Editors Ray Iles | Suzanne Docherty

Biomedical Sciences

Essential Laboratory Medicine

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Biomedical Sciences

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

Professor Ray K. Iles, B.Sc., M.Sc., Ph.D., CBiol, FSB, FRSC, Dr Iona Collins, BMedSci, MBBS, FRCS and 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.

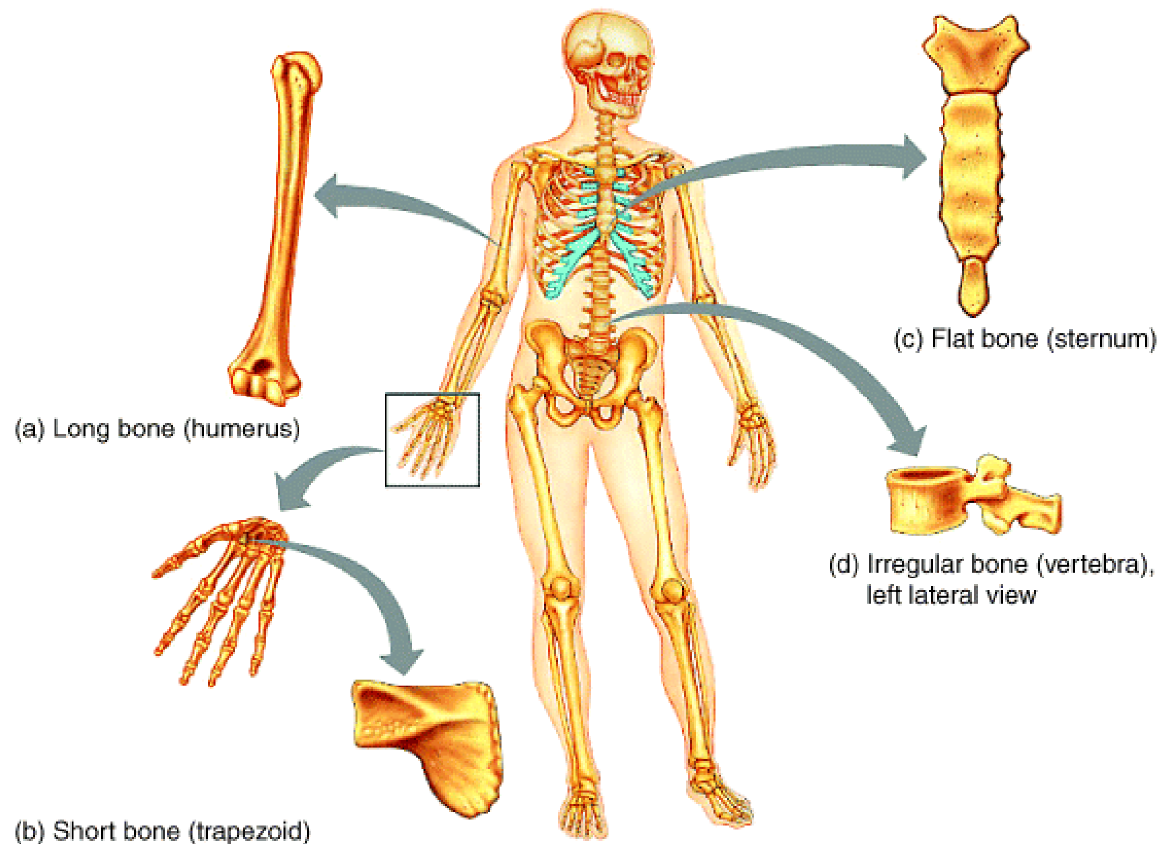
1.1 The Skeletal System

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.

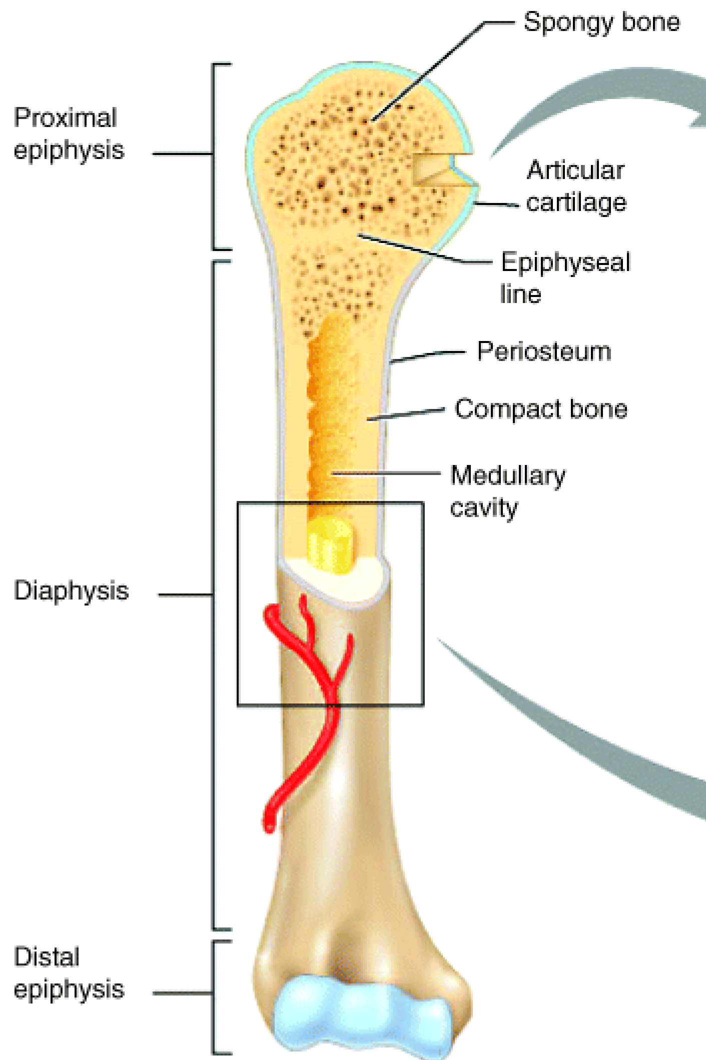
Figure 1.1 The human skeleton and the four bone categories which are shape descriptors. *Essentials of Human Anatomy & Physiology*, 9th Edition, Marieb, 2008 © Pearson Education Inc.



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 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).

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

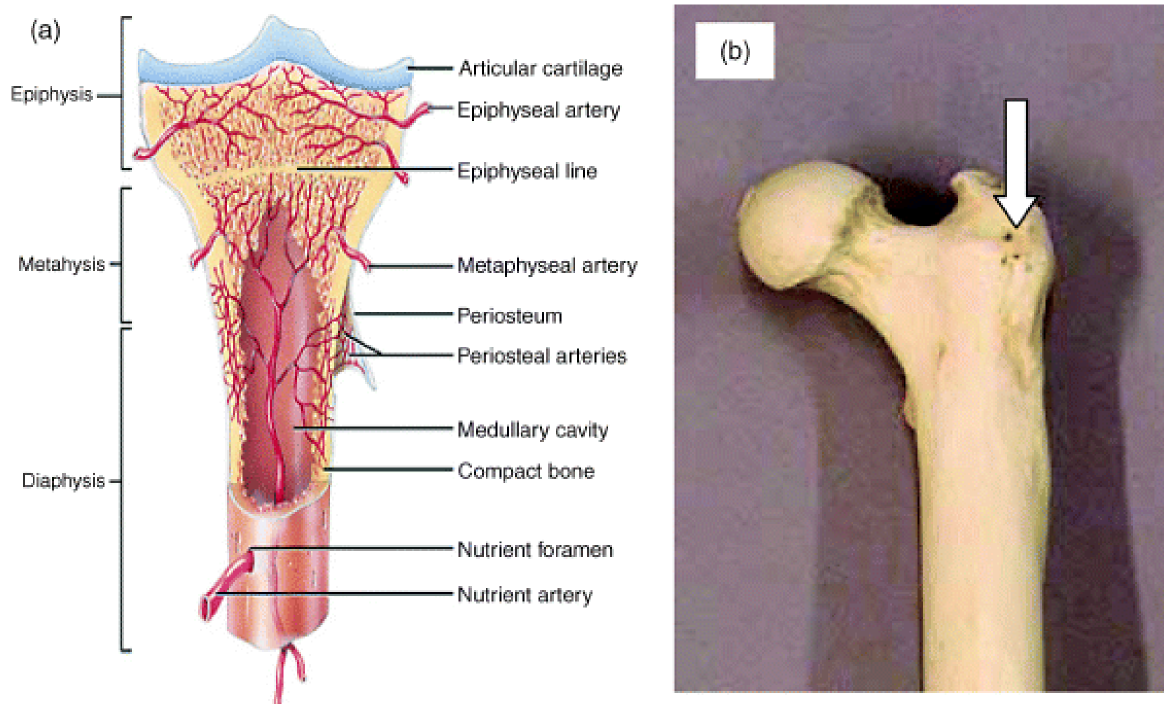


Bone is derived from connective tissue and there are two types of connective tissue in the skeletal system – calcified bone and cartilage. Cartilage tissue forms a covering of articular surfaces, ligaments and tendons, as well as sheaths around bone (periosteum).

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)).

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.

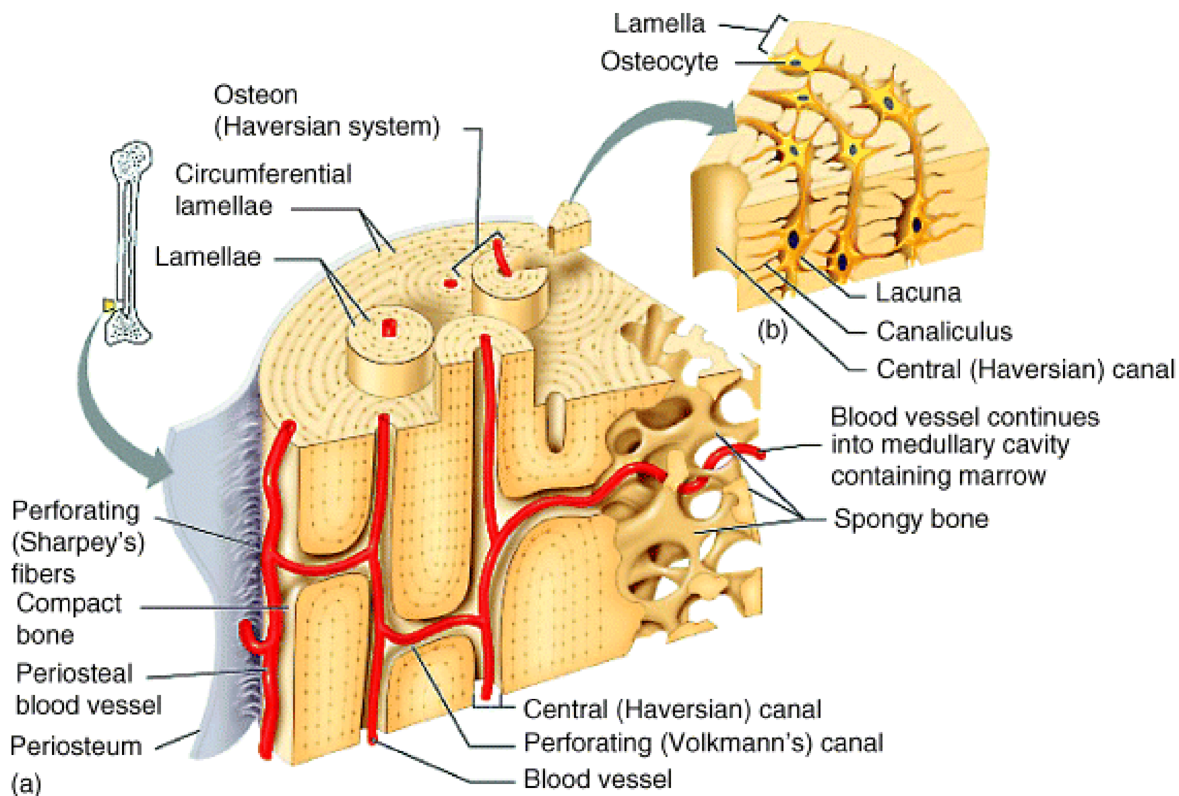


1.1.2 Spongy Bone and Compact Bone

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 1.4 Microanatomy of the 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.

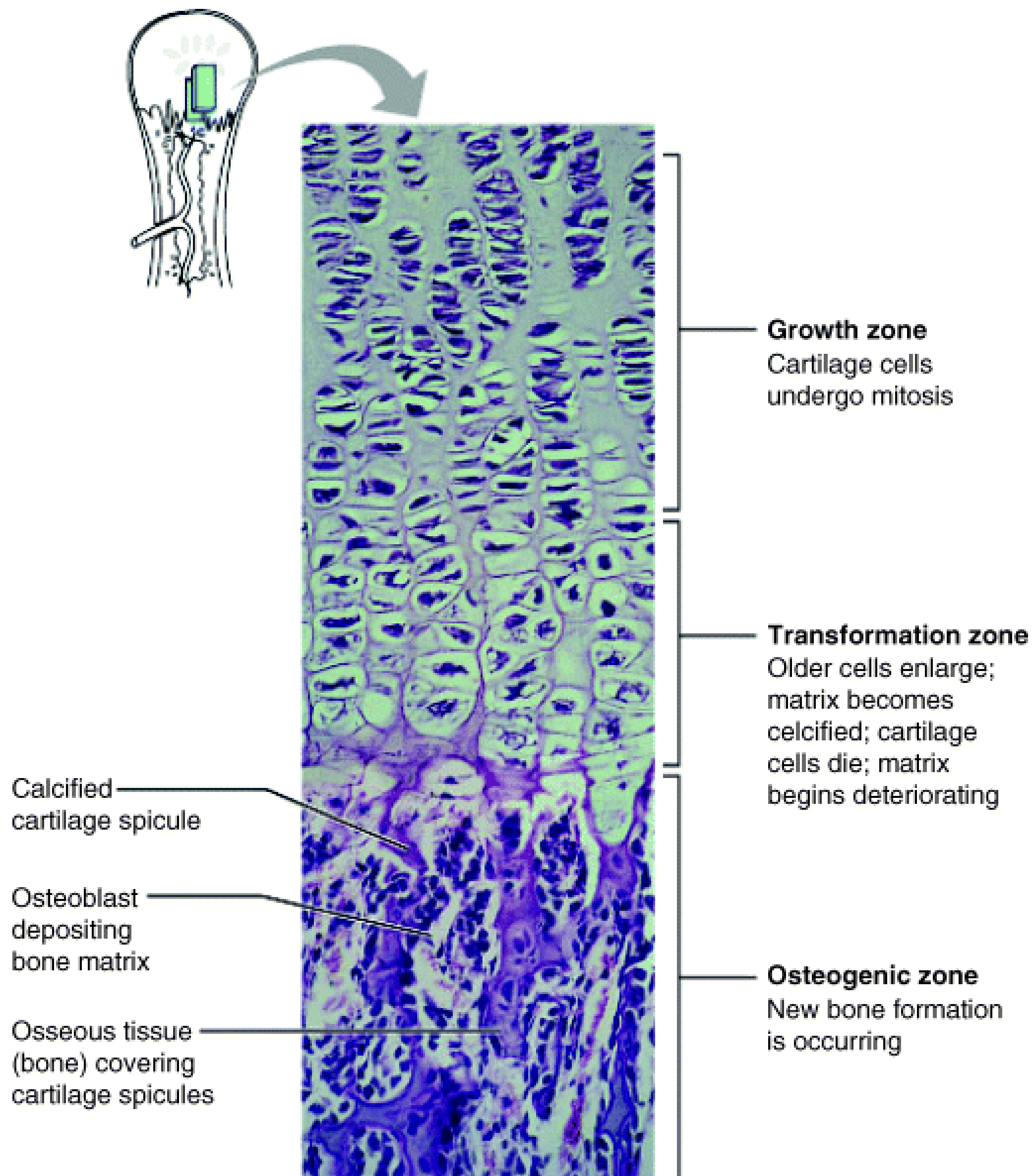
In the formation of new bone osteoblasts cover hyaline cartilage with bone matrix. Enclosed cartilage is digested away leaving the medullary cavity. Growth in width and length continues by the laying down of new bone matrix by osteoblasts. Remodelling to ensure the correct shape is effected by osteoclasts (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, 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).

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

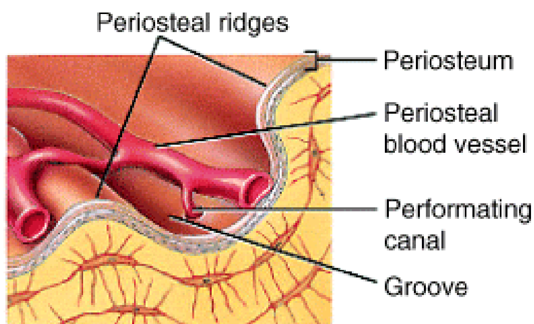


Cartilage cells are produced by mitosis on the epiphyseal side of plates (ends of bones) – this is continuous with articular cartilage at the end of the bone. Cartilage cells are destroyed and replaced by bone on the diaphyseal side of plates (middle of long bone) and a zone of resting cartilage anchors 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,

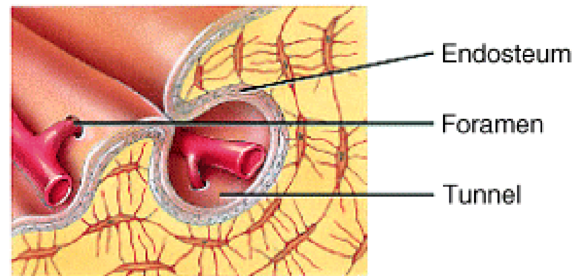
osteoblasts lay down a calcium phosphate matrix in and around the cartilage cells, ossifying the area. This gradually takes on the structure of bone. The epiphyseal plate cartilage is continuous with the articular cartilage at the end of the bone, and new cartilage (and bone formation) is occurring in 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.

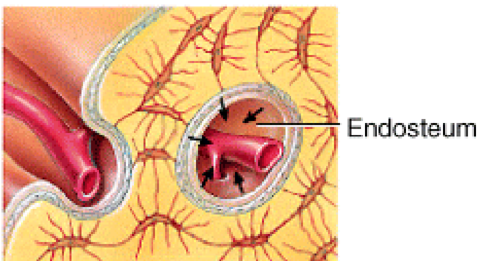
Figure 1.6 Appositional bone growth



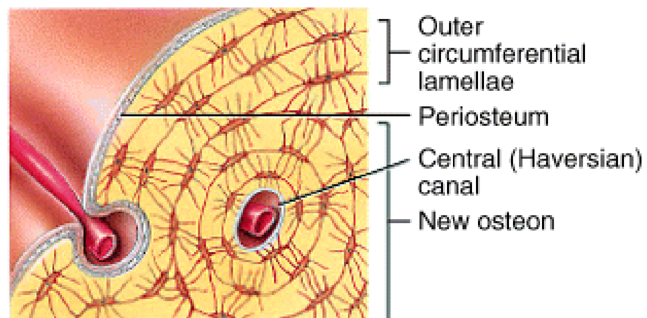
(a) Ridges in periosteum create groove for periosteal blood vessel.



(b) Periosteal ridges fuse, forming an endosteum-lined tunnel.



(c) Osteoblasts in endosteum build new concentric lamellae inward toward center of tunnel, forming a new osteon.



(d) Bone grows outward as osteoblasts in periosteum build new outer circumferential lamellae. Osteon formation repeats as new periosteal ridges fold over blood vessels.

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.

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

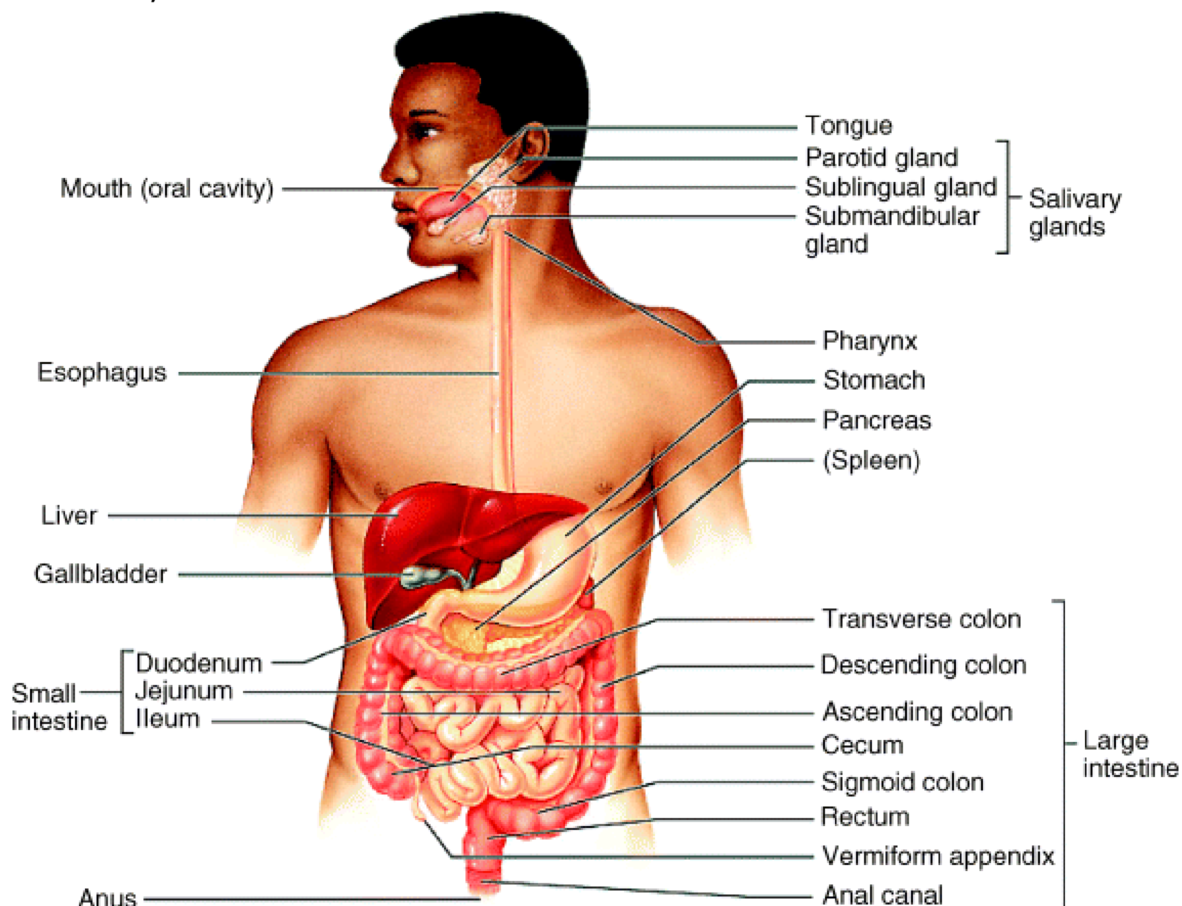
This section aims to give an overview of the anatomy of the digestive system, identifying the major organs of the

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.

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



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, 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.

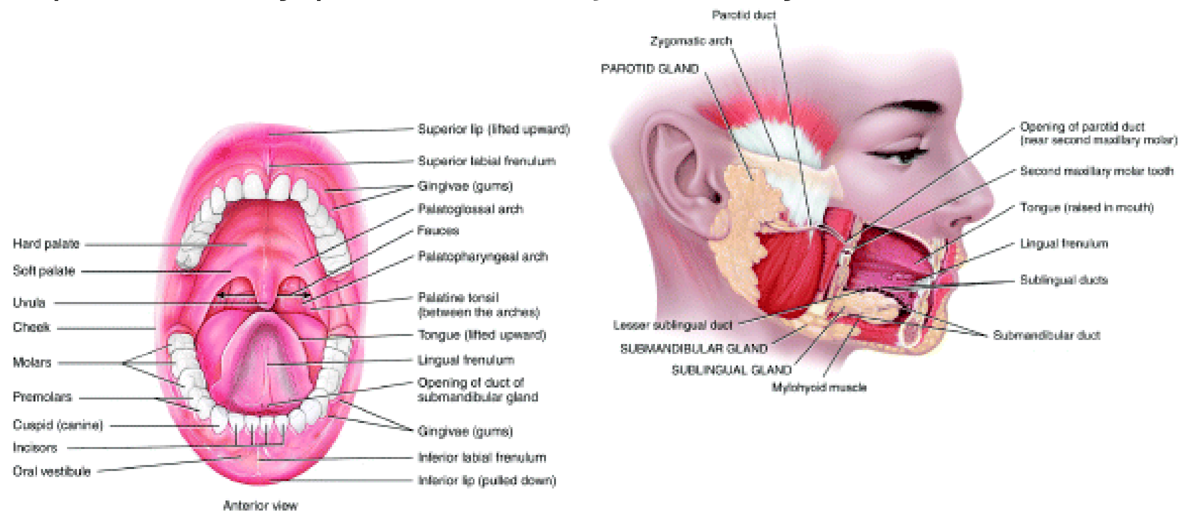
In order to extract macro- and micronutrients from food stuffs the digestive system must bring about ingestion, digestion (mechanical and chemical), enable movement through the digestive tract, facilitate absorption of nutrients and finally defaecation of the nondigestible elements and some waste products.

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).

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.



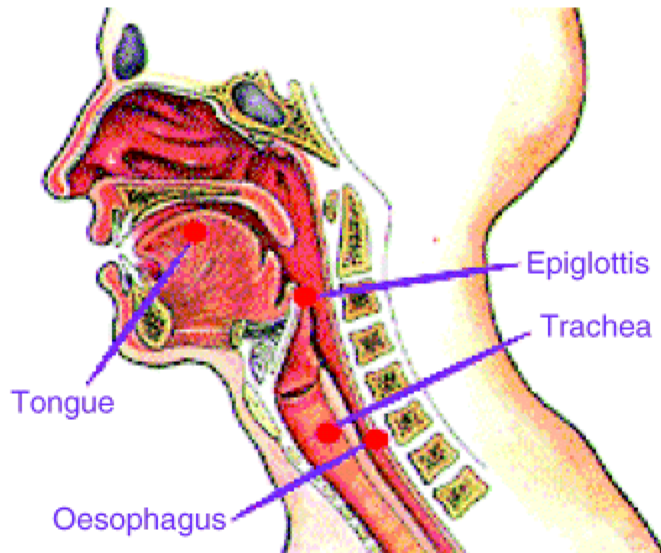
After chewing we swallow but there are two phases:

- 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 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.

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



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.