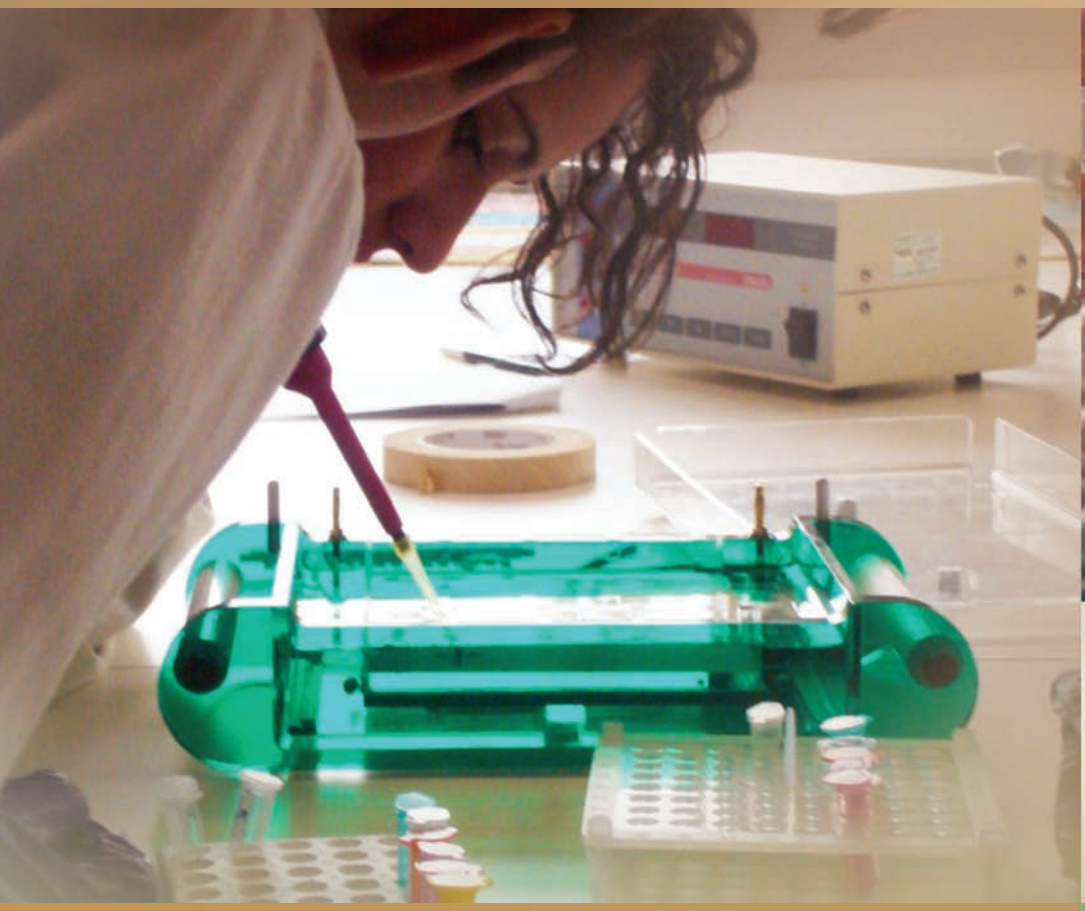
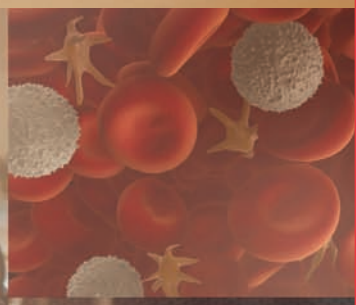
Editors Ray K. Iles | Suzanne M. Docherty

Biomedical Sciences

Essential Laboratory Medicine





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Essential Laboratory Medicine

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The editors would like to dedicate this book to the memory of Marion Docherty.

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Preface

The practice of clinical medicine and the diagnosis and management of human disease becomes ever more complex with each year that passes and our knowledge of the molecular basis of pathology expands seemingly exponentially. There is thus an ever greater need for well-trained, highly skilled biomedical scientists — the professionals who perform the vital laboratory tests and investigations that underpin the diagnosis of disorders and the evaluation of the effectiveness of treatment.

With this textbook on *Biomedical Sciences*, we set out to create a comprehensive — yet focused — resource that students can use at all levels of their study and career progression in biomedical science. After an overview of the anatomy and physiology of major organ systems, individual chapters cover those aspects of science that are relevant to the clinical laboratory: pathophysiology; clinical cell biology and genetics; cellular pathology; clinical chemistry; medical microbiology; clinical immunology; haematology and transfusion science, and then concludes with a chapter on professional practice. The book includes contributions from a number of registered Biomedical Scientists which greatly enhances its clinical relevance and interest as well as giving a sense of what happens in the real world, and at the bench in the working clinical laboratory.

We hope this textbook helps to take you successfully into a fulfilling career in biomedical science or an allied profession that you enjoy as much as the various contributors have to date.

R.K.I and S.M.D

Chapter 1

Anatomy and physiology of major organ systems

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Dr Suzanne M. Docherty, BmedSci, MBBS, Ph.D.

No area of medical science is truly self-contained; all systems interact, so as we study our chosen speciality we have to put this in a holistic context of human biology. This is as true for the clinical laboratory specialist as for any other medical professional. This introductory chapter is not aimed to be a comprehensive text on anatomy and physiology as there are numerous extremely good volumes published on this subject. However, the reader may wish to dip into these explanatory notes as a refresher or source of direction for further study. After all, students of clinical biomedical science will find they have to read around our specific substantive chapters on haematology, clinical chemistry, microbiology and especially histopathology if they do not have a grasp of anatomical systems.

1.1 The skeletal system

The obvious functions of the skeleton are to provide support, leverage and movement and protection of organs, for example the skull protects the brain, the rib cage the lungs, heart, liver and kidneys, and the pelvis the bladder. In addition, the skeletal system is a storage site for calcium and phosphate minerals and lipids (yellow marrow) and critically a site for the production of blood cells (red bone marrow).

The characteristics of bone are that they are very lightweight yet very strong – resistant to tensile and compressive forces. Interestingly, healthiness (bone density) depends on continuous stressing or loading (i.e. activity). Bones are characterized by their shape (Figure 1.1) into long bones, short bones, flat bones and irregular bones.

1.1.1 The anatomical structure of a bone

Best exemplified by long bones, the bone itself is subdivided by internal and external structures. The bone is covered by a layer of cartilage called the periosteum underneath which is a layer of dense compacted calcified compact bone: however, beneath this layer can either be a hollow chamber (medullary

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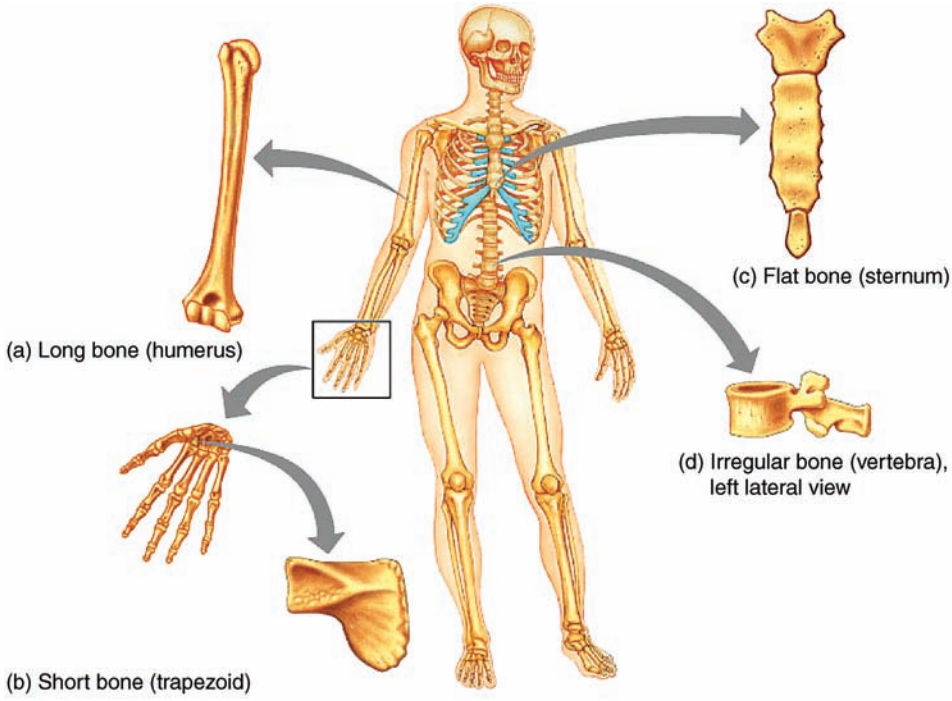


Figure 1.1 The human skeleton and the four bone categories which are shape descriptors. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

cavity) filled with the specialist tissue of the bone marrow or a spongy bone of small cavities. The spongy bone is always found at the end structures of articulating long bones and is a region of continued bone turnover lying above a line of active bone cells called the epiphyseal line. This spongy bone region is called the epiphysis, whilst the bone marrow dominant region between the two epiphyseal lines is termed the diaphysis where highly active bone turnover (remodelling) does not continuously occur (Figure 1.2).

Bone is derived from connective tissue and there are two types of connective tissue in the skeletal system — calcified bone and cartilage. Cartilage tissue forms a covering of articular surfaces, ligaments and tendons, as well as sheaths around bone (periosteum).

Bone tissue is calcium phosphate ($Ca_3(PO_4)$) crystals embedded in a collagen matrix peppered with bone cells. Thus bone is 60% minerals and collagen and 40% water where the collagen enables bones to resist tensile forces (i.e. are elastic) and minerals which enable bones to resist compressive forces, but this does makes them brittle.

Bone (osseous tissue) is, however, living tissue and therefore has an abundant blood and nerve supply: periosteal arteries supply the periosteum (see Figure 1.3 (a)); nutrient arteries enter through nutrient foramen supplies compact bone of the diaphysis and red marrow (see Figure 1.3(b)) and metaphyseal and epiphyseal arteries supply the red marrow and bone tissue of epiphyses (see Figure 1.3(a)).

1.1.2 Spongy bone and compact bone

Bone tissue is of two types — spongy and compact. Spongy bone forms 'struts' and 'braces' with spaces in between. Spaces contain bone marrow allowing production and storage of blood cells (red marrow) and the looser structure allows the bone to withstand compressive forces. Compact bone makes up the outer walls of bones, it appears smooth and homogenous and always covers spongy bone. Denser and stronger than spongy bone, compact bone gives bones their rigidity. Spongy and compact bone are biochemically similar, but are arranged differently. In compact bone the structural unit is the osteon (see Figure 1.4).

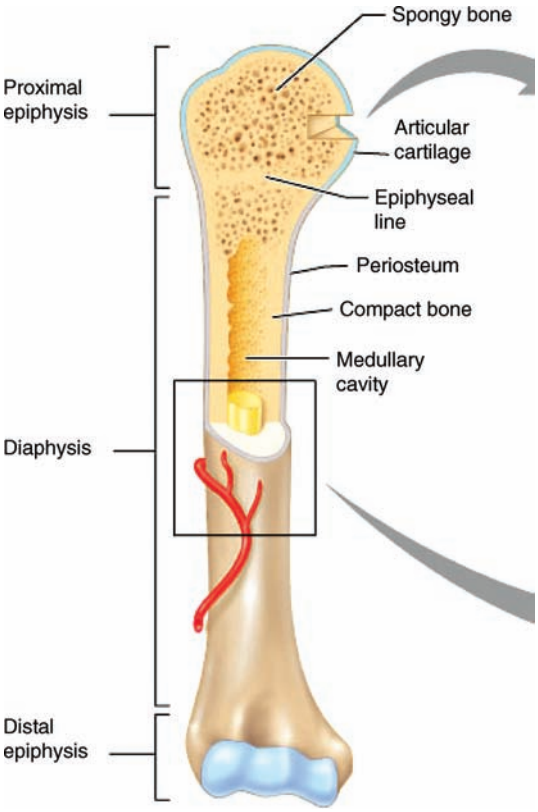


Figure 1.2 Structural components of the long bone. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

1.1.3 Osteocytes – mature bone cells

There are two types of bone cell:

- **Osteoblasts** – bone forming cells.
- **Osteoclasts** – bone destroying cells.

In the formation of new bone osteoblasts cover hyaline cartilage with bone matrix. Enclosed cartilage is digested away leaving the medullary cavity. Growth in width and length continues by the laying down of new bone matrix by osteoblasts. Remodelling to ensure the correct shape is effected by osteoclasts (bone-destroying cells). In mature bones osteoblast activity decreases whilst oesteoclast remodeling activity is maintained. However, bone remodelling requires both oesteocytes. Triggered in response to multiple signals stress on bones means that there is considerable normal 'turnover' – bone is a dynamic and active tissue; for example, the distal femur is fully remodelled every 4 months.

Osteoclasts carve out small tunnels and osteoblasts rebuild osteons: osteoclasts form a leak-proof seal around cell edges and then secrete enzymes and acids beneath themselves. The resultant digestion of the bone matrix releases calcium and phosphorus into interstitial fluid. Osteoblasts take over bone rebuilding,

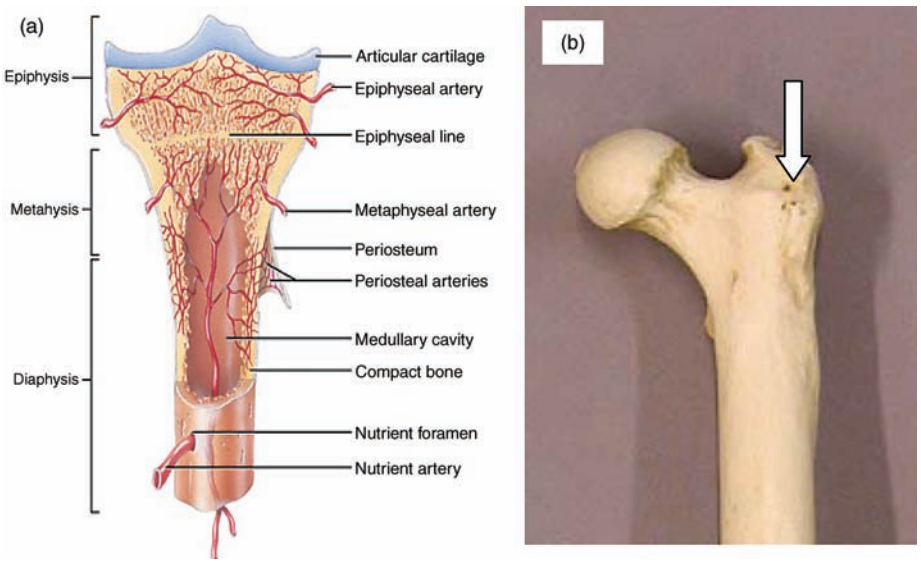


Figure 1.3 Detail of the blood supply of a long bone (a) and example of entry position, the nutrient foramina, is indicated in (b). *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

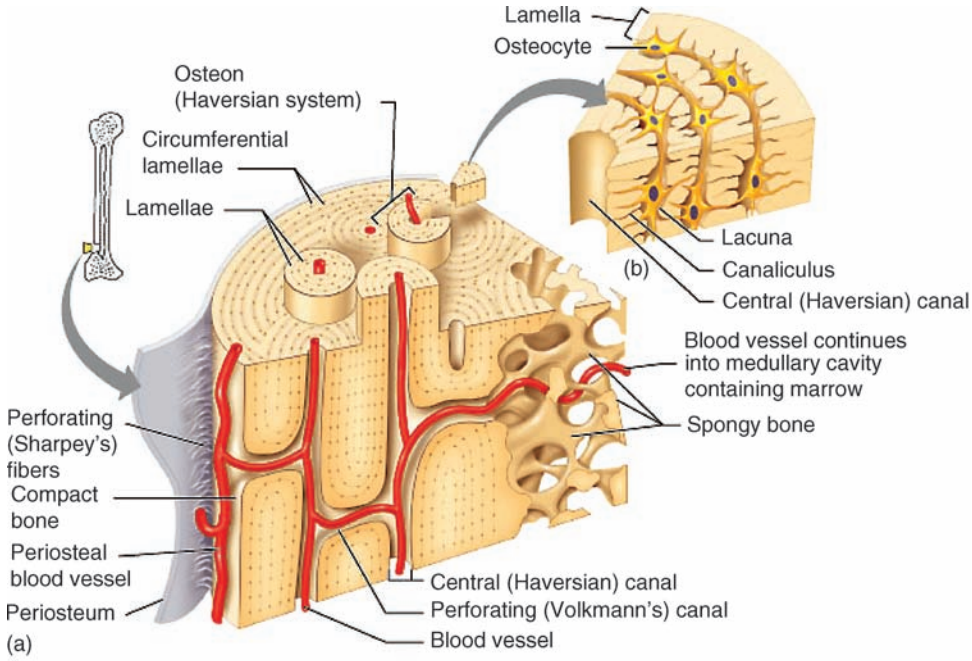


Figure 1.4 Microanatomy of the bone. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

continually redistributing bone matrix along lines of mechanical stress.

1.1.4 How bones grow

Bone growth only occurs in those young enough to still have an active, unfused epiphyseal plate (roughly < aged 16–19). The epiphyseal plates fuse earlier in females than in males — generally, females have stopped growing by around the age of 16, while for males this is around 18 to 19 (see Figure 1.5).

Cartilage cells are produced by mitosis on the epiphyseal side of plates (ends of bones) — this is continuous with articular cartilage at the end of the bone. Cartilage cells are destroyed and replaced by bone on the diaphyseal side of plates (middle of long bone)and a zone of resting cartilage anchors the growth plate to the bone. The epiphyseal plate is at the top of Figure 1.5, and this is where new cartilage cells are being created by mitosis. As they are 'pushed away' from the epiphyseal plate by new cartilage cells being created 'behind' them, osteoblasts lay down a calcium phosphate matrix in and around the cartilage cells, ossifying the area. This gradually takes on the structure of bone. The epiphyseal plate cartilage is continuous with the articular cartilage at the end of the bone, and new cartilage (and bone formation) is occurring in both areas rather than strictly just at the epiphyseal plate. Furthermore, the bone has to be remodelled as it increases in length, or the whole bone would be as wide as the epiphysis — but what you actually need is a narrower diaphysis (shaft) in the middle of the bone. The thick articular cartilage, at either end of the bone, is continuous with the thin (but tough) periosteum around the outside of the rest of the bone. Periosteum has a rich blood supply which is important when you consider bones grow not only in length but in width.

Periosteal cells (from membrane around the bone) differentiate into osteoblasts and form bony ridges and then a tunnel around a periosteal blood vessel. Concentric lamellae fill in the tunnel to form an osteon (see Figure 1.6). Blood vessels around the outside wall of the bone, on the periosteum, are 'walled in' as periosteal cells convert into osteoblasts and build new bone around them. This is why cortical bone is composed of osteons.

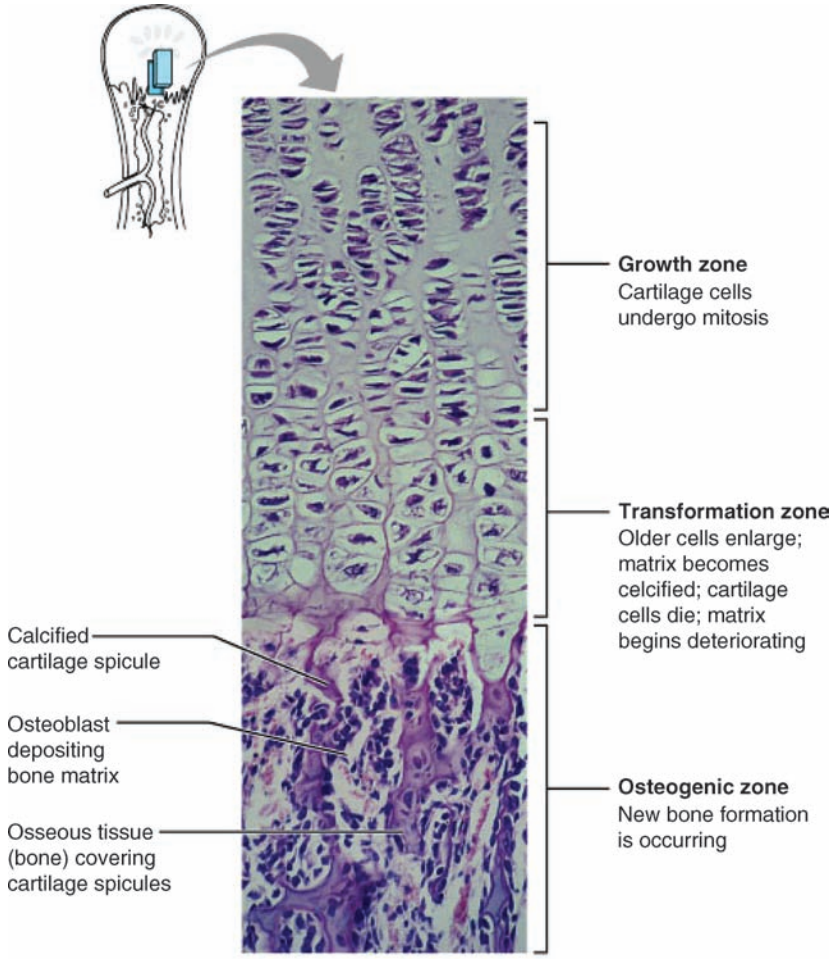


Figure 1.5 Histological appearance of epiphyseal plate. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

1.1.5 Endocrine regulation and nutritional requirement of bone growth

Several hormones are involved in endocrine control of bone growth: growth hormone, thyroid hormone, insulin and calcitonin. Before puberty growth hormone is the most important hormone involved in regulating bone growth. The metabolic hormones, thyroid hormones and insulin are involved in modulating the activity of growth hormone and ensuring proper proportions in the skeleton. Together these maintain the normal activity at the epiphyseal plate until the time of puberty. At puberty the increase in sex hormone production results in an acceleration of bone growth. These hormones promote the differences in the shape of the skeleton associated with males and females such as density and shape such as a flatter and wider pelvis in females. However, in both sexes the rate of ossification starts to outpace the rate of cartilage formation at the epiphyseal plates. Eventually the plates ossify and bone growth stops when the individual reaches sexual and physical maturity.

For adequate bone growth good nutrition is also required as are adequate levels of minerals and vitamins: calcium and phosphorus, vitamin D for bone formation, vitamin C for collagen formation and vitamins K and B_{12} for protein synthesis.

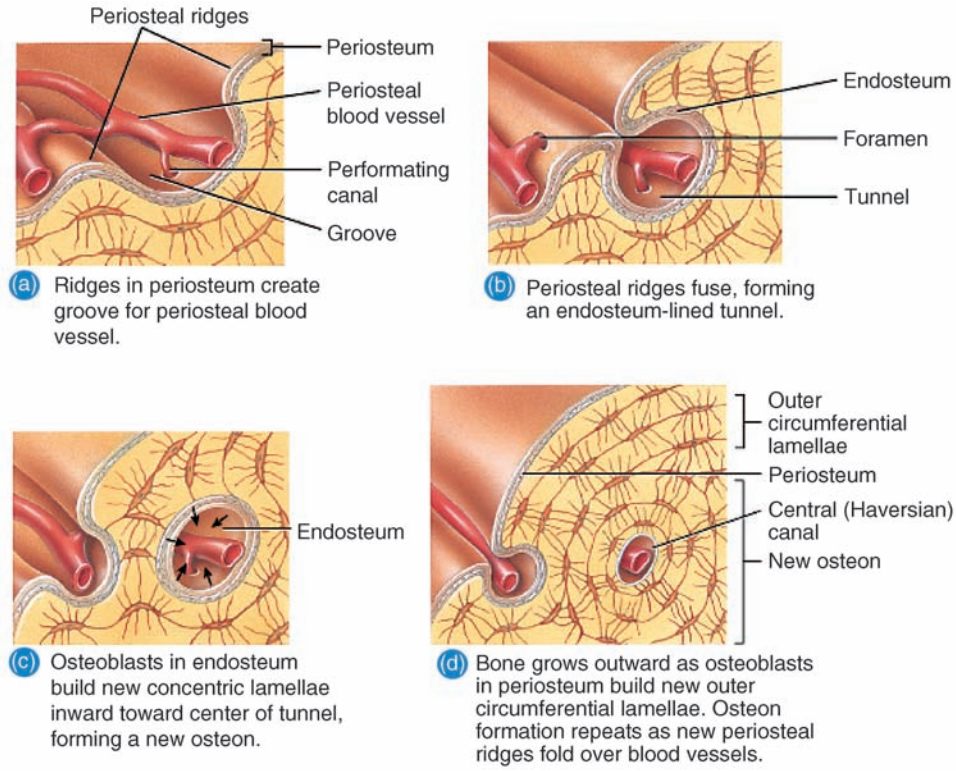


Figure 1.6 Appositional bone growth

1.1.6 The role of bone as a mineral store

A critical mineral which bones are involved in regulating is calcium as its ion concentrations in plasma must be very carefully controlled. Calcium homeostasis is affected by a negative feedback system involving the action of two primary hormones; calcitonin, produced from parafollicular cells of the thyroid gland in the neck and parathyroid hormone (PTH, also called parathormone) produced by the parathyroid glands (which lie on top of the thyroid gland). Responding to a fall in plasma calcium ions, released PTH, among other effects, induces the release of calcium by bone, whilst a rise in plasma calcium results in calcitonin which has the opposite effects, one of which is to promote increased deposition of calcium in bone.

1.2 The digestive system

This section aims to give an overview of the anatomy of the digestive system, identifying the major organs of the alimentary canal and the accessory digestive organs. In particular, the structure and function of the following organs and accessory organs of the alimentary canal are briefly described (see Figure 1.7):

- the oral cavity, pharynx and oesophagus;
- the stomach;
- the small intestine;
- the liver and gallbladder;
- the pancreas;
- the large intestine.

In so doing, it is possible to outline the major processes occurring during digestive system activity and give an overview of digestion and absorption.

1.2.1 Nutrition and absorption

The overall function of the digestive tract is to process not only the macronutrients (carbohydrates, proteins and fats) but also vitamins and minerals. Vitamins are complex organic substances essential for health,

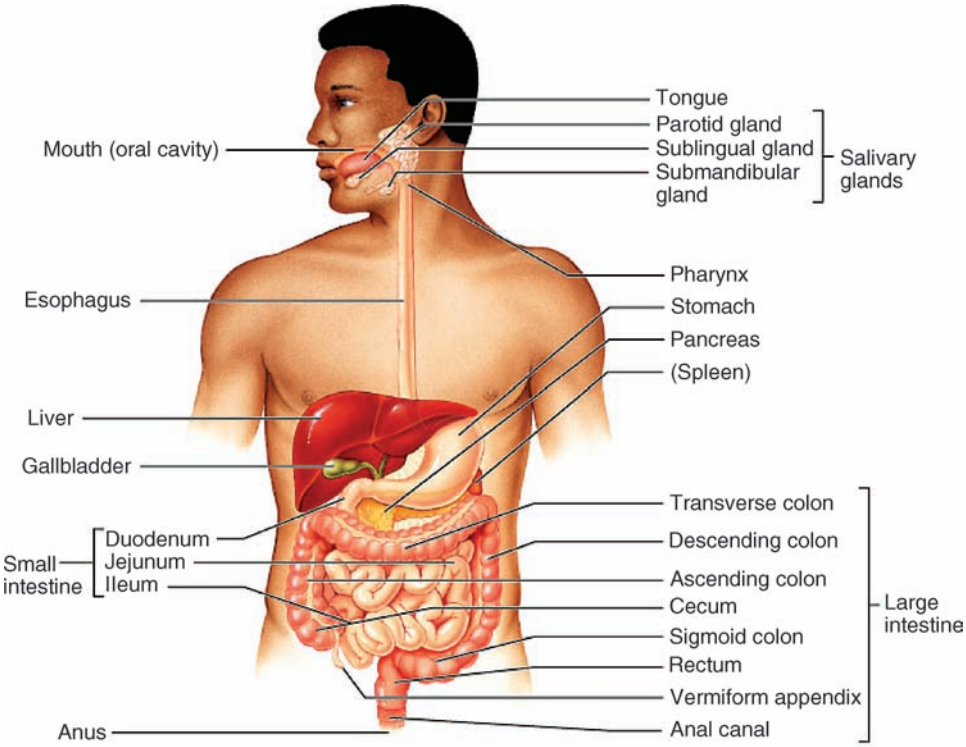


Figure 1.7 Overall anatomy of the digestive system. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

required in very small amounts (mg or µg per day) but most cannot be made by the body. They function as cofactors in enzyme activity, antioxidants to deal with free radicals generated during metabolism, and even as prohormone (i.e. vitamin D).

Minerals are inorganic compounds required by the body, like vitamins, for a variety of functions but often as cofactors or the reactive centres of functional proteins. Some minerals are needed in larger amounts than others, for example calcium, phosphorus, magnesium, sodium, potassium and chloride. Others are required in smaller quantities and are sometimes called trace minerals, for example iron, zinc, iodine, fluoride, selenium and copper. However, despite being required in smaller amounts, trace minerals are no less important than other minerals.

In order to extract macro- and micronutrients from food stuffs the digestive system must bring about ingestion, digestion (mechanical and chemical), enable movement through the digestive tract, facilitate absorption of nutrients and finally defaecation of the nondigestible elements and some waste products.

1.2.2 Ingestion

The oral cavity is a far more complex mechanism than just a set of teeth. You unconsciously analyse food when you put it in your mouth to check it isn't too large a chunk to sensibly chew, that it doesn't contain very hard bits, and that it isn't in some way mouldy or otherwise unpleasant. Only then do you start chewing properly and contemplating swallowing it. Thus the oral cavity analyses the food, mechanically processes (chews to smaller pieces), lubricates (saliva) and starts the process of chemical digestion via the enzymes secreted as part of saliva (see Figure 1.8).

After chewing we swallow but there are two phases:

- buccal phase (voluntary);
- pharyngeal phase (involuntary).

1.2.2.1 Pharynx and oesophagus

During the pharyngeal phase, the airways have to be shut off by the **epiglottis** to prevent food from going

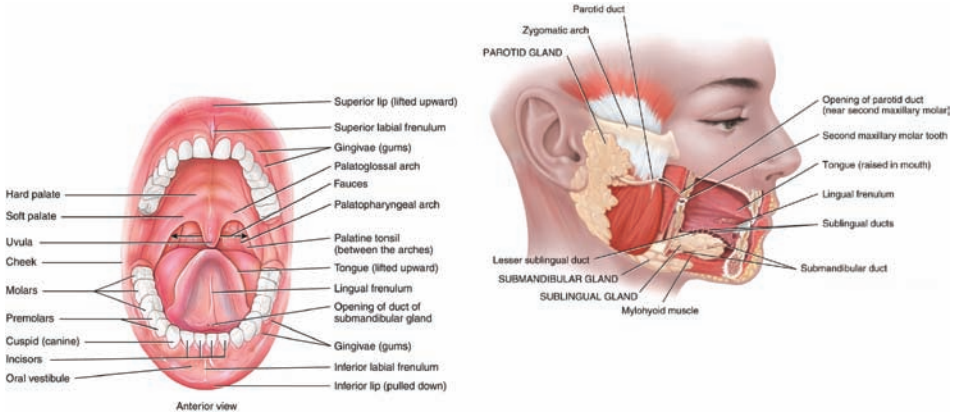


Figure 1.8 Structures and exocrine glands of the oral cavity. From Tortora and Derrickson, *Principles of Anatomy and Physiology*, Twelfth Edition, 2009, reproduced by permission of John Wiley & Sons Inc.

down the air passages/windpipe (see Figure 1.9). Babies don't have quite the same set up, and this allows them to breathe while drinking milk. Peristalsis carries food in one direction only — down, so you can eat and drink standing on your head if you want to; animals such as horses effectively do this by eating with their heads lower than the level of their stomach.

1.2.3 The stomach

Lying in the upper part of the abdominal cavity, this sac or balloon like stomach occupies a volume of 50 mL empty, but expands to 4 L when full. The different orientations of muscle layers in the stomach allow it to contract in different directions to maximize the effectiveness of mechanically breaking down food. The folds (rugae) increase the surface area for maximum absorption (see Figure 1.10). It is also important to note that there is a cardiac sphincter between the oesophagus and stomach, and a pyloric sphincter between the stomach and duodenum — sometimes the pyloric sphincter is malformed (this predominantly affects baby boys) and will not open, which causes projectile vomiting and failure to thrive until it is surgically corrected. At the other end the stomach sits below the diaphragm, but sometimes part of the stomach is squeezed up through the diaphragm, resulting in heartburn and reflux as acid enters the oesophagus.

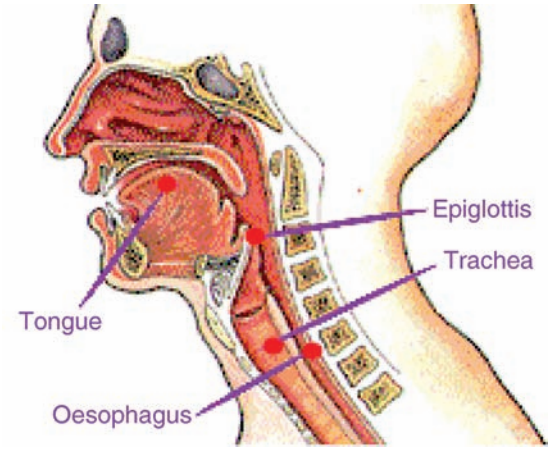


Figure 1.9 Position of the epiglottis in respect to closure of the trachea

1.2.3.1 Stomach mucosal lining

The gastric mucosa contain three predominant differentiated cell types: parietal cells which secrete hydrochloric acid and intrinsic factors facilitating the absorption of vitamin B12; chief cells which secrete pepsinogen (inactive form of pepsin) — which is activated by HCl and begins the digestion of protein; and mucous cells. The stomach secretes a thick mucus to protect itself from its own hydrochloric acid (see Figure 1.11).

1.2.3.2 The gastric digestive process

Swallowed food collects in the upper storage area. Starch (complex carbohydrate) continues to be digested until the mass has been mixed with gastric juice. Small portions of mashed food are pushed into the digesting area of the stomach where acid in gastric juice unwinds (denatures) the proteins and the enzyme pepsin breaks up the chains

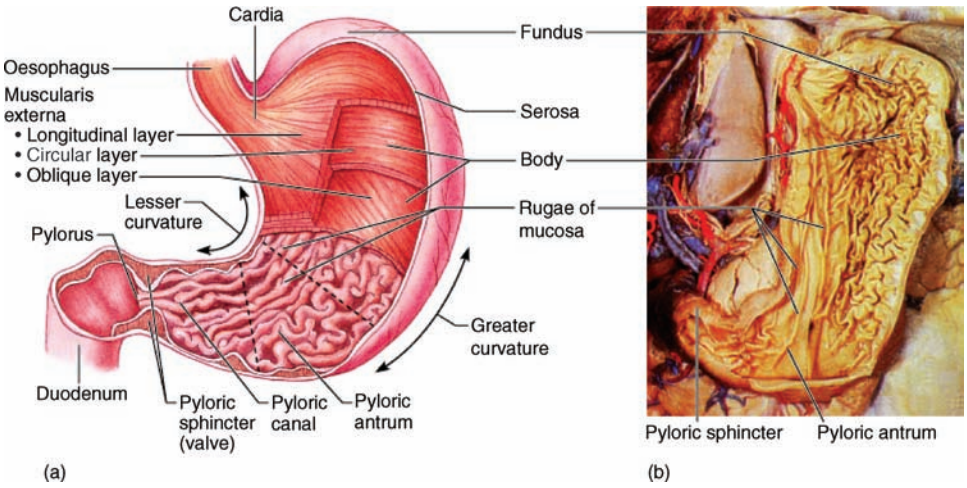


Figure 1.10 (a) Anatomy and (b) cross-sectional appearance of the stomach. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.

of amino acids. This all forms a thick liquid mass called chyme which moves on and enters the small intestine. Fat forms a separate layer on the top.

1.2.4 The small intestine

The small intestine consists of three distinct anatomical regions: the duodenum, pyloric sphincter to jejunum; jejunum, duodenum to ileum; and ileum, jejunum to large intestine. The small intestine is where most nutrients are absorbed, and it is all about surface area maximization (see Figure 1.12).

The mucosal folds of the small intestine are covered in villi (Figure 1.12(a) and (b)), and each villus in turn is lined with columnar cells that have a brush border (Figure 1.12(c)), all to give a large surface area for absorption. Note too that each villus has a rich blood supply to help with this too (see Figure 1.12(c)).

1.2.5 Liver and gall bladder

Positioned below the diaphragm and protected by the lower half of the rib cage, the liver is divided into a right and left lobe by the round ligament. The gall bladder nestles into it from underneath and in real life this is a dark green colour and really stands out. Among other functions the liver produces bile. Bile contains bile acids, which assist with the absorption of fats and fat-soluble vitamins in the small intestine. Many waste products, including bilirubin, are eliminated from the body by secretion into bile and elimination in faeces. Adult humans produce 400 to 800 mL of bile per day.

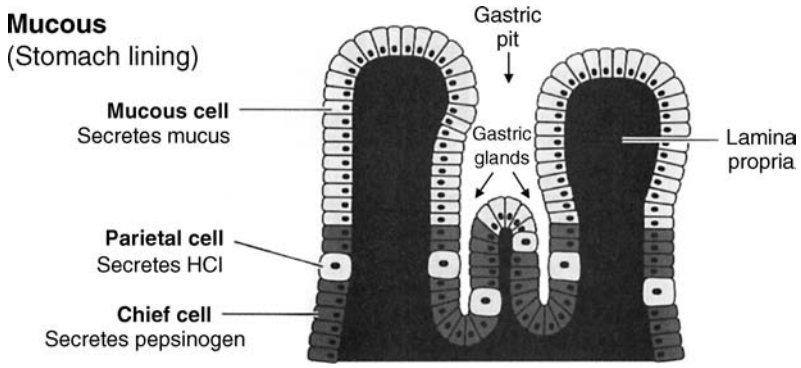


Figure 1.11 Microanatomy of the stomach lining

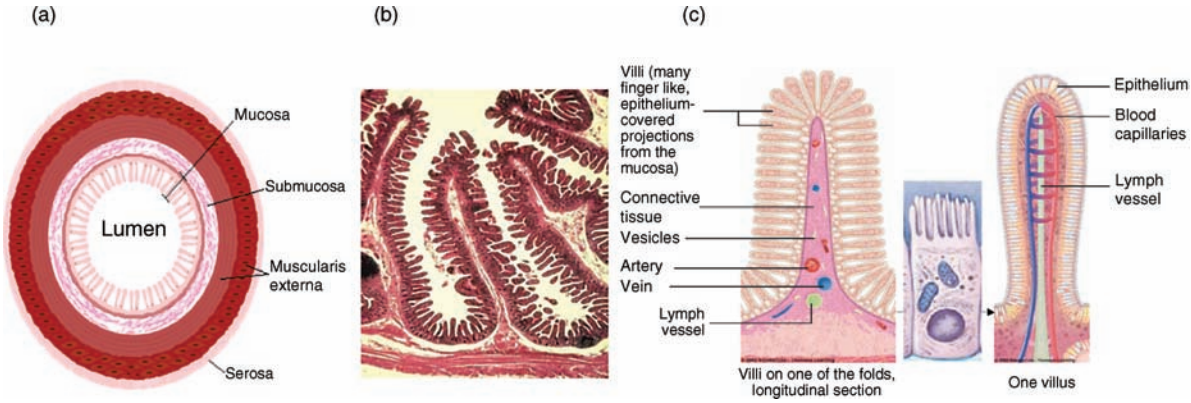


Figure 1.12 Small intestine: cross-sectional and microanatomy

Further modification of bile occurs in that organ. The gall bladder stores and concentrates bile during the fasting state. Typically, bile is concentrated fivefold in the gall bladder by absorption of water and electrolytes — virtually all of the organic molecules are retained. The liver drains bile out towards the gall bladder in the bile duct, and further down this is joined by secretions from the pancreas to form a common bile duct, which secretes a mixture of bile and pancreatic juices into the duodenum as food passes through (see Figure 1.13). The bile duct can become obstructed by small gallstones (and other things, like a tumour in the head of the pancreas), which causes jaundice and is described in several of the following chapters.

1.2.6 The pancreas

The pancreas is both an exocrine and endocrine gland. Its endocrine function is fulfilled by the pancreatic islets cells which secrete insulin and glucagon, whilst its digestive system exocrine function is to produce and secrete digestive enzymes: trypsin and chymotrypsin which break proteins into peptides (short chains of amino acids); pancreatic lipase which digests triglycerides into a monoglyceride and two free fatty acids; amylase which hydrolyses starch to maltose (a glucose—glucose disaccharide) and others such as nucleases (ribonuclease, deoxyribonuclease) and those that digest fibrous tissues (e.g. gelatinase and elastase). The pancreas is a highly sensitive organ and can become inflamed (pancreatitis) — this is caused by pancreatic enzymes from damaged pancreatic cells leaking into pancreatic tissue and digesting it.

1.2.7 Small intestine and associated organs and digestion

It must be remembered that the small intestine is a major site in the digestive process, the pancreas liver

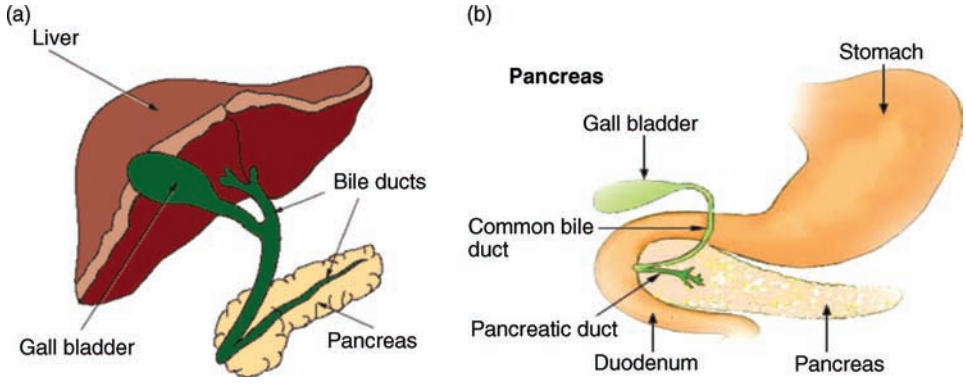


Figure 1.13 (a) Diagrammatic representation of the relative positional anatomy of the liver, gall bladder and pancreas, and (b) in relationship to the stomach and small intestine

and gall bladder all work in concert with the absorption function of the mucosal folds and villi cells found here. Thus, chyme squirts into the duodenum from the stomach and peristaltic movement pushes the chyme along and mixes with secretions for chemical digestion. In particular pancreatic juice and bile help to digest carbohydrate, lipids and proteins. All the while the macro- and microanatomy of the small intestine optimizes absorption and facilitates the transport of nutrient across the mucosal barrier and into the blood stream. Most digested food is absorbed in the small intestine so there is a rich and complex net of blood and lymphatic channels around and leading to and from the small intestine as it winds backwards and forwards.

1.2.8 The large intestine

The residual chyme moves from the small intestine via the Illeocecal valve (which prevents the contraction from these larger vessels forcing waste back into the small intestine) into the first pouch or haustra of the large intestine — the caecum. Herbivores have a large caecum and appendix that contain symbiotic bacteria that synthesize the enzyme cellulase, allowing them to digest plants cell walls, these pass through us as fibre. The human appendix is roughly the size of the little finger, but in some people it is relatively long and thin (with a small diameter that is more likely to block, possibly resulting in appendicitis).

The movement of this residual digestive chyme through the large intestine is slow and rather laborious in the mechanical mechanism that operates: pouches (or haustra) fill to capacity, when stretched they contract and force the contents into the next haustra (and section of the colon). During this slow passage water is absorbed or reabsorbed, and vitamins and minerals are absorbed along with it. As water is absorbed the residual chyme is dehydrated and compacted to form faeces. Mass peristalsis forces the contents into the rectum for the storage of faecal material prior to defecation (see Figure 1.14).

The average passage time of undigested food residues through the human gut is about 50 h in men and 57 h in women, but ranges from well under 20 to over 100 h. It also changes from one day to the next. However, about 80–90% of the entire transit time of food in the body is spent in the colon, so it needs to be large and have a good capacity. Thus, movement through the digestive tract varies dramatically section per section: Oesophageal peristalsis is fast with a transit time of about 3 s; time in the stomach is about 1–3 h; small intestine digestion and absorption is 2–6 h, whilst 12–48 h is spent in the large intestine prior to defecation.

1.3 The cardiovascular system

The function of the cardiovascular system is as a transport system of the body carrying:

- respiratory gases;
- nutrients;
- hormones and other material to and from the body tissues.

The fluid component of this system — blood — is a complex of specialized cells and solution of salts (electrolytes) and soluble proteins. At the centre of the cardiovascular system is the heart to which structurally distinct vessels — arteries — carry blood away, and equally structurally distinct vessels — veins — carry blood back to the heart.

However, the cardiovascular system has two divisions: pulmonary and systemic (see Figure 1.15). In the pulmonary division, blood flows from the right ventricle of the heart to alveolar capillaries of the lungs and back to the left atrium of the heart. In the systemic division the left ventricle pumps blood to the rest of the body and all other body capillaries, and the blood returns to the heart's right atrium. Hence there is an asymmetry in muscle mass between the two ventricles. In addition the two divisions have two different profiles with respect to the transport of respiratory gases; pulmonary arteries are low in O_2 high in CO_2 whilst the arteries of the systemic division are high in O_2 low in CO_2 (and the pulmonary–systemic veins vice versa). Capillaries, minute blood vessels found throughout tissues, connect the small arteries to the small veins. Exchange of respiratory gases and nutrients with the tissues occurs across the walls of the capillaries.

1.3.1 The heart

The heart is a complex structure of four chambers, powerful muscles, specialized valves that contract and

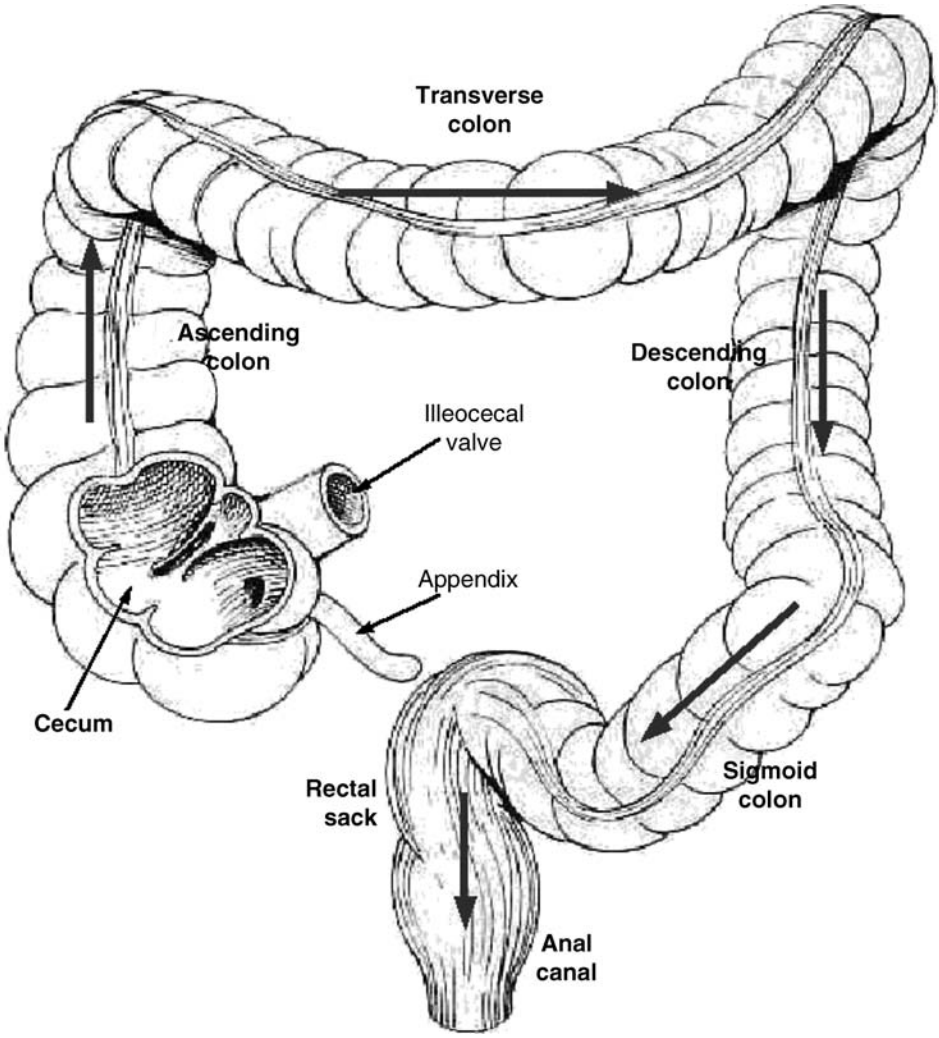


Figure 1.14 Diagrammatic representation of the structure of the large intestine

open/close in a coordinated manner, regulated by its own specialist sensory and responsive neurological system (see Figure 1.16). The entire organ is surrounded by a protective barrier called the pericardium. It is in fact a protective sac surrounding the heart consisting of an outer tissue layer called the parietal pericardium, a proteinacious (pericardial) fluid and a heart wall contacting tissue, the visceral pericardium also referred to as the epicardium.

The heart wall consists of two tissue layers the inner endocardium which is contiguous with blood vessel endothelium and the myocardium of specialist cardiac muscle. The heart has two structural classes of chambers: receiving chambers or atria (singular, atrium) and pumping chambers or ventricles. The right ventricle pumps for the pulmonary circulation, the left ventricle pumps for the systemic circulation. The 'Great Vessels' of the heart are the aorta and pulmonary trunk. Heart valves ensure the one-way flow of blood through the heart and there are two types: semilunar valves (pulmonary semilunar and aortic semilunar) lead from the ventricles and prevent back flow from pulmonary and systemic vasculature. The atrio-ventricular (AV) valves are the tricuspid — right atrium into the right ventricle; and bicuspid (mitral) — left atrium to the left ventricle. If a section is cut through the heart at the atrial ventricular boundary through the four valves a structural skeleton of (four) fibrous rings can be seen. These tough fibrous rings provide rigidity to prevent the dilation of valves and provide a point of

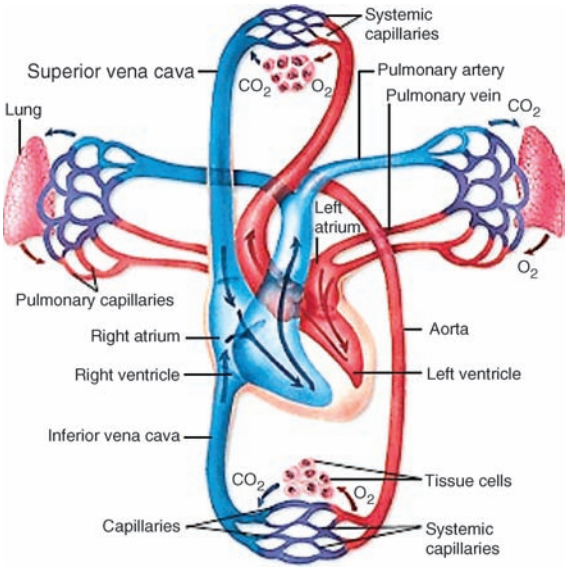


Figure 1.15 The systemic and pulmonary systems

attachment for valves. This fibrous skeleton also electrically isolates the atria from the ventricles. The AV bundle ('bundle of His') is the only electrical connection between the atria and the ventricles (see Figure 1.17).

The origin of heartbeat is located in a sinoatrial (SA) node of the heart, where a group of specialized cells continuously generates an electrical impulse. The SA node generates such impulses about 100–120 times per min at rest. However, in a healthy individual the resting heart rate (HR) would never be that high. This is due to continuous control of the autonomic nervous system (ANS) over the output of SA node activity, which net regulatory effect gives real HR. In a healthy subject at rest it is ranging between 50 and 70 beats per min.

The electrical impulse of the sino-atrial (SA), stimulated by blood flow, first induces the muscle tissue of the atrial chamber to contract. The electrical impulse travels to the atrio-ventricular node and synchronizes with this tissue's inherent but weaker electrical pulsivity. This combined and synchronized electrical pulse travels down the conductive fibres (bundle of His, bundle branches)of the noncontractive muscular cardiac septum (i.e. this tissue does not contract in response to this electrical signal) to the Purkinje fibres which originate at the base of the ventricle muscle walls and travel up towards the atrioventricular boundary. The result is that the signal is delayed, atria muscles are relaxing, but the impulses then induce waves of contraction of the ventricles from the bottom up. This efficiently empties the heart ventricles – like squeezing a toothpaste tube from the bottom and not the middle, whilst the atrium refill. The order of impulse spreading all over the heart muscle through specialized pathways creates synchronized heart muscle contraction between both atriums (first) and then the ventricles which contracts in a wave starting from the bottom of the heart to the top of the ventricles.

1.3.2 The vasculature

The blood vessels are the **arteries**, **arterioles**, **capillaries**, **venules** and **veins** and all blood vessels are lined with specialist cells of the endothelium (see Figure 1.18). The arteries which carry blood away from the heart are subject to the highest blood pressure and located deep within tissues. Subject to much lower pressures, veins return blood to the heart.

1.3.2.1 Structure of arteries and arterioles

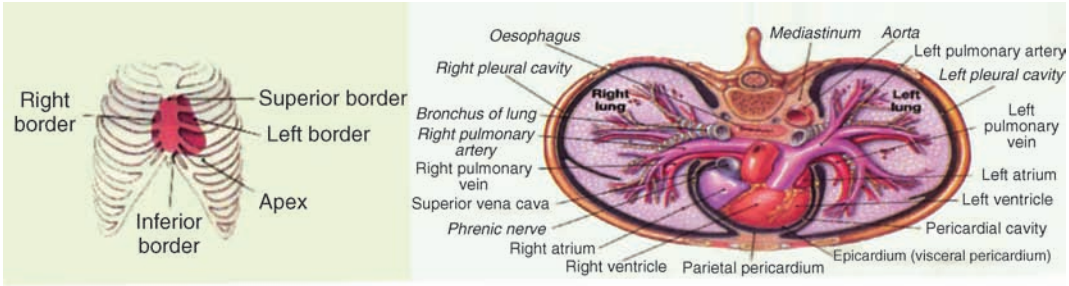
Arteries consist of three tissue layers: **tunica interna**, **tunica media** and **tunica externa**. However, there are two types of artery: elastic arteries, which contain elastic fibres in the tunica media and interna, which are the largest. Muscular arteries have little elasticity and abundant smooth muscle in the tunica media.

Arterioles are less than 1 mm in diameter and consist of endothelium and smooth muscle. It is the ability of arteries to contract by virtue of the dense smooth muscle layers that allows these vessels to regulate blood pressure in a general and locality specific manner. Indeed the **metarterioles** regulate the flow of blood into capillaries (see Figure 1.19).

Capillaries are the sites of exchange, they are very thin and permeable, allowing exchange between blood and tissue cells in systemic capillaries and the exchange between blood and air in pulmonary capillaries.

1.3.2.2 Structure of veins and venules

Veins are thinner than arteries, of a much larger diameter and located both deep and superficially



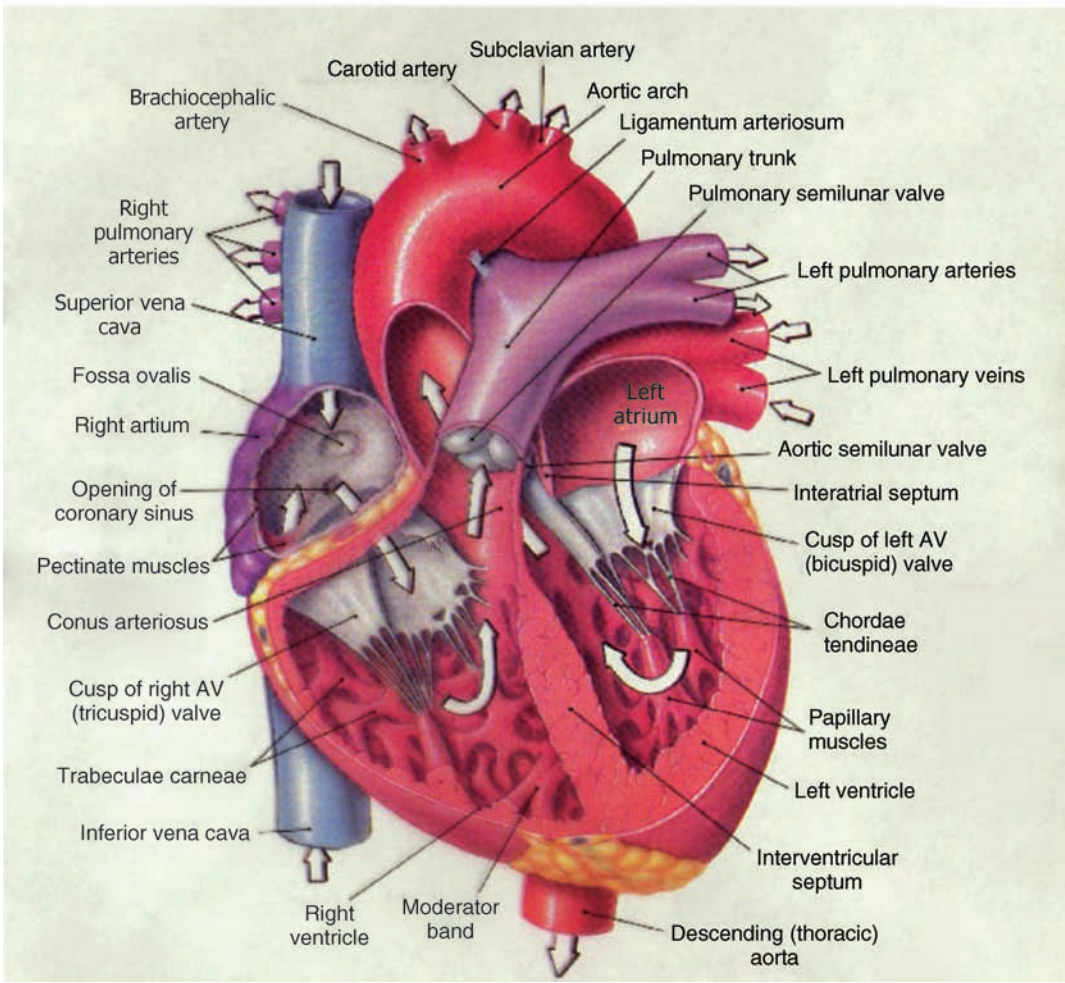


Figure 1.16 The heart, position associated organs and major vessels

within tissue. A key difference is that veins have valves. Since the blood in veins is under much lower pressure after a forward flow pressure beat from the left ventricle, the blood could flow backwards again. The valves prevent this backwards flow and veins within muscles are squeezed by external contraction of muscle tissue mass as a result of movement (and general muscle tone) to help return blood.