CHAPTER 12

The digestive system

ANIMATIONS

The digestive system describes the *alimentary canal*, its *accessory organs* and a variety of digestive processes that prepare food eaten in the diet for absorption. The alimentary canal begins at the mouth, passes through the thorax, abdomen and pelvis and ends at the anus (Fig. 12.1). It has a basic structure which is modified at different levels to provide for the processes occurring at each level (Fig. 12.2). The digestive processes gradually break down the foods eaten until they are in a form suitable for absorption. For example, meat, even when cooked, is chemically too complex to be absorbed from the alimentary canal. Digestion releases its constituents:

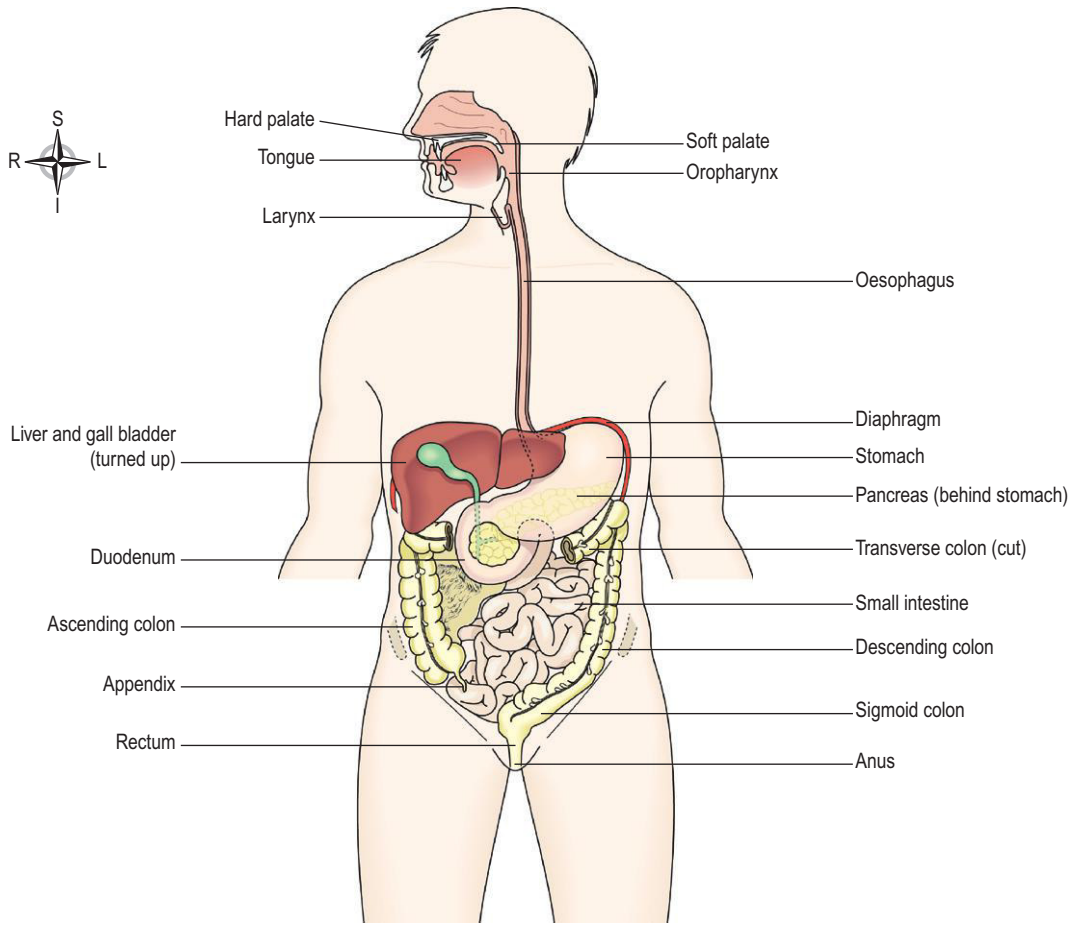

Figure 12.1 The digestive system (head turned to the right).

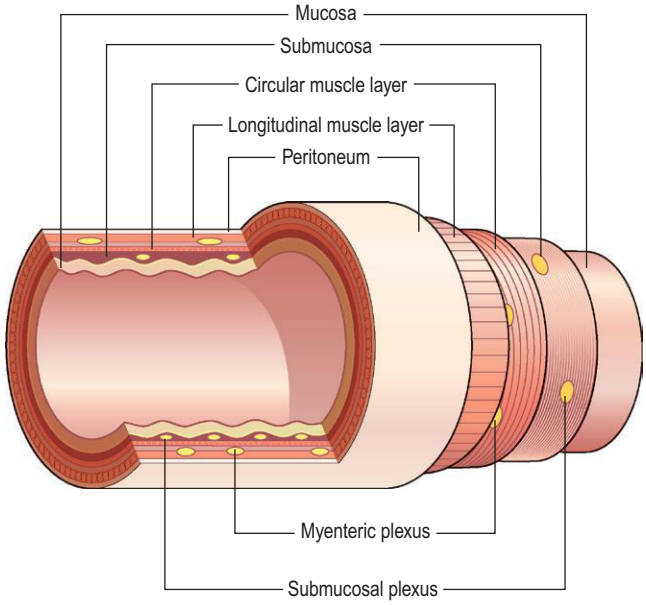

Figure 12.2 General structure of the alimentary canal.

amino acids, mineral salts, fat and vitamins. Digestive *enzymes* (p. 28) responsible for these changes are secreted into the canal by specialised glands, some of which are in the walls of the canal and some outside the canal, but with ducts leading into it. **12.1**

After absorption, nutrients provide the raw materials for the manufacture of new cells, hormones and enzymes. The energy needed for these and other processes, and for the disposal of waste materials, is generated from the products of digestion.

The activities of the digestive system can be grouped under five main headings.

Ingestion. This is the taking of food into the alimentary tract, i.e. eating and drinking.

Propulsion. This mixes and moves the contents along the alimentary tract.

Digestion. This consists of:

- *mechanical breakdown* of food by, e.g. mastication (chewing)
- *chemical digestion* of food into small molecules by enzymes present in secretions produced by glands and accessory organs of the digestive system.

Absorption. This is the process by which digested food substances pass through the walls of some organs of the alimentary canal into the blood and lymph capillaries for circulation and use by body cells.

Elimination. Food substances that have been eaten but cannot be digested and absorbed are excreted from the alimentary canal as *faeces* by the process of *defaecation*.

The fate of absorbed nutrients and how they are used by the body is explored and the effects of ageing on the digestive system are considered. In the final section disorders of the digestive system are explained.

Organs of the digestive system

(Fig. 12.1)

Learning outcomes

After studying this section, you should be able to:

- identify the main organs of the alimentary canal
- list the accessory organs of digestion.

Alimentary canal

Also known as the gastrointestinal (GI) tract, this is essentially a long tube through which food passes. It commences at the mouth and terminates at the anus, and the various organs along its length have different functions, although structurally they are remarkably similar. The parts are:

- mouth
- pharynx
- oesophagus
- stomach
- small intestine
- large intestine
- rectum and anal canal.

Accessory organs

Various secretions are poured into the alimentary tract, some by glands in the lining membrane of the organs, e.g. gastric juice secreted by glands in the lining of the stomach, and some by glands situated outside the tract. The latter are the accessory organs of digestion and their secretions pass through ducts to enter the tract. They consist of:

- three pairs of salivary glands
- the pancreas
- the liver and biliary tract.

The organs and glands are linked physiologically as well as anatomically in that digestion and absorption occur in stages, each stage being dependent upon the previous stage or stages.

Basic structure of the alimentary canal (Fig. 12.3)

Learning outcomes

After studying this section, you should be able to:

- describe the distribution of the peritoneum
- explain the function of smooth muscle in the walls of the alimentary canal
- discuss the structures of the alimentary mucosa
- outline the nerve supply of the alimentary canal.

The layers of the walls of the alimentary canal follow a consistent pattern from the oesophagus onwards. This basic structure does not apply so obviously to the mouth and the pharynx, which are considered later in the chapter.

In the organs from the oesophagus onwards, modifications of structure are found which are associated with specific functions. The basic structure is described here and any modifications in structure and function are described in the appropriate section.

The walls of the alimentary tract are formed by four layers of tissue:

- adventitia or serosa – outer covering
- muscle layer
- submucosa
- mucosa – lining.

Adventitia or serosa

This is the outermost layer. In the thorax it consists of *loose fibrous tissue* and in the abdomen the organs are covered by a serous membrane (serosa) called *peritoneum*.

Peritoneum

The peritoneum is the largest serous membrane of the body (Fig. 12.3A). It is a closed sac, containing a small amount of serous fluid, within the abdominal cavity. It is richly supplied with blood and lymph vessels, and contains many lymph nodes. It provides a physical barrier to local spread of infection, and can isolate an infective focus such as appendicitis, preventing involvement of other abdominal structures. It has two layers:

- the *parietal peritoneum*, which lines the abdominal wall
- the *visceral peritoneum*, which covers the organs (viscera) within the abdominal and pelvic cavities.

The parietal peritoneum lines the anterior abdominal wall.

The two layers of peritoneum are in close contact, and friction between them is prevented by the presence of serous fluid secreted by the peritoneal cells, thus the peritoneal cavity is only a potential cavity. A similar

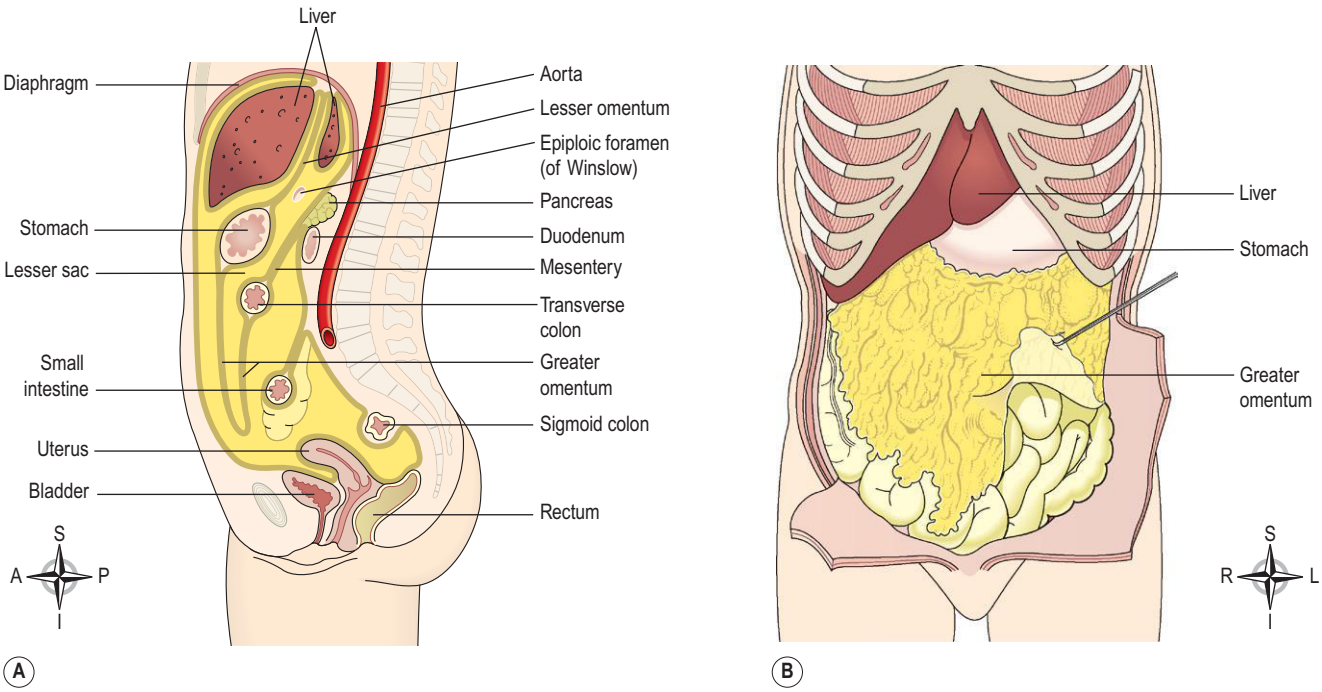

Figure 12.3 The peritoneum and associated structures. A. The peritoneal cavity (gold), the abdominal organs of the digestive system and the pelvic organs. **B.** The greater omentum.

arrangement is seen with the membranes covering the lungs, the pleura (p. 250). In the male, the peritoneal cavity is completely closed but in the female the uterine tubes open into it and the ovaries are the only structures inside (Ch. 18).

The arrangement of the peritoneum is such that the organs are invaginated (pushed into the membrane forming a pouch) into the closed sac from below, behind and above so that they are at least partly covered by the visceral layer, and attached securely within the abdominal cavity. This means that:

- pelvic organs are covered only on their superior surface
- the stomach and intestines, deeply invaginated from behind, are almost completely surrounded by peritoneum and have a double fold (the *mesentery*) that attaches them to the posterior abdominal wall. The fold of peritoneum enclosing the stomach extends beyond the greater curvature of the stomach, and hangs down in front of the abdominal organs like an apron (Fig. 12.3B). This is the *greater omentum*, which stores fat that provides both insulation and a long-term energy store
- the pancreas, spleen, kidneys and adrenal glands are invaginated from behind but only their anterior surfaces are covered and are therefore *retroperitoneal* (lie behind the peritoneum)
- the liver is invaginated from above and is almost completely covered by peritoneum, which attaches it to the inferior surface of the diaphragm
- the main blood vessels and nerves pass close to the posterior abdominal wall and send branches to the organs between folds of peritoneum.

Muscle layer

With some exceptions this consists of two layers of *smooth (involuntary) muscle*. The muscle fibres of the outer layer are arranged longitudinally, and those of the inner layer encircle the wall of the tube. Between these two muscle layers are blood vessels, lymph vessels and a plexus (network) of sympathetic and parasympathetic nerves, called the *myenteric plexus* (Fig. 12.2). These nerves supply the adjacent smooth muscle and blood vessels.

Contraction and relaxation of these muscle layers occurs in waves, which push the contents of the tract onwards. This type of contraction of smooth muscle is called *peristalsis* (Fig. 12.4) and is under the influence of sympathetic and parasympathetic nerves. Muscle contraction also mixes food with the digestive juices. Onward movement of the contents of the tract is controlled at various points by *sphincters*, which are thickened rings of circular muscle. Contraction of sphincters regulates forward movement. They also act as valves, preventing backflow in the tract. This control allows time for digestion and absorption to take place. **12.2**

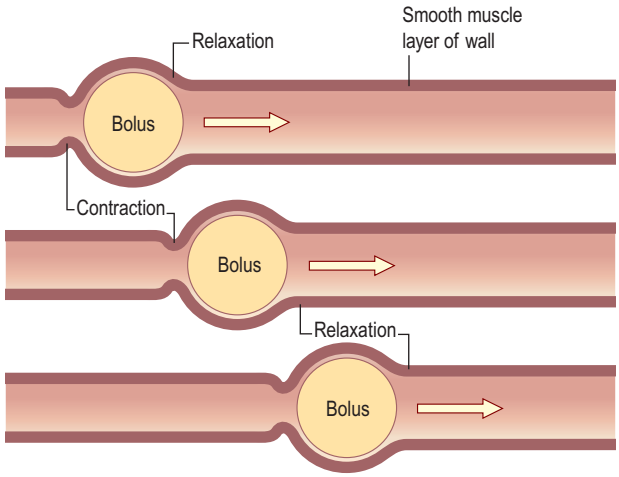

Figure 12.4 Movement of a bolus by peristalsis.

Submucosa

This layer consists of loose areolar connective tissue containing collagen and some elastic fibres, which binds the muscle layer to the mucosa. Within it are blood vessels and nerves, lymph vessels and varying amounts of lymphoid tissue. The blood vessels are arterioles, venules and capillaries. The nerve plexus is the *submucosal plexus* (Fig. 12.2), which contains sympathetic and parasympathetic nerves that supply the mucosal lining.

Mucosa

This consists of three layers of tissue:

- *mucous membrane* formed by columnar epithelium is the innermost layer, and has three main functions: *protection*, *secretion* and *absorption*
- *lamina propria* consisting of loose connective tissue, which supports the blood vessels that nourish the inner epithelial layer, and varying amounts of lymphoid tissue that protects against microbial invaders
- *muscularis mucosa*, a thin outer layer of smooth muscle that provides involutions of the mucosal layer, e.g. gastric glands (p. 299), villi (p. 302).

Mucous membrane

In parts of the tract that are subject to great wear and tear or mechanical injury, this layer consists of *stratified squamous epithelium* with mucus-secreting glands just below the surface. In areas where the food is already soft and moist and where secretion of digestive juices and absorption occur, the mucous membrane consists of *columnar epithelial cells* interspersed with mucus-secreting goblet cells (Fig. 12.5). Mucus lubricates the walls of the tract and provides a physical barrier that protects them from

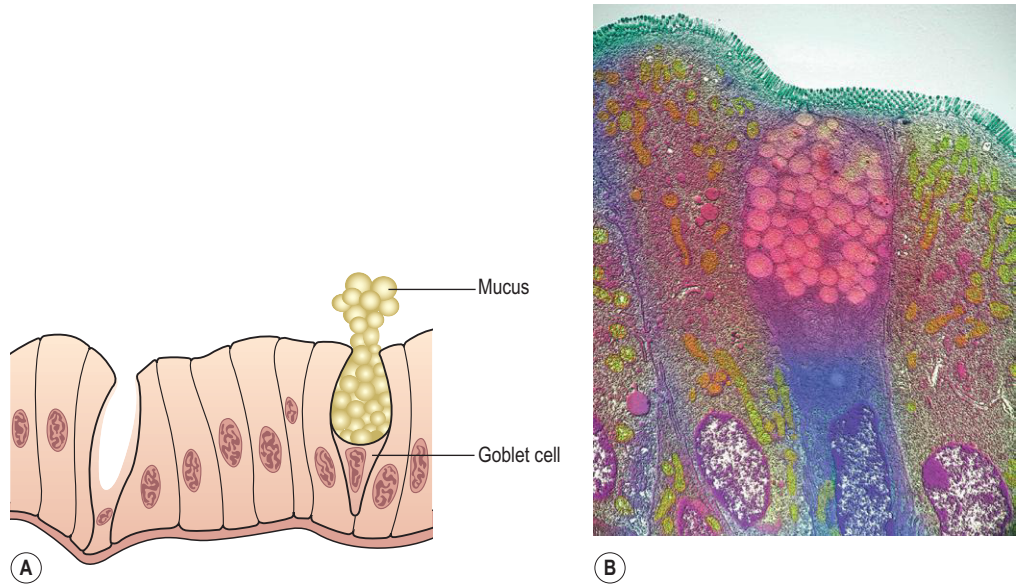

Figure 12.5 Columnar epithelium with a goblet cell. A. Diagram. **B.** Coloured transmission electron micrograph of a section through a goblet cell (pink and blue) of the small intestine.

the damaging effects of digestive enzymes. Below the surface in the regions lined with columnar epithelium are collections of specialised cells, or glands, which release their secretions into the lumen of the tract. The secretions include:

- *saliva* from the salivary glands
- *gastric juice* from the gastric glands
- *intestinal juice* from the intestinal glands
- *pancreatic juice* from the pancreas
- *bile* from the liver.

These are *digestive juices* and most contain enzymes that chemically break down food. Under the epithelial lining are varying amounts of lymphoid tissue that provide protection against ingested microbes.

Nerve supply

The alimentary canal and its related accessory organs are supplied by nerves from both divisions of the autonomic nervous system, i.e. both parasympathetic and sympathetic parts (Fig. 12.6). Their actions are generally antagonistic to each other and at any particular time one has a greater influence than the other, according to body needs, at that time. When digestion is required, this is normally through increased activity of the parasympathetic nervous system.

The parasympathetic supply. One pair of cranial nerves, the *vagus nerves*, supplies most of the alimentary canal and the accessory organs. Sacral nerves supply the most distal part of the tract. The effects of parasympathetic stimulation on the digestive system are:

- increased muscular activity, especially peristalsis, through increased activity of the myenteric plexus
- increased glandular secretion, through increased activity of the submucosal plexus (Fig. 12.2).

The sympathetic supply. This is provided by numerous nerves that emerge from the spinal cord in the thoracic and lumbar regions. These form plexuses (ganglia) in the thorax, abdomen and pelvis, from which nerves pass to the organs of the alimentary tract. The effects of sympathetic stimulation on the digestive system are to:

- decrease muscular activity, especially peristalsis, because there is reduced stimulation of the myenteric plexus
- decrease glandular secretion, as there is less stimulation of the submucosal plexus.

Mouth (Fig. 12.7)

Learning outcomes

After studying this section, you should be able to:

- list the principal structures associated with the mouth
- describe the structure of the mouth
- describe the structure and function of the tongue
- describe the structure and function of the teeth
- outline the arrangement of normal primary and secondary dentition.

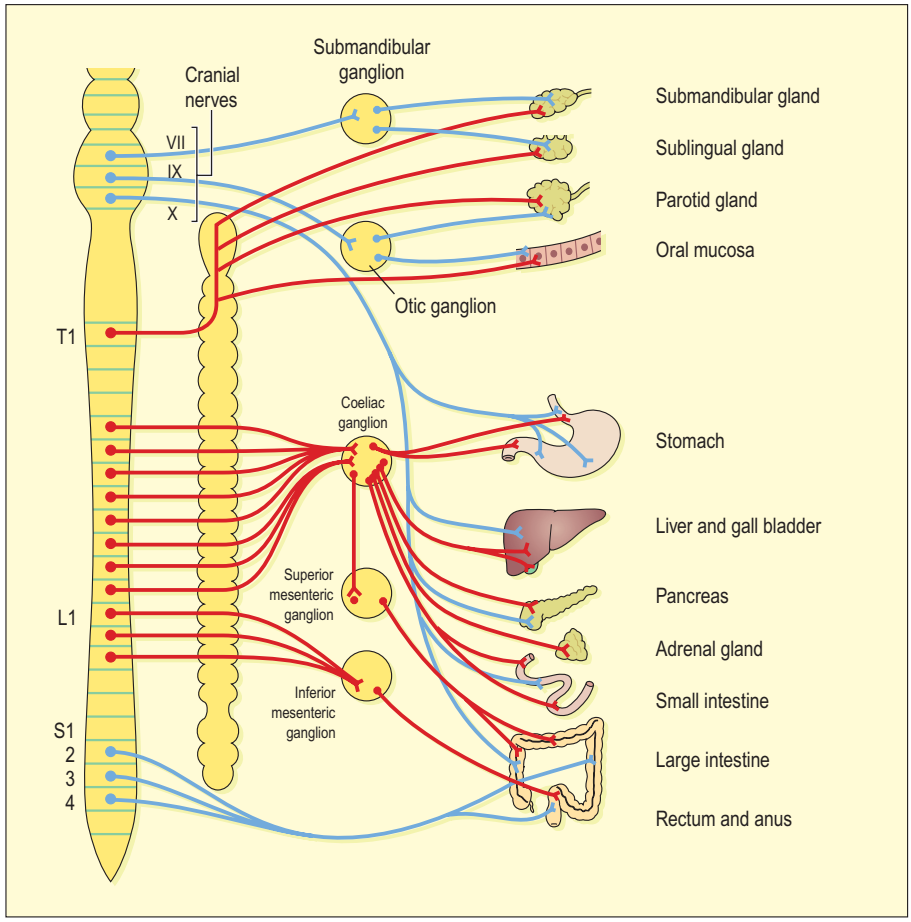

Figure 12.6 Autonomic nerve supply to the digestive system. Parasympathetic – blue; sympathetic – red.

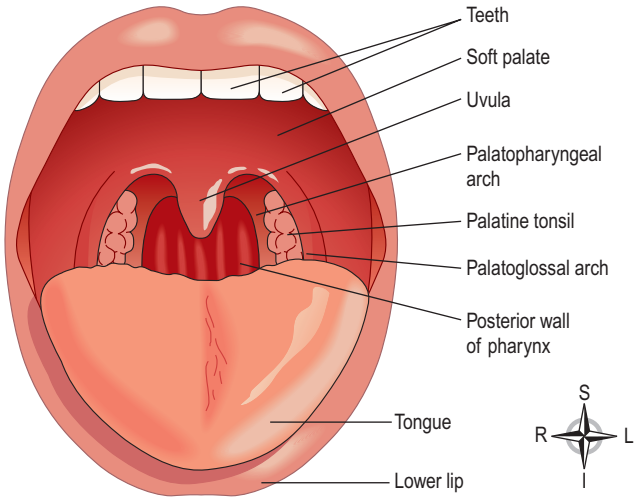

Figure 12.7 Structures seen in the widely open mouth.

The mouth or oral cavity is bounded by muscles and bones:

Anteriorly – by the lips
Posteriorly – it is continuous with the oropharynx
Laterally – by the muscles of the cheeks
Superiorly – by the bony hard palate and muscular soft palate
Inferiorly – by the muscular tongue and the soft tissues of the floor of the mouth.

The oral cavity is lined throughout with *mucous membrane*, consisting of stratified squamous epithelium containing small mucus-secreting glands.

The part of the mouth between the gums and the cheeks is the *vestibule* and the remainder of its interior is the *oral cavity*. The mucous membrane lining of the cheeks and the lips is reflected onto the gums or *alveolar ridges* and is continuous with the skin of the face.

The *palate* forms the roof of the mouth and is divided into the anterior *hard palate* and the posterior *soft palate* (Fig. 12.1). The hard palate is formed by the maxilla and the palatine bones. The soft palate, which is muscular, curves downwards from the posterior end of the hard palate and blends with the walls of the pharynx at the sides.

The *uvula* is a curved fold of muscle covered with mucous membrane, hanging down from the middle of the free border of the soft palate. Originating from the upper end of the uvula are four folds of mucous membrane,

two passing downwards at each side to form membranous arches. The posterior folds, one on each side, are the *palatopharyngeal arches* and the two anterior folds are the *palatoglossal arches*. On each side, between the arches, is a collection of lymphoid tissue called the *palatine tonsil*.

Tongue

The tongue is composed of voluntary muscle. It is attached by its base to the *hyoid bone* (see Fig. 10.4, p. 244) and by a fold of its mucous membrane covering, called the *frenulum*, to the floor of the mouth (Fig. 12.8). The superior surface consists of stratified squamous epithelium, with numerous *papillae* (little projections). Many of these contain sensory receptors (specialised nerve endings) for the sense of taste in the *taste buds* (see Fig. 8.24, p. 206).

Blood supply

The main arterial blood supply to the tongue is by the *lingual branch* of the *external carotid artery*. Venous drainage is by the *lingual vein*, which joins the *internal jugular vein*.

Nerve supply

The nerves involved are:

- the *hypoglossal nerves* (12th cranial nerves), which supply the voluntary muscle
- the *lingual branch of the mandibular nerves*, which arise from the 5th cranial nerves, are the nerves of somatic (ordinary) sensation, i.e. pain, temperature and touch
- the *facial* and *glossopharyngeal nerves* (7th and 9th cranial nerves), the nerves of taste.

Functions of the tongue

The tongue plays an important part in:

- chewing (mastication)
- swallowing (deglutition)
- speech (p. 245)
- taste (p. 207).

Nerve endings of the sense of taste are present in the papillae and widely distributed in the epithelium of the tongue.

Teeth

The teeth are embedded in the alveoli or sockets of the alveolar ridges of the mandible and the maxilla (Fig. 12.9). Babies are born with two sets, or *dentitions*, the *temporary* or *deciduous teeth* and the *permanent teeth* (Fig. 12.10). At birth the teeth of both dentitions are present, in immature form, in the mandible and maxilla.

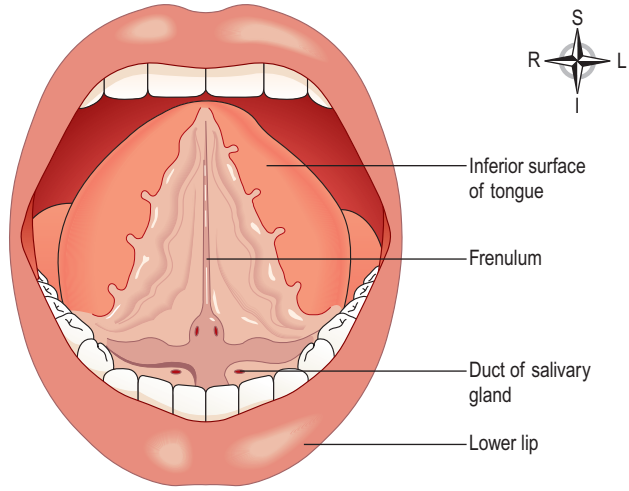

Figure 12.8 The inferior surface of the tongue.

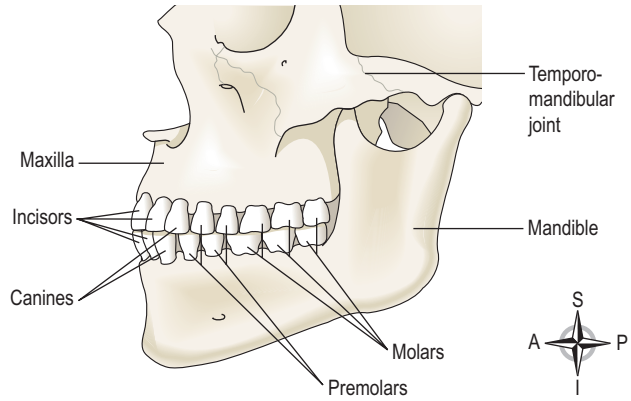

Figure 12.9 The permanent teeth and the jaw bones.

There are 20 temporary teeth, 10 in each jaw. They begin to erupt at about 6 months of age, and should all be present by 24 months (Table 12.1).

The permanent teeth begin to replace the deciduous teeth in the 6th year of age and this dentition, consisting of 32 teeth, is usually complete by the 21st year.

Functions of the teeth

Teeth have different shapes depending on their functions. *Incisors* and *canine* teeth are the cutting teeth and are used for biting off pieces of food, whereas the *premolar* and *molar* teeth, with broad, flat surfaces, are used for grinding or chewing food (Fig. 12.11).

Structure of a tooth (Fig. 12.12)

Although the shapes of the different teeth vary, the structure is the same and consists of:

- *the crown* – the part that protrudes from the gum
- *the root* – the part embedded in the bone

Table 12.1 Deciduous and permanent dentitions

Jaw	Molars	Premolars	Canine	Incisors	Incisors	Canine	Premolars	Molars
Deciduous teeth								
Upper	2	–	1	2	2	1	–	2
Lower	2	–	1	2	2	1	–	2
Permanent teeth								
Upper	3	2	1	2	2	1	2	3
Lower	3	2	1	2	2	1	2	3

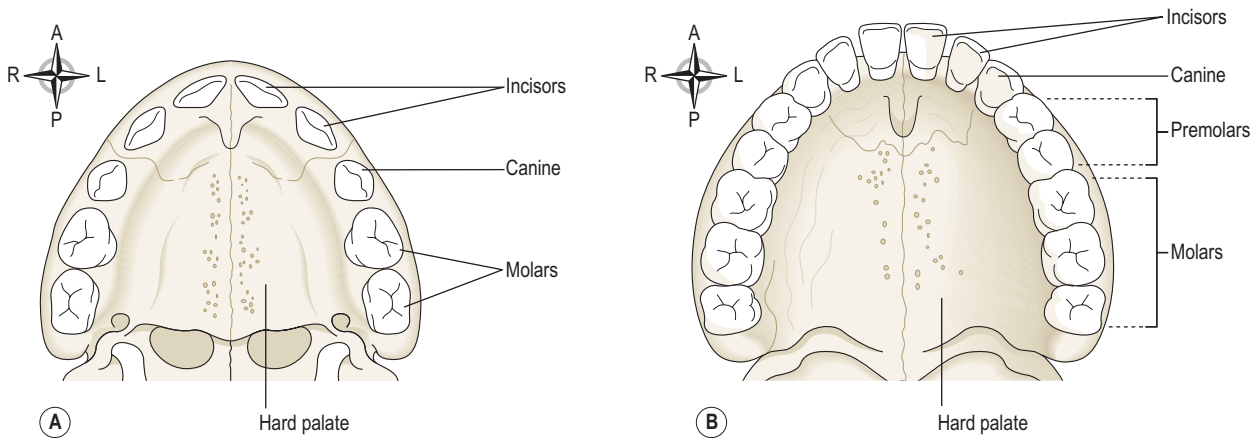

Figure 12.10 The roof of the mouth. A. The deciduous teeth – viewed from below. **B.** The permanent teeth – viewed from below.

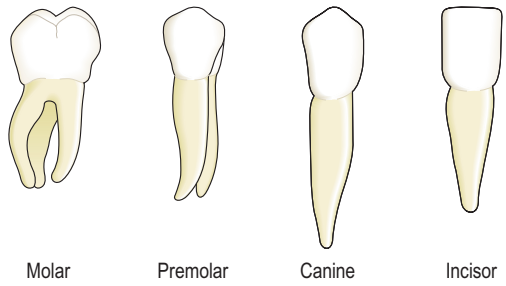

Figure 12.11 The shapes of the permanent teeth.

- *the neck* – the slightly narrowed region where the crown merges with the root.

In the centre of the tooth is the *pulp cavity* containing blood vessels, lymph vessels and nerves, and surrounding this is a hard ivory-like substance called *dentine*. The dentine of the crown is covered by a thin layer of very hard substance, *enamel*. The root of the tooth, on the other hand, is covered with a substance resembling bone, called *cementum*, which secures the tooth in its socket. Blood

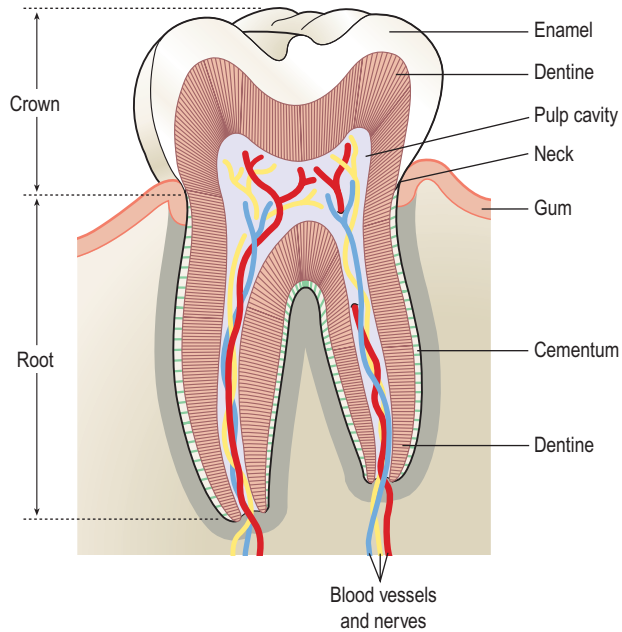

Figure 12.12 A section of a tooth.

vessels and nerves pass to the tooth through a small foramen (hole) at the apex of each root.

Blood supply
Most of the arterial blood supply to the teeth is by branches of the *maxillary arteries*. The venous drainage is by a number of veins which empty into the *internal jugular veins*.

Nerve supply
The nerve supply to the upper teeth is by branches of the *maxillary nerves* and to the lower teeth by branches of the *mandibular nerves*. These are both branches of the *trigeminal nerves* (5th cranial nerves) (Fig. 7.41, see p. 172).

Salivary glands (Fig. 12.13)

Learning outcomes

After studying this section, you should be able to:

- describe the structure and the function of the principal salivary glands
- explain the role of saliva in digestion.

Salivary glands release their secretions into ducts that lead to the mouth. There are three main pairs: the parotid glands, the submandibular glands and the sublingual glands. There are also numerous smaller salivary glands scattered around the mouth.

Parotid glands
These are situated one on each side of the face just below the external acoustic meatus (see Fig. 8.1, p. 192). Each gland has a *parotid duct* opening into the mouth at the level of the second upper molar tooth.

Submandibular glands
These lie one on each side of the face under the angle of the jaw. The two *submandibular ducts* open on the floor of the mouth, one on each side of the frenulum of the tongue.

Sublingual glands
These glands lie under the mucous membrane of the floor of the mouth in front of the submandibular glands. They have numerous small ducts that open into the floor of the mouth.

Structure of the salivary glands

The glands are all surrounded by a *fibrous capsule*. They consist of a number of *lobules* made up of small acini lined with secretory cells (Fig. 12.13B). The secretions are poured into ductules that join up to form larger ducts leading into the mouth.

Blood supply
Arterial supply is by various branches from the external carotid arteries and venous drainage is into the external jugular veins.

Composition of saliva
Saliva is the combined secretions from the salivary glands and the small mucus-secreting glands of the oral

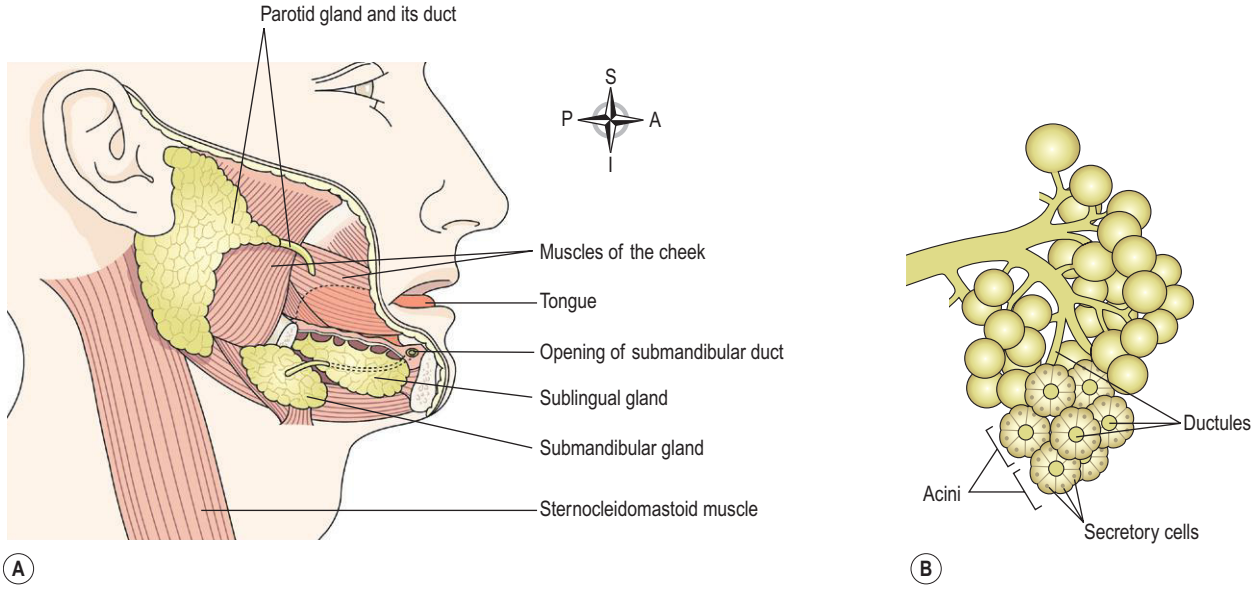

Figure 12.13 Salivary glands. A. The position of the salivary glands. **B.** Enlargement of part of a gland.

mucosa. About 1.5 litres of saliva is produced daily and it consists of:

- water
- mineral salts
- salivary amylase; a digestive enzyme
- mucus
- antimicrobial substances; immunoglobulins and the enzyme lysozyme.

Secretion of saliva

Secretion of saliva is controlled by the autonomic nervous system. Parasympathetic stimulation causes profuse secretion of watery saliva with a relatively low content of enzymes and other organic substances. Sympathetic stimulation results in secretion of small amounts of saliva rich in organic material, especially from the submandibular glands. Reflex secretion occurs when there is food in the mouth and the reflex can easily become *conditioned* so that the sight, smell and even the thought of food stimulates the flow of saliva.

Functions of saliva

Chemical digestion of polysaccharides

Saliva contains the enzyme *amylase* that begins the breakdown of complex sugars, including starches, reducing them to the disaccharide maltose. The optimum pH for the action of salivary amylase is 6.8 (slightly acid). Salivary pH ranges from 5.8 to 7.4 depending on the rate of flow; the higher the flow rate, the higher is the pH. Enzyme action continues during swallowing until terminated by the strongly acidic gastric juices (pH 1.5–1.8), which degrades the amylase.

Lubrication of food

The high water content means that dry food entering the mouth is moistened and lubricated by saliva before it can be made into a *bolus* ready for swallowing.

Cleaning and lubricating the mouth

An adequate flow of saliva is necessary to clean the mouth, and to keep it soft, moist and pliable. This helps to prevent damage to the mucous membrane by rough or abrasive food.

Non-specific defence

Lysozyme and immunoglobulins present in saliva combat invading microbes.

Taste

The taste buds are stimulated only by chemical substances in solution and therefore dry foods only stimulate the sense of taste after thorough mixing with saliva. The senses of taste and smell are closely linked and involved in the enjoyment, or otherwise, of food (see Ch. 8).

Pharynx

Learning outcome

After studying this section, you should be able to:

- describe the structure of the pharynx.

The pharynx is divided for descriptive purpose into three parts, the nasopharynx, oropharynx and laryngopharynx (see p. 245). The nasopharynx is important in respiration. The oropharynx and laryngopharynx are passages common to both the respiratory and the digestive systems. Food passes from the oral cavity into the pharynx then to the oesophagus below, with which it is continuous. The walls of the pharynx consist of three layers of tissue.

The *lining membrane* (mucosa) is stratified squamous epithelium, continuous with the lining of the mouth at one end and the oesophagus at the other. Stratified epithelial tissue provides a lining well suited to the wear and tear of swallowing ingested food.

The *middle layer* consists of connective tissue, which becomes thinner towards the lower end and contains blood and lymph vessels and nerves.

The *outer layer* consists of a number of involuntary muscles that are involved in swallowing. When food reaches the pharynx, swallowing is no longer under voluntary control.

Blood supply

The blood supply to the pharynx is by several branches of the facial arteries. Venous drainage is into the facial veins and the internal jugular veins.

Nerve supply

This is from the pharyngeal plexus and consists of parasympathetic and sympathetic nerves. Parasympathetic supply is mainly by the glossopharyngeal and vagus nerves and sympathetic from the cervical ganglia.

Oesophagus (Fig. 12.14)

Learning outcomes

After studying this section, you should be able to:

- describe the location of the oesophagus
- outline the structure of the oesophagus
- explain the mechanisms involved in swallowing, and the route taken by a bolus.

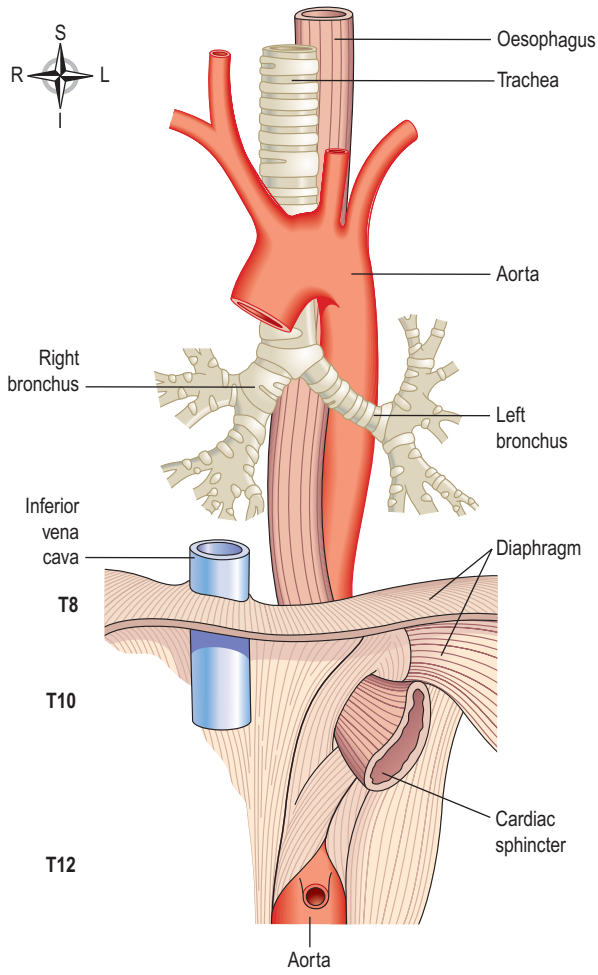

Figure 12.14 The oesophagus and some related structures.

The oesophagus is about 25 cm long and about 2 cm in diameter and lies in the median plane in the thorax in front of the vertebral column behind the trachea and the heart. It is continuous with the pharynx above and just below the diaphragm it joins the stomach. It passes between muscle fibres of the diaphragm behind the central tendon at the level of the 10th thoracic vertebra. Immediately the oesophagus has passed through the diaphragm it curves upwards before opening into the stomach. This sharp angle is believed to be one of the factors that prevents the regurgitation (backflow) of gastric contents into the oesophagus. The upper and lower ends of the oesophagus are closed by sphincters. The upper *cricopharyngeal* or *upper oesphageal sphincter* prevents air passing into the oesophagus during inspiration and the aspiration of oesophageal contents. The *cardiac* or *lower oesophageal sphincter* prevents the reflux of acid gastric contents into the oesophagus. There is no thickening of the circular muscle in this area and this sphincter is therefore 'physiological', i.e. this region can act as a sphincter without the presence of the anatomical features. When intra-abdominal pressure is raised, e.g. during inspiration and defaecation, the tone of the lower oesophageal sphincter increases. There is an added pinching effect by the contracting muscle fibres of the diaphragm. **12.3**

Structure of the oesophagus

There are four layers of tissue as shown in Figure 12.2. As the oesophagus is almost entirely in the thorax the outer covering, the adventitia, consists of *elastic fibrous tissue* that attaches the oesophagus to the surrounding structures. The proximal third is lined by stratified squamous epithelium and the distal third by columnar epithelium. The middle third is lined by a mixture of the two.

Blood supply

Arterial. The thoracic region is supplied mainly by the paired oesophageal arteries, branches from the thoracic aorta. The abdominal region is supplied by branches from the inferior phrenic arteries and the left gastric branch of the coeliac artery.

Venous drainage. From the thoracic region venous drainage is into the azygos and hemiazygos veins. The abdominal part drains into the left gastric vein. There is a venous plexus at the distal end that links the upward and downward venous drainage, i.e. the general and portal circulations.

Functions of the mouth, pharynx and oesophagus

Formation of a bolus

When food is taken into the mouth it is chewed (masticated) by the teeth and moved around the mouth by the tongue and muscles of the cheeks (Fig. 12.15). It is mixed with saliva and formed into a soft mass or bolus ready

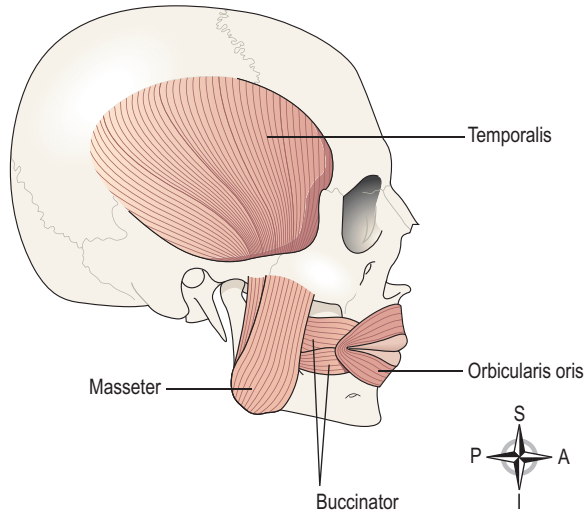

Figure 12.15 The muscles used in chewing.

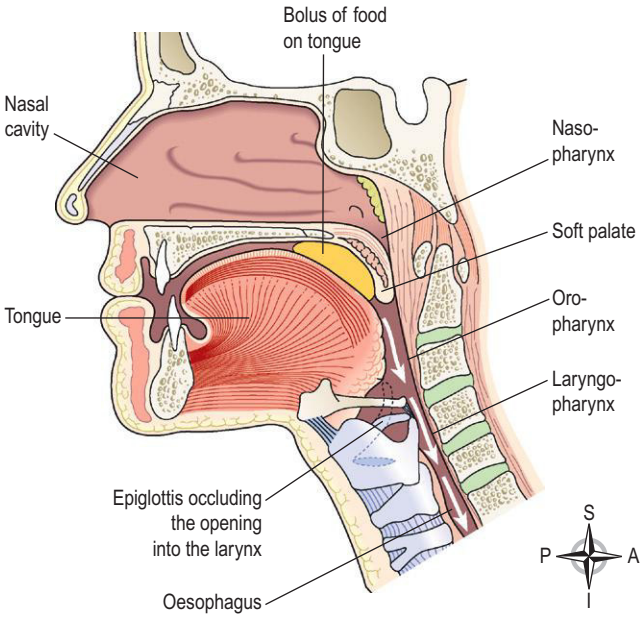

Figure 12.16 Section of the face and neck showing the positions of structures during swallowing.

for swallowing. The length of time that food remains in the mouth largely depends on the consistency of the food. Some foods need to be chewed longer than others before the individual feels that the bolus is ready for swallowing. **12.4**

Swallowing (deglutition) (Fig. 12.16)

This occurs in three stages after chewing is complete and the bolus has been formed. It is initiated voluntarily but completed by a reflex (involuntary) action.

1. Oral stage. With the mouth closed, the voluntary muscles of the tongue and cheeks push the bolus backwards into the pharynx.

2. Pharyngeal stage. The muscles of the pharynx are stimulated by a reflex action initiated in the walls of the oropharynx and coordinated by the *swallowing centre* in the medulla. Involuntary contraction of these muscles propels the bolus down into the oesophagus. All other routes that the bolus could take are closed. The soft palate rises up and closes off the nasopharynx; the tongue and the pharyngeal folds block the way back into the mouth; and the larynx is lifted up and forward so that its opening is occluded by the overhanging epiglottis preventing entry into the airway (trachea). **12.5**

3. Oesophageal stage. The presence of the bolus in the pharynx stimulates a wave of peristalsis that propels the bolus through the oesophagus to the stomach. **12.2**

Peristaltic waves pass along the oesophagus only after swallowing begins (see Fig. 12.4). Otherwise the walls are relaxed. Ahead of a peristaltic wave, the cardiac sphincter guarding the entrance to the stomach relaxes to allow the descending bolus to pass into the stomach. Usually, constriction of the cardiac sphincter prevents reflux of gastric acid into the oesophagus. Other factors preventing gastric reflux include:

- the attachment of the stomach to the diaphragm by the peritoneum
- the acute angle formed by the position of the oesophagus as it enters the fundus of the stomach, i.e. an acute cardio-oesophageal angle (see Fig. 12.18)
- increased tone of the cardiac sphincter when intra-abdominal pressure is increased and the pinching effect of diaphragm muscle fibres.

The walls of the oesophagus are lubricated by mucus which assists the passage of the bolus during the peristaltic contraction of the muscular wall.

Stomach

Learning outcomes

After studying this section, you should be able to:

- describe the location of the stomach with reference to surrounding structures
- explain the physiological significance of the layers of the stomach wall
- discuss the digestive functions of the stomach.

The stomach is a J-shaped dilated portion of the alimentary tract situated in the epigastric, umbilical and left hypochondriac regions of the abdominal cavity.

Organs associated with the stomach (Fig. 12.17)

Anteriorly – left lobe of liver and anterior abdominal wall
Posteriorly – abdominal aorta, pancreas, spleen, left kidney and adrenal gland
Superiorly – diaphragm, oesophagus and left lobe of liver
Inferiorly – transverse colon and small intestine
To the left – diaphragm and spleen
To the right – liver and duodenum.

Structure of the stomach (Fig. 12.18)

The stomach is continuous with the oesophagus at the cardiac sphincter and with the duodenum at the pyloric sphincter. It has two curvatures. The *lesser curvature* is short, lies on the posterior surface of the stomach and is

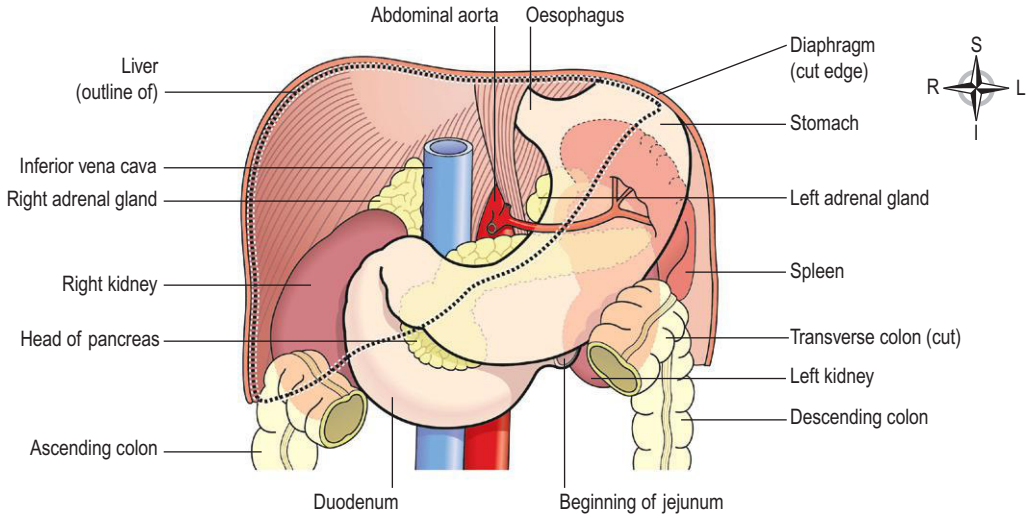

Figure 12.17 The stomach and its associated structures.

the downward continuation of the posterior wall of the oesophagus. Just before the pyloric sphincter it curves upwards to complete the J shape. Where the oesophagus joins the stomach the anterior region angles acutely upwards, curves downwards forming the *greater curvature* and then slightly upwards towards the pyloric sphincter.

The stomach is divided into three regions: the *fundus*, the *body* and the *pylorus*. At the distal end of the pylorus is the pyloric sphincter, guarding the opening between the stomach and the duodenum. When the stomach is inactive the pyloric sphincter is relaxed and open, and when the stomach contains food the sphincter is closed.

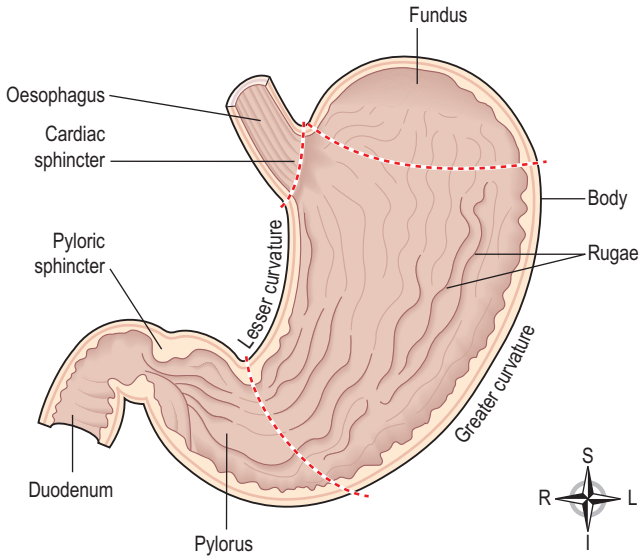

Figure 12.18 Longitudinal section of the stomach.

Walls of the stomach

The four layers of tissue that comprise the basic structure of the alimentary canal (Fig. 12.2) are found in the stomach but with some modifications.

Muscle layer. (Fig. 12.19). This consists of three layers of smooth muscle fibres:

- an outer layer of longitudinal fibres
- a middle layer of circular fibres
- an inner layer of oblique fibres.

In this respect, the stomach is different from other regions of the alimentary tract as it has three layers of muscle instead of two. This arrangement allows for the churning motion characteristic of gastric activity, as well as peristaltic movement. Circular muscle is strongest between the pylorus and the pyloric sphincter.

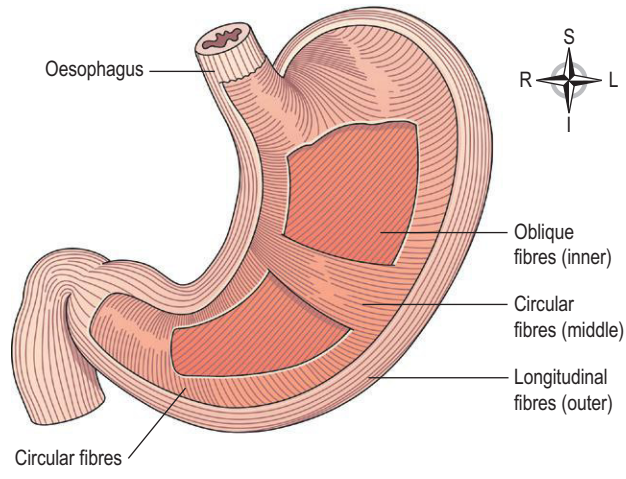

Figure 12.19 The muscle fibres of the stomach wall.
Sections have been removed to show the three layers.

Mucosa. When the stomach is empty the mucous membrane lining is thrown into longitudinal folds or *rugae*, and when full the rugae are 'ironed out' giving the surface a smooth, velvety appearance. Numerous *gastric glands* are situated below the surface in the mucous membrane and open on to it (Fig. 12.20). They consist of specialised cells that secrete *gastric juice* into the stomach.

Blood supply. Arterial supply to the stomach is by the left gastric artery, a branch of the coeliac artery, the right gastric artery and the gastroepiploic arteries. Venous drainage is through veins of corresponding names into the portal vein. Figures 5.38 and 5.40 (pp. 109 and 110) show these vessels.

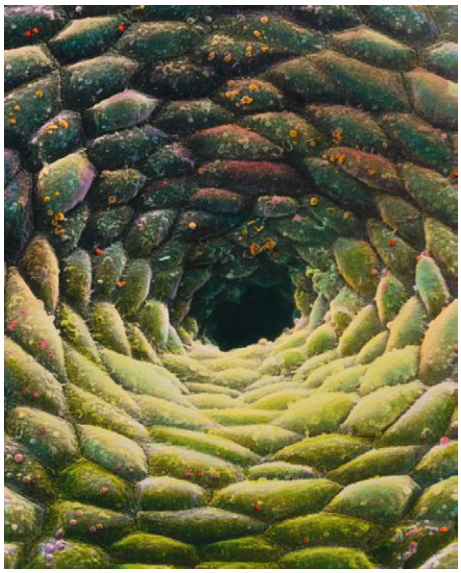

Figure 12.20 Coloured scanning electron micrograph of the mucous membrane lining the stomach showing the entrance to a gastric gland.

Gastric juice and functions of the stomach

Stomach size varies with the volume of food it contains, which may be 1.5 litres or more in an adult. When a meal has been eaten the food accumulates in the stomach in layers, the last part of the meal remaining in the fundus for some time. Mixing with the gastric juice takes place gradually and it may be some time before the food is sufficiently acidified to stop the action of salivary amylase.

The gastric muscle generates a churning action that breaks down the bolus and mixes it with gastric juice, and peristaltic waves that propel the stomach contents towards the pylorus. When the stomach is active the pyloric sphincter closes. Strong peristaltic contraction of the pylorus forces *chyme*, gastric contents after they are sufficiently liquefied, through the pyloric sphincter into the duodenum in small spurts. Parasympathetic stimulation increases the motility of the stomach and secretion of gastric juice; sympathetic stimulation has the opposite effect. **12.6**

Gastric juice

About 2 litres of gastric juice are secreted daily by specialised secretory glands in the mucosa (Fig. 12.21). It consists of:

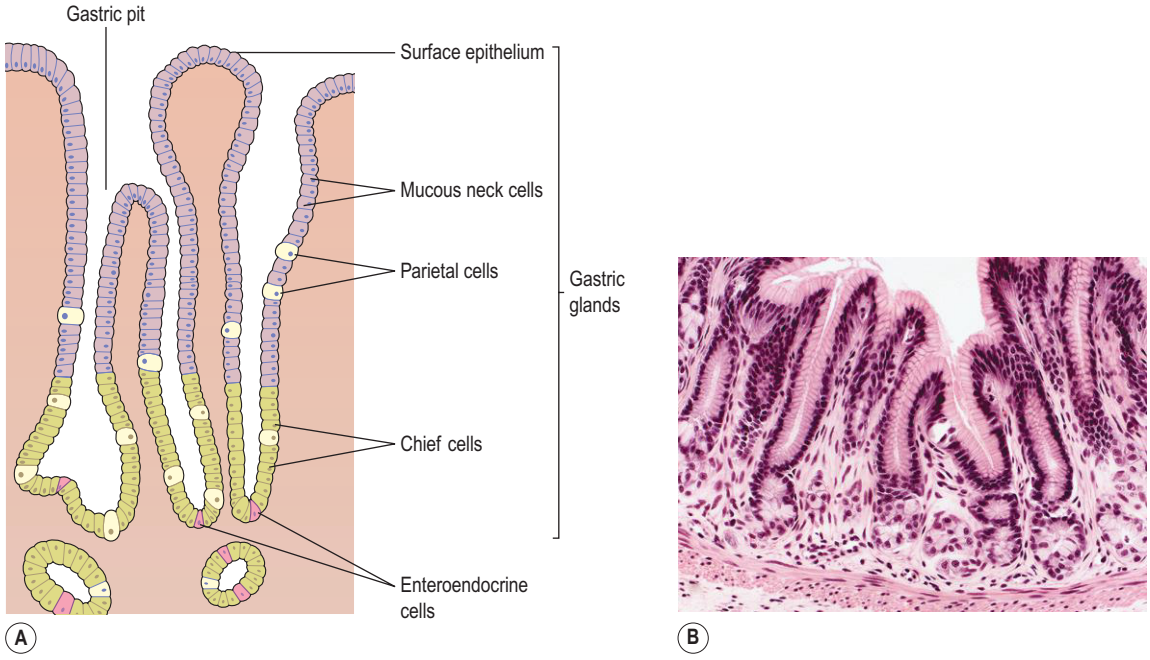

Figure 12.21 Structure of the gastric mucosa showing gastric glands. A. Diagram. **B.** Stained section of the pyloric region of the stomach (magnified x 150).

- water
- mineral salts
- mucus secreted by mucous neck cells in the glands and surface mucous cells on the stomach surface
- hydrochloric acid } secreted by *parietal cells* in the gastric glands
- intrinsic factor }
- inactive enzyme precursors: pepsinogens secreted by *chief cells* in the glands.

Functions of gastric juice

- *Water* further liquefies the food swallowed.
- *Hydrochloric acid*:
  - acidifies the food and stops the action of salivary amylase
  - kills ingested microbes
  - provides the acid environment needed for the action of pepsins.
- *Pepsinogens* are activated to *pepsins* by hydrochloric acid and by pepsins already present in the stomach. These enzymes begin the digestion of proteins, breaking them into smaller molecules. Pepsins have evolved to act most effectively at a very low pH, between 1.5 and 3.5. **12.7**
- *Intrinsic factor* (a protein) is necessary for the absorption of vitamin B_{12} from the ileum. (Deficiency leads to pernicious anemia p. 74.)
- *Mucus* prevents mechanical injury to the stomach wall by lubricating the contents. It also prevents chemical injury by acting as a barrier between the stomach wall and the corrosive gastric juice – hydrochloric acid is present in potentially damaging concentrations and pepsins would digest the gastric tissues.

Secretion of gastric juice

There is always a small quantity of gastric juice present in the stomach, even when it contains no food. This is known as fasting juice. Secretion reaches its maximum level about 1 hour after a meal then declines to the fasting level after about 4 hours.

There are three phases of secretion of gastric juice (Fig. 12.22).

1. Cephalic phase. This flow of juice occurs before food reaches the stomach and is due to reflex stimulation of the vagus (parasympathetic) nerves initiated by the sight, smell or taste of food. When the vagus nerves have been cut (vagotomy), this phase of gastric secretion stops. Sympathetic stimulation, e.g. during emotional states, also inhibits gastric activity.

2. Gastric phase. When stimulated by the presence of food the *enteroendocrine cells* in the pylorus (Fig. 12.21) and duodenum secrete the hormone *gastrin*, which passes directly into the circulating blood. Gastrin, circulating in the blood which supplies the stomach, stimulates the gastric glands to produce more gastric juice. In this way secretion of digestive juice is continued after completion of a meal and the end of the cephalic phase. Gastrin secretion is suppressed when the pH in the pylorus falls to about 1.5.

3. Intestinal phase. When the partially digested contents of the stomach reach the small intestine, two hormones, *secretin* and *cholecystokinin*, are produced by endocrine cells in the intestinal mucosa. They slow down the secretion of gastric juice and reduce gastric motility. By slowing the emptying rate of the stomach, the chyme in the duodenum becomes more thoroughly mixed with

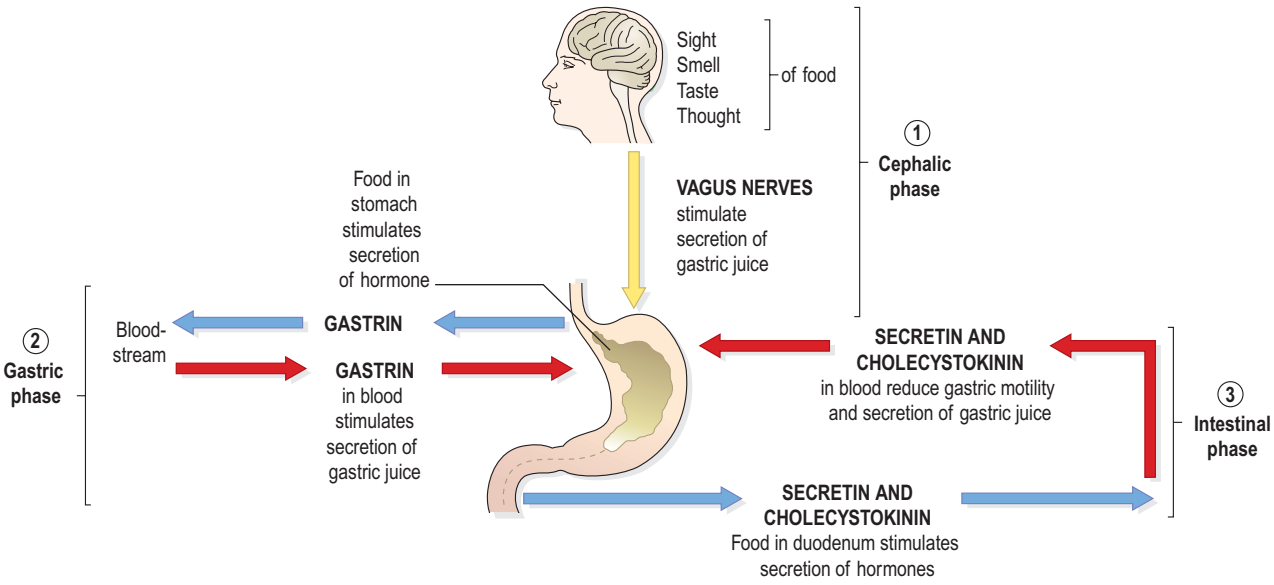

Figure 12.22 The three phases of secretion of gastric juice.

bile and pancreatic juice. This phase of gastric secretion is most marked following a meal with a high fat content.

The rate at which the stomach empties depends largely on the type of food eaten. A carbohydrate meal leaves the stomach in 2–3 hours, a protein meal remains longer and a fatty meal remains in the stomach longest.

Functions of the stomach

These include:

- temporary storage allowing time for the digestive enzymes, pepsins, to act
- chemical digestion – pepsins break proteins into polypeptides
- mechanical breakdown – the three smooth muscle layers enable the stomach to act as a churn, gastric juice is added and the contents are liquefied to chyme. Gastric motility and secretion are increased by parasympathetic nerve stimulation
- limited absorption – water, alcohol and some lipid-soluble drugs
- non-specific defence against microbes – provided by hydrochloric acid in gastric juice. Vomiting (Table 12.4) may occur in response to ingestion of gastric irritants, e.g. microbes or chemicals
- preparation of iron for absorption – the acid environment of the stomach solubilises iron salts, essential for iron absorption in the small intestine
- production and secretion of intrinsic factor needed for absorption of vitamin B_{12} in the terminal ileum
- regulation of the passage of gastric contents into the duodenum. When the chyme is sufficiently acidified and liquefied, the pylorus forces small jets of gastric contents through the pyloric sphincter into the duodenum. The sphincter is normally closed, preventing backflow of chyme into the stomach
- secretion of the hormone gastrin (see above).

Small intestine (Figs 12.23 and 12.24)

Learning outcomes

After studying this section, you should be able to:

- describe the location of the small intestine, with reference to surrounding structures
- sketch a villus, labelling its component parts
- discuss the digestive functions of the small intestine and its secretions
- explain how nutrients are absorbed in the small intestine.

The small intestine is continuous with the stomach at the pyloric sphincter. The small intestine is about 2.5 cm in diameter, a little over 5 metres long and leads into the large intestine at the *ileocaecal valve*. It lies in the abdominal cavity surrounded by the large intestine. In the small intestine the chemical digestion of food is completed and absorption of most nutrients takes place. The small intestine comprises three continuous parts.

Duodenum. This is about 25 cm long and curves around the head of the pancreas. Secretions from the gall bladder and pancreas merge in a common structure – the *hepatopancreatic ampulla* – and enter the duodenum at the *duodenal papilla*. The duodenal papilla is guarded by a ring of

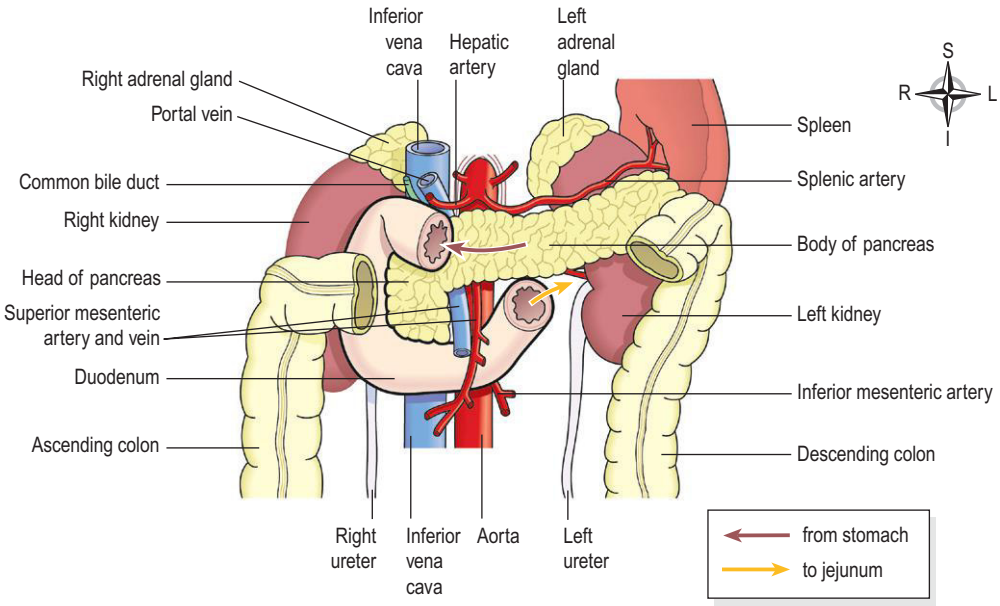

Figure 12.23 The duodenum and its associated structures.

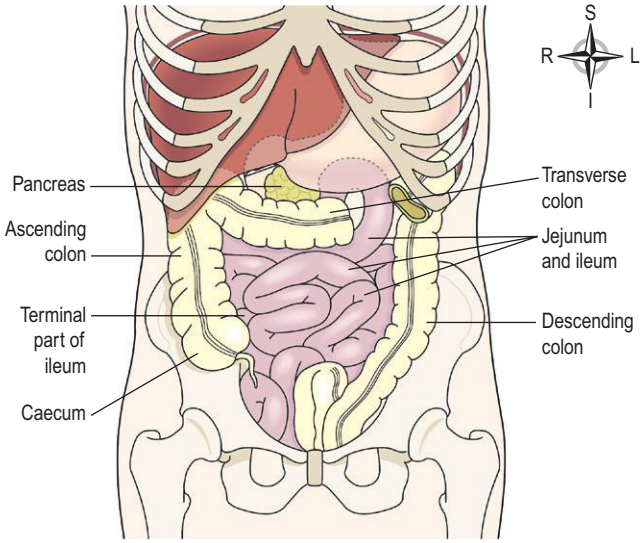

Figure 12.24 The jejunum and ileum and their related structures.

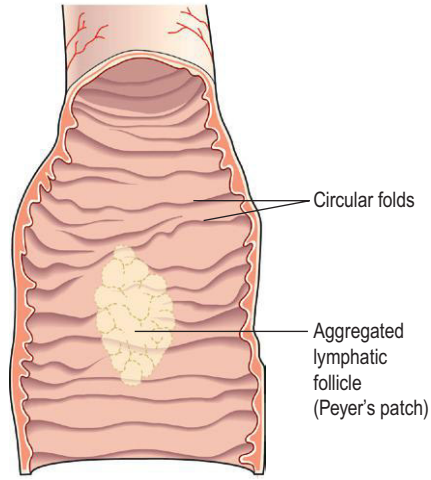

Figure 12.25 Section of a small piece of small intestine (opened out), showing the permanent circular folds.

smooth muscle, the *hepatopancreatic sphincter* (of Oddi) (see Fig. 12.38).

Jejunum. This is the middle section of the small intestine and is about 2 metres long.

Ileum. This terminal section is about 3 metres long and ends at the *ileocaecal valve*, which controls the flow of material from the ileum to the *caecum*, the first part of the large intestine, and prevents backflow.

Structure of the small intestine

The walls of the small intestine are composed of the four layers of tissue shown in Figure 12.2. Some modifications of the peritoneum and mucosa (mucous membrane lining) are described below.

Peritoneum

The *mesentery*, a double layer of peritoneum, attaches the jejunum and ileum to the posterior abdominal wall (see Fig. 12.3A). The attachment is quite short in comparison with the length of the small intestine, therefore it is fan shaped. The large blood vessels and nerves lie on the posterior abdominal wall and the branches to the small intestine pass between the two layers of the mesentery.

Mucosa

The surface area of the small intestine mucosa is greatly increased by permanent circular folds, villi and microvilli.

The *permanent circular folds*, unlike the rugae of the stomach, are not smoothed out when the small intestine is distended (Fig. 12.25). They promote mixing of chyme as it passes along.

The *villi* are tiny finger-like projections of the mucosal layer into the intestinal lumen, about 0.5–1 mm long (Fig. 12.26). Their covering consists of columnar epithelial cells, or *enterocytes*, with tiny *microvilli* (1 µm long) on their free border. *Goblet cells* (see Fig. 12.5) that secrete mucus are interspersed between the enterocytes. These epithelial cells enclose a network of blood capilliaries and a central lymph capillary. Lymph capillaries are called *lacteals* because absorbed fat gives the lymph a milky appearance. Absorption and some final stages of digestion of nutrients take place in the enterocytes before entering the blood and lymph capillaries. 12.8

The *intestinal glands* are simple tubular glands situated below the surface between the villi. The epithelial cells of the glands migrate upwards to form the walls of the villi replacing those at the tips as they are rubbed off by the passage of intestinal contents. The entire epithelium is replaced every 3 to 5 days. During migration, epithelial cells produce digestive enzymes that lodge in the microvilli and, together with intestinal juice, complete the chemical digestion of carbohydrates, protein and fats.

Numerous *lymph nodes* are found in the mucosa at irregular intervals throughout the length of the small intestine. The smaller ones are known as *solitary lymphatic follicles*, and collections of about 20 or 30 larger nodes situated towards the distal end of the ileum are called *aggregated lymphatic follicles* (Peyer's patches, Fig. 12.25). These lymphatic tissues, packed with defensive cells, are strategically located to neutralise ingested antigens (Ch. 15).

Blood supply

The *superior mesenteric artery* supplies the whole of the small intestine. Venous drainage is by the *superior mesenteric vein* that joins other veins to form the portal vein (see Figs 5.40 and 5.41, pp. 110 and 111). The portal vein contains a high concentration of absorbed nutrients and this blood passes through the liver before entering the hepatic veins and, ultimately, into the inferior vena cava (see Fig. 12.36).

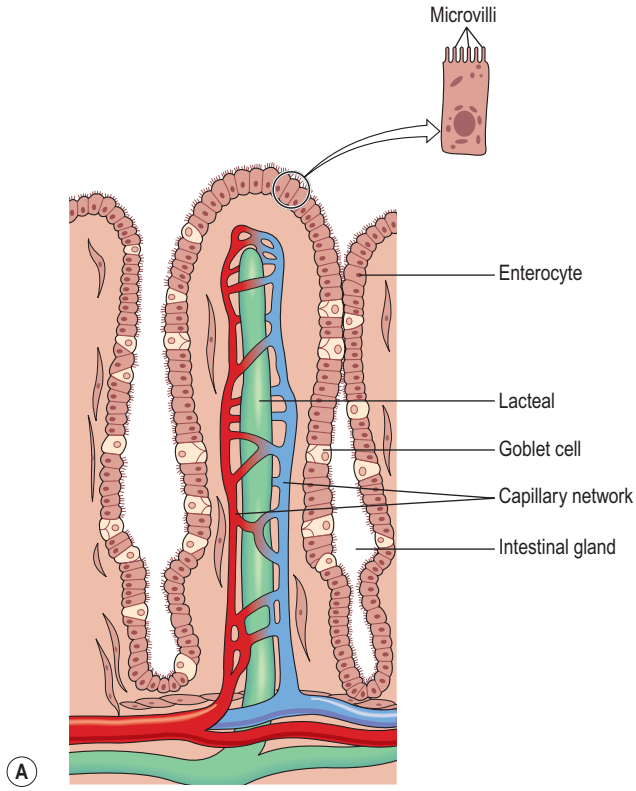

Figure 12.26 Villi. A. A highly magnified diagram of one complete villus in the small intestine. **B.** Coloured scanning electron micrograph showing many villi.

Intestinal juice

About 1500 mL of intestinal juice are secreted daily by the glands of the small intestine. It is slightly basic (alkaline) and consists of water, mucus and mineral salts.

Functions of the small intestine

The functions are:

- onward movement of its contents by peristalsis, which is increased by parasympathetic stimulation
- secretion of intestinal juice, also increased by parasympathetic stimulation
- completion of chemical digestion of carbohydrates, protein and fats in the enterocytes of the villi
- protection against infection by microbes that have survived the antimicrobial action of the hydrochloric acid in the stomach, by both solitary and aggregated lymph follicles
- secretion of the hormones cholecystokinin (CCK) and secretin
- absorption of nutrients.

Chemical digestion in the small intestine

When acid chyme passes into the small intestine it is mixed with *pancreatic juice*, *bile* and *intestinal juice*, and is in contact with the enterocytes of the villi. The digestion of all nutrients is completed:

- carbohydrates are broken down to monosaccharides
- proteins are broken down to amino acids
- fats are broken down to fatty acids and glycerol.

Pancreatic juice

Pancreatic juice is secreted by the exocrine pancreas (p. 308) and enters the duodenum at the duodenal papilla. It consists of:

- water
- mineral salts
- enzymes:
  - amylase
  - lipase
  - nucleases that digest DNA and RNA
- inactive enzyme precursors including:
  - trypsinogen
  - chymotrypsinogen.

Pancreatic juice is basic (alkaline, pH 8) because it contains significant quantities of bicarbonate ions, which are basic (alkaline) in solution. When acid stomach contents enter the duodenum they are mixed with pancreatic juice and bile and the pH is raised to between 6 and 8. This is the pH at which the pancreatic enzymes, amylase and lipase, act most effectively.

Functions

Digestion of proteins. Trypsinogen and chymotrypsinogen are inactive enzyme precursors activated by *enterokinase*, an enzyme in the microvilli, which converts them into the active proteolytic enzymes *trypsin* and *chymotrypsin*. These enzymes convert polypeptides to tripeptides, dipeptides and amino acids. It is important that they are produced as inactive precursors and are activated only upon their arrival in the duodenum, otherwise they would digest the pancreas.

Digestion of carbohydrates. *Pancreatic amylase* converts all digestible polysaccharides (starches) not acted upon by salivary amylase to disaccharides.

Digestion of fats. *Lipase* converts fats to fatty acids and glycerol. To aid the action of lipase, *bile salts* emulsify fats, i.e. reduce the size of the globules, increasing their surface area.

Control of secretion

The secretion of pancreatic juice is stimulated by secretin and CCK, produced by endocrine cells in the walls of the duodenum. The presence in the duodenum of acid chyme from the stomach stimulates the production of these hormones (see Fig. 12.22).

Bile

Bile, secreted by the liver, is unable to enter the duodenum when the hepatopancreatic sphincter is closed; therefore it passes from the *hepatic duct* along the *cystic duct* to the gall bladder where it is stored (see Fig. 12.38).

Bile has a pH of around 8 and between 500 and 1000 mL is secreted daily. It consists of:

- water
- mineral salts
- mucus
- bile salts
- bile pigments, mainly bilirubin
- cholesterol.

Functions

The functions of bile are explained further on page 311; in summary, these are:

- emulsification of fats in the small intestine – bile salts
- making cholesterol and fatty acids soluble, enabling their absorption along with the fat-soluble vitamins – bile salts
- excretion of *bilirubin* (a waste product from the breakdown of red blood cells), most of which is in the form of *stercobilin*.

Release from the gall bladder

After a meal, the duodenum secretes the hormones secretin and CCK during the intestinal phase of gastric secretion (p. 300). They stimulate contraction of the gall bladder and relaxation of the hepatopancreatic sphincter, expelling both bile and pancreatic juice through the duodenal papilla into the duodenum. Secretion is markedly increased when chyme entering the duodenum contains a high proportion of fat.

Intestinal secretions

The principal constituents of intestinal secretions are water, mucus and mineral salts.

Most of the digestive enzymes in the small intestine are contained in the enterocytes of the epithelium that covers the villi. Digestion of carbohydrate, protein and fat is completed by direct contact between these nutrients and the microvilli and within the enterocytes.

Chemical digestion associated with enterocytes

Alkaline intestinal juice (pH 7.8–8.0) assists in raising the pH of the intestinal contents to between 6.5 and 7.5. The enzymes that complete chemical digestion of food at the surface of the enterocytes are:

- peptidases
- lipase
- sucrase, maltase and lactase.

Peptidases such as trypsin break down polypeptides into smaller peptides and amino acids. Peptidases are secreted in an inactive form from the pancreas (to prevent them from digesting it) and must be activated by *enterokinase* in the duodenum.

The final stage of breakdown of all peptides to amino acids takes place at the surface of the enterocytes.

Lipase completes the digestion of emulsified fats to *fatty acids* and *glycerol* in the intestine.

Sucrase, maltase and *lactase* complete the digestion of carbohydrates by converting disaccharides such as sucrose, maltose and lactose to monosaccharides at the surface of the enterocytes.

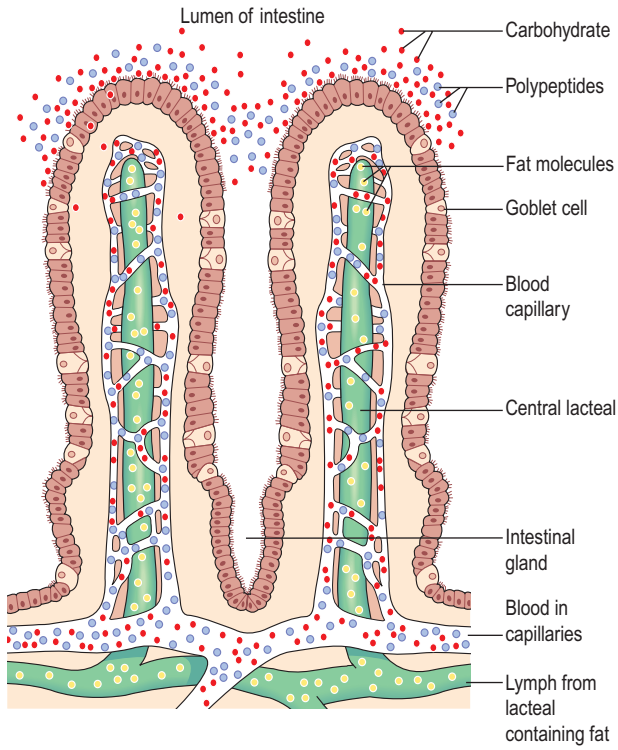

Figure 12.27 The absorption of nutrients into villi.

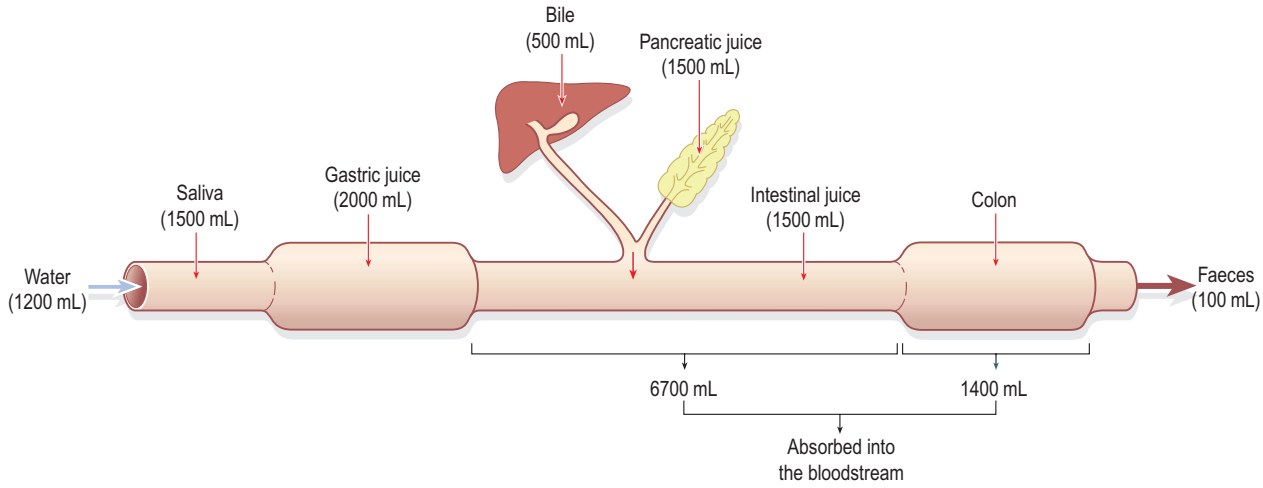

Figure 12.28 Average volumes of fluid ingested, secreted, absorbed and eliminated from the gastrointestinal tract daily.

Control of secretion

Mechanical stimulation of the intestinal glands by chyme is believed to be the main stimulus for the secretion of intestinal juice, although the hormone secretin may also be involved.

Absorption of nutrients (Fig. 12.27)

Absorption of nutrients from the small intestine through the enterocytes occurs by several processes, including diffusion, osmosis, facilitated diffusion and active transport. Water moves by osmosis; small fat-soluble substances, e.g. fatty acids and glycerol, are able to diffuse through cell membranes; while others are generally transported inside the villi by other mechanisms.

Monosaccharides and amino acids pass into the blood capillaries in the villi. Fatty acids and glycerol enter the lacteals and are transported along lymphatic vessels to the thoracic duct where they enter the circulation (Ch. 6).

A small number of proteins are absorbed unchanged, e.g. antibodies present in breast milk and oral vaccines, such as poliomyelitis vaccine.

Other nutrients such as vitamins, mineral salts and water are also absorbed from the small intestine into the blood capillaries. Fat-soluble vitamins are absorbed into the lacteals along with fatty acids and glycerol. Vitamin B_{12} combines with intrinsic factor in the stomach and is actively absorbed in the terminal ileum.

The surface area through which absorption takes place in the small intestine is greatly increased by the circular folds of mucous membrane and by the very large number of villi and microvilli present (Fig. 12.26). It has been calculated that the surface area of the small intestine is about five times that of the whole body surface.

Large amounts of fluid enter the alimentary tract each day (Fig. 12.28). Of this, only about 1500 mL is not absorbed by the small intestine, and passes into the large intestine. **12.9**

Large intestine, rectum and anal canal

Learning outcomes

After studying this section, you should be able to:

- identify the different sections of the large intestine
- describe the structure and functions of the large intestine, the rectum and the anal canal.

The large intestine is about 1.5 metres long, beginning at the *caecum* in the right iliac fossa and terminating at the *rectum* and *anal canal* deep within the pelvis. Its lumen is about 6.5 cm in diameter, larger than that of the small intestine. It forms an arch round the coiled-up small intestine (Fig. 12.29).

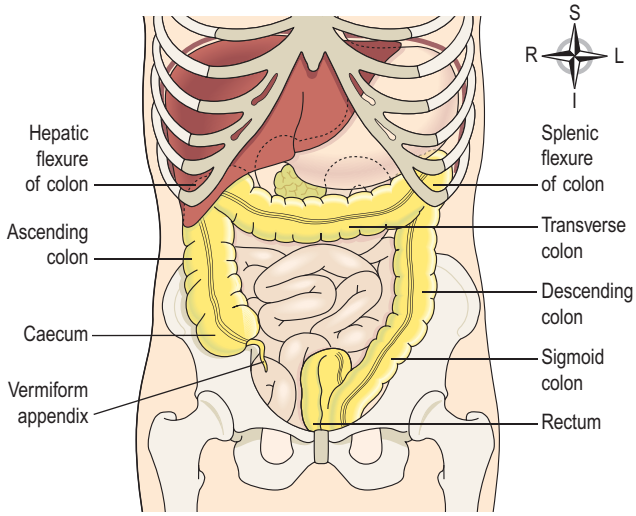

Figure 12.29 The parts of the large intestine and their positions.

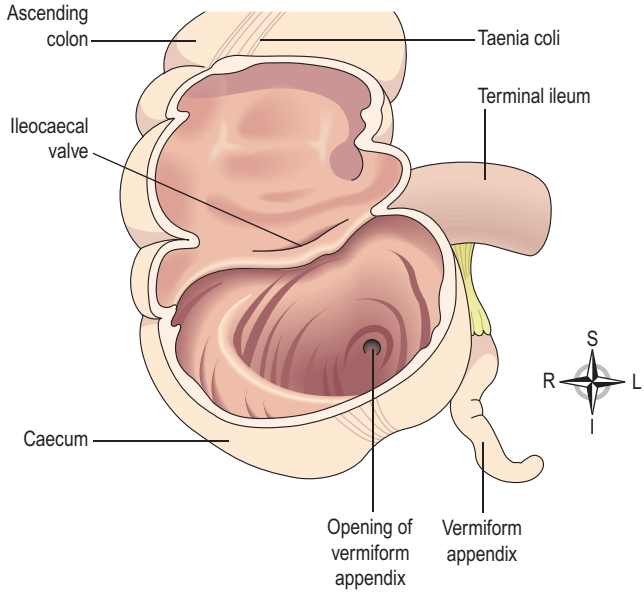

Figure 12.30 Interior of the caecum.

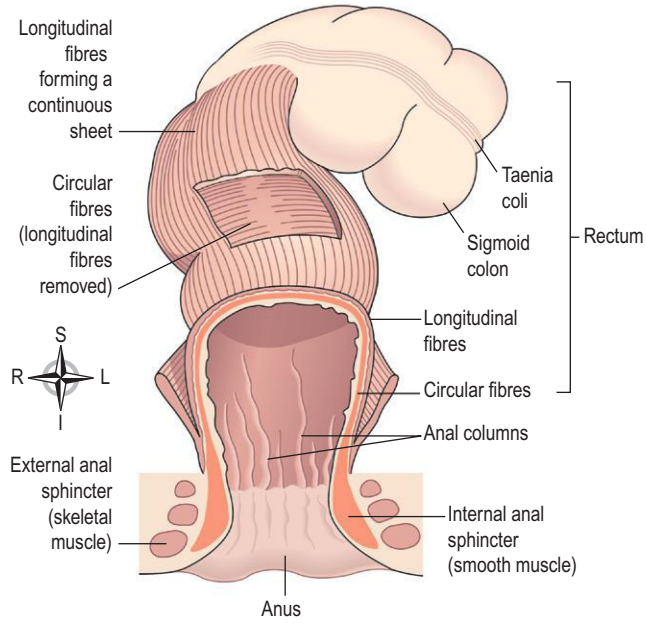

Figure 12.31 Arrangement of muscle fibres in the large intestine, rectum and anus. Sections have been removed to show the layers.

For descriptive purposes the large intestine is divided into the caecum, colon, sigmoid colon, rectum and anal canal.

The caecum

This is the first part of the large intestine (Fig. 12.30). It is a dilated region which has a blind end inferiorly and is continuous with the ascending colon superiorly. Just below the junction of the two the *ileocaecal valve* opens from the ileum. The *vermiform appendix* is a fine tube, closed at one end, which leads from the caecum. It is about 8–9 cm long and has the same structure as the walls of the large intestine but contains more lymphoid tissue. The appendix has no digestive function but can cause significant problems when it becomes inflamed (*appendicitis*, p. 325).

The colon

The colon has four parts which have the same structure and functions.

The ascending colon. This passes upwards from the caecum to the level of the liver where it curves acutely to the left at the *hepatic flexure* to become the transverse colon.

The transverse colon. This part extends across the abdominal cavity in front of the duodenum and the stomach to the area of the spleen where it forms the *splenic flexure* and curves acutely downwards to become the descending colon.

The descending colon. This passes down the left side of the abdominal cavity then curves towards the midline. At the level of the iliac crest it is known as the sigmoid colon.

The sigmoid colon. This part describes an S-shaped curve in the pelvic cavity that continues downwards to become the rectum.

The rectum

This is a slightly dilated section of the large intestine about 13 cm long. It leads from the sigmoid colon and terminates in the anal canal.

The anal canal

This is a short passage about 3.8 cm long in the adult and leads from the rectum to the exterior. Two sphincter muscles control the anus; the *internal sphincter*, consisting of smooth muscle, is under the control of the autonomic nervous system and the *external sphincter*, formed by skeletal muscle, is under voluntary control (Fig. 12.31). **12.10**

Structure

The four layers of tissue described in the basic structure of the gastrointestinal tract (Fig. 12.2) are present in the caecum, colon, the rectum and the anal canal. The arrangement of the longitudinal muscle fibres is modified in the caecum and colon. They do not form a continuous layer of tissue but are instead collected into three bands, called *taeniae coli*, which run lengthways along the caecum and colon. They stop at the junction of the sigmoid colon and the rectum. As these bands of muscle tissue are slightly shorter than the total length of the caecum and colon they give it a sacculated or puckered appearance (Fig. 12.31).

In the rectum the longitudinal muscle fibres spread out as in the basic structure and this layer therefore

completely surrounds the rectum and anal canal. The anal sphincters are formed by thickening of the circular muscle layer.

In the submucosal layer there is more lymphoid tissue than in any other part of the alimentary tract, providing non-specific defence against invasion by resident and other potentially harmful microbes.

In the mucosal lining of the colon and the upper region of the rectum are large numbers of mucus-secreting goblet cells (see Fig. 12.5B) within simple tubular glands. They are not present beyond the junction between the rectum and the anal canal.

The lining membrane of the anal canal consists of stratified squamous epithelium continuous with the mucous membrane lining of the rectum above and which merges with the skin beyond the external anal sphincter. In the upper section of the anal canal the mucous membrane is arranged in 6–10 vertical folds, the *anal columns*. Each column contains a terminal branch of the superior rectal artery and vein.

Blood supply

Arterial supply is mainly by the superior and inferior mesenteric arteries (see Fig. 5.39, p. 109). The *superior mesenteric artery* supplies the caecum, ascending and most of the transverse colon. The *inferior mesenteric artery* supplies the remainder of the colon and the proximal part of the rectum. The *middle* and *inferior rectal arteries*, branches of the internal iliac arteries, supply the distal section of the rectum and the anus.

Venous drainage is mainly by the *superior* and *inferior mesenteric veins* which drain blood from the parts supplied by arteries of the same names. These veins join the splenic and gastric veins to form the portal vein (see Fig. 5.41, p. 111). Veins draining the distal part of the rectum and the anus join the *internal iliac veins*, meaning that blood from this region returns directly to the inferior cava, bypassing the portal circulation.

Functions of the large intestine, rectum and anal canal

Absorption

The contents of the ileum which pass through the ileocaecal valve into the caecum are fluid, even though a large amount of water has been absorbed in the small intestine. In the large intestine absorption of water, by osmosis, continues until the familiar semisolid consistency of faeces is achieved. Mineral salts, vitamins and some drugs are also absorbed into blood capillaries from the large intestine.

Microbial activity

The large intestine is heavily colonised by certain types of bacteria, which synthesise vitamin K and folic acid. They include *Escherichia coli*, *Enterobacter aerogenes*, *Streptococcus faecalis* and *Clostridium perfringens*. These microbes are commensals, i.e. normally harmless, in humans. However, they may become pathogenic if transferred to another part of the body, e.g. *E. coli* may cause cystitis if it gains access to the urinary bladder.

Gases in the bowel consist of some of the constituents of air, mainly nitrogen, swallowed with food and drink. Hydrogen, carbon dioxide and methane are produced by bacterial fermentation of unabsorbed nutrients, especially carbohydrate. Gases pass out of the bowel as *flatus* (wind).

Mass movement

The large intestine does not exhibit peristaltic movement as in other parts of the digestive tract. Only at fairly long intervals (about twice an hour) does a wave of strong peristalsis sweep along the transverse colon forcing its contents into the descending and sigmoid colons. This is known as *mass movement* and it is often precipitated by the entry of food into the stomach. This combination of stimulus and response is called the *gastrocolic reflex*.

Defaecation

Usually the rectum is empty, but when a mass movement forces the contents of the sigmoid colon into the rectum the nerve endings in its walls are stimulated by stretch. In infants, defaecation occurs by reflex (involuntary) action. However, during the second or third year of life children develop voluntary control of bowel function. In practical terms this acquired voluntary control means that the brain can inhibit the reflex until it is convenient to defaecate. The external anal sphincter is under conscious control through the *pudendal nerve*. Thus, defaecation involves involuntary contraction of the muscle of the rectum and relaxation of the internal anal sphincter. Contraction of the abdominal muscles and lowering of the diaphragm increase the intra-abdominal pressure (Valsalva's manoeuvre) and so assist defaecation. When the need to pass faeces is voluntarily postponed, it tends to fade until the next mass movement occurs and the reflex is initiated again. Repeated suppression of the reflex may lead to *constipation* (hard faeces, p. 282) as more water is absorbed.

Constituents of faeces. The faeces consist of a semisolid brown mass. The brown colour is due to the presence of stercobilin (p. 311 and Fig. 12.37).

Even though absorption of water takes place in the small and large intestines, water still makes up about 60–70% of the weight of the faeces. The remainder consists of:

- fibre (indigestible cellular plant and animal material)
- dead and live microbes
- epithelial cells shed from the walls of the tract
- fatty acids
- mucus secreted by the epithelial lining of the large intestine.

Mucus helps to lubricate the faeces and an adequate amount of dietary non-starch polysaccharide (NSP, fibre and previously known as roughage) ensures that the contents of the large intestine are sufficiently bulky to stimulate defaecation.

Pancreas (Fig. 12.32)

Learning outcome

After studying this section, you should be able to:

- differentiate between the structures and functions of the exocrine and endocrine pancreas.

The pancreas is a pale grey gland weighing about 60 grams. It is about 12–15 cm long and is situated in the epigastric and left hypochondriac regions of the abdominal cavity (see Figs 3.37 and 3.38, p. 52). It consists of a broad head, a body and a narrow tail. The head lies in the curve of the duodenum, the body behind the stomach and the tail lies in front of the left kidney and just reaches the spleen. The abdominal aorta and the inferior vena cava lie behind the gland.

The pancreas is both an exocrine and endocrine gland.

The exocrine pancreas

This consists of a large number of *lobules* made up of small acini, the walls of which consist of secretory cells. Each lobule is drained by a tiny duct and these unite eventually to form the *pancreatic duct*, which extends along the whole length of the gland and opens into the duodenum. Just before entering the duodenum the pancreatic duct joins the *common bile duct* to form the hepatopancreatic ampulla. The duodenal opening of the ampulla is controlled by the hepatopancreatic sphincter (of Oddi) at the duodenal papilla.

The function of the exocrine pancreas is to produce *pancreatic juice* containing enzymes, some in the form of inactive precursors, that digest carbohydrates, proteins and fats (p. 303). As in the alimentary tract, parasympathetic stimulation increases the secretion of pancreatic juice and sympathetic stimulation depresses it.

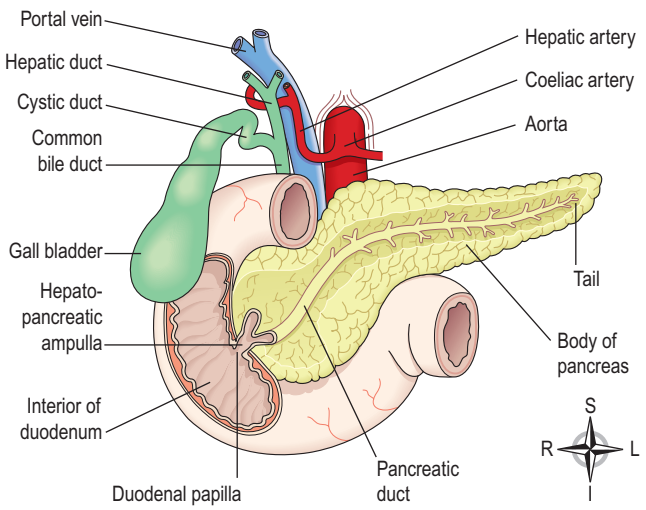

Figure 12.32 The pancreas in relation to the duodenum and biliary tract. Part of the anterior wall of the duodenum has been removed.

The endocrine pancreas

Distributed throughout the gland are groups of specialised cells called the pancreatic islets (of Langerhans). The islets have no ducts so the hormones diffuse directly into the blood. The endocrine pancreas secretes the hormones *insulin* and *glucagon*, which are principally concerned with control of blood glucose levels (see Ch. 9).

Blood supply

The splenic and mesenteric arteries supply the pancreas, and venous drainage is by veins of the same names that join other veins to form the portal vein.

Liver

Learning outcomes

After studying this section, you should be able to:

- describe the location of the liver in the abdominal cavity
- describe the structure of a liver lobule
- outline the functions of the liver.

The liver is the largest gland in the body, weighing between 1 and 2.3 kg. It is situated in the upper part of the abdominal cavity occupying the greater part of the right hypochondriac region, part of the epigastric region and extending into the left hypochondriac region. Its upper and anterior surfaces are smooth and curved to fit the under surface of the diaphragm (Fig. 12.33); its posterior surface is irregular in outline (Fig. 12.34).

Organs associated with the liver

Superiorly and anteriorly – diaphragm and anterior abdominal wall
Inferiorly – stomach, bile ducts, duodenum, hepatic flexure of the colon, right kidney and adrenal gland
Posteriorly – oesophagus, inferior vena cava, aorta, gall bladder, vertebral column and diaphragm
Laterally – lower ribs and diaphragm.

The liver is enclosed in a thin inelastic capsule and incompletely covered by a layer of peritoneum. Folds of peritoneum form supporting ligaments that attach the liver to

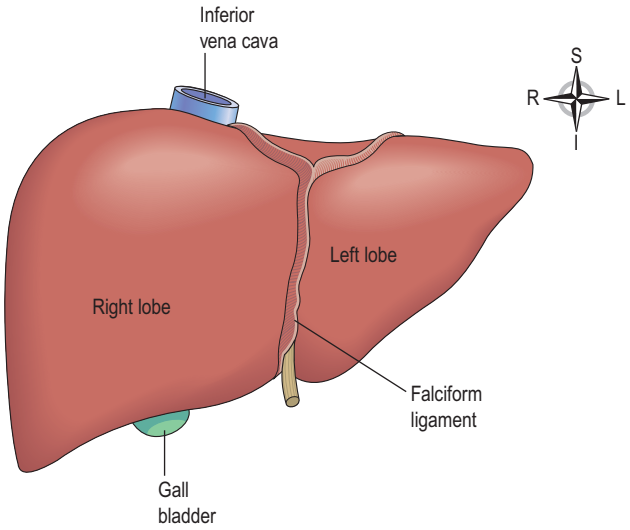

Figure 12.33 The liver. Anterior view.

the inferior surface of the diaphragm. It is held in position partly by these ligaments and partly by the pressure of the organs in the abdominal cavity.

The liver has four lobes. The two most obvious are the large *right lobe* and the smaller, wedge-shaped, *left lobe*. The other two, the *caudate* and *quadrate* lobes, are areas on the posterior surface (Fig. 12.34).

The portal fissure

This is the name given to the region on the posterior surface of the liver where various structures enter and leave the gland.

The *portal vein* enters, carrying blood from the stomach, spleen, pancreas and the small and large intestines. **12.11**

The *hepatic artery* enters, carrying arterial blood. It is a branch from the coeliac artery, which branches from the abdominal aorta.

Nerve fibres, sympathetic and parasympathetic, enter here.

The *right* and *left hepatic ducts* leave, carrying bile from the liver to the gall bladder.

Lymph vessels leave the liver, draining lymph to abdominal and thoracic nodes.

Blood supply (see Figs 5.38 and 5.40)

The hepatic artery and the portal vein take blood to the liver (see Fig. 12.36). Venous return is by a variable number of hepatic veins that leave the posterior surface and immediately enter the inferior vena cava just below the diaphragm.

Structure

The lobes of the liver are made up of tiny functional units, called *lobules*, which are just visible to the naked eye (Fig. 12.35A). Liver lobules are hexagonal in outline and are formed by cuboidal cells, the *hepatocytes*, arranged in pairs of columns radiating from a central vein. Between two pairs of columns of cells are *sinusoids* (blood vessels with incomplete walls, Ch. 5) containing a mixture of blood from the tiny branches of the portal vein and hepatic artery (Fig. 12.35B). This arrangement allows the arterial blood and portal venous blood (with a high concentration of nutrients) to mix and come into close contact with the liver cells. Amongst the cells lining the sinusoids are hepatic macrophages (Kupffer cells) whose function is to ingest and destroy worn out blood cells and any foreign particles present in the blood flowing through the liver.

Blood drains from the sinusoids into *central* or *centrilobular veins*. These then merge with veins from other lobules, forming larger veins, until eventually they become the hepatic veins, which leave the liver and empty into the inferior vena cava. Figure 12.36 shows the system

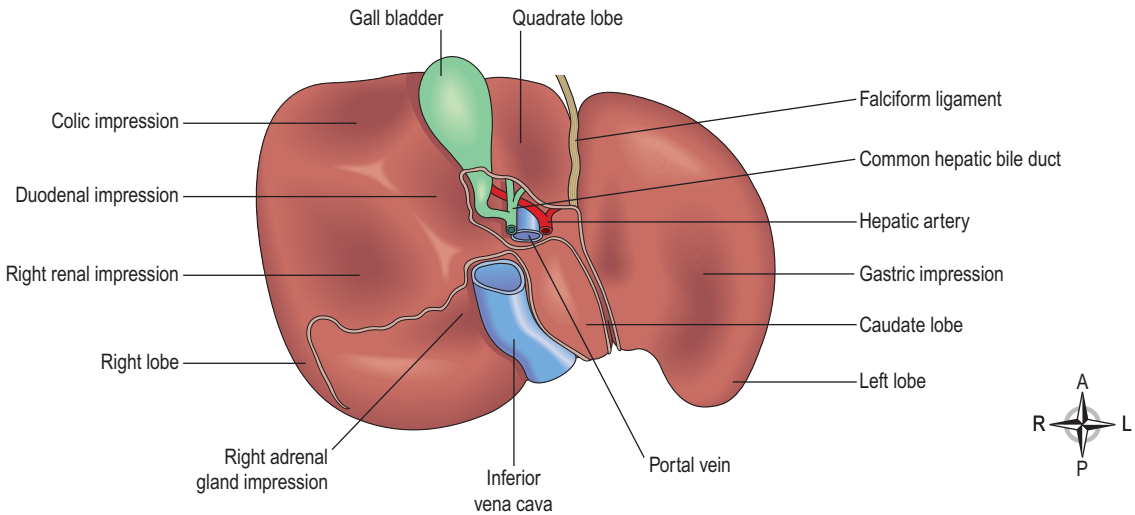

Figure 12.34 The liver. Inferior view (turned up to show the posterior surface).

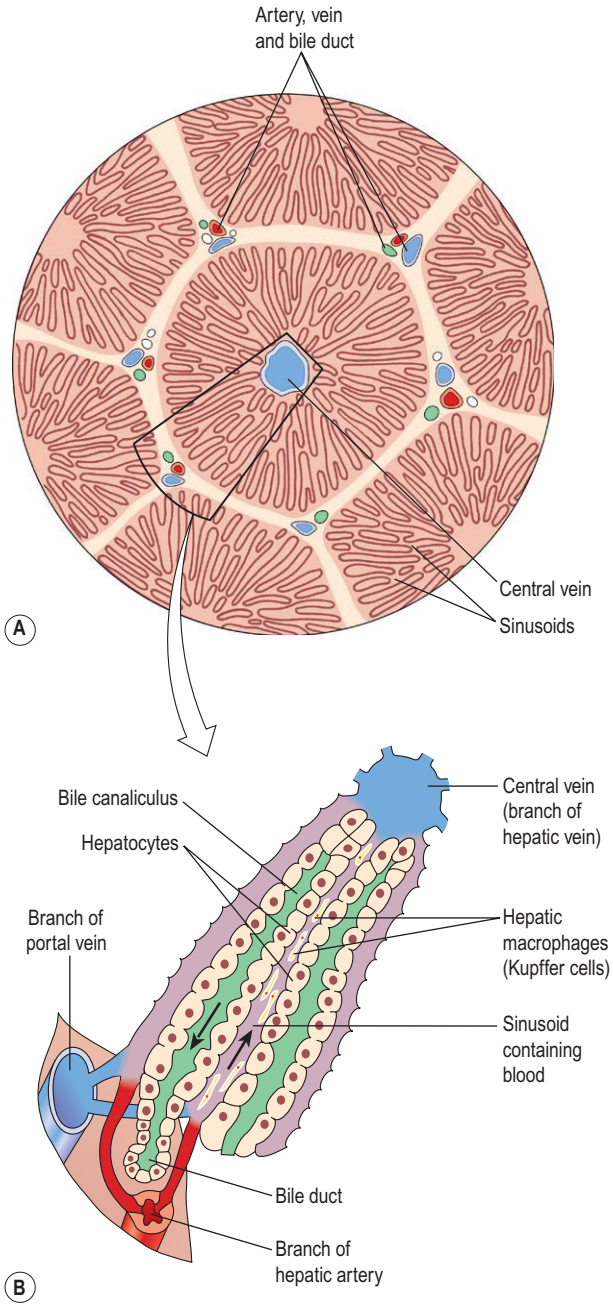

Figure 12.35 The liver lobule. A. A magnified transverse section of a liver lobule. **B.** Direction of the flow of blood and bile in a liver lobule.

of blood flow through the liver. One of the functions of the liver is to secrete bile. In Figure 12.35B it is seen that *bile canaliculi* run between the columns of liver cells. This means that each column of hepatocytes has a blood sinusoid on one side and a bile canaliculus on the other. The canaliculi join up to form larger bile canals until eventually they form the *right and left hepatic ducts*, which drain bile from the liver.

Lymphoid tissue and a network of lymph vessels are also present in each lobule.

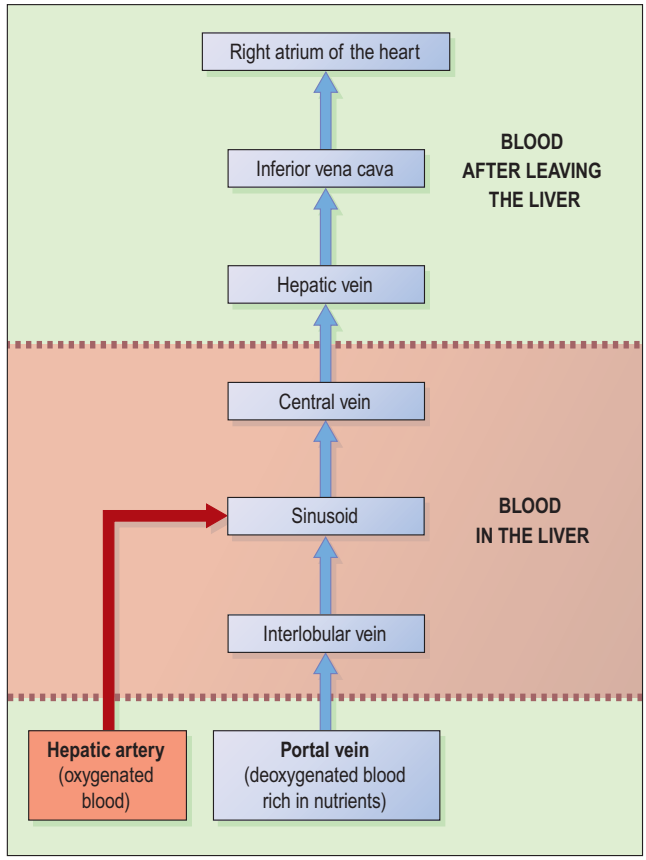

Figure 12.36 Scheme of blood flow through the liver.

Functions of the liver

The liver is an extremely active organ, which has many important functions that are described below.

Carbohydrate metabolism

The liver has an important role in maintaining plasma glucose levels. After a meal when levels rise, glucose is converted to glycogen for storage under the influence of the hormone insulin. Later, when glucose levels fall, the hormone glucagon stimulates conversion of glycogen into glucose again, keeping levels within the normal range (see Fig 12.39).

Fat metabolism

Stored fat can be converted to a form in which it can be used by the tissues to provide energy (see Fig. 12.44).

Protein metabolism

Deamination of amino acids. This process:

- removes the nitrogenous portion from amino acids that are not required for the formation of new protein; *urea* is formed from this nitrogenous portion and is excreted in urine
- breaks down nucleic acids (genetic material, e.g. DNA, see p. 438) to form *uric acid*, which is excreted in the urine.

Transamination. Removes the nitrogenous portion of amino acids and attaches it to other carbohydrate molecules forming new non-essential amino acids (see Fig. 12.42).

Synthesis of plasma proteins. These are formed from amino acids and include albumins, globulins and blood clotting factors (p. 62).

Breakdown of erythrocytes and defence against microbes

This is carried out by phagocytic hepatic macrophages (Kupffer cells) in the sinusoids although breakdown of red blood cells also takes place in the spleen and bone marrow.

Detoxification of drugs and toxic substances

These include ethanol (alcohol), waste products and microbial toxins. Some drugs are extensively inactivated by the liver and are not very effective when given by mouth (orally), e.g. glyceryl trinitrate. This is because after absorption from the alimentary tract, they travel in the blood to the liver where they are largely metabolised so that levels in the blood leaving the liver and which enters the systemic circulation are inadequate to achieve therapeutic effects. This is known as *'first pass metabolism'*.

Inactivation of hormones

These include insulin, glucagon, cortisol, aldosterone, thyroid and sex hormones.

Production of heat

The liver uses a considerable amount of energy, has a high metabolic rate and consequently produces a great deal of heat. It is the main heat-producing organ of the body.

Secretion of bile

The hepatocytes synthesise the constituents of bile from the mixed arterial and venous blood in the sinusoids. These include bile salts, bile pigments and cholesterol (see below).

Storage

Stored substances include:

- glycogen (see p. 315)
- fat-soluble vitamins: A, D, E, K
- iron, copper
- some water-soluble vitamins, e.g. vitamin B_{12}.

Composition of bile

Between 500 and 1000 mL of bile is secreted by the liver daily. Bile consists of:

- water
- mineral salts
- mucus
- bile pigments, mainly bilirubin
- bile salts
- cholesterol.

Functions of bile

Fat digestion. The bile acids, *cholic* and *chenodeoxycholic acid*, are synthesised by hepatocytes from cholesterol, then secreted into bile as sodium or potassium salts. In the small intestine they emulsify fats, aiding their digestion. Fatty acids are insoluble in water, which makes them very difficult to absorb through the intestinal wall. Bile salts make cholesterol and fatty acids more water-soluble, enabling both these and the fat-soluble vitamins (vitamins A, D, E and K) to be readily absorbed.

In the terminal ileum most of the bile salts are reabsorbed and return to the liver in the portal vein. This *enterohepatic circulation*, or recycling of bile salts, ensures that large amounts of bile salts enter the small intestine daily from a relatively small bile acid pool (Fig. 12.37).

Excretion of bilirubin. Bilirubin is one of the products of haemolysis of erythrocytes by hepatic macrophages (Kupffer cells) in the liver and by other macrophages in the spleen and bone marrow. Bilirubin is insoluble in water and is carried in the blood bound to the plasma protein albumin. In hepatocytes it is *conjugated* (combined) with glucuronic acid and becomes water-soluble enough to be excreted in bile. Microbes in the large

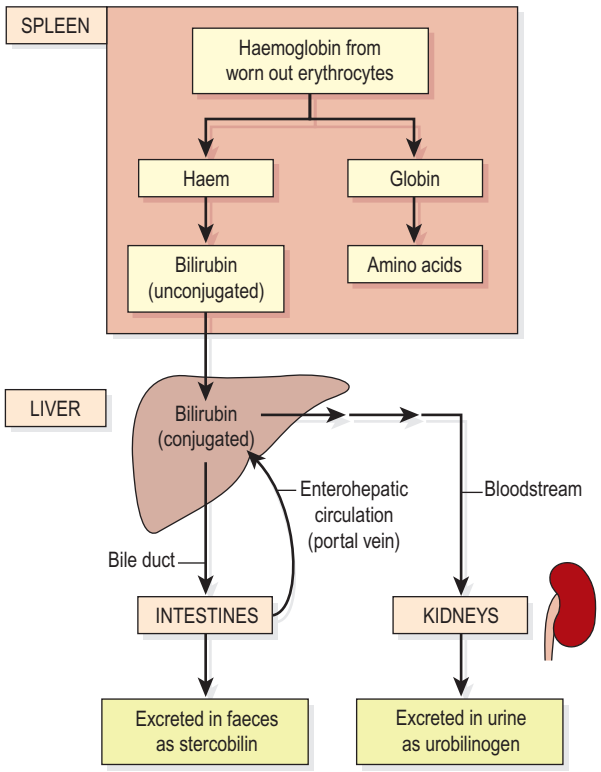

Figure 12.37 Fate of bilirubin from breakdown of worn-out erythrocytes.

intestine convert bilirubin into *stercobilin*, which is excreted in the faeces. Stercobilin colours and deodorises the faeces. A small amount is reabsorbed and excreted in urine as *urobilinogen* (Fig. 12.37). Jaundice is yellow pigmentation of the tissues, seen in the skin and conjunctiva, caused by excess blood bilirubin (p. 336).

Biliary tract

Learning outcomes

After studying this section, you should be able to:

- describe the route taken by bile from the liver, to the gall bladder, and then to the duodenum
- outline the structure and functions of the gall bladder.

Bile ducts (Fig. 12.38) 12.12

The *right* and *left hepatic ducts* join to form the *common hepatic duct* just outside the portal fissure. The hepatic duct passes downwards for about 3 cm where it is joined by the *cystic duct* from the gall bladder. The cystic and hepatic ducts merge forming the *common bile duct*, which passes downwards behind the head of the pancreas. This is joined by the main pancreatic duct at the hepatopancreatic ampulla. It opens into the duodenum, at the duodenal papilla, which is controlled by the hepatopancreatic sphincter (of Oddi). The common bile duct is about 7.5 cm long and has a diameter of about 6 mm.

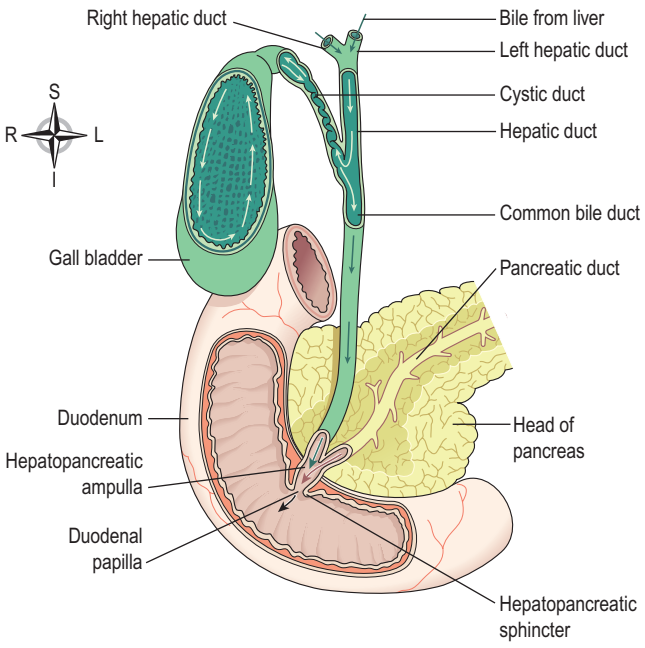

Figure 12.38 Direction of the flow of bile from the liver to the duodenum.

Structure

The walls of the bile ducts have the same layers of tissue as those of the basic structure of the alimentary canal (Fig. 12.2). In the cystic duct the mucous membrane lining is arranged in irregular circular folds, which have the effect of a spiral valve. Bile passes through the cystic duct twice – once on its way into the gall bladder and again when it is expelled from the gall bladder into the common bile duct and then on to the duodenum.

Gall bladder

The gall bladder is a pear-shaped sac attached to the posterior surface of the liver by connective tissue. It has a *fundus* or expanded end, a *body* or main part and a *neck*, which is continuous with the cystic duct.

Structure

The wall of the gall bladder has the same layers of tissue as those of the basic structure of the alimentary canal, with some modifications.

Peritoneum. This covers only the inferior surface because the upper surface of the gall bladder is in direct contact with the liver and held in place by the visceral peritoneum that covers the liver.

Muscle layer. There is an additional layer of oblique muscle fibres.

Mucous membrane. This displays small rugae when the gall bladder is empty that disappear when it is distended with bile.

Blood supply

The *cystic artery*, a branch of the hepatic artery, supplies the gall bladder. Blood is drained away by the *cystic vein* that joins the portal vein.

Functions of the gall bladder

These include:

- reservoir for bile
- concentration of the bile by up to 10- or 15-fold, by absorption of water through the walls of the gall bladder
- release of stored bile.

When the muscle wall of the gall bladder contracts, bile passes through the bile ducts to the duodenum. Contraction is stimulated by the hormone cholecystokinin (CCK), secreted by the duodenum and the presence of fat and acid chyme in the duodenum.

Relaxation of the hepatopancreatic sphincter (of Oddi) is caused by CCK and is a reflex response to contraction of the gall bladder.

Summary of digestion and absorption of nutrients

Learning outcomes

After studying this section, you should be able to:

- list the principal digestive enzymes, their sites of action, their substrates and their products
- describe the sites of absorption of the main nutrient groups.

Table 12.2 summarises the main digestive processes of the principal nutrient groups, the locations where these processes occur and the enzymes involved.

Metabolism

Learning outcomes

After studying this section, you should be able to:

- discuss general principles of metabolism, including anabolism, catabolism, units of energy and metabolic rate
- compare and contrast the metabolic rates of the body's main energy sources (carbohydrate, protein and fat)
- describe in simple terms the central metabolic pathways; glycolysis, citric acid cycle and oxidative phosphorylation.

Metabolism constitutes all the chemical reactions that occur in the body, using nutrients to:

- provide energy by chemical oxidation of nutrients
- make new or replacement body substances.

Table 12.2 Summary showing the sites of digestion and absorption of nutrients

			Small intestine		
	Mouth	**Stomach**	***Digestion***	***Absorption***	**Large intestine**
Carbohydrate	*Salivary amylase:* digestible starches to disaccharides	*Hydrochloric acid*: denatures and stops action of salivary amylase	*Pancreatic amylase*: digestible starches to disaccharides *Sucrase, maltase, lactase* (in enterocytes): disaccharides to monosaccharides (mainly glucose)	Into blood capillaries of villi	–
Proteins		*Hydrochloric acid*: pepsinogen to pepsin *Pepsin*: proteins to polypeptides	*Enterokinase* (in enterocytes): chymotrypsinogen and trypsinogen (from pancreas) to chymotrypsin and trypsin *Chymotrypsin and trypsin*: polypeptides to di- and tripeptides *Peptidases* (in enterocytes): di- and tripeptides to amino acids	Into blood capillaries of villi	–
Fats	–	–	*Bile* (from liver): bile salts emulsify fats *Pancreatic lipase*: fats to fatty acids and glycerol *Lipases* (in enterocytes): fats to fatty acids and glycerol	Into the lacteals of the villi	–
Water	–	Small amount absorbed here		Most absorbed here	Remainder absorbed here
Vitamins	–	Intrinsic factor secreted for vitamin B_{12} absorption	–	Water-soluble vitamins absorbed into capillaries; fat-soluble ones into lacteals of villi	Bacteria synthesise vitamin K in colon; absorbed here

Two types of process are involved:

large molecules ⇌ small molecules (catabolism / anabolism)

Catabolism. Catabolic processes break down large molecules into smaller ones releasing *chemical energy*, which is stored as adenosine triphosphate (ATP), and *heat*. Heat generated maintains core body temperature at the optimum level for chemical activity (36.8°C). Excess heat is lost, mainly through the skin (Ch. 14).

Anabolism. This is building up, or synthesis, of large molecules from smaller ones and requires a source of energy, usually ATP.

Metabolic pathways

Anabolism and catabolism usually involve a series of chemical reactions, known as metabolic pathways. These consist of 'small steps' that permit controlled, efficient and gradual transfer of energy from ATP rather than large intracellular 'explosions'. Metabolic pathways (see below) are switched on and off by hormones, providing control of metabolism and meeting individual requirements.

Both catabolic and anabolic processes occur continually in all cells. Very active tissues, such as muscle or liver, need a large energy supply to support their requirements.

Energy

The energy produced in the body may be measured and expressed in units of work (*joules*) or units of heat (*kilocalories*).

A kilocalorie (kcal) is the amount of heat required to raise the temperature of 1 litre of water by 1 degree Celsius (1°C). On a daily basis, the body's collective metabolic processes generate a total of about 3 million kilocalories.

1 kcal = 4184 joules (J) = 4.184 kilojoules (kJ)

The nutritional value of carbohydrates, protein and fats eaten in the diet may be expressed in either *kilojoules per gram* or kcal per gram.

1 gram of carbohydrate provides 17 kilojoules (4 kcal)
1 gram of protein provides 17 kilojoules (4 kcal)
1 gram of fat provides 38 kilojoules (9 kcal)

Chapter 11 provides examples of foods providing these nutrients.

Energy balance

Energy balance is important as it determines changes in body weight. Body weight remains constant when energy intake is equal to energy use. When intake exceeds requirement, body weight increases, which may lead to obesity. Conversely, body weight decreases when nutrient intake does not meet energy requirements.

Table 12.3 Factors affecting metabolic rate

Factor	Effect on metabolic rate
Age	Gradually reduced with age
Gender	Higher in men than women
Height, weight	Relatively higher in larger people
Pregnancy, menstruation, lactation	Increased
Ingestion of food	Increased
Muscular activity, physical exertion	Increased
Elevated body temperature (fever)	Increased
Excess thyroid hormones	Increased
Starvation	Decreased
Emotional states	Increased

Metabolic rate 12.13

The metabolic rate is the rate at which energy is released from the fuel molecules inside cells. As most of the processes involved require oxygen and produce carbon dioxide as waste, the metabolic rate can be estimated by measuring oxygen uptake or carbon dioxide excretion.

The *basal metabolic rate* (BMR) is the rate of metabolism when the individual is at rest in a warm environment and is in the *postabsorptive state*, i.e. has not had a meal for at least 12 hours. In this state the release of energy is sufficient to meet only the essential needs of vital organs, such as the heart, lungs, nervous system and kidneys. Some of the many factors that affect metabolic rate are shown in Table 12.3. The postabsorptive state is important because the intake of food, especially protein, increases metabolic rate.

Central metabolic pathways

Much of the metabolic effort of cells is concerned with energy production to fuel cellular activities. Certain common pathways are central to this function. Fuel molecules enter these central energy-producing pathways and in a series of steps, during which a series of intermediate molecules are formed and energy is released, these fuel molecules are chemically broken down. The end results of these processes are production of energy and carbon dioxide and water (called *metabolic water*). Much of the energy is stored as ATP, although some is lost as heat. The carbon dioxide is excreted through the lungs and excess water excreted as urine.

The preferred fuel molecule is glucose, but alternatives should glucose be unavailable include amino acids,

fatty acids, glycerol and occasionally nucleic acids. Each of these may enter the central energy-producing pathways and be converted to energy, carbon dioxide and water. There are three central metabolic pathways (see Fig. 12.44):

- glycolysis
- the citric acid (Krebs) cycle
- oxidative phosphorylation.

Products from glycolysis enter the citric acid cycle, and products from the citric acid cycle proceed to oxidative phosphorylation. The fates of the different fuel molecules entering the central metabolic pathways are discussed in the following sections.

Carbohydrate metabolism

Erythrocytes and neurones can use only glucose for fuel and therefore maintenance of blood glucose levels is needed to provide a constant energy source to these cells. Most other cells can also use other sources of fuel.

Digested carbohydrate, mainly glucose, is absorbed into the blood capillaries of the villi of the small intestine. It is transported by the portal circulation to the liver, where it is dealt with in several ways (Fig. 12.39):

- glucose may be oxidised to provide the chemical energy, in the form of ATP, necessary for the considerable metabolic activity which takes place in the liver itself (p. 310)
- some glucose may remain in the circulating blood to maintain the normal blood glucose of about 3.5–8 millimoles per litre (mmol/L) (63–144 mg/100 mL).

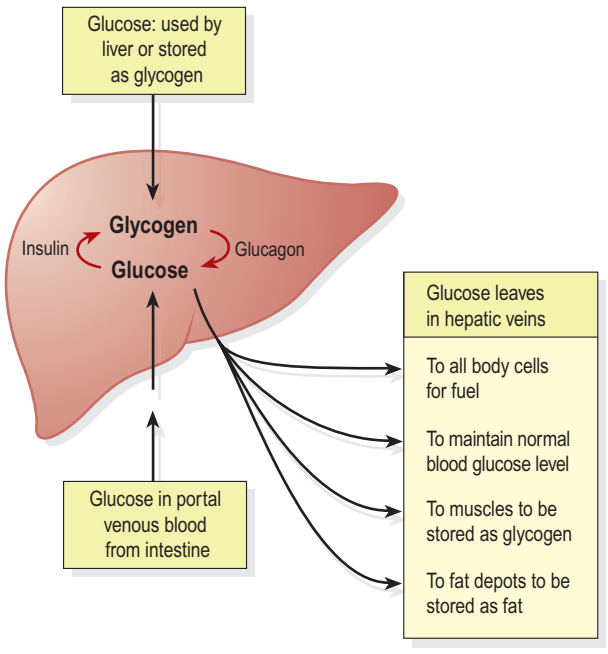

Figure 12.39 Summary of the source, distribution and use of glucose.

- some glucose, if in excess of the above requirements, may be converted by the hormone *insulin* to the insoluble polysaccharide, *glycogen*, in the liver and in skeletal muscles. The formation of glycogen inside cells is a means of storing carbohydrate without upsetting the osmotic equilibrium. Before it can be used to maintain blood levels or to provide ATP it must be broken down again into its constituent glucose units. Liver glycogen constitutes a store of glucose used for liver activity and to maintain the blood glucose level. Muscle glycogen stores provide the glucose requirement of muscle activity. *Glucagon*, *adrenaline* (*epinephrine*) and *thyroxine* are the main hormones associated with the breakdown of glycogen to glucose. These processes can be summarised:

$$\text{glucose} \underset{\text{glucagon}}{\overset{\text{insulin}}{\rightleftharpoons}} \text{glycogen}$$

- carbohydrate in excess of that required to maintain the blood glucose level and glycogen stores in the tissues is converted to fat and stored in the fat depots.

All body cells require energy to carry out their metabolic processes including multiplication for replacement of worn out cells, muscle contraction and synthesis of glandular secretions. The oxidation of carbohydrate and fat provides most of the energy required by the body. When glycogen stores are low and more glucose is needed, the body can make glucose from non-carbohydrate sources, e.g. amino acids, glycerol. This is called *gluconeogenesis* (formation of new glucose).

Carbohydrate and energy release (Fig. 12.40)

Glucose is broken down in the body releasing energy, carbon dioxide and metabolic water. Catabolism of glucose occurs in a series of steps with a little energy being released at each stage. The total number of ATP molecules which may be generated from the complete breakdown of one molecule of glucose is 38, but for this to be achieved the process must occur in the presence of oxygen (aerobically). In the absence of oxygen (anaerobically) this number is greatly reduced; the process is therefore much less efficient. **12.14**

Aerobic respiration (catabolism). Aerobic catabolism of glucose can occur only when the oxygen supply is adequate, and is the process by which energy is released during prolonged, manageable exercise. When exercise levels become very intense, the energy requirements of muscles outstrip the oxygen supply, and anaerobic breakdown then occurs. Such high levels of activity can be sustained for only short periods, because there is accumulation of wastes (mainly lactic acid) and reduced efficiency of the energy production process.

The first stage of glucose catabolism is *glycolysis*. This is an anaerobic process that takes place in the cytoplasm

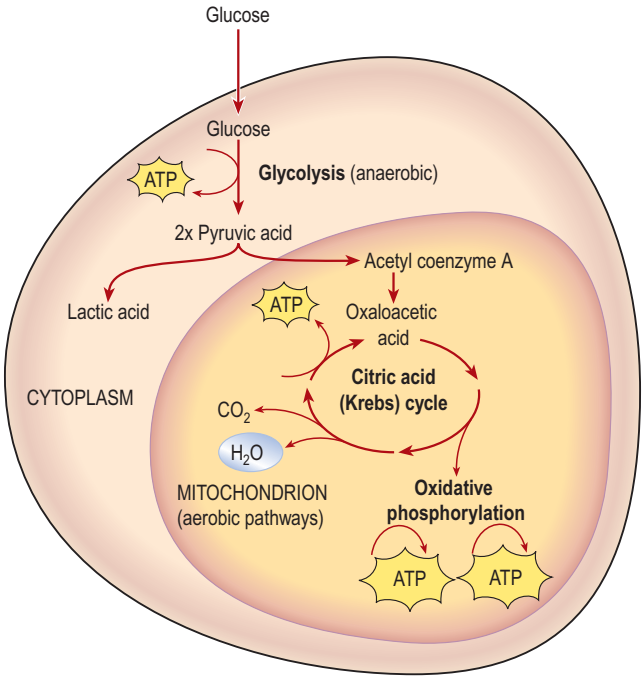

Figure 12.40 Oxidation of glucose.

of the cell. Through a number of intermediate steps one glucose molecule is converted to two molecules of pyruvic acid, with the net production of two molecules of ATP. The remainder of the considerable energy stores locked up in the original molecule of glucose is released only if there is enough oxygen to allow the pyruvic acid molecules to enter the biochemical roundabout called the *citric acid cycle* (Fig. 12.40). This takes place in the mitochondria of the cell and is oxygen dependent. For every two molecules of pyruvic acid entering the citric acid cycle, a further two molecules of ATP are formed but this is still far short of the maximum possible 38 ATP molecules. The remaining 34 molecules of ATP come from the third energy-generating process, *oxidative phosphorylation*, a process dependent on hydrogen atoms released during earlier stages of glucose breakdown. Oxidative phosphorylation, like the citric acid cycle, can occur only in the presence of oxygen and takes place in the mitochondria.

Anaerobic catabolism. When oxygen levels in the cell are low, the molecule of glucose still undergoes glycolysis and is split into two molecules of pyruvic acid, because glycolysis is an anaerobic process. However, the pyruvic acid does not enter the citric acid cycle or progress to oxidative phosphorylation; instead it is converted anaerobically to lactic acid. Build-up of lactic acid causes the pain and cramps of overexercised muscles. When oxygen levels are restored, lactic acid is reconverted to pyruvic acid, which may then enter the citric acid cycle.

Fate of the end products of carbohydrate metabolism

Lactic acid. Some of the lactic acid produced by anaerobic catabolism of glucose may be oxidised in the cells to carbon dioxide and water but first it must be changed back to pyruvic acid. If complete oxidation does not take place, lactic acid passes to the liver in the circulating blood where it is converted to glucose and may then take any of the pathways open to glucose (Fig. 12.39).

Carbon dioxide. This is excreted from the body as a gas by the lungs.

Metabolic water. This is added to the considerable amount of water already present in the body; excess is excreted as urine by the kidneys.

Protein metabolism

Dietary protein consists of a number of amino acids. About 20 amino acids have been named and nine of these are described as *essential* because they cannot be synthesised in the body. The others are *non-essential* amino acids because they can be synthesised by many tissues. The enzymes involved in this process are called *transaminases*. Digestion breaks down dietary protein into its constituent amino acids in preparation for absorption into the blood capillaries of the villi in the small intestine. Amino acids are transported in the portal circulation to the liver and then into the general circulation, thus making them available to all body cells and tissues. Different cells choose from those available the particular amino acids required for building or repairing their specific type of tissue and for synthesising their secretions, e.g. antibodies, enzymes or hormones.

Amino acids not required for building and repairing body tissues cannot be stored and are broken down in the liver (see deamination below).

Amino acid pool (Fig. 12.41)

A small pool of amino acids is maintained within the body. This is the source from which the body cells draw the amino acids they need to synthesise their own materials, e.g. new cells or cell components, secretions such as enzymes, hormones and plasma proteins.

Sources of amino acids

Exogenous. These are derived from dietary protein.

Endogenous. These are obtained from the breakdown of existing body proteins. In adults, about 80–100 g of protein are broken down and replaced each day. The entire intestinal mucosa is replaced about every 5 days.

Loss of amino acids

Deamination. Amino acids not needed by the body are broken down, or deaminated, mainly in the liver. The

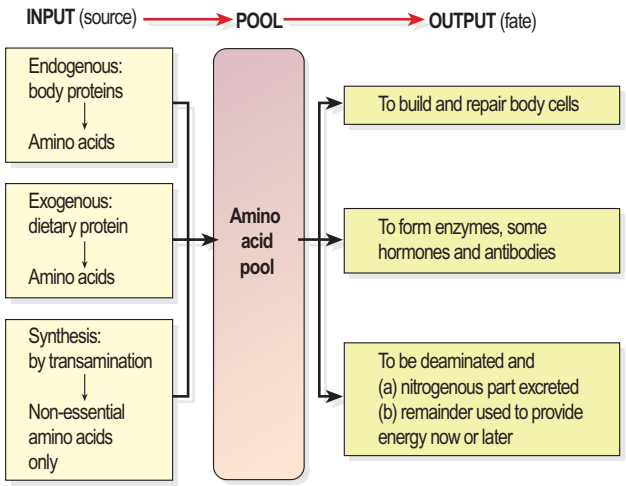

Figure 12.41 Sources and use of amino acids in the body.

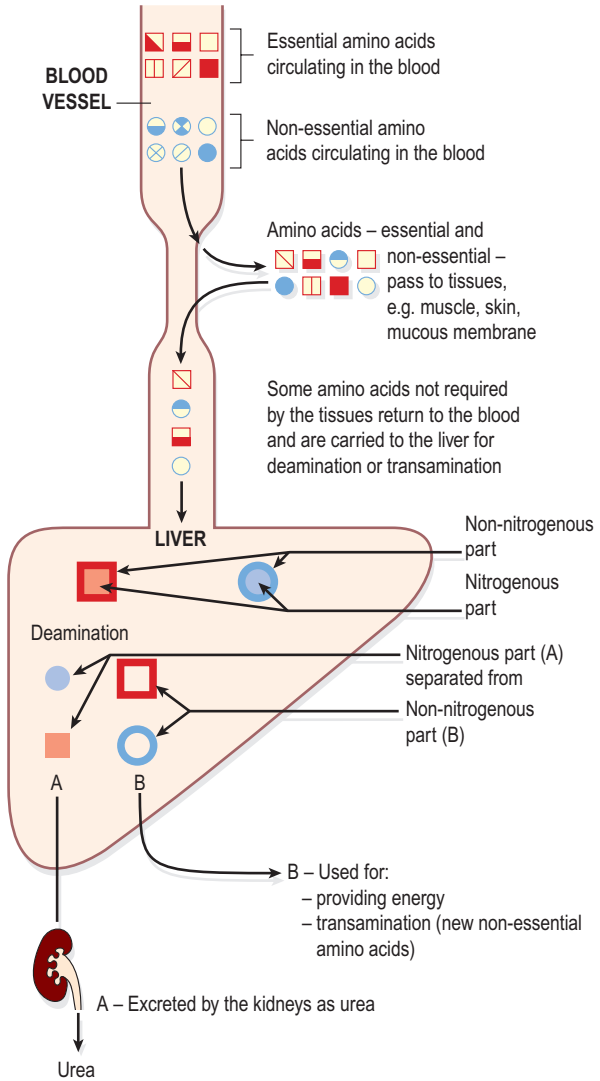

Figure 12.42 The fate of amino acids in the body.

nitrogenous part, the amino group (NH_2), is converted to ammonia (NH_3) and then combined with carbon dioxide forming *urea*, which is excreted in the urine. The remaining part is used to provide energy, as glucose by gluconeogenesis, or stored as fat, if in excess of immediate requirements.

Excretion. The faeces contain a considerable amount of protein within cells shed from the lining of the alimentary tract.

Endogenous and exogenous amino acids are mixed in the 'pool' and the body is said to be in *nitrogen balance* when the rate of removal from the pool is equal to the additions to it. Unlike carbohydrates, the body has no capacity for the storage of amino acids except for this relatively small pool. Figure 12.42 depicts what happens to amino acids in the body.

Amino acids and energy release (see Fig. 12.44)

Proteins, in the form of amino acids, are potential fuel molecules that are used by the body only when other energy sources are low, e.g. in starvation. To supply the amino acids for use as fuel, in extreme situations, the body breaks down muscle, its main protein source. Some amino acids can be converted directly to glucose, which enters glycolysis. Other amino acids are changed to intermediate compounds of the central metabolic pathways, e.g. acetyl coenzyme A or oxaloacetic acid, and therefore enter the system at a later stage.

Fat metabolism (Fig. 12.43)

Fat is synthesised from excess dietary carbohydrates and proteins, and stored in the fat depots, i.e. under the skin, in the omentum or around the kidneys.

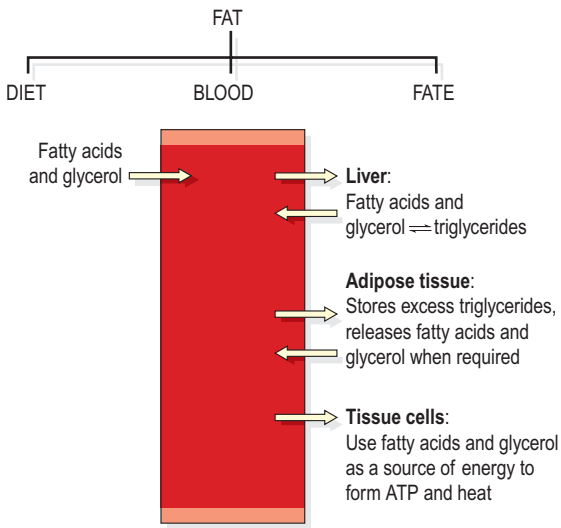

Figure 12.43 Sources, distribution and use of fats in the body.

Fats that have been digested and absorbed as fatty acids and glycerol into the lacteals are transported via the cisterna chyli and the thoracic duct of the lymphatic system (Ch. 6) to the bloodstream and so, by a circuitous route, to the liver. Fatty acids and glycerol circulating in the blood are used by the cells to provide energy and to synthesise some of their secretions. In the liver some fatty acids and glycerol are used to provide energy and heat, and some are recombined forming *triglycerides*, the form in which fat is stored. A triglyceride consists of three fatty acids chemically combined with a glycerol molecule (see Fig. 2.9, p. 27). When required, triglycerides are converted back to fatty acids and glycerol and used to provide energy. The end products of fat metabolism are chemical energy, heat, carbon dioxide and water.

Fatty acids and energy release

When body tissues are deprived of glucose, as occurs in prolonged fasting, starvation, energy-restricted diets or during strenuous exercise, the body uses alternative energy sources, mainly fat stores. Fatty acids may be converted to acetyl coenzyme A, and enter the energy production pathway in that form. One consequence of this is accumulation of *ketone bodies*, which are produced in the liver from acetyl coenzyme A when levels are too high for processing through the citric acid cycle (see Fig. 12.44). Ketone bodies then enter the blood and can be used by other body tissues, including the brain (which is usually glucose dependent) as a source of fuel. However, at high concentrations, ketone bodies are toxic, particularly to the brain. Ketone bodies include acetone and some weak organic acids. Normally levels are low because they are used as soon as they are produced. When production exceeds use, in the situations mentioned above, levels rise causing *ketosis*. Ketosis is associated with acidosis, which can lead to coma or even death if severe. Excretion of excess ketone bodies is via:

- the urine (ketonuria)
- the lungs, giving the breath a characteristic sweet smell of acetone or 'pear drops'.

In ketosis, compensation is required to maintain acid–base balance. This is achieved by buffer systems that excrete excess acid (hydrogen ions) by the lungs, through hyperventilation, or kidneys. In health, ketosis is self-limiting and ketone body production stops when fasting or exercise ceases. Ketoacidosis is associated with uncontrolled type 1 diabetes mellitus (p. 237).

Glycerol and energy release (Fig. 12.44)

The body converts glycerol from the degradation of fats into one of the intermediary compounds produced during glycolysis, and in this form it enters the central metabolic pathways.

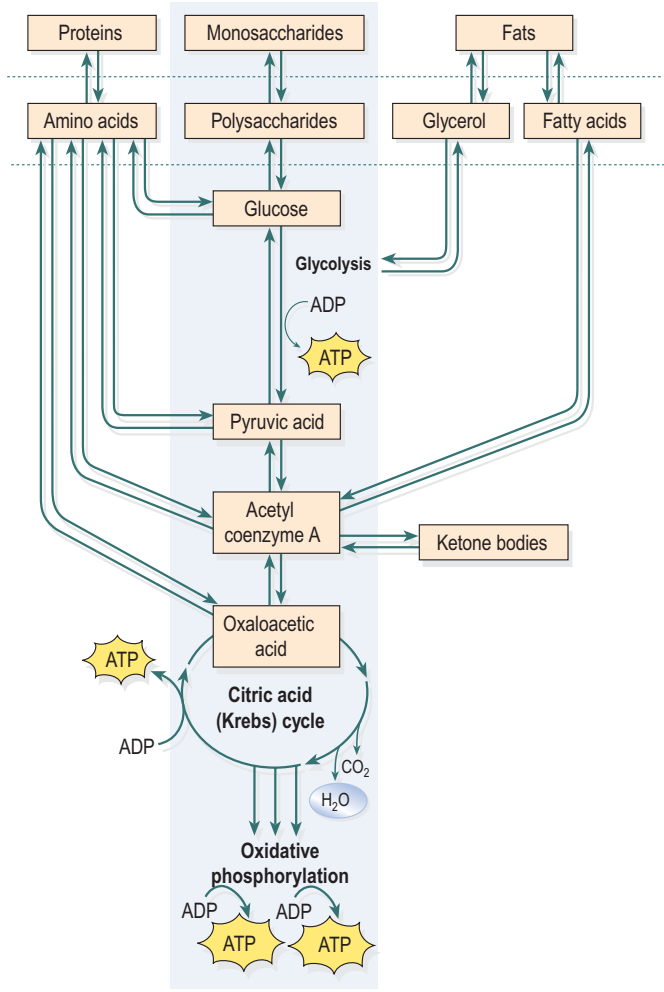

Figure 12.44 Summary of the fates of the three main energy sources in the central metabolic pathways.

Effects of ageing on the digestive system

Learning outcome

After studying this section you, should be able to:

- describe the effects of ageing on the digestive system.

Loss of many teeth, e.g. through periodontal disease, may cause difficulty chewing which it turn restricts dietary choices. A reduction in the muscle mass of the tongue and lessened salivation can exacerbate this. The sensitivity of taste buds declines with age (p. 207).

Peristalsis within the alimentary canal reduces, which predisposes to constipation (p. 319). Other features of ageing such as lessened mobility or poor cognitive

function also contribute to constipation unless dietary NSP (fibre) is increased and an adequate fluid intake is maintained.

Liver mass decreases with age and this is accompanied by a variable decline in its reserve capacity which can impair metabolism, including breakdown of drugs that may lead to toxicity.

In older adults there is a reduction in skeletal muscle mass and also responsiveness to hormones; including adrenaline, noradrenaline and thyroid hormones, contributing to a lower basal metabolic rate (BMR). Limited physical activity or inactivity also reduce BMR. A reduction in BMR that is not accompanied by a lower dietary intake predisposes to obesity and its consequences (p. 284).

Table 12.4 Common signs and symptoms of gastrointestinal disorders

Sign/symptom	Definition and description
Abdominal pain	This is caused by stretching of smooth muscle or organ capsules. The location is described with reference to the regions of the abdomen (see Fig. 3.38).
Anorexia	Loss of appetite which prevents or markedly reduces eating. When severe and ongoing, it is accompanied by weight loss.
Constipation	Passing faeces less frequently than normal and/or passing hard faeces. Normal frequency varies greatly between individuals between 3 times daily and 3 times per week.
Diarrhoea	Unusually frequent passing of loose or watery faeces. Normally most fluid in the GI tract is reabsorbed (see Fig. 12.28). Diarrhoea arises when water reabsorption from the intestines is reduced and/or intestinal motility is increased.
Dysphagia	Difficulty swallowing
Haematemesis	Vomiting of blood, either fresh blood or partly digested (described as '*coffee grounds*').
Melaena	Passing blood in the faeces. Very small amounts are only found by testing for *faecal occult* (hidden) *blood* (FOB).
Nausea	Feeling of sickness, which usually precedes vomiting. It may be accompanied by profuse salivation and tachycardia.
Vomiting	An (involuntary) reflex in which there is forceful ejection of stomach contents through the mouth. Vomiting follows stimulation of, for example the pharynx, oesophagus, stomach or the vomiting centre in the medulla, e.g. by drugs. Co-ordinated by the medulla; the glottis closes, the diaphragm contacts, the upper oesophageal sphincter relaxes; strong waves of reverse peristalsis in the stomach then expel its contents upwards. If severe, consequences include disturbance of fluid, electrolyte and acid-base balance (metabolic alkalosis, as excessive H^+ is lost).

This section considers disorders of the digestive system. Table 12.4 lists some common signs and symptoms of gastrointestinal disorders.

Diseases of the mouth

Learning outcomes

After studying this section, you should be able to:

- discuss the main inflammatory and infectious conditions of the mouth
- outline the sites and effects of oral squamous cell carcinoma
- distinguish between cleft lip and cleft palate, including describing the anatomical abnormalities involved.

Inflammatory and infectious conditions

Injury may be caused to tissues in and around the mouth by food and other ingested substances, if they are corrosive, abrasive or excessively hot or cold. The mouth contains a large number and variety of normally harmless commensal micro-organisms. The antibacterial action of saliva helps to limit their growth, but the presence of dental plaque and residual foodstuffs, especially sugars, in the mouth can promote infection. Inflammation of the mouth is known as *stomatitis*, and inflammation of the gums as *gingivitis*.

Thrush (oral candidiasis)

This acute fungal infection is caused by the yeast *Candida albicans*, which occurs when the commensal microbe grows in white patches on the tongue and oral mucosa. In adults it causes opportunistic infection mainly in debilitated people and in those whose immunity is lowered by, e.g., steroids, antibiotics or cytotoxic drugs. In children it occurs most commonly in bottle-fed babies. *Chronic thrush* may develop, affecting the roof of the mouth in people who wear dentures. The fungus survives in fine grooves on the upper surface of the denture and repeatedly reinfects the oral mucosa. The same fungus is also responsible for sexually transmitted infections (p. 466).

Gingivitis

This is inflammation of the gums, which may be acute or, much more commonly, chronic. Chronic gingivitis is a common inflammatory condition that occurs in response to accumulation of bacterial plaque around the teeth. It causes bleeding gums and gradually destroys the tissues that support the teeth, which eventually loosen and may fall out.

Recurrent aphthous ulceration

This common condition features extremely painful ulcers that occur singly or in crops in any part of the mouth. The cause is unknown.

Viral infections

These are usually caused by one type of herpes simplex virus, HSV-1.

Acute herpetic gingivostomatitis. Inflammation of the mouth and gums is caused by herpes simplex-1 virus and is the most common oral virus infection. It is characterised by extensive and very painful ulceration.

Secondary or recurrent herpes lesions (cold sores). Lesions, caused by herpes simplex-1 virus, occur round the nose and on the lips. After an outbreak the viruses remain dormant within local nerves. Later outbreaks, usually at the same site, are precipitated by a variety of stimuli including exposure to UV rays (strong sunlight) and impaired immune response.

Tumours of the mouth

Squamous cell carcinoma

This is the most common type of malignant tumour in the mouth. It affects mainly older adults and carries a poor prognosis. The usual sites are the floor of the mouth and the edge of the tongue. Ulceration occurs frequently and there is early spread to surrounding tissues and cervical lymph nodes, in which case, the prognosis is poor.

Congenital disorders

Cleft palate and cleft lip (harelip)

During embryonic development, the roof of the mouth (hard palate) develops as two separate (right and left) halves; this occurs from the lips anteriorly to the uvula posteriorly. Before birth, these two halves normally fuse along the midline (Fig. 12.45A). If fusion is incomplete, a cleft (division) remains, which may be very minor, or it may be substantial. *Cleft lip* (Fig. 12.45B) ranges from a minor notch in the upper lip to a more extensive condition when the lip is completely split in one or two places and the nose is involved. In *cleft palate*, there is a gap between the two halves of the palate, which creates a channel of communication between the mouth and the nasal cavity (Fig. 12.45C). Contributing factors include genetic abnormalities, and certain drugs or poor nutrition between weeks 7 and 12 of pregnancy.

Drinking, eating and development of speech cannot take place normally until the defect has been surgically repaired.

Dental caries

Tooth decay starts with discolouration and then formation of cavities (caries). It arises when bacteria present in

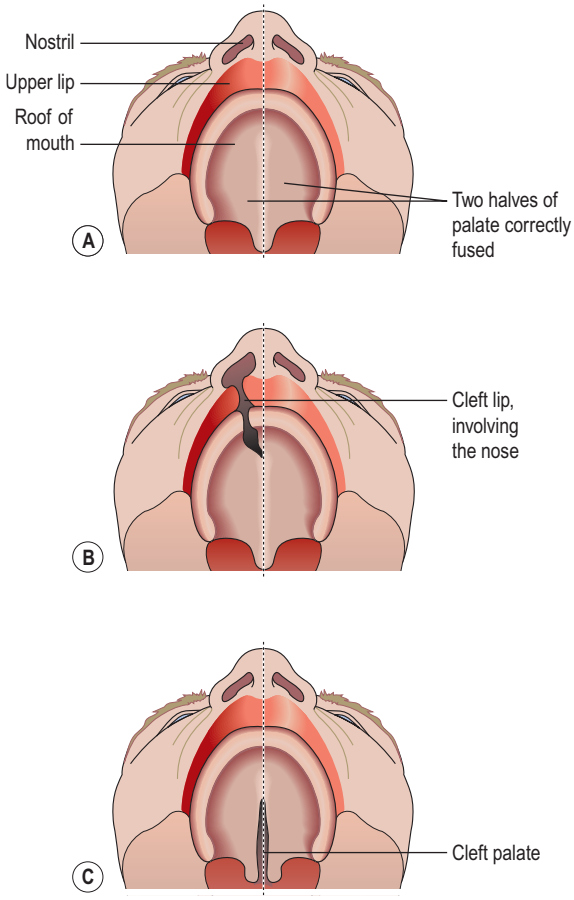

Figure 12.45 Cleft lip and cleft palate. A. Normal hard palate. **B.** Cleft lip. **C.** Cleft palate.

plaque on the teeth act on sugars forming acid, which may eventually destroy the hard parts of the teeth. Caries can be prevented by good oral hygiene.

Diseases of the pharynx

See tonsillitis and diphtheria (p. 262).

Diseases of salivary glands

Learning outcomes

After studying this section, you should be able to:

- outline the pathophysiology of mumps
- describe the most common tumours of the salivary glands.

Mumps

This is an acute inflammatory condition of the salivary glands, especially the parotids. It is caused by the mumps virus, one of the parainfluenza group. The virus is spread by inhalation of infected droplets. Viruses multiply elsewhere in the body before spreading to the salivary glands. The virus is most infectious for 1–2 days before and 5 days after symptoms appear. Complications may affect:

- the brain, causing meningitis (see Ch. 7) or meningoencephalitis
- the testes, causing orchitis (testicular inflammation) after puberty and sometimes atrophy of the glands and sterility.

In developed countries, children are usually vaccinated against mumps in their preschool years.

Tumours of the salivary glands

Salivary adenoma

This benign tumour occurs mainly in the parotid gland and is the most common tumour of the salivary glands. A second tumour may develop in the same gland several years after the first has been removed and it occasionally undergoes malignant change.

Carcinoma

Malignant tumours most commonly affect the parotid glands. Some forms have a tendency to infiltrate nerves in the surrounding tissues, causing severe pain. Lymph spread is to the cervical nodes.

Diseases of the oesophagus

Learning outcomes

After studying this section, you should be able to:

- explain how oesophageal varices develop
- discuss the main inflammatory conditions of the oesophagus
- describe the main oesophageal tumours
- define oesophageal atresia and tracheo-oesophageal fistula.

Oesophageal varices (Fig. 12.46)

In conditions such as cirrhosis (p. 334) or venous thrombosis, blood flow into the liver via the portal vein is impeded and blood pressure within the portal system rises (*portal hypertension*). This forces blood from the portal vein into anastomotic veins, which redirect (shunt) blood into the systemic venous circulation, bypassing the liver. Fifty percent or more of the portal blood may be shunted into anastomotic veins, leading to rising pressure in these veins too. One route taken by the shunted blood is into veins of the lower oesophagus, which become distended and weakened by the abnormally high volume of blood. *Varices* (localised dilations of veins) develop when

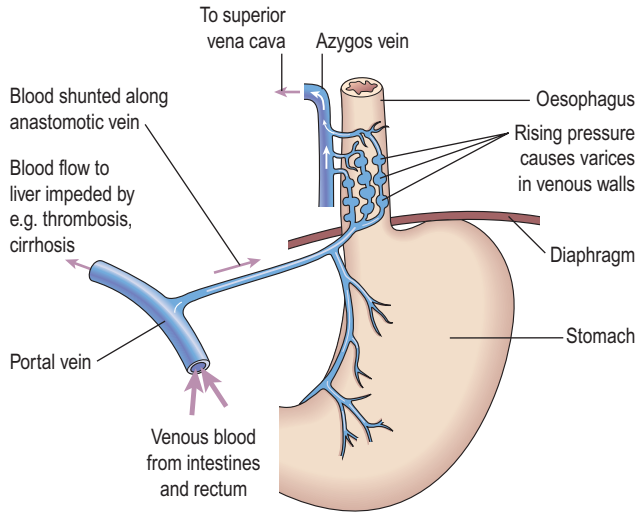

Figure 12.46 Oesophageal varices.

the weakest regions of the vessel wall bulge outwards into the lumen of the oesophagus, and, being thin walled and fragile, they are easily eroded or traumatised by swallowed food. Bleeding may be slight, but chronic, leading to iron deficiency anaemia (p. 74); however, sudden rupture can cause life-threatening haemorrhage.

Inflammatory and infectious conditions

Acute oesophagitis

This arises after caustic materials are swallowed and also if immunocompromised people acquire severe fungal infections, typically candidiasis (p. 320), or viral infections, e.g. herpes simplex. *Dysphagia* (difficulty in swallowing) is usually present. Following severe injury, healing often causes fibrosis, and there is a risk of oesophageal stricture developing later, as the fibrous tissue shrinks.

Gastro-oesophageal reflux disease (GORD)

This condition, the commonest cause of indigestion (or 'heartburn'), is caused by persistent regurgitation of acidic gastric juice into the oesophagus, causing irritation, inflammation and painful ulceration. Haemorrhage occurs when blood vessels are eroded. Persistent reflux leads to chronic inflammation and if damage is extensive, secondary healing with fibrosis occurs. Shrinkage of mature fibrous tissue may cause stricture of the oesophagus. This condition sometimes gives rise to Barrett's oesophagus (see below). Reflux of gastric contents is associated with:

- increase in the intra-abdominal pressure, e.g. in pregnancy, constipation and obesity
- low levels of secretion of the hormone gastrin, leading to reduced sphincter action at the lower end of the oesophagus
- the presence of hiatus hernia (p. 329).

Barrett's oesophagus

This condition develops after long-standing reflux oesophagitis. Columnar cells resembling those found in the stomach replace the squamous epithelium of the lower oesophagus. This is a premalignant state carrying an increased risk of subsequent malignancy.

Achalasia

This may occur at any age but is most common in middle life. Peristalsis of the lower oesophagus is impaired and the lower oesophageal sphincter fails to relax during swallowing, causing dysphagia, regurgitation of gastric contents and aspiration pneumonia. The oesophagus becomes dilated and the muscle layer hypertrophies. Autonomic nerve supply to the oesophageal muscle is abnormal, but the cause is not known.

Tumours of the oesophagus

Benign tumours are rare, accounting for only 5% of oesophageal tumours.

Malignant tumours

These occur more often in males than females. They are most common in the lower oesophagus but can arise at any level. Both types of tumour, described below, tend to begin as an ulcer that spreads round the circumference causing a stricture that results in dysphagia. By the time of diagnosis, local spread has usually occurred and the prognosis is very poor.

The geographical incidence of *squamous cell carcinoma* varies greatly worldwide. It is associated with long-term high alcohol intake and cigarette smoking. Other predisposing factors are believed to include obesity, low fruit and vegetable consumption, and chewing betel nuts or tobacco.

Adenocarcinoma usually develops from Barrett's oesophagus (see above).

Congenital abnormalities

The most common congenital abnormalities of the oesophagus are:

- *oesophageal atresia*, in which the lumen is narrow or blocked
- *tracheo-oesophageal fistula*, in which there is an opening (fistula) between the oesophagus and the trachea through which milk or regurgitated gastric contents are aspirated.

One or both abnormalities may be present. The causes are unknown.

Diseases of the stomach

Learning outcomes

After studying this section, you should be able to:

- compare the main features of chronic and acute gastritis
- discuss the pathophysiology of peptic ulcer disease
- describe the main tumours of the stomach and their consequences
- define the term congenital pyloric stenosis.

Gastritis

Inflammation of the stomach can be an acute or chronic condition.

Acute gastritis

This is usually a response to irritant drugs or alcohol. The drugs most commonly implicated are non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin, even at low doses, although many others may also be involved. Other causes include the initial response to *Helicobacter pylori* infection (see below) and severe physiological stress, e.g. extensive burns and multiple organ failure.

There are varying degrees of severity. Mild cases can be asymptomatic or may present with nausea and vomiting associated with inflammatory changes of the gastric mucosa. Erosions, which are characterised by tissue loss affecting the superficial layers of the gastric mucosa may also occur. In more serious cases, multiple erosions may result in life-threatening haemorrhage causing *haematemesis* (vomiting of frank blood or black 'coffee grounds' when there has been time for digestion of blood to occur) and *melaena* (passing black tarry faeces), especially in older adults.

The outcome depends on the extent of the damage. In many cases recovery is uneventful after the cause is removed. Where there has been extensive tissue damage, healing is by fibrosis causing reduced elasticity and peristalsis.

Chronic gastritis

Chronic gastritis is a milder but longer-lasting condition. It is usually associated with *Helicobacter pylori* but is sometimes due to autoimmune disease or chemical injury. It is more common in later life.

***Helicobacter*-associated gastritis.** *Helicobacter pylori* is a bacterium that can survive in the gastric mucosa and is commonly associated with gastric conditions, especially chronic gastritis and peptic ulcer disease.

Autoimmune chronic gastritis. This is a progressive disease. Destructive inflammatory changes that begin on the surface of the mucous membrane may extend to affect its whole thickness, including the gastric glands. When this stage is reached, secretion of hydrochloric acid and intrinsic factor are markedly reduced. The antigens are the gastric parietal cells and the intrinsic factor they secrete. When the parietal cells are destroyed as a result of this autoimmune condition, the inflammation subsides. The causes of the autoimmunity are not known but there is a familial predisposition and an association with thyroid disorders. Secondary consequences include:

- pernicious anaemia due to lack of intrinsic factor (p. 74)
- increased risk of cancer of the stomach.

Peptic ulcer disease

Ulceration involves the full thickness of the gastrointestinal mucosa and penetrates the muscle layer (Fig. 12.47). It is caused by disruption of the normal balance between the corrosive effect of gastric juice and the protective effect of mucus on the gastric epithelial cells. It may be viewed as an extension of the gastric erosions found in acute gastritis. The most common sites for ulcers are the stomach and the first few centimetres of the duodenum. More rarely they occur in the oesophagus and round the anastomosis of the stomach and small intestine, following gastrectomy. The incidence of peptic ulcers is greater in men than women and increases with age. The underlying causes are not known but there is a strong association with *H. pylori* infection. It is believed that *H. pylori,* some drugs, e.g. non-steroidal anti-inflammatory drugs (NSAIDs), and smoking may impair the gastric mucosal defences in some people. However, *H. pylori* is present in many people who show no signs of peptic ulcer disease.

If gastric mucosal protection is impaired, the epithelium can be exposed to gastric acid causing the initial cell

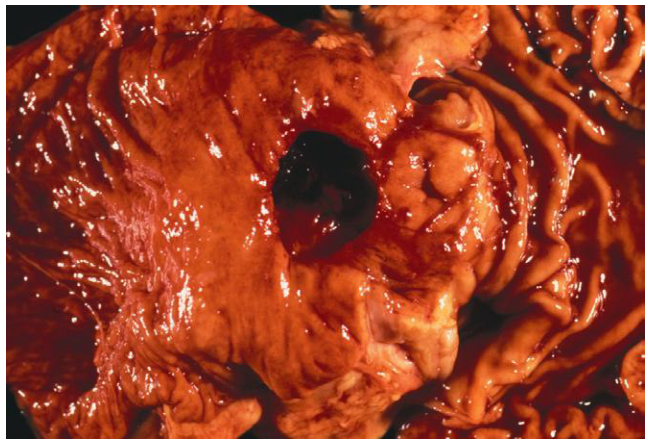

Figure 12.47 Peptic ulceration: a large duodenal ulcer.

damage that leads to ulceration. The main protective mechanisms are: a good blood supply, adequate mucus secretion and efficient epithelial cell replacement.

Blood supply. Reduced blood flow and ischaemia may be caused by cigarette smoking and severe stress, either physical or mental. In stressful situations the accompanying sympathetic activity causes constriction of the blood vessels supplying the alimentary tract.

Secretion of mucus. The composition and the amount of mucus may be altered, e.g.:

- by regular and prolonged use of aspirin and other anti-inflammatory drugs
- by the reflux of bile acids and salts
- in chronic gastritis.

Epithelial cell replacement. There is normally a rapid turnover of gastric and intestinal epithelial cells. This may be reduced:

- by raised levels of steroid hormones, e.g. in response to stress or when they are used as drugs
- in chronic gastritis
- by radiotherapy and cytotoxic drugs.

Acute peptic ulcers

These lesions may be single or multiple. They are found in many sites in the stomach and in the first few centimetres of the duodenum. Their development is often associated with acute gastritis, severe stress, e.g. severe illness, shock, burns, severe emotional disturbance and following major surgery. Healing without the formation of fibrous tissue usually occurs when the stressor is removed, although haemorrhage, which may be life-threatening, can be a complication.

Chronic peptic ulcers

These ulcers are 2–3 times more common in the duodenum than the stomach. They usually occur singly in the pylorus of the stomach or in the duodenum. *H. pylori* is found in 90% of people with duodenal ulcers and in 70% of those with gastric ulcers. The remaining gastric ulcers are almost entirely due to NSAIDs. Smoking predisposes to peptic ulceration and delays healing. Healing occurs with the formation of fibrous tissue and its subsequent shrinkage may cause:

- stricture of the lumen of the stomach
- gastric outflow obstruction or stenosis of the pyloric sphincter
- adhesions to adjacent structures, e.g. pancreas, liver, transverse colon.

Complications of peptic ulcers

Haemorrhage When a major artery is eroded a serious and possibly life-threatening haemorrhage may occur, causing shock (p. 118), haematemesis and/or melaena.

Perforation When an ulcer erodes through the full thickness of the wall of the stomach or duodenum their contents enter the peritoneal cavity, causing acute peritonitis (p. 325).

Infected inflammatory material may collect under the diaphragm, forming a *subphrenic abscess* (see Fig. 12.48) and the infection may spread through the diaphragm to the pleural cavity.

Anaemia Chronic persistent low level bleeding from an ulcer may lead to development of iron deficiency anaemia (p. 74).

Gastric outflow obstruction Also known as *pyloric stenosis*, fibrous tissue formed as an ulcer in the pyloric region heals, causes narrowing of the pylorus that obstructs outflow from the stomach and results in persistent vomiting.

Malignancy This is frequently associated with chronic gastritis caused by *H. pylori*.

Tumours of the stomach

Benign tumours of the stomach are rare.

Malignant tumours

This is a common malignancy that occurs more frequently in men than women and the incidence increases sharply after 50 years of age. The causes have not been established, but there appears to be a link with *Helicobacter pylori* infection in some 60–70% of cases. Smoking, alcohol and diets high in salted, smoked and pickled food have also been implicated. Local growth of the tumour gradually destroys the normal tissue so that achlorhydria (reduced hydrochloric acid secretion) and pernicious anaemia are frequently secondary features. As the tumour grows, the surface may ulcerate and become infected, especially when achlorhydria develops.

This condition carries a poor prognosis because spread has often already occurred prior to diagnosis. Local spread is to adjacent organs, e.g. the oesophagus, duodenum and pancreas and also to the peritoneal cavity when the outermost layer, the serosa, is affected. Spread via the blood is by the hepatic portal vein to the liver where tumour cells may lodge causing metastases. Lymphatic spread is also common, initially to nearby nodes and later to more distant ones.

Congenital pyloric stenosis

In this condition there is spasmodic constriction of the pyloric sphincter, characteristic projectile vomiting and failure to put on weight. In an attempt to overcome the spasms, hypertrophy of the muscle of the pylorus develops, causing pyloric obstruction 2–3 weeks after birth. The cause is not known but there is a familial tendency and this condition is more common in boys.

Diseases of the intestines

Learning outcomes

After studying this section, you should be able to:

- describe appendicitis and its consequences
- discuss the principal infectious disease of the intestines
- compare and contrast the features of Crohn's disease and ulcerative colitis
- distinguish between diverticulitis and diverticulosis
- describe the main tumours of the intestines
- describe the abnormalities present in hernia, volvulus and intussusception
- list the main causes of intestinal obstruction
- compare the causes and outcomes of primary and secondary malabsorption.

Diseases of the small and large intestines are described together because they have certain characteristics in common and some conditions affect both.

Appendicitis

The lumen of the appendix is very small and there is little room for swelling when it becomes inflamed. The initial cause of inflammation is not always clear. Microbial infection is commonly superimposed on obstruction by, for example, hard faecal matter (*faecoliths*), kinking or a foreign body. Inflammatory exudate, with fibrin and phagocytes, causes swelling and ulceration of the mucous membrane lining. In the initial stages, the pain of appendicitis is usually located in the central area of the abdomen. After a few hours, the pain typically shifts and becomes localised to the region above the appendix (the right iliac fossa). In mild cases the inflammation subsides and healing takes place. In more severe cases microbial growth progresses, leading to suppuration, abscess formation and further congestion. The rising pressure inside the appendix occludes first the veins, then the arteries and ischaemia develops, followed by gangrene and rupture.

Complications of appendicitis

Peritonitis. The peritoneum becomes acutely inflamed, the blood vessels dilate and excess serous fluid is secreted. It occurs as a complication of appendicitis when:

- microbes spread through the wall of the appendix and infect the peritoneum
- an appendix abscess (Fig. 12.48) ruptures and pus enters the peritoneal cavity

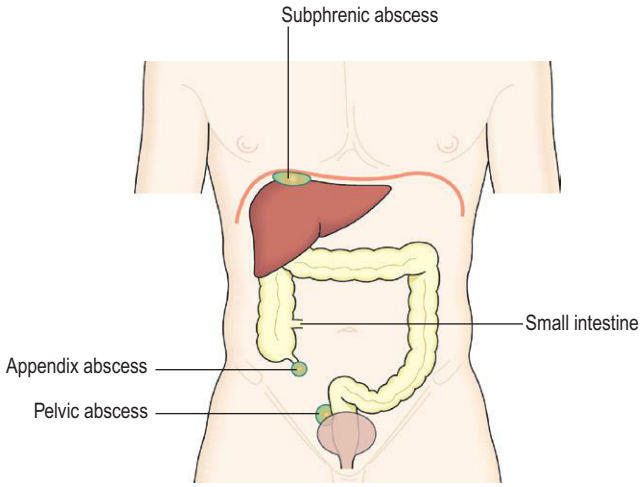

Figure 12.48 Abscess formation: complication of appendicitis.

- the appendix becomes gangrenous and ruptures, discharging its contents into the peritoneal cavity.

Abscess formation. The most common are:

- *subphrenic abscess*, between the liver and diaphragm, from which infection may spread upwards to the pleura, pericardium and mediastinal structures
- *pelvic abscess* from which infection may spread to adjacent structures (Fig. 12.48).

Adhesions. When healing takes place bands of fibrous scar tissue (adhesions) form and later shrinkage may cause:

- stricture or obstruction of the bowel
- limitation of the movement of a loop of bowel, which may twist around the adhesion causing a type of bowel obstruction called a volvulus (p. 330).

Gastrointestinal infections

The incidence of these diseases varies considerably but they represent a major cause of morbidity and mortality worldwide. Public health measures including clean, safe drinking water and effective sewage disposal, and safe food hygiene practices greatly reduce their spread: many are highly contagious. As many are spread by the faecal–oral route, meticulous handwashing after defaecation and contact between the hands and any potentially contaminated material is essential, especially in healthcare facilities. Contamination of drinking water results in diarrhoeal diseases that are a major cause of illness in all age groups and infant death in developing countries.

Typhoid and paratyphoid (enteric) fever

Typhoid and paratyphoid fevers are caused by *Salmonella typhi* and *S. paratyphi A* or *B*, respectively. Both are common in some tropical countries and both are spread by the faecal–oral route from food, water or fomites

contaminated by individuals either suffering from the illness or who are carriers (see below).

The incubation period is about 10–14 days during which time bacteria invade the lymphoid tissue of the small intestine, especially the aggregated lymph follicles (Peyer's patches). Thereafter, the microbes spread via the blood to the liver, spleen and gallbladder. A bacteraemic period (febrile illness) follows accompanied by malaise, headache, drowsiness and aching limbs. The intestinal lymphoid tissue becomes acutely inflamed and ulcerated although healing usually follows. The spleen becomes enlarged (splenomegaly) and red spots are typically seen on the skin, especially of the chest and back.

Without treatment, severe, and often fatal, illness is common 2 weeks after the onset of illness. Complications due to spread of microbes during the bacteraemic phase include pneumonia, meningitis and typhoid cholecystitis in which microbes multiply in the gall bladder and are secreted in the bile, reinfecting the intestine (Fig. 12.49). Bacterial toxins can cause disorders of the heart (myocarditis, Ch. 5) and kidneys (nephritis, Ch.13). In the bowel, ulcers may perforate a blood vessel wall resulting in haemorrhage or erode the intestinal wall causing acute peritonitis.

A few individuals (up to 5%) may become carriers where there is asymptomatic but chronic infection of the gall bladder. Continued release of microbes into the bile for months or years after recovery leads to infection of the faeces; much less often the urinary system is also involved and microbes are released into the urine. Carriers may transmit the infection to others through contact with their infected faeces or urine.

Paratyphoid fever follows a similar course but is usually milder and of shorter duration although the onset can be more sudden; complications are less frequent. Some people may become carriers, but fewer than in typhoid fever.

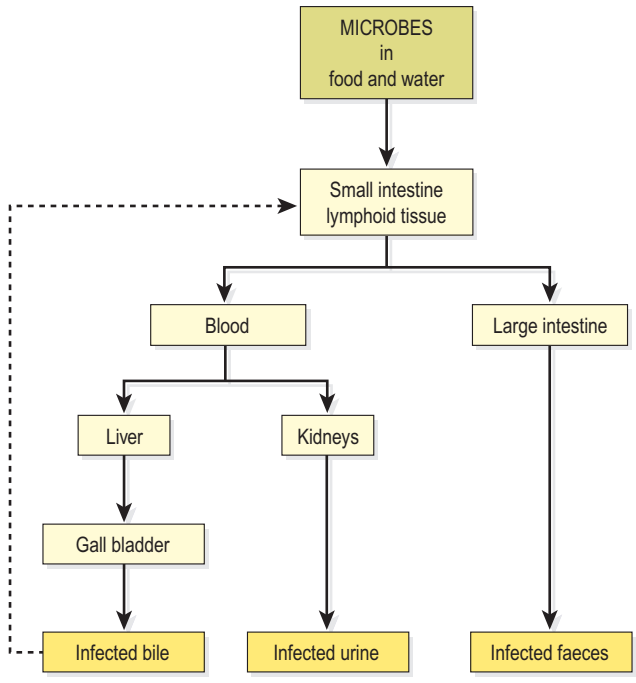

Figure 12.49 The routes of excretion of microbes in typhoid and paratyphoid (enteric) fever.

Other Salmonella infections

Salmonella typhimurium and *S. enteritidis* are the most common bacteria in this group. Generally the effects are confined to the gastrointestinal tract, unlike the *Salmonella* infections above. In addition to humans their hosts are domestic animals and birds. The microbes may be present in meat, poultry, eggs and milk, causing infection if cooking does not achieve sterilisation. Mice and rats also carry the organisms and may contaminate food before or after cooking.

The incubation period is 12–72 hours; enteritis is usually short lived and accompanied by acute abdominal pain and diarrhoea, which may cause dehydration and electrolyte imbalance. Sometimes vomiting is present. In children and debilitated older adults the infection may be severe or even fatal.

Escherichia coli (E. coli) food poisoning

Common sources of these bacteria include undercooked meat and unpasteurised milk; adequate cooking and pasteurization kill *E. coli*. The severity of the disease depends on the type of *E. coli* responsible; some types are more virulent than others. Outbreaks of *E. coli* food poisoning can cause fatalities, particularly in young children and older adults.

Staphylococcal food poisoning

After eating contaminated food, *Staphylococcus aureus* releases toxins that cause acute gastroenteritis (rather than the bacteria that cause the condition). Although cooking kills the bacteria, the toxins are heat resistant.

There is usually short-term acute inflammation with violent vomiting occurring 2–4 hours after ingestion, which may cause dehydration and electrolyte imbalance. Diarrhoea may not be significant. In most cases complete recovery occurs within 24 hours.

Clostridium perfringens food poisoning

These commensal bacteria are normally present in the intestines of humans and animals, but can cause food poisoning when ingested in large numbers. Meat may be contaminated at any stage between slaughter and the consumer. Outbreaks of food poisoning are associated with large-scale cooking, e.g. in institutions. Slow cooling after cooking and/or slow reheating allow microbial multiplication. When they reach the intestines, the bacteria release a toxin that causes watery diarrhoea and severe abdominal pain. The illness is usually self-limiting.

Antibiotic-associated diarrhoea

The bacterium *Clostridium difficile* is already present in the large intestine, but after antibiotic therapy many other commensal intestinal bacteria die. This allows *C. difficile* to take over and multiply, releasing toxins that damage the mucosa of the large intestine causing profound diarrhoea. Significant inflammation of the large intestine (colitis), which is often fatal in older adults and debilitated people, may occur as a complication.

Campylobacter food poisoning

These Gram-negative bacilli are a common cause of gastroenteritis accompanied by fever, acute pain and sometimes bleeding. They affect mainly young adults and children under 5 years. The bacteria are present in the intestines of birds and animals, and are spread in undercooked poultry and meat. They may also be spread in water and milk. Pets, such as cats and dogs, may be a source of infection. There is an association with Guillain–Barré syndrome (Ch. 7).

Cholera

Cholera is caused by *Vibrio cholerae*, which is spread by contaminated drinking water, faeces, vomit, food, hands and fomites. The only known hosts are humans. In some infected people, known as subclinical cases, no symptoms occur, although these people can transmit the condition to others while their infection remains. A very powerful toxin is released by the bacteria, which stimulates the intestinal glands to secrete large quantities of water, bicarbonate and chloride. This leads to persistent diarrhoea, severe dehydration and electrolyte imbalance, and may cause death due to hypovolaemic shock.

Dysentery

Bacillary dysentery. This infection of the large intestine is caused by bacteria of the *Shigella* group. The severity of the condition depends on the organisms involved. In the UK it is usually a relatively mild condition caused by *Shigella sonnei*. *Shigella dysenteriae* causes the most severe type of infection and it occurs mainly in developing countries. Children and older debilitated adults are particularly susceptible. The only host is humans and the organisms are spread by faecal contamination of food, drink, hands and fomites.

The intestinal mucosa becomes inflamed, ulcerated and oedematous with excess mucus secretion. In severe infections, the acute diarrhoea, that contains blood and excessive mucus, causes dehydration, electrolyte imbalance and anaemia. When healing occurs the mucous membrane is fully restored.

Amoebiasis (amoebic dysentery). This disease is caused by the protozoan *Entamoeba histolytica*. The only known hosts are humans and it is spread by faecal contamination of food, water, hands and fomites. Although many infected people do not develop symptoms they may become asymptomatic carriers.

The amoebae grow, divide and invade the mucosal cells, causing inflammation within the colon (colitis). Without treatment the condition frequently becomes chronic with mild, intermittent diarrhoea and abdominal pain. This may progress with ulceration of the colon accompanied by persistent and debilitating diarrhoea that contains mucus and blood. Complications are unusual but include severe haemorrhage from ulcers and liver abscesses.

Viral gastroenteritis

Several viruses, including rotavirus and norovirus, are known to cause vomiting and/or diarrhoea.

Rotavirus. This is a major cause of diarrhoea in young children. It is easily spread in healthcare facilities.

Norovirus. Also known as the '*winter vomiting virus*', this is responsible for outbreaks of acute but self-limiting enteritis with vomiting as the main symptom. Most common in the winter months, it spreads easily in families and in child and healthcare facilities. Spread is by the faecal–oral route but airborne transmission by inhalation may also occur.

Inflammatory bowel disease (IBD)

This term includes Crohn's disease and ulcerative colitis. A comparison of the main features is shown in Table 12.5; however, it is not always possible to distinguish these conditions in practice. Their aetiology is unknown but is thought to involve environmental and immune factors in genetically susceptible individuals. Both conditions typically have a pattern of relapse and remission.

Crohn's disease

This chronic inflammatory condition of the alimentary tract usually occurs in young adults. The terminal ileum and the rectum are most commonly affected but the disease may affect any part of the tract. There is chronic patchy inflammation with oedema of the full thickness of the intestinal wall, causing partial obstruction of the lumen, sometimes described as *skip lesions*. There are periods of remission of varying duration. The main symptoms are diarrhoea, abdominal pain and weight loss. Complications include:

- secondary infections, occurring when inflamed areas ulcerate
- fibrous adhesions and subsequent intestinal obstruction caused by the healing process
- fistulae between intestinal lesions and adjacent structures, e.g. loops of bowel, surface of the skin (p. 370)
- perianal fistulae, fissures and skin tags
- cancer of the small or large intestine.

Table 12.5 Comparison of the main features of Crohn's disease and ulcerative colitis

	Crohn's disease	Ulcerative colitis
Incidence	Usually between 20 and 40 years of age (mean 26 years); both sexes affected equally; smokers at higher risk	Usually between 20 and 40 years of age (mean 34 years); both sexes affected equally; smoking not a risk factor
Main sites of lesions	Anywhere in digestive tract from mouth to anus; common in terminal ileum	Rectum always involved, with variable spread along colon
Tissue involved	Entire thickness of the wall affected; ulcers and fistulae common	Only mucosa involved
Nature of lesions	'Skip' lesions, i.e. diseased areas interspersed with regions of normal tissue; ulcers and fistulae common	Continuous lesion; mucosa is red and inflamed
Prognosis	In severe cases, surgery may improve condition, but relapse rate very high, slightly increased risk of cancer	Surgical removal of entire colon cures the condition, significantly increased risk of cancer

Ulcerative colitis

This is a chronic inflammatory disease of the mucosa of the colon and rectum, which may ulcerate and become infected. It usually occurs in young adults and begins in the rectum. From there it may spread proximally to involve a variable proportion of the colon and, sometimes, the entire colon. The main symptom is bloody diarrhoea. There are periods of remission lasting weeks, months or years. Individuals may develop other systemic problems affecting, for example, the joints (ankylosing spondylitis, p. 433), skin and liver. In long-standing cases, cancer sometimes develops.

Toxic megacolon is an acute complication where the colon loses its muscle tone and dilates. There is a high risk of electrolyte imbalance, perforation and hypovolaemic shock, which may be fatal if untreated.

Diverticular disease

Diverticula are small pouches of mucosa that protrude (herniate) into the peritoneal cavity through the circular muscle fibres of the colon between the taeniae coli (Fig. 12.50). The walls consist of mucous membrane with a covering of visceral peritoneum. They occur at the weakest points of the intestinal wall, i.e. where the blood vessels enter, most commonly in the sigmoid colon.

The causes of *diverticulosis* (presence of diverticuli) are not known but it is associated with deficiency of dietary fibre. In Western countries, diverticulosis is fairly common after middle age but is usually asymptomatic.

Diverticulitis arises as a consequence of diverticulosis when faeces impact the diverticula. The walls become inflamed and oedematous as secondary infection develops. This reduces the blood supply causing ischaemic abdominal pain. Occasionally, rupture occurs resulting in peritonitis (p. 325).

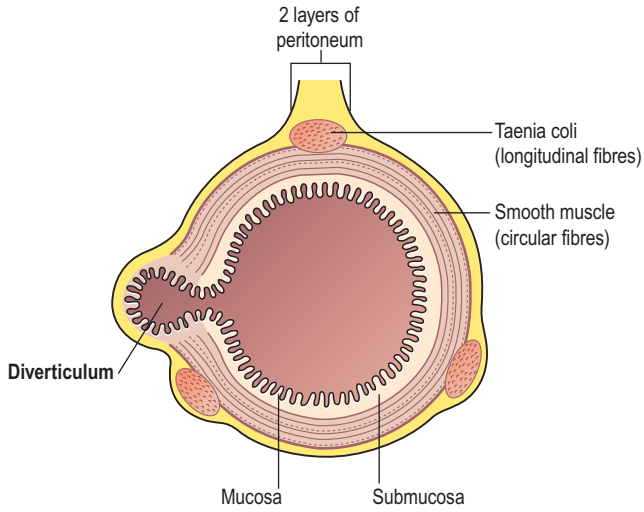

Figure 12.50 Diverticular disease: cross-section of bowel showing one diverticulum.

Tumours of the small and large intestines

Benign and malignant tumours of the small intestine are rare, especially compared with their occurrence in the stomach, large intestine and rectum.

Benign tumours

Benign neoplasms may form a broad-based mass or polyp, i.e. develop a pedicle. Occasionally polyps twist upon themselves, causing ischaemia, necrosis and, sometimes, gangrene. Malignant changes may occur in adenomas, which are mostly found in the large intestine. The incidence is high in developed countries.

Colorectal cancer

This is the most common malignancy of the alimentary tract in Western countries and, as a cause of cancer-related death, is second only to lung cancer in the UK.

The most important predisposing factor for colorectal cancer is thought to be diet. In cultures eating a high-fibre, low-fat diet, the disease is virtually unknown, whereas in Western countries, where large quantities of red meat and saturated animal fat and insufficient fibre are eaten, the disease is much more common. Slow movement of bowel contents may result in conversion of unknown substances present into carcinogenic agents. Genetic factors are also implicated. Predisposing diseases include ulcerative colitis and some benign tumours (usually adenomas).

The tumours are adenocarcinomas with about half arising in the rectum, one-third in the sigmoid colon and the remainder elsewhere in the colon. The tumour may be:

- a soft polypoid mass, projecting into the lumen of the colon or rectum with a tendency to ulceration, infection and bleeding
- a hard fibrous mass encircling the colon, causing narrowing of the lumen and, eventually, obstruction.

Local spread of intestinal tumours occurs early but may not be evident until there is severe ulceration and haemorrhage or obstruction. Spread can be outwards through the wall into the peritoneal cavity and adjacent structures.

Lymph-spread metastases occur in mesenteric lymph nodes, the peritoneum and other abdominal and pelvic organs. Pressure caused by enlarged lymph nodes may cause obstruction or damage other structures.

Blood-spread metastases are most common in the liver, brain and bones.

Hernias

A hernia is a protrusion of an organ or part of an organ through a weak point or aperture in the surrounding structures. In those affecting the digestive system, a piece of bowel protrudes through a weak point in either the musculature of the anterior abdominal wall or an existing opening (Fig. 12.51A). It occurs when there are intermittent increases in intra-abdominal pressure, most commonly in men who lift heavy loads at work. Outcomes include:

- spontaneous reduction, i.e. the loop of bowel slips back to its correct place when the intra-abdominal pressure returns to normal
- manual reduction, i.e. by applying gentle pressure over the abdominal swelling
- *strangulation* (Fig. 12.51B), when reduction is not possible and the venous drainage from the herniated loop of bowel is impaired, causing congestion, ischaemia and gangrene. In addition there is intestinal obstruction (p. 330).

Sites of hernias (Fig. 12.51A)

Inguinal hernia. The weak point is the inguinal canal, which contains the spermatic cord in the male and the

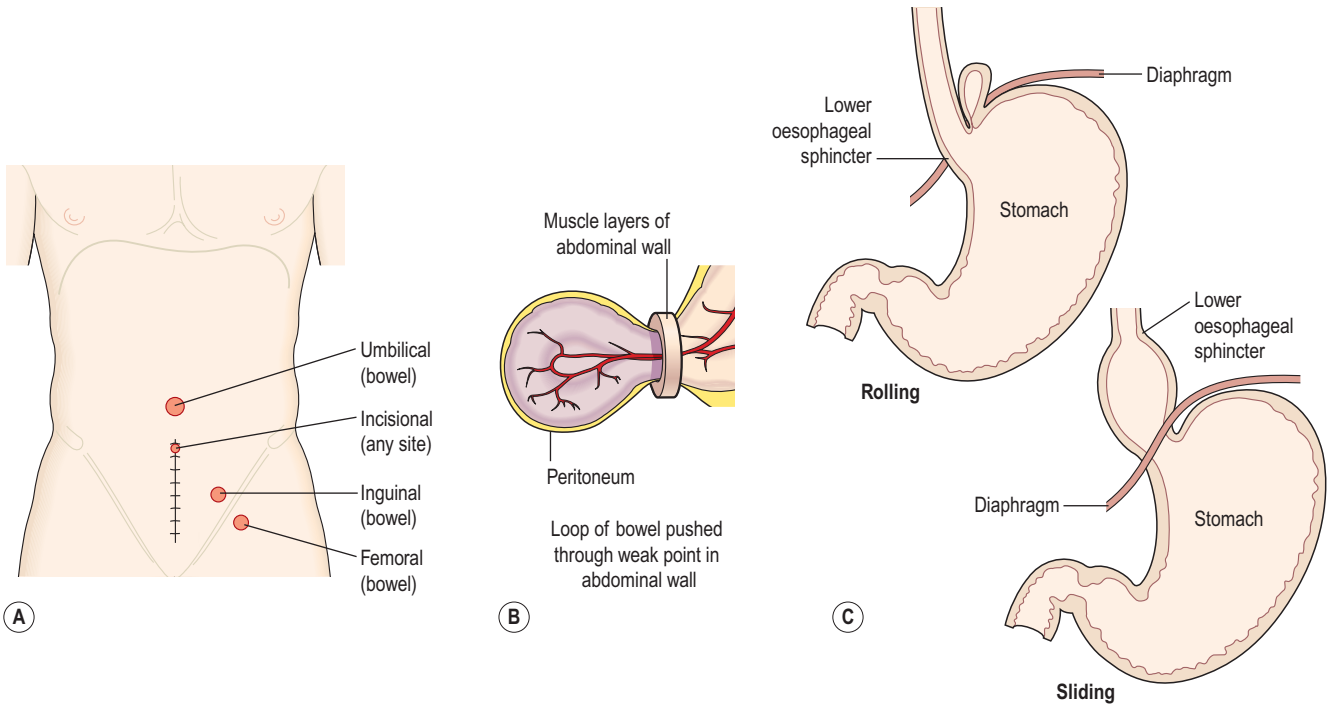

Figure 12.51 Hernias. A. Common sites of herniation. **B.** Strangulated hernia formation. **C.** Hiatus hernia.

round ligament in the female. It occurs more commonly in males than in females.

Femoral hernia. The weak point is the femoral canal through which the femoral artery, vein and lymph vessels pass from the pelvis to the thigh.

Umbilical hernia. The weak point is the umbilicus where the umbilical blood vessels from the placenta entered the fetus before birth.

Incisional hernia. This is caused by repeated stretching of fibrous (scar) tissue formed after previous abdominal surgery.

Hiatus hernia. This is the protrusion of a part of the fundus of the stomach through the oesophageal opening in the diaphragm (Fig. 12.51C). Although often asymptomatic, irritation of the oesophagus only occurs when there is reflux of acid gastric juice, especially when the individual lies flat or bends down. The long-term effects may be oesophagitis, fibrosis and narrowing of the oesophagus, causing dysphagia. Strangulation does not occur.

Rolling hiatus hernia An abnormally large opening in the diaphragm allows a pouch of stomach to 'roll' upwards into the thorax beside the oesophagus. This is associated with obesity and increased intra-abdominal pressure.

Sliding hiatus hernia Part of the stomach is pulled upwards into the thorax. The abnormality may be caused by shrinkage of fibrous tissue formed during healing of a previous oesophageal injury. The sliding movement of the stomach in the oesophageal opening is due to shortening of the oesophagus by muscular contraction during swallowing.

Peritoneal hernia. A loop of bowel may herniate through the epiploic foramen (of Winslow, Fig. 12.3A), the opening in the lesser omentum that separates the greater and lesser peritoneal sacs.

Congenital diaphragmatic hernia. Incomplete formation of the diaphragm, usually on the left side, allows abdominal organs such as the stomach and loops of intestine into the thoracic cavity, preventing normal development of the fetal lungs.

Volvulus

This occurs when a loop of bowel twists occluding its lumen resulting in obstruction. It is usually accompanied by *strangulation*, where there is interruption of the blood supply causing gangrene. It occurs in parts of the intestine that are attached to the posterior abdominal wall by the mesentery (a long double fold of visceral peritoneum. The most common site in adults is the sigmoid colon and in children the small intestine. Predisposing factors include:

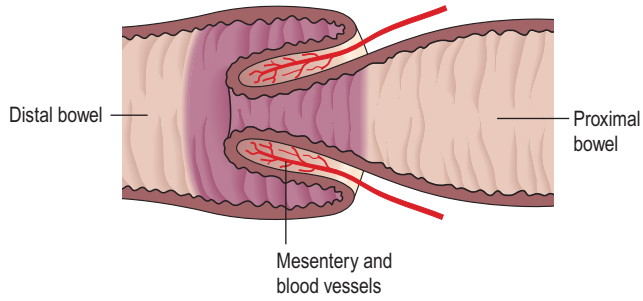

Figure 12.52 Intussusception.

- an unusually long mesentery
- heavy loading of the sigmoid colon with faeces
- a slight twist of a loop of bowel, causing gas and fluid to accumulate, which promotes further twisting
- adhesions formed following surgery or peritonitis.

Intussusception

In this condition a length of intestine is invaginated into itself causing intestinal obstruction (Fig. 12.52). It occurs most commonly in children when a piece of terminal ileum is pushed through the ileocaecal valve. The overlying mucosa bulges into the lumen, creating a partial obstruction and a rise in pressure inside the intestine proximal to the swelling. Strong peristaltic waves develop in an attempt to overcome the partial obstruction. These push the swollen piece of bowel into the lumen of the section immediately distal to it, creating the intussusception. The pressure on the veins in the invaginated portion is increased, causing congestion, further swelling, ischaemia and possibly gangrene. Complete intestinal obstruction may occur. In adults, tumours that bulge into the lumen, e.g. polyps, together with the strong peristalsis, may be the cause.

Intestinal obstruction

This is not a disease in itself but arises as a consequence of many other conditions. The summary below outlines effects and main causes of obstruction.

Mechanical causes

These include:

- constriction or blockage of the intestine by, for example, a strangulated hernia, intussusception, volvulus, peritoneal adhesions; partial obstruction (narrowing of the lumen) that suddenly becomes complete
- stenosis and thickening of the intestinal wall, e.g. in diverticulosis, Crohn's disease and malignant tumours; there is usually

a gradual progression from partial to complete obstruction
- physical causes where the obstruction is by, for example, a large gallstone or a tumour growing into the lumen
- pressure on the intestine from outside, e.g. from a large tumour in any pelvic or abdominal organ, such as a uterine fibroid; this is most likely to occur inside the confined space of the pelvic cavity.

Neurological causes of obstruction

Partial or complete loss of peristaltic activity produces the effects of obstruction. *Paralytic ileus* is the most common form. The mechanisms are not clear but there are well-recognised predisposing conditions including major surgery requiring considerable handling of the intestines and peritonitis.

Secretion of water and electrolytes continues although intestinal mobility is lost and absorption impaired. This causes distension and electrolyte imbalance, leading to hypovolaemic shock.

Vascular causes of obstruction

When the blood supply to a segment of bowel is cut off, ischaemia is followed by infarction and gangrene. The damaged bowel becomes unable to function. The causes may be:

- atheromatous changes in the blood vessel walls, with thrombosis (p. 119)
- embolism (p. 120)
- mechanical obstruction of the bowel, e.g. strangulated hernia (p. 329).

Effects of intestinal obstruction

Symptoms include abdominal pain, vomiting and constipation. When the upper gastrointestinal tract is affected vomiting may be profuse, although it may be absent in lower bowel obstruction. There are neither bowel sounds present nor passing of flatus (wind) as peristalsis ceases. Without treatment, irrespective of the cause, this condition is fatal.

Malabsorption

Impaired absorption of nutrients and water from the intestines is not a disease in itself, but the result of abnormal changes in one or more of the following:

- villi in the small intestine, e.g. coeliac disease, tropical sprue (see below)
- digestion of food
- absorption or transport of nutrients from the small intestine.

Intestinal conditions that impair normal digestion and/or absorption and transport of nutrients include:

- extensive resection of the small intestine
- 'blind loop syndrome' where there is microbial overgrowth in a blind end of intestine following surgery
- lymphatic obstruction by diseased or absent (following surgical excision) lymph nodes.

Coeliac disease

This disease is the main cause of malabsorption in Western countries. It is due to an abnormal, genetically determined autoimmune reaction to the protein gluten, present in wheat, barley and rye. When it is removed from the diet, there is complete remission of symptoms. There is marked villous atrophy, especially in the jejunum, and malabsorption characterised by the passage of loose, pale-coloured, fatty stools (*steatorrhoea*).

T-cell function may be disordered causing abnormal immune reactions to other antigens as well. Atrophy of the spleen is common and malignancy of the small intestine is a rarer consequence. Sometimes other autoimmune conditions are also present. It often presents in infants after weaning but can affect people of any age.

Tropical sprue

This disease is endemic in subtropical and tropical countries except Africa. After visiting an endemic area most travellers suffering from sprue recover, but others may not develop symptoms until months or even years later.

There is partial villous atrophy with malabsorption, chronic diarrhoea, a variable degree of weight loss and pernicious anaemia due to deficient absorption of vitamin B_{12} and folic acid. The cause is unknown but it may be that microbial infection is a factor.

Diseases of the pancreas

Learning outcomes

After studying this section, you should be able to:

- compare and contrast the causes and effects of acute and chronic pancreatitis
- outline the main pancreatic tumours and their consequences.

Pancreatitis

Proteolytic enzymes produced by the pancreas are secreted in inactive forms, which are not activated until they reach the intestine; this protects the pancreas from digestion by its own enzymes. If these precursor enzymes are activated while still in the pancreas, pancreatitis results.

Acute pancreatitis

The severity of the disease is directly related to the amount of pancreatic tissue involved. Mild forms are more common and damage only those cells near the ducts. Recovery is usually complete.

Severe forms cause widespread damage with necrosis and haemorrhage. Common complications include infection, suppuration, and local venous thrombosis. Pancreatic enzymes, especially amylase, enter and circulate in the blood, causing similar damage to other structures. In severe cases there is a high mortality rate.

The causes of acute pancreatitis are not clear but known predisposing factors are gallstones and excessive use of alcohol. Other associated conditions include:

- pancreatic cancer (see below)
- viral infections, notably mumps
- kidney and liver transplantation
- hypercalcaemia
- severe hypothermia
- drugs, e.g. corticosteroids, some cytotoxic agents.

Chronic pancreatitis

This is either due to repeated attacks of acute pancreatitis or may arise gradually without evidence of pancreatic disease. This form is associated with irreversible structural changes. It is more common in men and is frequently associated with fibrosis and distortion of the main pancreatic duct. There is intestinal malabsorption when pancreatic secretions are reduced and diabetes mellitus (p. 236) occurs when damage affects the β-islet cells.

Protein material secreted by the acinar cells blocks the tiny acinar ducts. This eventually leads to the formation of encapsulated cysts, which are a feature of acute and chronic pancreatitis.

The most common cause in the Western world is excessive alcohol consumption. In developing countries dietary factors and malnutrition have been implicated. It is also associated with cystic fibrosis.

Cystic fibrosis (see p. 266)

Tumours of the pancreas

Benign tumours are very rare.

Malignant tumours

These are relatively common and affect more men than women. There is an association with cigarette smoking, excessive alcohol intake, use of aspirin and co-existing conditions, e.g. diabetes mellitus and chronic pancreatitis.

They occur most frequently in the head of the pancreas, obstructing the flow of bile and pancreatic juice into the duodenum. Jaundice, sometimes accompanied by itching, develops. Weight loss is the result of impaired digestion and absorption of fat, although anorexia and metabolic effects of the tumour may also play a role. Tumours in the body and tail of the gland rarely cause symptoms until the disease is advanced.

Irrespective of the site, metastases are often recognised before the primary tumour and therefore the prognosis is generally poor.

Diseases of the liver

Learning outcomes

After studying this section, you should be able to:

- compare and contrast the causes, forms and effects of chronic and acute hepatitis
- describe the main non-viral inflammatory conditions of the liver
- discuss the causes and consequences of liver failure
- describe the main liver tumours.

Liver tissue has a remarkable capacity for regeneration and therefore damage is usually extensive before it is evident. The effects of disease or toxic agents are seen when:

- regeneration of hepatocytes (liver cells) does not keep pace with damage, leading to hepatocellular failure
- there is a gradual replacement of damaged cells by fibrous tissue, leading to portal hypertension.

In most liver disease both conditions are present.

Acute hepatitis

Areas of necrosis develop as groups of hepatocytes die and the eventual outcome depends on the size and number of these areas. Causes of the damage may be a variety of conditions, including:

- viral infections
- toxic substances
- circulatory disturbances.

Viral hepatitis

Viral infections are the commonest cause of acute liver injury and different types are recognised. The types are distinguished serologically, i.e. by the antibodies produced to combat the infection. The severity of the ensuing disease caused by the different virus types varies considerably, but the pattern is similar. The viruses enter the liver cells, causing degenerative changes. An inflammatory reaction ensues, accompanied by production of an exudate containing lymphocytes, plasma cells and granulocytes. There is reactive hyperplasia of the hepatic macrophages (Kupffer cells) in the walls of the sinusoids.

As groups of cells die, necrotic areas of varying sizes develop, phagocytes remove the necrotic material and the lobules collapse. The basic lobule framework (Fig. 12.35) becomes distorted and blood vessels develop kinks. These changes interfere with the circulation of blood to the remaining hepatocytes and the resultant hypoxia causes further damage locally. Fibrous tissue develops in the damaged area and adjacent hepatocytes proliferate. The effect of these changes on the overall functioning of the liver depends on the size of the necrotic areas, the amount of fibrous tissue formed and the extent to which the blood and bile channels are distorted.

Hepatitis A

Previously known as 'infectious hepatitis', this type often occurs as epidemics in all parts of the world. It affects mainly children, causing a mild illness although it is often asymptomatic. Infection is spread by the faecal–oral route, e.g. via contaminated hands, food, water and fomites. Viruses are excreted in the faeces for 7–14 days before clinical symptoms appear and for about 7 days after. Symptoms may include general malaise followed by a period of jaundice (p. 336) that is accompanied by passing of dark urine and pale faeces. Antibodies develop and confer lifelong immunity after recovery. Subclinical disease may occur but not carriers.

Hepatitis B

Previously known as 'serum hepatitis', infection occurs at any age, but mostly in adults. The incubation period is from 50 to 180 days. The virus enters the blood and is spread by contaminated blood and blood products. People at greatest risk of infection are those who come in contact with blood and blood products in the course of their work, e.g. health-care workers. The virus is also spread by body fluids, i.e. saliva, semen, vaginal secretions, and from mother to fetus (vertical transmission). Others at risk include intravenous drug users and men who have sex with men. Antibodies are formed and immunity persists after recovery. Infection usually leads to severe illness lasting from 2 to 6 weeks, often followed by a protracted convalescence. Carriers may, or may not, have had clinical disease. Hepatitis B virus may cause massive liver necrosis and death. In less severe cases recovery may be complete. In others chronic hepatitis (see opposite) may develop; live viruses continue to circulate in the blood and other body fluids. The condition also predisposes to cirrhosis (see below) and liver cancer.

Hepatitis D. This virus contains no RNA and can only replicate in the presence of hepatitis B virus. It most often infects intravenous drug users who already have hepatitis B but also affects others with hepatitis B.

Box 12.1 Some hepatotoxic substances

Predictable group (dose related)	Unpredictable group (individual idiosyncrasy)
Alcohol	Phenothiazine compounds
Chloroform	Halothane
Cytotoxic drugs	Methyldopa
Tetracyclines	Indometacin
Anabolic steroids	Chlorpropamide
Paracetamol	Thiouracil
Some fungi	Sulphonamides

Hepatitis C

This virus is spread by blood and blood products, which accounts for the infection of many people with haemophilia. In countries, including the UK, where blood donors are now screened for the virus this route of transmission is now rare although it is prevalent in intravenous drug users. The infection is very frequently asymptomatic although a carrier state occurs. Infection is usually diagnosed later in life when cirrhosis (p. 334) or chronic liver failure becomes evident.

Toxic substances

Many drugs undergo chemical change in the liver before excretion in bile or by other organs. They may damage the liver cells in their original form or while in various intermediate stages. Some substances always cause liver damage (predictably toxic) while others only do so when hypersensitivity to normal doses develops (unpredictably toxic). In both types the extent of the damage depends on the size of the dose and/or the duration of exposure (Box 12.1).

Circulatory disturbances

The intensely active hepatocytes are particularly vulnerable to damage by hypoxia, which is usually due to impaired blood supply caused by:

- fibrosis in the liver following inflammation
- compression of the portal vein, hepatic artery or vein by a tumour
- acute general circulatory failure and shock
- venous congestion caused by acute or chronic right-sided heart failure (Ch. 5).

Chronic hepatitis

This is defined as any form of hepatitis which persists for more than 6 months. It may be caused by viruses, alcohol or drugs, but sometimes the cause is unknown.

Mild, persistent inflammation may follow acute viral hepatitis. There is usually little or no fibrosis.

There may be continuing progressive inflammation with cell necrosis and formation of fibrous tissue that may lead to cirrhosis of the liver. Distortion of the liver blood vessels causes localised hypoxia, leading to further hepatocyte damage. This condition is commonly associated with hepatitis B and C, some forms of autoimmunity and unpredictable (idiosyncratic) drug reactions.

Cirrhosis of the liver

This is the result of long-term injury caused by a variety of agents. The most common causes are:

- excessive alcohol consumption
- hepatitis B and C infections
- recurrent obstruction of the biliary tract.

Chronic liver damage results in inflammation, necrosis and, in time, affected tissue is replaced with fibrous tissue. Hyperplasia of hepatocytes occurs in areas adjacent to the damaged tissue in an attempt to compensate for destroyed cells, which leads to formation of nodules. The normal structure of the liver lobules becomes increasingly abnormal, usually over several years, which interferes with blood flow resulting in portal hypertension and its consequences (see p. 321), and impairment of liver cell function.

Liver failure may occur when cell regeneration is unable to keep pace with cell destruction, and there is increased risk of liver cancer developing.

Liver failure

This occurs when liver function is markedly impaired. It can be acute or chronic and may be the outcome of a wide variety of disorders, e.g.:

- acute viral hepatitis
- extensive necrosis due to poisoning, e.g. some drug overdoses, hepatotoxic chemicals, adverse drug reactions
- cirrhosis of the liver.

Liver failure has serious effects on other parts of the body.

Hepatic encephalopathy

This condition is characterised by apathy, disorientation, confusion and muscular rigidity, progressing to coma. The cells affected are the astrocytes in the brain and several factors may be involved, e.g.:

- nitrogenous bacterial metabolites absorbed from the colon, which are normally detoxified in the liver, reach the brain via the bloodstream
- other metabolites, normally present only in trace amounts, e.g. ammonia, may reach toxic concentrations and change the permeability of the cerebral blood vessels and the effectiveness of the blood–brain barrier
- hypoxia and electrolyte imbalance.

Blood coagulation defects

The liver fails to synthesise adequate supplies of blood clotting factors, i.e. prothrombin, fibrinogen and factors II, V, VII, IX and X; purpura, bruising and bleeding may occur.

Oliguria and renal failure

Portal hypertension may cause oesophageal varices (p. 321). If these rupture, severe haemorrhage may lead to a fall in blood pressure sufficient to reduce the renal blood flow, causing progressive oliguria and renal failure (p. 352).

Oedema and ascites

These may arise from one or both of the following factors:

- portal hypertension raises the capillary hydrostatic pressure in the organs drained by the tributaries of the portal vein (see Fig. 5.40, p. 110)
- diminished production of serum albumin and clotting factors reduces the plasma osmotic pressure.

Together these changes cause the movement of excess fluid into the interstitial spaces where it causes *oedema* (p. 125) as the fluid cannot leave the tissue. Eventually free fluid accumulates in the peritoneal cavity and the resultant *ascites* may be severe.

Jaundice

The following factors may cause jaundice as liver failure develops:

- inability of the hepatocytes to conjugate and excrete bilirubin
- obstruction to the movement of bile through the bile channels by fibrous tissue that has distorted the structural framework of liver lobules.

Tumours of the liver

Benign tumours are very rare.

Malignant tumours

Cancer of the liver is frequently associated with cirrhosis but the relationship between them is not clear. It may be that both cirrhosis and cancer are caused by the same agents or that the carcinogenic action of an agent is promoted by cirrhotic changes. Malignancy sometimes develops following hepatitis B and C. The most common sites of metastases are the abdominal lymph nodes, the peritoneum and the lungs.

Secondary malignant tumours (metastases) in the liver are more common than primary liver tumours. They usually spread there from primary tumours in the gastrointestinal tract, the lungs and the breast. These tumours tend to grow rapidly and are often the cause of death.

Diseases of the gall bladder and bile ducts

Learning outcomes

After studying this section, you should be able to:

- describe the causes and consequences of gallstones
- compare and contrast acute and chronic cholecystitis
- briefly outline the common sites and consequences of biliary tract tumours
- discuss the main causes and effects of jaundice.

Gallstones (cholelithiasis)

Gallstones consist of deposits of the constituents of bile, most commonly cholesterol. Many small stones or one or more large stones may form but they do not necessarily produce symptoms. Predisposing factors include:

- changes in the composition of bile that affect the solubility of its constituents
- high blood cholesterol levels
- diabetes mellitus
- female gender
- obesity
- several pregnancies in young women, especially when accompanied by obesity.

Cholecystitis

This is usually associated with the presence of gallstones.

Acute cholecystitis

This is acute inflammation of the gall bladder that occurs when a gallstone becomes impacted (stuck) in the cystic duct (Fig. 12.53), often after a fatty meal. Strong peristaltic contractions of the smooth muscle in the wall of the cystic duct that occur in an attempt to move the stone onwards result in *biliary colic*, severe acute pain in the epigastrium or right hypochondrium. This does not cause jaundice because bile from the liver can still pass directly into the duodenum. However, bile is unable to leave the gall bladder and an inflammatory reaction follows.

This may be complicated by bacterial infection and distension of the gall bladder, which carries the risk of perforation and peritonitis.

Chronic cholecystitis

The onset is usually insidious, sometimes following repeated acute attacks. Gallstones are invariably present and there may be accompanying biliary colic. Secondary infection with suppuration may develop. Without treatment, ulceration of the tissues between the gall bladder and the duodenum or colon may occur with fistula formation and, later, fibrous adhesions. This condition is associated with cancer of the gall bladder.

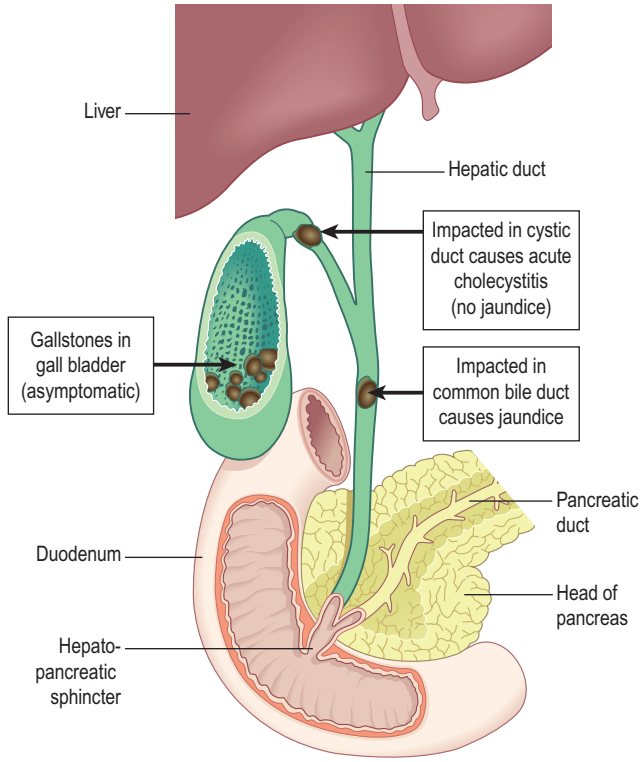

Figure 12.53 Effects of gallstones in different locations.

Cholangitis

This is inflammation of bile ducts caused by bacterial infection which is typically accompanied by abdominal pain, fever and jaundice (because the flow of bile into the duodenum is blocked). Infection can spread upwards in the biliary tree to the liver (*ascending cholangitis*) causing liver abscesses.

Tumours of the biliary tract

Benign tumours are rare.

Malignant tumours

These are relatively rare and gallstones are nearly always present. Local spread to the liver, the pancreas and other adjacent organs is common. Lymph and blood spread lead to widespread metastases. The tumour has often spread by the time of diagnosis and, therefore, the prognosis is poor.

Jaundice

This is not a disease in itself, but yellowing of the skin and mucous membrane is a sign of abnormal bilirubin metabolism and excretion. Bilirubin, produced from the breakdown of haemoglobin, is normally conjugated in the liver and excreted in the bile (Fig. 12.37). Conjugation makes bilirubin water-soluble and greatly enhances its removal from the blood, an essential step in excretion.

Unconjugated bilirubin, which is fat-soluble, has a toxic effect on brain cells. However, it is unable to cross the blood–brain barrier until the plasma level rises above 340 µmol/L, but when it does it may cause neurological damage, seizures (fits) and cognitive impairment. Serum bilirubin may rise to 40–50 µmol/L before the yellow coloration of jaundice is evident in the skin and conjunctiva (normal 3–13 µmol/L). Jaundice is often accompanied by *pruritus* (itching) caused by the irritating effects of bile salts on the skin.

Jaundice develops when there is an abnormality of bilirubin processing and the different types are considered below.

Types of jaundice

Whatever stage in bilirubin processing is affected, the end result is rising blood bilirubin levels.

Pre-hepatic jaundice

This is due to increased haemolysis of red blood cells (see Fig. 12.37) that results in production of excess bilirubin. Because the excess bilirubin is unconjugated it cannot be excreted in the urine, which therefore remains normal in colour.

Neonatal haemolytic jaundice occurs in many babies, especially in those born prematurely where the normally high rate of haemolysis is coupled with a shortage of conjugating enzymes in the hepatocytes of the still immature liver.

Intra-hepatic jaundice

This is the result of damage to the liver itself by, e.g.:

- viral hepatitis (p. 332)
- toxic substances, such as drugs
- amoebiasis (amoebic dysentery) (p. 327)
- cirrhosis (p. 334).

Excess bilirubin accumulates in the liver. Because it is mainly in the conjugated form, it is water-soluble and excreted in the urine making it dark in colour.

Post-hepatic jaundice

Causes of obstruction to the flow of bile in the biliary tract include:

- gallstones in the common bile duct (Fig. 12.53)
- tumour of the head of the pancreas
- fibrosis of the bile ducts, following cholangitis or injury by the passage of gallstones.

In this situation excess bilirubin is also conjugated and is therefore excreted in the urine. The effects of raised serum bilirubin include:

- pruritus (itching)
- pale faeces due to absence of stercobilin (p. 311)
- dark urine due to the presence of increased amounts of bilirubin.

For a range of self-assessment exercises on the topics in this chapter, visit Evolve online resources: https://evolve.elsevier.com/Waugh/anatomy/