6 Cells and tissues

After reading this chapter you should have gained an understanding of:

- The principal tissue types:
  - Blood and lymph
  - Connective tissue
  - Nervous tissue
  - Muscle
  - Epithelia and glandular tissue
- Cell–cell adhesion and the extracellular matrix
- Cell–cell recognition

6.1 Introduction

The basic features of mammalian cells were discussed in Chapter 4. This chapter is concerned with the arrangement of cells into functional aggregates known as **tissues**. There are five main types of tissue:

1. Blood and lymph
2. Connective tissue
3. Nervous tissue
4. Muscle tissue
5. Epithelial tissue.

Each type of tissue has its own characteristics and the organs of the body, such as the brain, the heart, the lungs, the intestines and the liver, are built from these basic types of tissue. For example, the stomach is lined by epithelial tissue; its wall consists mainly of connective tissue and smooth muscle, which are supplied with blood vessels and nerve fibres. The organs themselves are parts of distinct physiological systems: the heart and blood vessels form the cardiovascular system; the lungs, trachea and bronchi together with the chest wall and diaphragm form the respiratory system; the skeleton and skeletal muscles form the musculoskeletal system; the brain, spinal cord, autonomic nerves and ganglia, and peripheral somatic nerves form the nervous system, and so on.

6.2 Histological features of the main tissue types

Blood and lymph

Blood and lymph are characterized by having cells dispersed within a fluid. As the cells of blood and lymph do not form a continuous mass but are dispersed within the fluid phase, these tissues are sometimes classed as connective tissue (see below). In the case of blood, the fluid phase is known as **plasma**. The vast majority of blood cells are **red cells** or **erythrocytes**, which have no nucleus (Figure 6.1). The red cells contain the oxygen-binding protein haemoglobin and their chief function is to transport oxygen from the lungs to the tissues and return the carbon dioxide generated by the cells to the lungs. There are five different kinds of white blood cell (**leukocyte**). These are the granulocytes (basophils, eosinophils and neutrophils), the monocytes and the lymphocytes. Examples of some of these can be seen in Figure 6.1. The leukocytes play a major role in the defence against infection. In addition, the blood contains small cell fragments known as **platelets**, which play a crucial role in blood clotting. The detailed properties of blood are discussed in Chapter 20.

Lymph is a clear fluid formed in the tissues. It contains many fewer cells than blood and its main cells are lymphocytes, although a small number of red blood cells may also be present. The cell count is significantly increased after the lymph has passed through a lymph node from which it acquires many lymphocytes (see p. 333).

KEY POINT:

- Blood and lymph are specialized tissues that are characterized by having cells dispersed within a fluid medium.

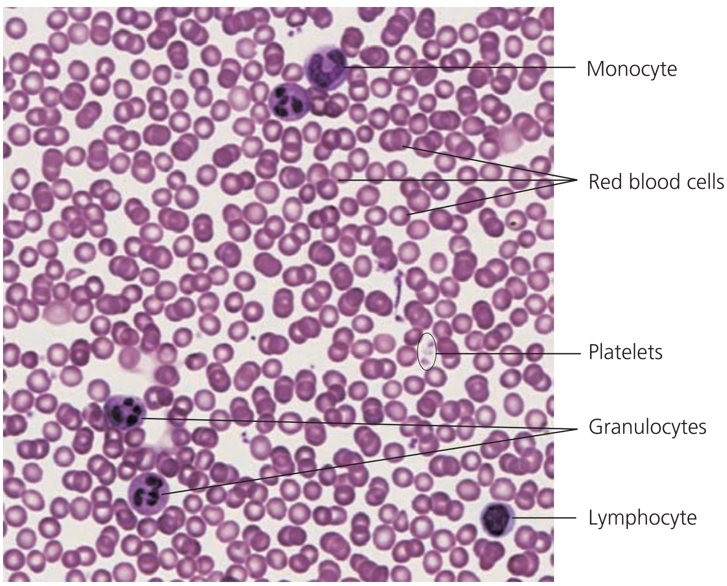


Figure 6.1 A blood film showing the main classes of cell. Note the large number of red blood cells relative to the number of white blood cells. The granulocytes have lobed nuclei – for that reason they are also called polymorphs. The small densely staining fragments are platelets.

Connective tissue

The connective tissues provide structural support to the various organs of the body. For this reason, they are sometimes called **structural tissues**. Connective tissues are very variable in appearance as each type is adapted to perform a specific function, but all are characterized by having cells that are dispersed within an extensive extracellular matrix. The main cells of connective tissues are **fibroblasts**, which synthesize and secrete the extracellular matrix (often called ground substance, and the fibres that provide the mechanical strength of the connective tissues. The extracellular matrix consists of polysaccharides known as **glycosaminoglycans**. Most connective tissues contain fat cells (**adipocytes**) and are well supplied with blood vessels (the exception being cartilage).

Most connective tissue fibres are formed of **collagen**, which exists in a variety of forms. Examples are the dense type I collagen fibres found in the ligaments and tendons (Figure 6.2) and the delicate fibrils found interspersed between the cells of organs such as the liver (known as type III collagen). In many tissues, such as the kidney, the connective tissue acts as a loose packing material with little mechanical strength (Figure 6.3). In others, for example the dermis of the skin, the connective tissue provides a tough, protective layer. The tough outer capsule of the liver and kidneys is formed of connective tissue, as is the mesentery of the gastrointestinal tract. Bone and cartilage are highly specialized forms of supporting tissue and will be discussed in Chapter 10 (pp. 154–160). Many tissues have fibres of **elastin**, which provide the elasticity that allows tissues to resume their original shape after they have been stretched. Elastin fibres are found in the skin, lungs and in the walls of elastic arteries (Figure 6.4).

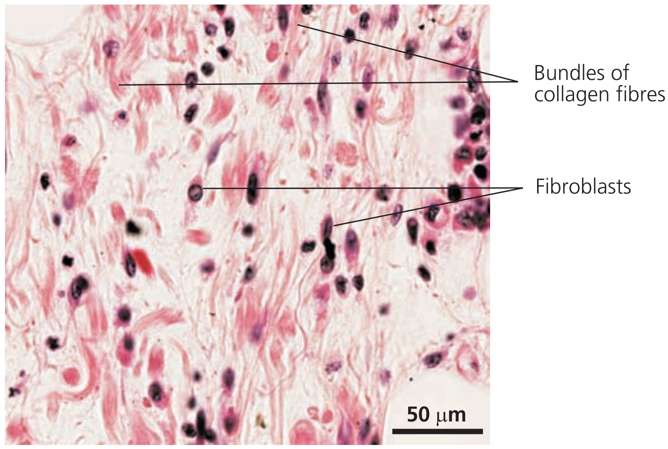


Figure 6.3 Loose connective tissue stained to show the fibroblasts and the bundles of collagen. Note the random arrangement of the collagen bundles.

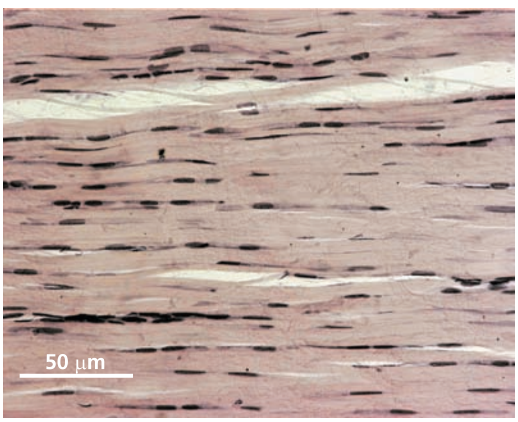


Figure 6.2 A section of tendon stained to reveal the nuclei of the fibroblasts. Note the alignment of the fibroblast nuclei with the bundles of collagen fibres, which are less intensely stained.

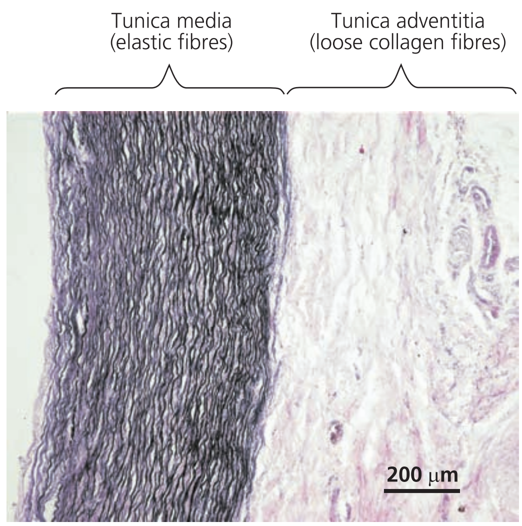


Figure 6.4 A section of the wall of an elastic artery stained to show the elastic fibres of the tunica media. The section also shows the loose arrangement of the collagen bundles of the tunica adventitia.

There are two main forms of fatty connective tissue: **white adipose tissue** and **brown adipose tissue**, more commonly called **brown fat**. The white adipose tissue is widely dispersed throughout the body and forms its main energy reserve. The fat is stored within adipocytes as a single large droplet that forces the cytoplasm into a thin layer around the cell. The nucleus is compressed and forced to one side of the cell, as shown in Figure 6.5. In contrast, the cells of brown adipose tissue store their fat in a number of small vesicles surrounded by a large number of mitochondria, which give the tissue its characteristic brown coloration. The distribution of brown fat is more restricted than that of white adipose tissue. It is especially important in neonates, where it plays an important role in the maintenance of body temperature (see Chapter 33).

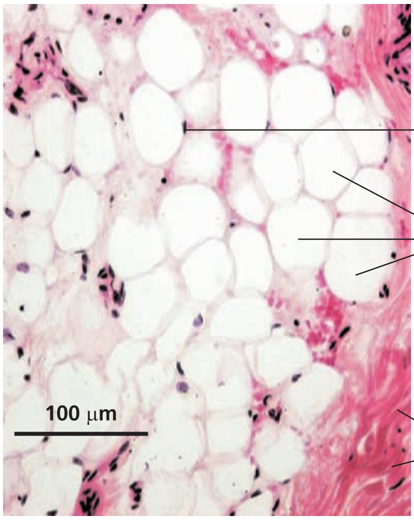


Figure 6.5 The appearance of white adipose tissue in a histological section. The nuclei are stained blue and appear on the edges of large spaces, which contained fat droplets that have been removed in the processing of the section.

KEY POINTS:

- The connective tissues provide structural support to the various organs of the body. They are also called structural tissues.
- They are very variable in appearance, but all are characterized by having cells that are dispersed within an extensive extracellular matrix.

Nervous tissue

The brain and spinal cord constitute the **central nervous system** (CNS) while the nervous tissues that lie outside the CNS make up the **peripheral nervous system**. The CNS is made up of two main types of cell, **nerve cells** (also called **neurones**) and **glial cells**. The nerve cells provide rapid and discrete signalling over long distances (from millimetres to a metre or more) while the glial cells have a complex supporting role. The nerve cell bodies are very varied in both size and shape, but all stain strongly with basic dyes, as shown in Figure 6.6. The material is called **Nissl substance** and corresponds to the RNA of the rough endoplasmic reticulum described in Chapter 4 (p. 44). Figure 6.6 also shows the nuclei of glial cells, which are more widespread and plentiful than the nerve cells.

Each nerve cell has an extensive set of fine branches called **dendrites** that receive information from other neurones, integrate it and transmit it to its target cells via a delicate extension of the cell body called an **axon** (Figure 6.7). Axons and dendrites are collectively called neuronal processes. The space between the nerve cell bodies is known as the **neuropil**. It contains the cytoplasmic extensions of both neurones and glia.

The peripheral nervous system consists of nerve trunks and ganglia. The nerve trunks contain large numbers of axons while the ganglia contain nerve cell bodies, as in the example shown in Figure 6.8. Both the peripheral and central nervous system are well provided with blood vessels and both are protected with layers of connective tissue, which will be described in detail in Chapters 8 and 11.

KEY POINTS:

- Nervous tissue consists mainly of neurones and glial cells.
- It is found mainly in the brain and spinal cord, but small ganglia are scattered throughout the body.
- Nerve trunks connect the CNS to the various organ systems.

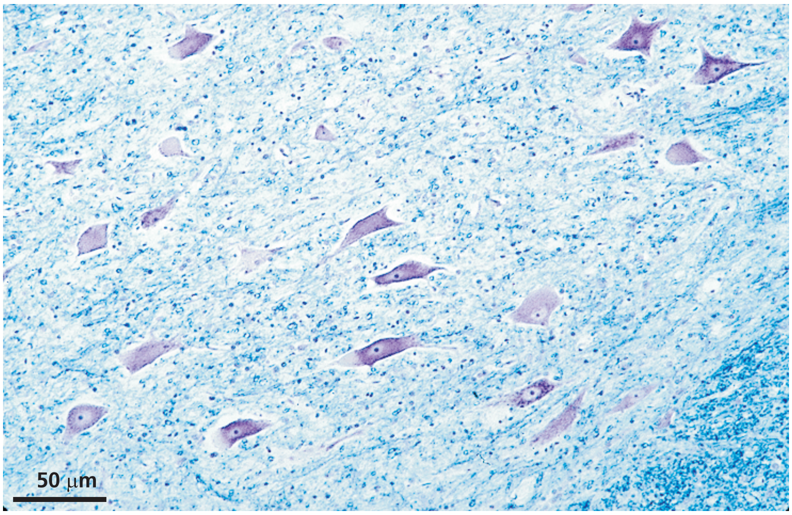


Figure 6.6 A section of the grey matter of the spinal cord stained to show the motoneurones (violet) and the glial cells of the neuropil (blue). The cell bodies of the neurones are well defined and are much larger than those of the glial cells. However, glial cells vastly outnumber the neurones.

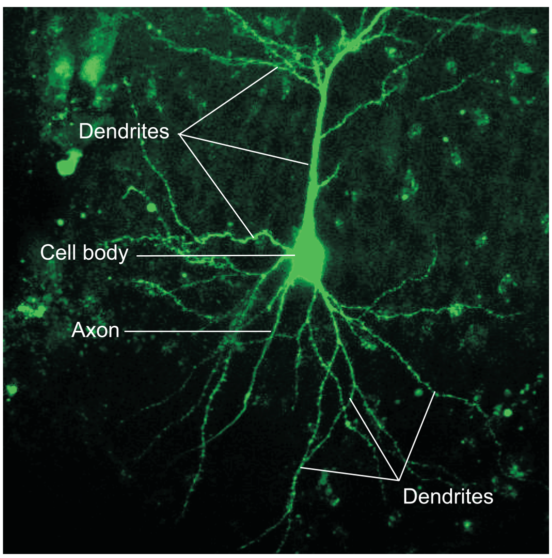


Figure 6.7 A pyramidal cell (a type of neurone) from the CNS stained with a green fluorescent dye. Note the extensive dendrites, which have a roughened appearance and arise from both the apex and base of the cell. A single axon emerges from the base of the cell.

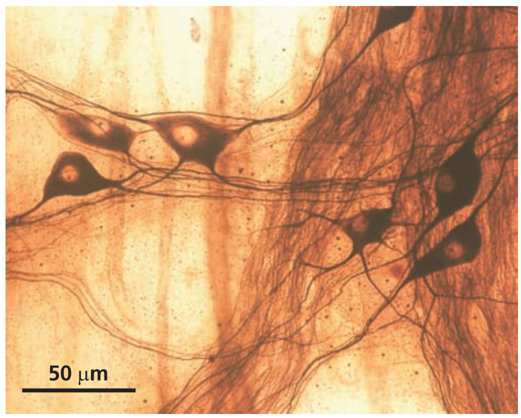


Figure 6.8 This image shows neurones in a ganglion from the wall of the gastrointestinal tract. The main processes of the individual cells are clearly visible.

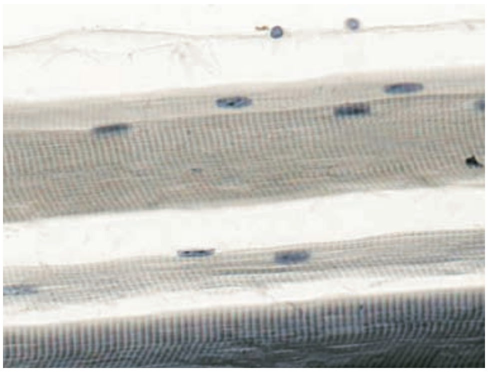
Muscle tissue

Muscle tissue is characterized by its ability to contract in response to an appropriate stimulus. Muscle cells are also known as **myocytes**. There are three main types of muscle: skeletal muscle, cardiac muscle and smooth muscle. **Skeletal muscle** is the muscle directly attached to the bones of the skeleton, **cardiac muscle** is the muscle of the heart and **smooth muscle** is the muscle that lines the blood vessels and the hollow organs of the body.

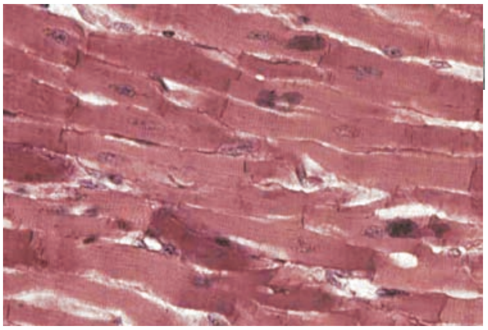
The appearance of the different kinds of muscle tissue is shown in Figure 6.9. Their detailed structure and function will be discussed in Chapter 9.

When the cells of skeletal and cardiac muscle are viewed down a microscope, they are seen to have characteristic striations – small regular stripes running across the individual muscle cells (Figure 6.9a and b). For this reason, skeletal and cardiac muscles are sometimes called **striated muscles**. Smooth muscle lacks striations and consists of sheets of spindle-shaped cells. Between the muscle cells are layers of delicate connective tissue that bind them together into bundles called fascicles. The individual fascicles are bound together in a denser wrapping of connective tissue that provides support for the blood vessels and nerve fibres as they course through the tissue. The connective tissues of muscle will be described in more detail in Chapter 9. In skeletal and cardiac muscle, the smaller blood vessels run parallel to the main course of the bundles of muscle fibres, as shown in Figure 6.10.

(a)



(b)



(c)

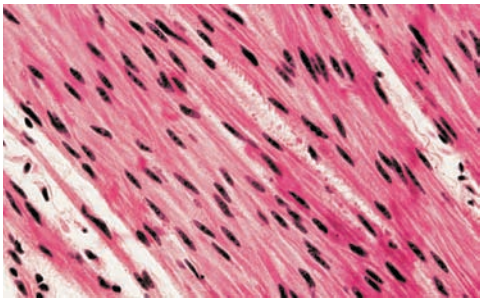


Figure 6.9 The appearance of the three principal types of muscle. (a) This shows the appearance of skeletal muscle with its characteristic striations. Note the large size of the individual fibres and the distribution of the nuclei on the outside of each fibre. (b) The appearance of cardiac muscle. Note the prominent intercalated disks and the centrally place nuclei. (c) Smooth muscle from the gastrointestinal tract. Note the absence of striations and the elongated nuclei within the spindle-shaped cells.

KEY POINTS:

- There are three kinds of muscle tissue: skeletal, cardiac and smooth muscle.
- Skeletal and cardiac muscle fibres are striated while smooth muscle cells are not.
- Muscle fibres are bound together with layers of connective tissue and are well supplied with blood vessels.

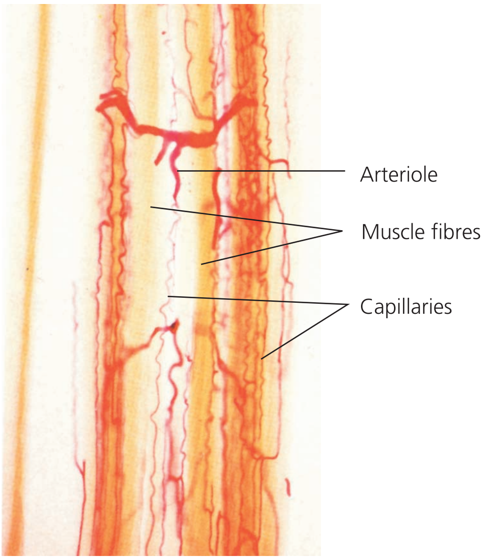


Figure 6.10 The blood supply of skeletal muscle revealed by perfusing the blood vessels with a red dye. The larger vessels enter the body of the muscle and branch to give rise to a series of capillaries that run alongside the bundles of muscle fibres.

Epithelia

Continuous sheets of cells are known as **epithelia.** They form the epidermis of the skin and line the hollow organs of the body, such as the gut, lungs and urinary tract, as well as the fluid-filled spaces such as the peritoneal cavity. However, the cell layer that lines the blood vessels is called the vascular **endothelium** and the epithelial coverings of the pericardium, pleura and peritoneal cavity are known as **mesothelium**, reflecting their origins from the embryonic mesoderm. Nevertheless, all three separate one compartment of the body from another. Their detailed structure reflects their differing functional requirements. For example, the epithelium of the skin is thick and tough to resist abrasion, and to prevent the loss of water from the body. In contrast, the epithelial lining of the alveoli of the lungs is very delicate and thin to permit free exchange of the respiratory gases.

Despite their differences in form and function, all epithelia share certain features:

- Firstly, they are composed of cells that are tightly joined together via specialized cell–cell junctions to form a continuous sheet (see p. 77).
- Secondly, epithelial cells lie on a matrix of connective tissue fibres called the **basement membrane**. The basement membrane provides physical support and separates the epithelium from the underlying vascular connective tissue, which is known as the **lamina propria**.
- Thirdly, to replace damaged and dead cells, all epithelia undergo continuous cell replacement. The rate of replacement depends on the physiological role of the epithelium and is highest in the skin and gut, both of which are continually subjected to abrasive forces.
- Finally, unlike cells scattered throughout a tissue, the arrangement of cells into epithelial sheets permits the directional transport of materials either into or out of a compartment. In the gut, kidney and many glandular tissues, this feature of epithelia is of great functional significance. The surface of an epithelial layer that is oriented towards the central space of a gland or hollow organ is known as the **apical surface**. The surface that is oriented towards the basement membrane and the interior of the body is called the **basolateral surface**.

The classification of epithelia

The main types are known as **simple**, **stratified** and **pseudostratified**. Simple epithelia consist of a single cell layer and are classified according to the shape of the constituent cell type. Stratified epithelia are also classified according to the appearance of their constituent cells. They are characterized by having more than one cell layer. Pseudostratified epithelia consist of a single layer of cells in contact with the basement membrane, but the varying height and shape of the constituent cells gives the appearance of more than one cell layer.

The morphological characteristics of the main types of epithelium are shown in Figure 6.11 and are summarized below:

- Simple squamous epithelium (squamous = flattened) consists of thin and flattened cells, as shown in Figure 6.11 (i) and (ii). These epithelia are adapted for the exchange of small molecules between the separated compartments. The walls of the alveoli of the lungs and the endothelium of the blood vessels are squamous epithelia.
- Simple cuboidal epithelium, as the name implies, consists of a single layer of cuboidal cells whose width is approximately equal to their height (Figure 6.11 (iii)). A simple cuboidal epithelium forms the walls of the small collecting ducts of the kidneys.
- Simple columnar epithelium is adapted to perform secretory or absorptive functions. In this form of epithelium, the height of the cells is much greater than their width, as shown in Figure 6.11 (iv). It occurs in the large-diameter collecting ducts of the kidneys. It is also found lining the small intestine.
- Ciliated epithelium consists of cells that have cilia on their apical surface. Non-ciliated cells are also interspersed between the ciliated cells, as illustrated in Figure 6.11 (v). Ciliated epithelia line the Fallopian tubes.
- Pseudostratified columnar ciliated epithelium consists of cells of differing shapes and height, as shown in Figure 6.11 (vi). This type of epithelium predominates in the upper airways (trachea and bronchi).
- Stratified squamous epithelium is adapted to withstand chemical and physical stresses. The best-known stratified epithelium is the epidermis of the skin. In

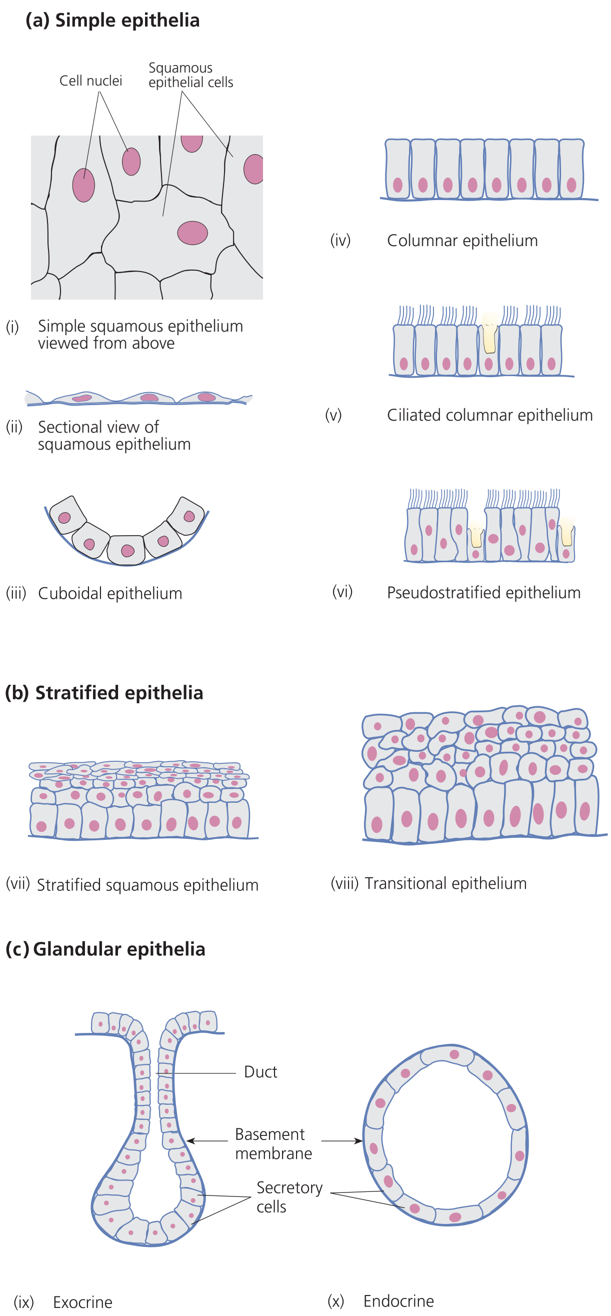


Figure 6.11 A diagrammatic representation of the principal types of epithelium. Panel (a) shows the general structure of the common types of simple epithelia. Note that when viewed from the apical surface there are no gaps between the cells (i). Pseudostratified epithelia (vi) have cells of differing shape and size, so giving a false appearance of multiple cell layers. The nuclei are found at many levels within the epithelium. Panels (b) and (c) show the general structure of stratified, transitional and glandular epithelia. See text for further details.

this case, the flattened epithelial cells form many layers, only the lowest layer being in direct contact with the basement membrane (Figure 6.11 (vii)). The more superficial cells are filled with a special protein called keratin, which renders the skin almost impervious to water and provides an effective barrier against invading organisms such as bacteria.

- Transitional epithelium is found in the bladder and ureters. It is similar in structure to stratified squamous epithelium except that the superficial cells are larger and rounded (Figure 6.11 (viii)). This adaptation allows stretching of the epithelial layer as the bladder fills.

KEY POINTS:

- Epithelia are formed entirely from sheets of cells and consist of one or more cell layers.
- They separate one compartment of the body from another.
- An epithelium consisting of a single cell layer is known as a simple epithelium while those with more than one layer are called stratified epithelia.

Glandular epithelia

Glandular epithelia are specialized for secretion. The epithelia that line the airways and part of the gut are covered with a thick layer of mucus that is secreted by specialized secretory cells, known as goblet cells, which discharge their contents directly onto an epithelial surface. Glands, known as **exocrine glands**, secrete material via a specialized duct onto an epithelial surface, as shown in Figure 6.11 (ix). Examples are the salivary glands and sweat glands. Other glandular epithelia lack a duct and secrete material across their basolateral surfaces from where it passes into the blood. These are the **endocrine glands**. Examples include the thyroid gland and the irregular clusters of epithelial cells that constitute the islets of Langerhans of the pancreas.

The exocrine glands may be grouped into various classes according to the arrangement of their duct system. Some examples are shown in Figure 6.12. The gastric glands in the body of the stomach are simple tubular glands. The sweat glands are simple, coiled, tubular glands. Other exocrine glands have a system of branching ducts that link groups of secretory cells called **acini** (singular **acinus**). The acinar cells of an individual acinus are held in a tight ball by a capsule of connective tissue. This type of organization is found in the pancreas and salivary glands.

Serous membranes enclose a fluid-filled space such as the peritoneal cavity. The peritoneal membranes consist of a layer of epithelial cells (called the mesothelium) overlying a thin basement membrane, beneath which is a narrow band of connective tissue. The pleural membranes that separate the lungs from the wall of the thoracic cavity are another example of serous epithelia. Not all fluid-filled spaces are lined by an epithelium: while the articular surfaces of joints such as the knee are lubricated by synovial fluid, they are not lined by a continuous layer of cells. Instead, the synovial cells form a discontinuous layer up to four cells deep, which does not constitute a true epithelium.

KEY POINTS:

- Glandular epithelia are specialized for secretion.
- If their secretion is via a duct, they form part of an exocrine gland.
- If their secretion passes directly into the blood, they form part of an endocrine gland.

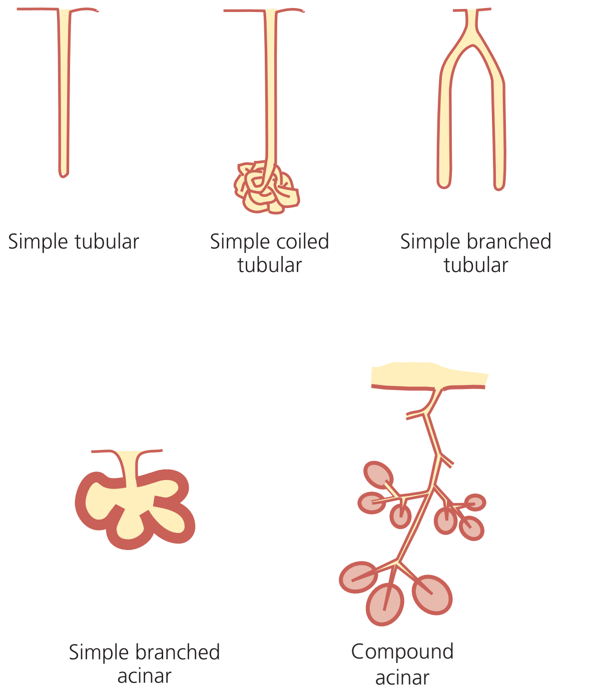


Figure 6.12 This figure shows the duct arrangement of several types of exocrine gland. The compound glands all have a set of branching ducts.

6.3 Cell–cell adhesion

To form complex tissues, different cell types must aggregate together. As all cells have their origin in the fertilized egg, some cells must migrate from their point of origin to another part of the body during development. When they arrive at the appropriate region, they must recognize their target cells and participate in the differentiation of the tissue. To do so, they must attach to other cells and to the extracellular matrix. What signals are employed by developing cells to establish their correct positions and why do they cease their migrations when they have found their correct target?

Unlike adult cells, embryonic cells do not form strong attachments to each other. Instead, when they interact, their cell membranes become closely apposed to each other leaving a very small gap of only 10–20 nm. Exactly how cells are able to recognize their correct associations is not fully understood, but each type of cell has a specific marker on its surface. When cell membranes touch each other, these marker proteins can interact and allow the cells to adhere. This must be an early step in tissue formation. It has been shown that cells will associate only if they recognize the correct surface markers. Thus, if differentiated embryonic liver cells are dispersed by treatment with enzymes and grown in culture with cells from the retina, the two cell types aggregate with others of the same kind. Thus, liver cells aggregate together and exclude the retinal cells and vice versa.

KEY POINTS:

- For cells to assemble into tissues, they need to adhere to other cells of the correct type. This recognition requires tissue-specific cell-surface marker molecules.
- Cell–cell adhesion and cell–matrix interactions play an important role in tissue maintenance and development.

6.4 Specialized cell attachments

Epithelial cells are joined together by a characteristic structure known as the **junctional complex** (Figure 6.13), which consists of three structural components: the **tight junction** (also known as the zonula occludens), the **adherens junction** (or zonula adherens) and the **desmosomes**. Within the junctional complexes, specialized regions of contact, called **gap junctions**, are found. Gap junctions allow small molecules to diffuse between adjacent cells. In this way, they play a role in communication between neighbouring cells (see Chapter 7, p. 94).

The tight junction forms a continuous band in which the membranes of adjacent cells are fused together. Indeed, the adjacent cells are held so closely apposed that the extracellular space is eliminated. As a result, the tight junction separates the space above the apical surface of an epithelial cell from that surrounding the basolateral surface and prevents ions and water-soluble molecules from leaking between the cells. The proteins responsible for linking the epithelial cells so closely together are transmembrane proteins called **claudins**.

As the tight junctions have little structural rigidity, they are supported by protein filaments in the cytoskeleton. These filaments form the adherens junctions and desmosomes. The adherens junctions form a continuous band around each epithelial cell. On the cytoplasmic side of the membrane, anchor proteins link to the actin and intermediate filaments of the cytoskeleton. This is known as an attachment plaque and appears as a densely staining band in electron micrographs. The anchor proteins are connected to transmembrane adhesion proteins called **cadherins**, which bind neighbouring cells together.

The desmosomes are points of contact between the adjacent cells. They consist of various anchoring proteins that link intermediate filaments of the cytoskeleton to the cadherins. The cadherins of one cell bind to those of its neighbours to form focal attachments of great mechanical strength, rather as spot welds can be used to secure sheets of metal to one another.

Hemidesmosomes, as their name implies, have a similar appearance to half a desomosome as seen in an electron micrograph. However, they are formed by different anchoring proteins that bind cytoskeletal intermediate filaments to transmembrane adhesion proteins known as **integrins**. The integrins fix the epithelial cells to the basal lamina, so linking the cell layer to the underlying connective tissue. The integrins also play an important role in development and wound repair. The cadherins, integrins and immunoglobulin-like cell adhesion molecules (e.g. **N-CAM**) are also involved in non-junctional cell–cell adhesion, which must play an important role in the formation of integrated tissues. Other proteins that promote cell adhesion are the **selectins**, which are a family of adhesion molecules that mediates the initial attachment of a white blood cell to the wall of a blood vessel before it can migrate to a site of tissue injury.

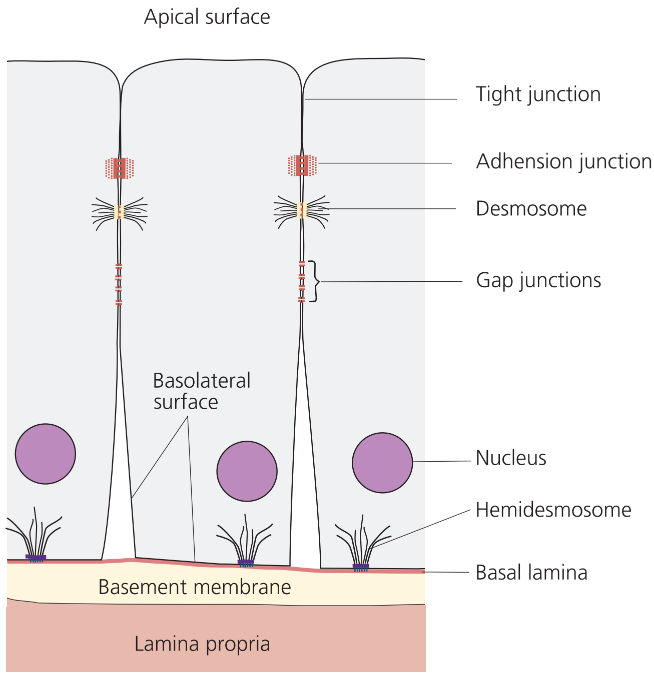


Figure 6.13 A diagram that shows the main structural features of the junctional complexes of epithelia. The tight junctions and adhesion junction form continuous bands around each cell, linking it with its neighbours. The desomosomes give great mechanical strength and the hemidesmosomes link the cells firmly to the underlying tissues.

Recommended reading

Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K. and Walter, P. (2008). *Molecular Biology of the Cell*, 5th edn. Garland: New York. Chapter 19.

Junquieira, L.C. and Carneiro, J. (2005). *Basic Histology*, 11th edn. McGraw-Hill. Chapters 2–4.

Young, B. and Heath, J.W. (2000). *Wheater's Functional Histology*, 4th edn. Churchill-Livingstone: Edinburgh. Chapters 3–7.

Self-assessment questions

Which of the following statements are true and which are false? Answers are given at the end of the book (p. 755).

1 a) An organ usually contains a single tissue type.
b) Connective tissues are characterized by an extensive extracellular matrix.
c) The principal cells of connective tissue are called fibroblasts.
d) Epithelia are connective tissues.
e) The CNS contains a large number of collagen fibres.

2 a) Connective tissues contain either collagen or elastic fibres.
b) Fibroblasts secrete the proteins that make up the fibres of the extracellular matrix.

c) Elastic fibres provide the supporting framework for the cells of the liver.
d) Bone is a type of connective tissue.
e) Adipocytes (fat cells) are commonly found in loose connective tissue.

3 a) Epithelia consist of cells that lie on a basement membrane.
b) The lung alveoli are lined with ciliated columnar epithelium.
c) The epidermis of the skin is a stratified squamous epithelium.
d) Epithelia separate body compartments from each other.
e) The joints are lined with an epithelium.

4 a) The cells of an epithelium are linked together by hemidesmosomes.
b) Epithelial cells communicate with their immediate neighbours via gap junctions.
c) The tight junctions between epithelial cells seal off one body compartment from another.
d) The cadherins are membrane proteins that bind neighbouring cells together.
e) The intermediate filaments of the cytoskeleton are linked to the basal lamina by integrins.