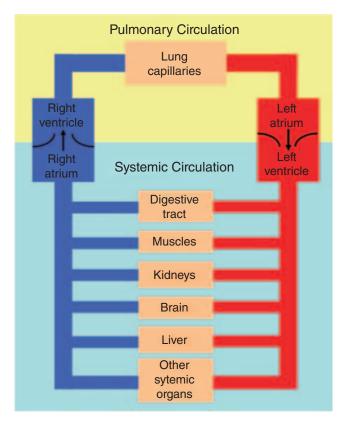


Fig. 13.8. Systemic and pulmonary circulation. The right side of the heart pumps deoxygenated blood to the pulmonary circuit while the left side of the heart pumps oxygenated blood throughout the body.

tendineae allows regurgitation of blood through the AV valves.

Semilunar valves

The semilunar valves include the aortic and pulmonary valves, which allow blood to pass from the ventricles into the aorta and pulmonary vein, respectively. These valves are made of three crescent-shaped cusps. As the pressure in the ventricles exceed that in the arteries, blood passes from the heart into the arteries. As the ventricles relax, the backflow of blood catches the cusps and causes these valves to close, thus preventing the movement of blood back into the ventricles.

There are no valves located at the entrance of the venae cavae into the right atrium or pulmonary veins into the left atrium. So as the atria contract, a small amount of blood can backflow into these veins. However, contraction of the atria compresses the area where the veins attach, thus minimizing the backflow of blood.

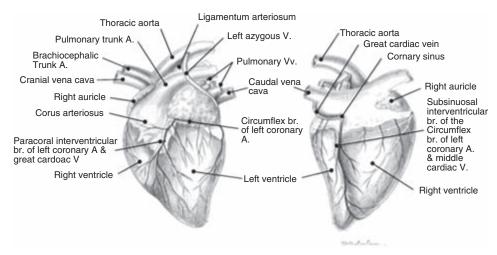


Fig. 13.9. Coronary circulation of goat heart. (Reprinted from Constantinescu, 2001. Used by permission of the publisher.)

Pulmonary, systemic, and coronary circulation

Pulmonary circulation

The pulmonary circulation transports deoxygenated blood from the right ventricle to the lungs where it picks up O_2 while delivering CO_2 . The right side of the heart is responsible for the pulmonary circuit. Deoxygenated blood returning from the body enters the right atrium and passes into the right ventricle. The right ventricle pumps the blood into the pulmonary artery and into the pulmonary capillaries. Oxygenated blood is returned to the left atrium via the pulmonary vein.

Systemic circulation

The systemic circulation distributes oxygenated blood throughout the body. Blood is pumped from the left ventricle into the aorta, and then into smaller systemic arteries. These arteries give rise to arterioles that lead to systemic capillaries. Exchange of nutrients occurs across the capillary walls. Blood enters the systemic venules and then into systemic veins that return the blood to the right atrium.

Coronary circulation

The myocardium, or heart muscle, receives nutrients via the coronary circulation (Fig. 13.9). Blood leaves the aorta and passes into the left and right coronary arteries arising at the base of the aorta and encircling the heart in the atrioventricular groove. The left coronary artery has two branches. The anterior interventricular artery travels in the anterior interventricular sulcus and supplies the interventricular septum and ventral walls of both ventricles. The circumflex artery supplies the left atrium and dorsal walls of the left ventricle.

The right coronary artery also divides into two branches. The marginal artery supplies the lateral right side of the heart, and the posterior interventricular artery travels to the heart apex and supplies the posterior ventricular walls.

After passing through the capillaries, venous blood in the heart collects in the cardiac veins. These veins carry blood to the coronary sinus, which empties into the right atrium.

Cardiac muscle and the cardiac conduction system

Cardiac muscle

Cardiac muscle is also called involuntary, striated muscle. Cardiac muscle fibers are shorter and less circular than skeletal muscle fibers. They generally contain a single nucleus, although occasionally two are present. Cardiac muscle fibers connect with neighboring fibers via thickening of the sarcolemma called intercalated discs (Fig. 13.10). These discs contain desmosomes that hold the fibers together and gap junctions that allow action potentials to move among cardiac muscle fibers. The gap junctions allow the cardiac muscle fibers to act as a functional syncytium, so that the atria and ventricles can contract as a unit.

Cardiac muscle fibers contain larger, more numerous mitochondria than skeletal muscle. The mitochondria account for 25% of the cell volume in cardiac muscle while only occupying 2% in skeletal muscle. Like skeletal muscle fibers, cardiac muscle contains

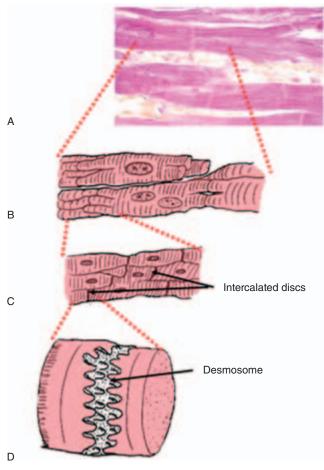


Fig. 13.10. Cardiac muscle A) Histological section of cardiac muscle. B) Drawing of a longitudinal section of cardiac muscle showing the branched cardiac muscle fibers. C) A close-up of the intersection of adjacent cardiac muscle fibers and their intervening intercalated discs. D) A close-up of the intercalated disc showing a desmosome.

sarcomeres. However, the T tubules in cardiac muscle fibers are wider and less abundant than in skeletal muscle. In addition, there is only one T tubule per sarcomere in cardiac fibers, entering at the Z disc, whereas there are two per sarcomere in skeletal muscle fibers entering at the junction of the A and I bands. The sarcoplasmic reticulum is also less extensive in cardiac muscle fibers.

The conduction system

The heart contains specialized cardiac muscle fibers that can self-generate an action potential, and are therefore called autorhythmic fibers. These cells do not require extrinsic neural input, and they can continue to generate an action potential even when the heart is removed from the body. These autorhythmic cells act as a pacemaker, establishing the basic electrical activity in the heart. In addition, there are specialized cardiac muscle fibers that form a conduction system that provides a path for electrical excitation to travel throughout the heart (Fig. 13.11). This conduction system helps the heart pump in a coordinated manner so that blood can be pumped throughout the body.

Cardiac electrical activity is propagated through the heart conduction system in the following manner:

- 1. Located in the wall of the right atria near the entrance of the inferior vena cava is the sinoatrial (SA) node. The cells in the SA node do not maintain a stable resting membrane potential, but instead spontaneously depolarize 75 times/min. Since this is faster than in other areas of the heart, the SA node becomes the pacemaker, establishing the sinus rhythm.
- 2. Depolarization of the SA node results in an action potential that is propagated throughout the atria via the gap junctions between neighboring cardiac muscle fibers.
- 3. The action potential reaches the atrioventricular (AV) node, located in the inferior portion of the interatrial septum, above the tricuspid valve. The AV node delays the action potential about 0.1 sec before it travels to the ventricles. The delay occurs because the AV fibers are smaller, and have fewer gap junctions. This delay allows the atria time to complete their contraction before the ventricles contract.
- 4. From the AV node, the action potential moves to the AV bundle, also called the bundle of His, located in the superior portion of the interventricular septum. There are no gap junctions between the atria and the ventricles, which are instead insulated from each other by the fibrous skeleton of the heart. This necessitates that the action potential travel through the AV node to reach the ventricles.
- 5. The action potential continues in the right and left branches. These continue through the inferior portion of the interventricular septum toward the apex of the heart.
- 6. The right and left branches carry the action potential to the Purkinje fibers, which complete the pathway to the heart apex and then turn superiorly, running up the outer walls of the ventricles toward the atria. Purkinje fibers supply the papillary muscles as well as the ventricular muscles.

The rate at which the SA node depolarizes can be influenced by hormones and the autonomic nervous system. If acetylcholine is released by the parasympathetic nervous system, the SA node slows while release of epinephrine by the sympathetic nervous system accelerates the SA node.

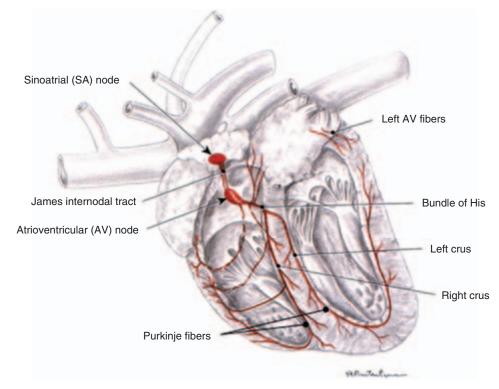


Fig. 13.11. Excitation and conducting system of the dog heart. The pacemaker of the heart is the sinoatrial (SA) node. A wave of depolarization spreads from the SA node throughout the atria. This wave of depolarization then passes through the atrioventricular (AV) node where it is delayed from proceeding to the ventricles. From the AV node, the wave of depolarization travels down the bundle of His located in the intraventricular septum, and then into the Purkinje fibers. (Modified from Constantinescu, 2002.)

Mechanisms of heart contraction

Action potentials generated in the heart by the SA node travel throughout the heart via the conduction system as described above. The mechanism of contraction of cardiac muscle fibers is described below (Fig.13.12):

- Depolarization. As a cardiac muscle fiber is stimulated by a neighboring action potential, voltagegated fast Na⁺ channels open. This allows a rapid influx of Na+ from the extracellular fluid, which results in depolarization of the cardiac muscle fiber from -90 mV to +30 mV. These channels quickly become inactivated and close.
- 2. Plateau. As the voltage-gated fast Na⁺ channels close, voltage-gated slow Ca²⁺ channels open in the sarcolemma and sarcoplasmic reticulum (SR). The influx of Ca²⁺ from the extracellular space (20%) causes a large release (80%) of Ca²⁺ from the SR. Simultaneously, the membrane permeability to K⁺ decreases. As a result, the membrane remains depolarized at around 0 mV for about 0.25 sec, compared to about 0.001 sec in skeletal muscle.
- 3. Repolarization. After the relatively long plateau phase, voltage-gated K⁺ channels open, allowing

potassium ions to flow out of the cell and the membrane to repolarize. The cell returns to its resting membrane potential of about –90 mV.

4. Refractory period. The refractory period, or time during which the next contraction cannot be triggered, is relatively long in cardiac muscle compared to skeletal muscle. The refractory period prevents cardiac muscle from developing tetanus, and thereby it allows the heart to act as an effective pump rather than developing a sustained contraction.

The mechanism of contraction of cardiac muscle fibers is similar to that in skeletal muscle fibers. As intracellular Ca^{2+} concentrations increase, Ca^{2+} binds to troponin, causing the tropomyosin to move and thus uncovering the myosin binding sites on the actin filaments. Myosin then binds to actin, and the actin is pulled across the myosin filament. Drugs that alter the movement of calcium into the cardiac muscle fibers can affect the strength of heart contraction.

ATP production

Cardiac muscle has little capacity for anaerobic cellular respiration; thus, cardiac muscle relies almost

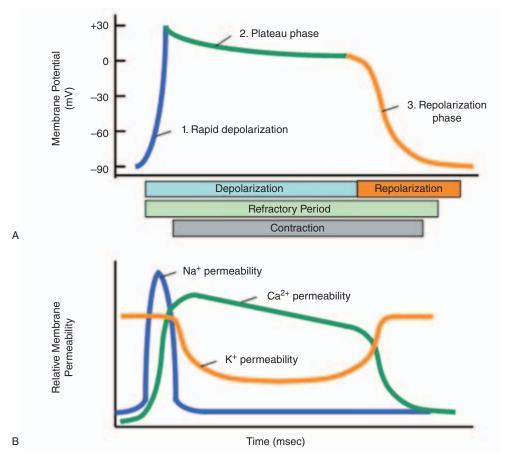


Fig. 13.12. Action potential in cardiac muscle fibers. A) The action potential in cardiac muscle fibers has a plateau phase not seen in skeletal muscle fibers. B) The influx of Na⁺ causes the rapid depolarization phase while increased Ca²⁺ permeability leads to the plateau phase. Efflux of K⁺ results in repolarization.

entirely on aerobic respiration. Therefore, cardiac muscle needs a continuous supply of O_2 , which arrives via the coronary circulation or is released from myoglobin inside the cardiac muscle fibers. Cardiac muscle can produce ATP from the oxidation of fatty acids, glucose, lactic acid, amino acids, and ketone bodies.

Cardiac muscle also contains creatine phosphate, which can be used to produce ATP. The enzyme creatine kinase can catalyze the transfer of a phosphate group from creatine phosphate to ADP to produce a new molecule of ATP. If the heart is damaged, it releases creatine kinase into the bloodstream, which is often measured as an indicator of heart damage.

Electrocardiogram

The propagation of the action potentials through the heart produces electrical currents that can be detected on the surface of the body. A recording of these electrical activities is called an electrocardiogram (ECG or EKG). An ECG represents all of the electrical activity in the heart rather than a single action potential (Fig. 13.13).

Two electrodes are generally placed on each forelimb, and one on the left hindlimb. The potential difference between electrodes is measured using different combinations of electrodes. By comparing these various recordings, it is possible to determine whether there are abnormalities in the conduction system or whether the heart is damaged.

Each segment of the ECG is generated from a specific area of the heart in sequential manner (Fig. 13.14). A typical ECG has three characteristic waves with each heart beat. The first, or P wave, is a small upward deflection reflecting atrial depolarization (Fig. 13.13). It is generated as the SA node depolarizes, and the action potential spreads throughout the atria. The second wave, or QRS complex, begins with a downward deflection, and then rises sharply and ends with a downward deflection. The QRS complex represents ventricular depolarization. Its shape is complex because the movement of the wave of depolarization through the ventricle changes direction throughout

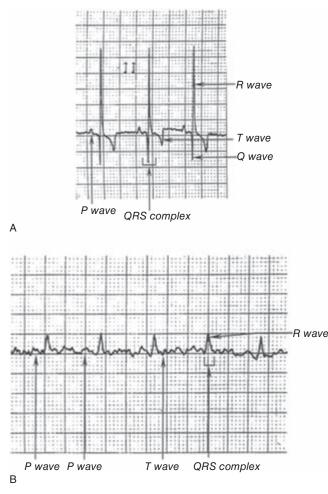


Fig. 13.13. Normal electrocardiogram. A) Dog. B) Cat. (Reprinted from Constantinescu, 2002. Used by permission of the publisher.)

the wave. The third wave is the T wave, and it represents ventricular repolarization. Since repolarization is slower than depolarization, the T wave is longer than the QRS complex.

Within the ECG, it is also possible to examine various intervals or segments. The P-Q interval is the time between the beginning of atrial excitation and the beginning of ventricular excitation. Therefore, it represents the time for the action potential to travel through the atria, the AV node, and the remainder of the conduction system. This interval can lengthen if there is coronary heart disease or scar tissue in the heart. The S-T segment begins with the S wave and ends with the beginning of the T wave. It represents the time when the ventricle is depolarized during the plateau phase. The T wave can be elevated in acute myocardial infarction. The Q-T interval is the period from the beginning of ventricular depolarization through ventricular repolarization. It can be lengthened by myocardial damage or myocardial ischemia.

Heart sounds

Auscultation involves listening to body sounds, usually with a stethoscope. Four sounds are created during each heart beat, and two of these sounds are clearly audible. These sounds are typically described as "lub-dup." The first sound, *lub*, is the AV valves closing. This occurs at the beginning of systole as the ventricular pressure increases above the atria pressure, causing the AV valves to close as blood begins returning to the atria. This sound is louder and longer than the second sound. The *dup* sound is caused by the semilunar valves closing at the beginning of ventricular diastole. The two other sounds, which are less audible, are due to the blood turbulence during ventricular filling and atrial systole.

Heart murmurs include clicking, rushing, or gurgling sounds. Although not always due to a problem, heart murmurs generally indicate a valve disorder. If the valve is stenotic, meaning it has a narrowed opening, a click may be audible when the valve should be fully opened. In contrast, if a swishing sound is heard when the valve should be closed, it may indicate that blood is able to backflow through the valve.

The cardiac cycle

The total of events associated with the movement of blood during one heartbeat is called the cardiac cycle (Fig. 13.15). The contraction and relaxation periods are called systole and diastole, respectively. The following steps describe the cardiac cycle:

- 1. Mid-to-late diastole. While the heart is relaxed, blood passively returns to the atria and into the ventricles through the opened AV valves. Approximately 70% of ventricular filling occurs during this time.
- 2. Atrial systole. During atrial systole, the atria contract while the ventricles remain relaxed. Atrial systole begins with depolarization of the SA node, causing an action potential to spread throughout the atria, appearing as the P wave on an ECG. As the atria contract, the remaining 30% of blood is forced through the opened AV valves and into the ventricles. The volume of blood in the ventricles is referred to as the end diastolic volume (EDV).
- 3. Ventricular systole. While the atria are relaxed (atrial diastole), the ventricles contract, appearing as the QRS complex on an ECG. As the volume in the ventricles decreases, ventricular pressure increases, causing the AV valves to close. For a fraction of a second, all the heart valves are closed, resulting in the isovolumetric contraction phase. When ventricular pressure exceeds the pressure in

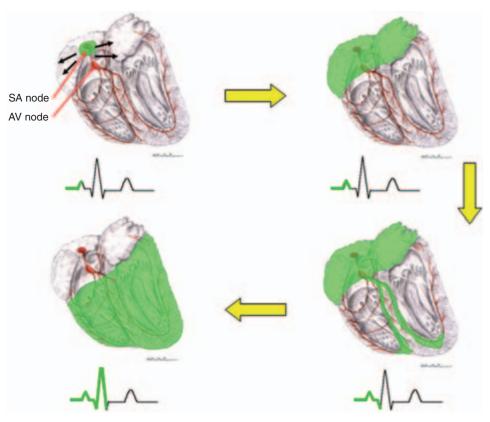


Fig. 13.14. Heart excitation and the ECG tracing. The green shading indicates the relationship between the area of the heart depolarizing coincident with the portion of the ECG produced by that depolarization. (Figure modified from Constantinescu, 2002.)

the large arteries, the semilunar valves are forced open, leading to the ventricular ejection phase.

4. Early diastole. Immediately following the T wave (i.e., ventricle repolarization), the ventricles relax, and the amount of blood remaining in the ventricles is referred to as the end systolic volume (ESV). As the pressure in the ventricles decreases, blood in the aorta and pulmonary arteries begins to return to the heart, causing closure of the semilunar valves. As these valves close, it causes a transient increase in aortic blood pressure called the dicrotic notch.

If the heart rate is 75 beats/min, the cardiac cycle is about 0.8 sec. Atrial systole lasts about 0.1 sec, ventricular systole lasts about 0.3 sec, and the remainder of the cycle is the quiescent period.

Cardiac output

The amount of blood pumped by the heart can be altered in response to metabolic changes caused by such factors as exercise, environmental temperature changes, or blood loss. The amount of blood pumped by either the right or left ventricle per minute is called the cardiac output (CO). CO is equal to stroke volume (SV), the amount of blood pumped by the ventricle per heart beat multiplied by the heart rate:

$$CO = SV \times HR$$

(mL/min) (mL/beat) (beats/min)

SV is equal to end diastolic volume (EDV) minus end systolic volume (ESV). The heart pumps approximately 60% of the blood in its chambers with each beat.

Factors that can alter stroke volume will alter CO. Cardiac reserve is the difference between an animal's maximum CO and its resting CO.

Box 13.7 Canine heartworms

Canine heartworms, *Dirofilaria immitus*, are common in the hearts and major heart blood vesicles of dogs throughout the world. The male worms are a few inches in length; the female worms are about double the size and cause most of the damage. The worms are transferred from dog to dog through the bite of an infected mosquito. Mosquitoes transfer microscopic larva that migrate through the body and arrive at the heart several months later where they mature into adult worms. Damage to the dog's heart is due to adult worms.

The first sign of heartworm disease is often premature aging in which dogs gray prematurely around the muzzle and forelegs. Then their activity level decreases and their coats lack luster. Further progression results in a chronic dry cough most noticeable at night when the dog is resting or in a sitting position. At the same time, the dog's heart and pulmonary arteries enlarge due to mechanical obstruction of the worms, inflammation, and valvular damage to the heart.

Until recently, the only medicine available to cure infected dogs of heartworms contained arsenic. More recent medications have an added ingredient, pyrantel pamoate, which prevents infestation with hookworms and roundworms as well.

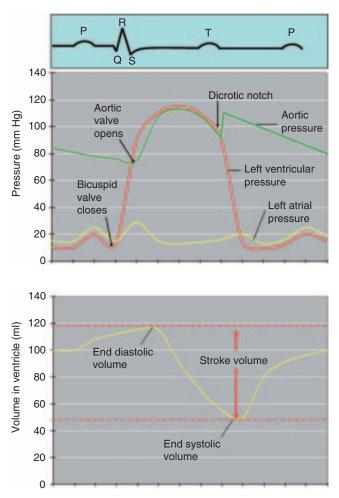


Fig. 13.15. Cardiac cycle. The top of the figure shows a typical ECG. The middle graph displays simultaneous changes in left atrial and ventricle pressure, and aortic pressure. The bottom graph shows changes in ventricular volume during the cardiac cycle.

Regulation of stroke volume

The heart will pump all the blood returning during systole. Three factors regulate stroke volume: preload, contractility, and afterload.

Preload

Preload is the amount of stretch on the heart prior to contraction. Within limits, greater stretch of the heart results in more forceful contraction. This is known as the Frank-Starling law of the heart. Cardiac muscle fibers are normally shorter than their optimal length for generating force. As a result, stretch of these fibers results in increased contractile force.

The preload is directly proportional to the volume of blood in the ventricles, or EDV. Two factors affect EDV: 1) duration of ventricular diastole, and 2) venous return, the amount of blood returning to the heart. As heart rate increases, duration of diastole shortens, resulting in a smaller EDV and a smaller SV. Although the decreased stroke volume can be offset by the increased heart rate, if heart rate becomes too rapid, there is insufficient preload and cardiac output declines. In contrast, during exercise, venous return increases because of increased squeezing of skeletal muscle on the veins. Consequently, SV increases.

Contractility

Contractility is the strength of contraction at a given preload, and it is independent of muscle stretch and EDV. Although preload is the major intrinsic factor regulating SV, contractility is influenced by extrinsic factors. Substances that increase contractility are called positive inotropic agents while those that decrease contractility are called negative inotropic agents.

Positive inotropic agents generally stimulate Ca²⁺ influx into the cytosol of cardiac muscle fibers, strengthening the force of contraction. Such agents include digitalis, glucagon, thyroxine, norepinephrine, and epinephrine (Fig. 13.16). Negative inotropic agents, which impair Ca²⁺ inflow, include anoxia, acidosis, increased extracellular K⁺ levels, and calcium channel blockers.

Afterload

The pressure that must be exceeded by the ventricles before blood can be ejected through the semilunar valves is called afterload. Any factor that increases afterload will increase ESV and decrease stroke volume. Such factors include hypertension or narrowing of the arteries, as in arteriosclerosis.

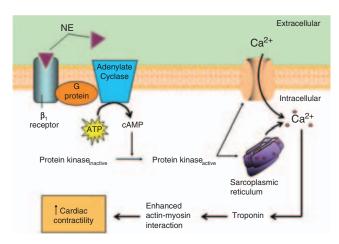


Fig. 13.16. Mechanism of norepinephrine-induced increase in heart contractility. Norepinephrine (NE), or epinephrine, binds to β 1-adrenoreceptor on the cardiac muscle fibers. That activates a G protein, which activates adenylate cyclase, thus producing cAMP. cAMP then activates protein kinase, which causes increased cytosolic Ca²⁺, coming both from the extracellular space and the sarcoplasmic reticulum. Ca²⁺ increases contractility.

Regulation of heart rate

Cardiac output depends on heart rate and stroke volume. Changes in heart rate (HR) are important in short-term regulation of cardiac output. Factors that increase HR are positive chronotropic factors; those that decrease heart rate are negative chronotropic factors. The most important factor controlling heart rate is the autonomic nervous system.

Autonomic nervous system regulation

The cardiovascular center in the medulla oblongata influences heart rate. This center receives input from sensory receptors, the limbic system, and the cerebral cortex. It directs the output from both the parasympathetic and sympathetic divisions of the autonomic nervous system.

The cardiovascular center receives sensory input from several areas. Proprioceptors monitor the positions of the limbs and joints. Increased movement of joints such as during exercise sends signals resulting in a rapid rise in heart rate. Chemoreceptors monitor blood chemical changes that can lead to changes in heart rate. Baroreceptors are located in the aortic arch and carotid arteries. Sudden changes in pressure in these regions cause changes in heart rate.

Activation of the sympathetic nervous system by either emotional or physical factors causes increased heart rate. This activation occurs via the cardiovascular center, which can stimulate heart rate via fibers from the spinal cord that stimulate the cardiac accelerator nerves extending from the spinal cord to the SA node, to the AV node, and throughout the myocardium. The sympathetic nerve fibers release norepinephrine (NE), which binds to β_1 adrenergic receptors in the heart. NE accelerates the rate of depolarization of the SA node and increases Ca²⁺ influx into cardiac myofibers, increasing contractility. Both of these effects result in enhanced pumping of blood during systole.

Although large increases in heart rate decrease end diastolic volume and stroke volume, moderate increases in heart rate are associated with increased contractility, which maintains stroke volume, and therefore CO increases.

Activation of the parasympathetic nervous system sends signals to the heart via the vagus nerve (cranial nerve X). The vagus nerve terminates in the SA node, AV node, and atrial myocardium. Parasympathetic fibers release acetylcholine, which decreases the spontaneous rate of depolarization of the SA node. Parasympathetic input has little affect on contractility.

Chemical regulation of heart rate

Chemicals can have a profound affect on the heart. The major chemicals affecting the heart are hormones and cations.

Hormones

Epinephrine and norepinephrine are both released from the adrenal medulla, and, acting as neurohormones, increase heart rate and contractility. Thyroid hormones also increase heart rate and contractility.

Cations

Extracellular and intracellular cation concentrations are important in maintaining resting membrane potentials. Therefore, it should come as no surprise that alterations in cation concentrations will affect heart function. Elevated blood Na⁺ concentrations decrease heart rate and contractility by interfering with Ca²⁺ influx into the cardiac muscle fiber. Increased blood K⁺ also decreases heart rate and contractility, but it does so by inhibiting the formation of the action potential. Increasing blood Ca²⁺ levels increases heart rate and contractility by leading to increased intracellular Ca²⁺.

Blood vessels and hemodynamics

Structure and function of blood vessels

There are five main types of blood vessels: arteries, arterioles, capillaries, venules, and veins. Arteries carry blood away from the heart as they branch or

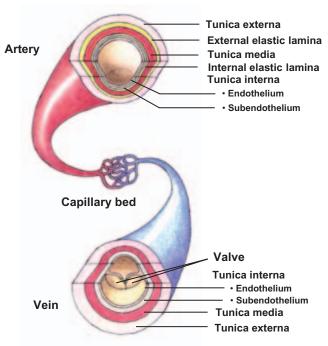


Fig. 13.17. Blood vessel walls.

diverge into smaller arterioles that then carry blood to the capillaries. Blood leaving the capillaries enters venules, which merge into the larger veins that ultimately enter the heart.

Blood vessel walls

Except in the smallest vessels, there are three layers, or tunics, surrounding the blood vessel lumen (Fig. 13.17). The tunica interna, or tunica intima, is the innermost layer. In intimate contact with the blood, this layer contains the endothelium consisting of simple squamous epithelium lining the lumen. These epithelial cells sit on a loose connective tissue basement membrane called the subendothelial layer. The endothelium is continuous with the endocardium lining the inside of the heart.

The middle layer, or tunica media, consists of a circular layer of smooth muscle, and elastin. Stimulation of the vasomotor nerve fibers by the sympathetic nervous system causes vasoconstriction in which the lumen diameter decreases. Relaxation of the smooth muscle results in vasodilation, or an increase in lumen diameter.

The outer layer is the tunica externa, or tunica adventitia, is composed of loosely woven collagen fibers. This layer reinforces and protects the vessels, and it is the site where nerve fibers and lymphatic vessels enter to provide nourishment.

Arteries

The arteries near the heart are called elastic arteries because they contain a large proportion of elastic fibers in the tunica media. They are large in diameter, therefore providing little resistance to blood flow. They expand to accommodate blood ejected from the ventricles. As the blood pressure decreases, these vessels recoil, thus helping to maintain pressure. They are sometimes called conducting arteries because they carry blood to more muscular, medium-sized vessels. Elastic arteries include the aorta, and the brachiocephalic, common carotid, subclavian, vertebral, pulmonary, and common iliac arteries.

The medium-sized arteries are called muscular arteries because they contain more muscle and less elastic fibers in the tunica media. Being more muscular, they have greater capacity to vasoconstrict. They are sometimes called distributing arteries because they deliver blood to various parts of the body.

Arterioles

The smallest of the arteries, arterioles deliver blood to the capillaries. Large arterioles contain all three tunics, with the tunica media having considerable smooth muscle and few elastic fibers. The smallest arterioles consist of simply a layer of endothelial cells surrounded by scattered smooth muscle cells. A metarteriole connects an arteriole with 10–100 capillaries making a capillary bed.

Capillaries

Capillaries, also called exchange vessels, are the smallest vessels. Their walls consist of only a tunica interna. Although capillaries are found in most places in the body, they are lacking in epithelium, the cornea and lens of the eye, and cartilage.

True capillaries originate from arterioles or metarterioles. At their origin is a ring of smooth muscle called the precapillary sphincter (Fig. 13.18). When contracted, the sphincter restricts the flow of blood into the capillary bed. Normally, blood flow within a capillary bed is intermittent due to changing vasomotor tone in the precapillary sphincter.

There are three types of capillaries: continuous, fenestrated, and sinusoidal (Fig. 13.19). Found in skin and muscles, the most common type is continuous, in which the endothelial cells form an uninterrupted layer with tight junctions between cells. However, there are intercellular clefts, or gaps, between neighboring cells allowing for exchange of nutrients. Within the brain, continuous capillaries lack intercellular clefts, and therefore form a structural barrier between the blood and brain, called the blood-brain barrier.

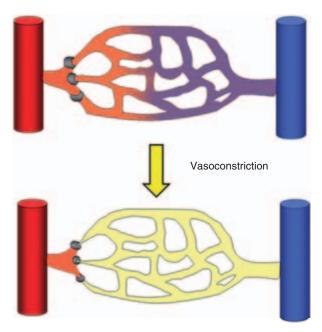


Fig. 13.18. Precapillary sphincters. Constriction of precapillary sphincters restricts the blood flow within a capillary bed.

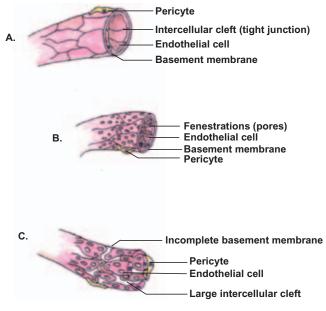


Fig. 13.19. Types of capillaries.

Fenestrated capillaries are similar to continuous capillaries, but they also have pores, or fenestrations, in the endothelial cells that allow substances to move out of the vessels. Such capillaries are found in the kidneys, villi of the small intestine, choroids plexus, ciliary processes of the eyes, and endocrine glands.

Sinusoidal capillaries have large, irregularly shaped lumens, and their endothelial cells have large fenestrations. They also lack a complete basement membrane, and thus they are very leaky. Such capillaries are found in the liver, bone marrow, lymphoid tissue such as the spleen, anterior pituitary, and parathyroid glands.

Venules

The smallest venules found close to capillaries consist of a tunica interna and a tunica media with a few smooth muscle cells. As the venules enlarge, they may contain a tunica externa.

Veins

Veins have the same three layers as arteries, but their thicknesses vary. The tunica interna and tunica media are thinner. The tunica externa is the thickest layer, containing collagen and elastic fibers. In the largest veins, the tunica externa also contains a longitudinal smooth muscle layer.

Unlike other vessels, veins also contain venous valves (Fig. 13.20). Formed from the tunica interna,

these one-way valves point toward the heart. The contraction of skeletal muscle during movement and increased thoracic pressure associated with respiration squeezes the veins, forcing blood towards the heart. As the skeletal muscle relaxes, the backflow of blood is prevented by the venous valves.

Because veins have a large lumen and thin walls, they can contain a large blood volume. Because veins can contain up to 65% of blood volume, they are called capacitance vessels.

Anastomoses

Most tissues receive blood from multiple arteries. The merging of these multiple sources results in an anastomosis. Such mergers provide alternate routes by which tissue can receive blood. If blood flow through one artery is prevented by an occlusion or loss of a vessel, blood still goes to the tissue through an anastomosis, thus providing collateral circulation.

Portal systems

In several places throughout the body, there are also vessels that link one capillary bed to another. These are known as portal vessels. Such vessels have the histological structure of veins. The complex of two capillary beds and the intervening portal vessel is known as a portal system.

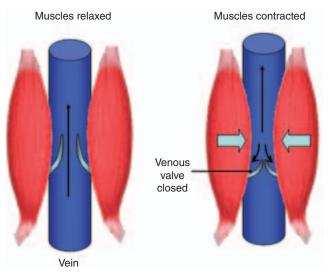


Fig. 13.20. Venous blood flow. Contraction of skeletal muscle and increased thoracic pressure due to respiration squeezes the veins, which causes the blood to move toward the heart. The blood is prevented from flowing backward, away from the heart, by one-way venous valves located in the veins.

One such portal system, called the hypophyseal portal system, consists of a capillary network in the median eminence supplied by the superior hypophyseal artery. This capillary network unites to form a series of vessels that spiral around the infundibulum and carry blood to a second capillary network located in the anterior pituitary.

A second example of a portal system is the hepatic portal system. The capillaries along the digestive system deliver blood into the inferior mesenteric vein, the splenic vein, and the superior mesenteric vein. These all deliver blood to the hepatic portal vein, which forms from a fusion of the superior mesenteric and splenic veins. The hepatic portal vein then carries blood to a capillary bed located in the liver. While carrying blood to the liver, the hepatic portal vein receives more blood from the gastric veins draining the stomach and the cystic vein coming from the gallbladder.

Capillary exchange

The purpose of the circulatory system is to deliver nutrients and remove wastes from tissues. This occurs through capillary exchange, in which substances move between the blood and interstitial fluid.

Diffusion

Capillary exchange generally occurs by simple diffusion, where chemicals move along their concentration gradient moving from an area of higher concentration to an area of lower concentration. O_2 and nutrients are generally in higher concentrations within the blood and therefore pass into the tissue; waste products are in higher concentration in the interstitial space and pass into the blood.

In all capillaries except sinusoids, the space between endothelial cells prevents the movement of plasma proteins from leaving the capillaries. In contrast, water-soluble chemicals, including glucose and amino acids, pass out of the capillaries through fenestrations of intercellular clefts. Lipid-soluble materials such as O_2 , CO_2 , and steroid hormones pass directly through the endothelial cell wall. In liver sinusoids, the gaps between the endothelial cells are large enough to allow proteins synthesized in the liver to enter the blood.

Bulk flow

The passive movement of large numbers of materials across a membrane is called bulk flow. Bulk flow moves from an area of higher pressure to an area of lower pressure. Diffusion accounts for most nutrient exchange across the capillary wall; bulk flow controls blood and interstitial fluid volume. The movement of fluid and solutes from capillaries into the interstitial space is called filtration, and the movement from interstitial fluid into the capillaries is called reabsorption.

Capillary hydrostatic pressure (HP_C) is the force exerted by blood against the capillary wall. This pressure tends to force fluid out of the capillary at the arteriole end of a capillary bed. HP_C is opposed by the interstitial fluid hydrostatic pressure (HP_{IF}), which pushes inward against the capillary. Therefore, the net hydrostatic pressure (Net HP) acting on a capillary is HP_C minus HP_{IF}. However, HP_{IF} is generally zero, so the effective hydrostatic pressure acting on a capillary is equal to HP_C. HP_C is larger at the arterial end of a capillary than at the venule end of the capillary.

 HP_C is also opposed by the colloid osmotic pressure (OP_C) , or oncotic pressure. This is the osmotic pressure inside the capillary caused by the presence of large plasma proteins that cannot leave the capillaries. The main protein responsible for OP_C is albumin. OP_C does not vary between the arterial and venule end of the capillary. Since the interstitial fluid has a few proteins, there is also an interstitial fluid osmotic pressure (OP_{IF}) opposing OP_C . OP_{IF} is generally only around 1 mm Hg.

Net filtration pressure (NFP), which is an interaction of hydrostatic and osmotic pressures, determines the direction of movement of fluids across the capillary wall (Fig. 13.21). NFP is calculated as follows:

$$NFP = (HP_C - HP_{IF}) - (OP_C - OP_{IF})$$

If we assume that at the arterial end of a capillary HP_C is 40 mm Hg, OP_C is 25 mm Hg, and OP_{IF} is 1 mm Hg, then:

$$NFP = (40 - 0) - (25 - 1) = 16 \text{ mm Hg}$$

If, at the venule end of the capillary, HP_C is 20 mm Hg, OP_C is 25 mm Hg, and OP_{IF} is 1 mm Hg, then:

$$NFP = (20 - 0) - (25 - 1) = -4 \text{ mm Hg}$$

Since HP_c varies along the capillary, there is a net movement of materials out of the capillary at the arterial end of the capillary and a net movement inward at the venule end. About 85% of the fluid filtered at the capillary is reabsorbed. The remaining fluid enters the lymphatic capillaries and eventually returns to the circulation at the subclavian vein.

Lack of reabsorption or an increase in filtration leads to edema, an abnormal increase in interstitial fluid volume. Lack of reabsorption can be caused by a decreased concentration of plasma proteins as is seen during liver disease, burns, malnutrition, or kidney disease. An increase in filtration can result from increased capillary pressure or damage to the endothelial wall caused by chemical, mechanical, or bacterial agents.

Factors affecting blood flow

Flow, pressure, and resistance

Blood flow (F) refers to the volume of blood flowing through a tissue during a given period of time. Total blood flow is equal to cardiac output. Blood flow is directly proportional to the difference in blood pressure (BP) between two points, and is inversely proportional to the resistance (R) to blood flow in the vessels:

$$F = \frac{\Delta BP}{R}$$

Since blood vessels have a great capacity to vasoconstrict and vasodilate, *R* has a greater affect on *F* than does *BP*. Since total blood flow is equal to cardiac output, CO equals Δ BP/R.

Blood pressure

Blood flow occurs because of the pumping action of the heart. Blood pressure is the hydrostatic pressure exerted by the blood against the blood vessel wall. BP occurs because there is resistance to blood flow. BP is highest in the arteries, and decreases as blood moves through the circulatory system (Fig. 13.22).

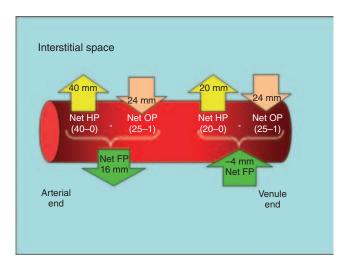


Fig. 13.21. Fluid flow across the capillary wall. At the arteriole end of a capillary, the hydrostatic pressure inside the capillary exceeds the oncotic pressure inside the capillary, which results in a net outward filtration pressure. In contrast, at the venule end of the capillary, the oncotic pressure inside the capillary exceeds the outwardly directed hydrostatic pressure, causing a net inwardly directed filtration pressure. The interstitial fluid that does not return to the capillary enters the lymphatic system.

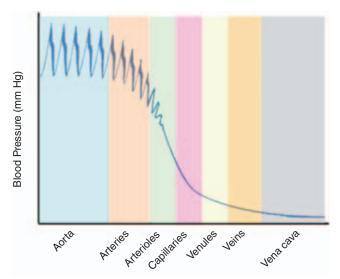


Fig. 13.22. Blood pressure throughout the circulatory system. The pulse pressure in the large arteries is substantial. As the blood moves through the circulatory system, pulse pressure declines. Although capillaries have a small cross-sectional area, blood pressure drops in the capillary bed due to the large numbers of capillaries. Blood pressure within the veins is low. (Modified from Marieb, 2004.)

BP is highest at the end of ventricular contraction, which is called systolic blood pressure. During diastole, the semilunar valves close, preventing blood from returning to the heart, and the elastic recoil in the large arteries maintains pressure that keeps blood flowing. At the end of diastole, the BP is at its lowest point, which is called diastolic blood pressure.

Pulse pressure is the difference between systolic and diastolic blood pressure. Mean arterial pressure (MAP) is the pressure that propels blood. Since the heart spends more time in diastole than systole, MAP is not simply the mean of diastolic and systolic blood pressure. Instead, MAP is equal to diastolic blood pressure plus one-third of pulse pressure:

MAP = Diastolic blood pressure + $\frac{Pulse pressure}{3}$

Resistance

Vascular resistance opposes blood flow, and is due to the friction between blood and the vessel walls. As shown in Figure 13.22, MAP and pulse pressure decline with increasing distance from the heart. This is due to the increased friction between the blood and vessel walls, and the decreasing elasticity of the vessel walls farther from the heart.

Vascular resistance is dependent on the size of the blood vessel lumen, blood viscosity, and total blood vessel length.

Blood vessel lumen

As lumen size decreases, resistance to blood flow increases. Resistance is inversely proportional to the fourth power of the lumen diameter. Therefore:

$$R\cong \frac{1}{d^4}$$

where d = lumen diameter. A small change in blood vessel diameter results in a large change in resistance. Decreasing the diameter of a vessel by one-half will increase resistance by 2⁴, or sixteenfold. Therefore, vasodilation and vasoconstriction have a large affect on vascular resistance.

Blood viscosity

Blood viscosity is affected by the concentration of erythrocytes. Increasing the erythrocyte concentration, i.e., increasing the hematocrit, increases blood viscosity. This can be a result of dehydration or polycythemia. In contrast, decreased viscosity can result from hemorrhage or anemia.

Total blood vessel length

Resistance to blood flow is proportional to the blood vessel length. The longer the blood vessel, the greater the resistance. Hence, obesity in animals can result in hypertension due to increased length of blood vessels associated with adipose tissue.

Venous blood return

Blood pressure within the veins is relatively low due to the cumulative effects of peripheral resistance throughout the vascular system (Fig. 13.21). Therefore, there are other factors besides the heart that are important in venous circulation. First, the respiratory pump involves increases in abdominal pressure associated with inhalation. This increase in pressure squeezes venous blood toward the heart. As abdominal pressure is increasing, thoracic pressure is decreasing during inhalation, further allowing blood to enter the right atrium.

Second, there is a muscular pump that aids in venous return. As an animal moves, the skeletal muscle squeezes the veins, thus moving the blood toward the heart. As the muscles relax, the one-way valves in the veins prevent the backflow of blood.

Maintaining blood pressure

There are both short- and long-term mechanisms controlling blood pressure and blood flow. These mechanisms are responsible for controlling heart rate, stroke volume, systemic vascular resistance, and blood volume.

Neural regulation

The cardiovascular center is located in the medulla oblongata and is responsible for controlling heart rate and stroke volume. As discussed above, the cardiovascular center sends sympathetic signals via the cardiac accelerator nerve that increases heart rate and contractility. Conversely, parasympathetic signals from the cardiovascular center are carried via the vagus nerve and decrease heart rate and contractility. The cardiovascular center also sends signals to blood vessels via the vasomotor nerves, resulting in vasomotor tone, or a moderate amount of constriction within the vessels. The vasomotor tone can be altered by either vasoconstriction or vasodilation.

The cardiovascular center is involved in two reflexes controlling blood pressure: the baroreceptor reflex and chemoreceptor reflex.

Baroreceptor reflex

There are pressure-sensitive mechanoreceptors located in swellings within the internal carotid arteries, known as the carotid sinuses, the aortic arch, and the walls of most large arteries in the neck and thorax. In response to stretch, these receptors send signals resulting in inhibition of the cardiovascular center. This results in vasodilation and a decrease in blood pressure. Conversely, a sudden decrease in blood pressure results in stimulation of the cardiovascular center, a resulting vasoconstriction, and an increase in blood pressure.

This reflex is important in making rapid adjustments in blood pressure in response to acute changes. For example, as an animal stands, the pressure in the neck may decrease. The baroreceptor reflex quickly increases blood pressure to maintain adequate flow to the brain.

Chemoreceptor reflex

Chemoreceptors located in the carotid bodies and aortic bodies monitor blood O_2 , CO_2 , and H^+ concentrations. Hypoxia, acidosis, or hypercapnia (i.e., increased blood CO_2) stimulate the chemoreceptors. The resulting signals stimulate sympathetic output from the cardiovascular center, causing vasoconstriction and increased blood pressure.

Chemical regulation of blood pressure: Short-term control

There are several hormones and neurotransmitters that have significant affects on blood pressure. Some act directly on blood vessels, and others have differential affects on organs.

Renin-angiotensin-alsdosterone (RAA) system

A decrease in blood pressure or blood flow to the kidneys causes the juxtaglomerular cells of the kidneys to secrete renin. Renin acts on angiotensinogen produced in the liver to produce angiotensin I (ANG I). As ANG I travels through the lungs, it is converted to angiotensin II (ANG II), which raises blood pressure two ways (Fig. 13.23). First, it causes vasoconstriction, which increases vascular resistance, thereby increasing blood pressure. Second, it causes the release of aldosterone from the adrenal cortex. Aldosterone increases sodium and water reabsorption by the kidneys. This results in an increase in blood volume and thereby raises blood pressure.

Epinephrine and norepinephrine

Sympathetic stimulation causes the adrenal medulla to secrete both norepinephrine and epinephrine. These

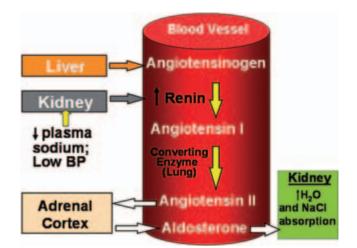


Fig. 13.23. Production and action of renin. Renin is produced by the juxtaglomerular cells in the kidney in response to low blood pressure. Renin converts angiotensinogen, produced by the liver, to angiotensin I, which is then converted to angiotensin II (ANG II) by a converting enzyme located in the lungs. ANG II acts on the adrenal cortex to cause the release of aldosterone, causing the kidneys to reabsorb Na⁺, thus raising blood volume and blood pressure. ANG II also acts directly on blood vessels causing vasoconstriction.

neurohormones increase the rate and force of heart contractions, thereby increasing cardiac output. They also have a differential effect on various vascular beds, causing vasoconstriction in the skin and visceral organs, while causing vasodilation in skeletal muscle.

Antidiuretic hormone (ADH)

ADH is secreted from the posterior pituitary. It acts in the kidneys to increase water reabsorption, and it also acts directly on blood vessels to cause vasoconstriction. Both these effects cause an increase in blood pressure.

Atrial naturiuretic peptide (ANP)

ANP is released from the atria of the heart in response to high blood pressure, i.e., stretching of the atria. This hormone decreases sodium reabsorption from the kidneys, thereby decreasing water reabsorption from the kidneys. This results in decreased blood volume and blood pressure.

Endothelial-derived factors

Several chemicals affecting vasomotor tone are produced from the endothelial lining of blood vessels. Endothelin release is stimulated by angiotensin II, ADH, thrombin, cytokines, reactive oxygen species, and shearing forces acting on the vascular endothelium. Its release is inhibited by nitric oxide, prostacyclin, and ANP. Endothelin causes vasoconstriction (Fig. 13.24).

Endothelial cells also release a potent vasodilator called nitric oxide (NO). Originally called endothelial-

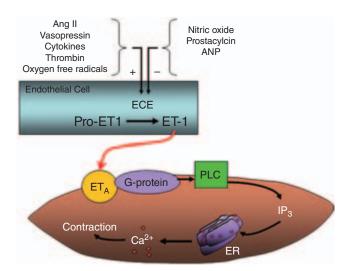


Fig. 13.24. Endothelin production and action. Endothelin is produced by endothelial cells lining the blood vessels. Various stimuli activate endothelin-converting enzyme (ECE), which converts Pro-endothelin-1 (Pro-ET1) to endothelin-1 (ET-1). ET-1 diffuses to vascular smooth muscle cells and binds to the ET_A receptors. These receptors are coupled to a G-protein that activates phospholipase C (PLC), which results in the production of inositol triphosphate (IP₃). IP₃ causes the release of ET_A Ca²⁺ from the endoplasmic reticulum, which leads to smooth muscle contraction.

derived relaxation factor, NO is a gas produced in response to high blood pressure, acetylcholine, and bradykinin. It diffuses to the neighboring smooth muscle cells where it causes the production of cGMP resulting in relaxation and vasodilation.

Inflammatory chemicals

Erythemia, or vasodilation, is associated with inflammation. A number of chemicals are involved in this response, including histamine, prostacyclin, and kinins. This response allows monocytes and neutrophils to leave the bloodstream and move toward the site of inflammation.

Renal regulation of blood pressure: Long-term control

Although most short-term blood pressure control mechanisms work by altering peripheral resistance, long-term renal control alters blood volume (Fig. 13.25). Blood volume has a direct affect on cardiac output, and therefore affects blood pressure. An increase in end diastolic volume increases cardiac output, thus increasing blood pressure.

Direct renal mechanism

An increase in blood pressure or blood volume causes an increased filtration rate in the kidney. As the filtra-

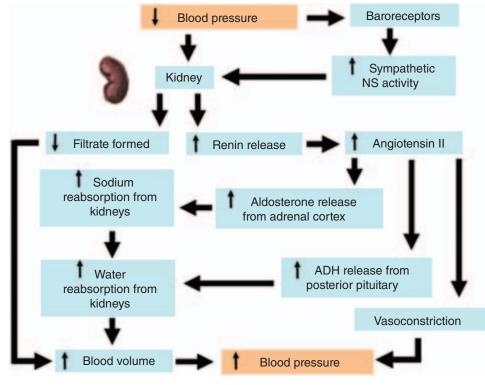


Fig. 13.25. Renal control of blood pressure.

tion rate exceeds the kidney tubules reabsorption rate, more urine is produced, resulting in increased fluid loss and decreased blood volume.

Indirect renal mechanism

If arterial blood pressure declines, the kidneys release the enzyme renin into the bloodstream. As shown in Figure 13.23, renin induces angiotensin II (ANG II) production. ANG II has three affects that increase blood pressure. First, it causes vasoconstriction. Second, it stimulates the adrenal cortex to secrete aldosterone, a hormone that stimulates sodium reabsorption from the kidney tubules. Third, ANG II stimulates ADH release from the posterior pituitary. ADH increases water reabsorption from the kidney tubules. Increased sodium and water reabsorption from the kidneys leads to increased blood volume and blood pressure.

Autoregulation of blood pressure

Local oxygen needs change throughout the body. In order to accommodate these local needs, capillary beds can alter their vasomotor tone in response to local physical and chemical factors.

Physical factors

Increased local temperature, such as occurs during inflammation or exercise, causes vasodilation. Decreased local temperature causes vasoconstriction. In addition, the smooth muscles in arteriole walls display myogenic responses, in which increased stretch causes enhanced contraction while decreased stretch caused relaxation. Such responses help regulate local blood flow as follows: If blood flow through an arteriole decreases, the arteriole wall is stretched less, resulting in smooth muscle relaxation and vasodilation. The vasodilation increases blood flow through the arteriole.

Chemical factors

Cells such as platelets, blood cells, smooth muscle, macrophages, and endothelial cells release a variety of chemicals that modify blood vessel diameter. Metabolically derived vasodilators include K⁺, H⁺, lactic acid, and ATP. Other tissue-synthesized vasodilators include nitric oxide (NO) produced by endothelial cells, histamine from mast cells, and monocytes and kinins produced during inflammation. Vasoconstrictors include thromboxane A2 and serotonin from platelets, superoxide radicals, and endothelins from endothelial cells.

Note that the systemic and pulmonary circulatory systems respond differently to changes in O₂ levels.

Systemic blood vessels dilate in response to low O_2 , whereas pulmonary blood vessels constrict. Therefore, systemic vessels dilate in order to deliver more O_2 to needed areas while pulmonary vessels constrict so that blood is diverted from poorly ventilated alveoli.

Shock and homeostasis

Circulatory shock includes any condition in which blood vessels are unable to deliver adequate O_2 and nutrients to meet cellular needs. This results in hypoxia in the affected tissue, leading to a switch to anaerobic metabolism, lactic acid accumulation, and possibly tissue death.

Types of shock

The most common type of shock is hypovolemic shock resulting from massive blood loss. Blood loss can occur internally from the rupture of an artery, or externally from trauma. Excessive loss of body fluids such as occurs in profuse sweating, diarrhea, or vomiting can also cause hypovolemic shock. Treatment involves the restoration of fluids.

Cardiogenic shock occurs when the heart fails to adequately pump. This can be caused by a myocardial infarction, ischemia of the heart, heart valve problems, impaired contractility of the heart, or arrhythmias.

Vascular shock is a result of abnormal expansion of the vascular bed. Although there is no change in blood volume, there is a drastic drop in peripheral resistance leading to a drop in blood pressure. Causes can include anaphylactic shock from an allergic reaction or neurogenic shock resulting from head trauma damaging the cardiovascular center. Another cause can be septic shock resulting from bacterial toxins.

Circulatory routes

Pulmonary circulation

The pulmonary circulation functions to carry deoxygenated blood to the alveoli (air sacs) in the lungs where gas exchange occurs (Fig. 13.26). The blood picks up oxygen in exchange for carbon dioxide. The blood is pumped from the right ventricle into the pulmonary trunk, which then divides into the right and left pulmonary arteries. The pulmonary arteries divide into lobar arteries following the bronchi into the lungs. They then branch, eventually forming pulmonary capillaries in the air sacs. These capillary beds drain into the pulmonary veins. The pulmonary veins return to the left atria from which the blood enters the left ventricle and is then delivered to the body.

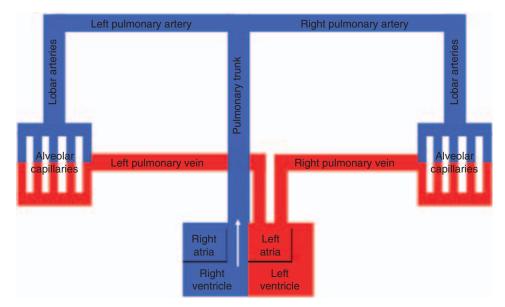


Fig. 13.26. Schematic diagram of pulmonary circulation. The pulmonary circulation carries deoxygenated blood to the lungs where the blood picks up oxygen in exchange for carbon dioxide. The blood returns to the left side of the heart where it enters the systemic circulation.

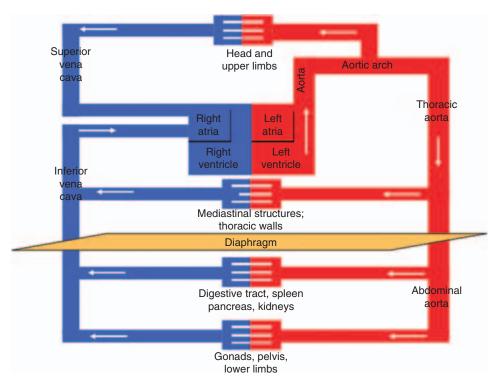


Fig. 13.27. Schematic diagram of systemic circulation. Blood delivered to the left side of the heart from the pulmonary circulation (pulmonary circulation has been omitted from this figure) leaves via the aorta to be circulated throughout the body. After passing through the capillary beds, the blood returns to the right side of the heart via the superior or inferior vena cava.

Systemic circulation

The systemic circulation includes vessels that deliver oxygenated blood from the left ventricle, throughout the body, and returns deoxygenated blood to the right atrium (Fig. 13.27). The systemic circulatory system includes vessels supplying the tissue needs of the lungs, as well as all the remaining tissues in the body. So, while the pulmonary circulatory system supplies blood only to the gas exchange portion of the lungs, the systemic circulation must supply blood to every tissue of the body. This is why the left ventricle has a thicker muscular wall than the right ventricle. Systemic circulation begins with blood traveling through the aorta, and ends with the blood returning via the superior vena cava, inferior vena cava, or coronary sinus.

The aorta has four major divisions: the ascending aorta, arch of the aorta, thoracic aorta and abdominal aorta. The ascending aorta emerges from the left ventricle and runs posterior to the pulmonary trunk. It gives rise to two coronary arteries that supply the myocardium (Fig. 13.28). It then curves left, giving rise to the aortic arch. It then continues caudally running close to the vertebral bodies. As it courses caudally, it is called the thoracic aorta until it passes through the diaphragm becoming the abdominal aorta.

The aortic arch is a continuation of the ascending aorta. It gives rise to three major arteries: the brachiocephalic trunk, the left common carotid, and the left subclavian (Fig. 13.29). The brachiocephalic trunk gives rise to the right subclavian artery and right common carotid artery. These vessels provide the arterial supply to the head, neck, front limbs, and a portion of the thoracic spine (Fig. 13.30).

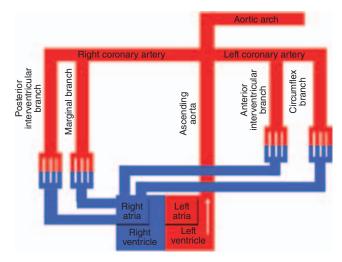


Fig. 13.28. Ascending aorta. The ascending aorta begins at the aortic valve and ascends dorsal to the aortic arch. It gives rise to vessels supplying the heart.

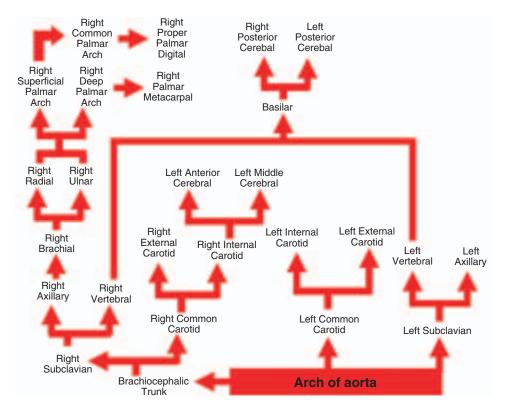


Fig. 13.29. Aortic arch. The thoracic aorta gives rise to visceral and parietal branches supplying the thorax wall and viscera (Fig. 13.30). The abdominal aorta supplies the abdominal walls and viscera. It ends in the right and left common iliac arteries supplying the pelvis and hindlimbs.

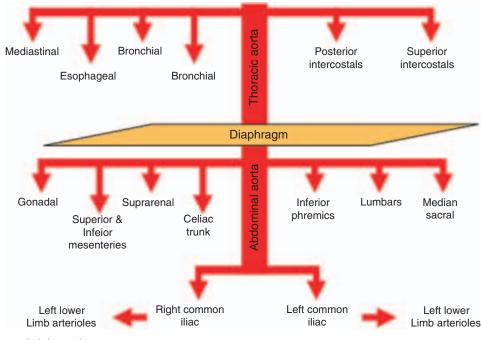


Fig. 13.30 Thoracic and abdominal aorta.

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