11 Introduction to nutrition

Before discussing the digestive system it is necessary to have an understanding of the nutritional needs of the body, i.e. the dietary constituents and their functions within the body.

A *nutrient* is any substance that is digested, absorbed and utilised to promote body function. These substances are:

- carbohydrates
- proteins
- fats
- vitamins
- mineral salts
- water.

Many foods contain a number of nutrients, e.g. potatoes and bread are mainly carbohydrate but both contain protein and some vitamins. Foods are described as carbohydrate or protein because they contain a higher proportion of one or the other. *Fibre* consists of indigestible material. It is not a nutrient, as it is not digested, absorbed or utilised, but it has many beneficial effects on the digestive tract.

The *diet* is the selection of foods eaten by an individual. A *balanced diet* is essential for health. It provides the appropriate amounts of all nutrients in the correct proportions to meet the requirements of the body cells. An *essential nutrient* is a substance that cannot be made by the body and must therefore be included in the diet.

THE BALANCED DIET

Learning outcome

After studying this section, you should be able to:

- list the constituent food groups of a balanced diet.

A balanced diet contains all nutrients required for health in appropriate proportions, and is normally achieved by eating a variety of foods. If any nutrient is eaten in excess, or is deficient, health may be adversely affected. For example, a calorie-rich diet can lead to obesity, and an iron-deficient one to anaemia. Ensuring a balanced diet requires a certain amount of knowledge and planning. Recommendations for daily food intake sort foods of similar origins and nutritive values into food groups, and advise that a certain number of servings from each group be eaten daily (Fig. 11.1). If this plan is followed, the resulting dietary intake is likely to be well balanced.

The five main food groups are:

- bread, rice, cereal and pasta
- fruit and vegetables
- meat and fish
- dairy products, e.g. milk and cheese
- fats, oils and sweets.

Bread, rice, cereal and pasta

Most (50–60%) of the daily calorie requirements should come from these sources. In practice this means eating 6–11 servings from this food group every day. These foods contain large amounts of complex carbohydrates, which provide sustained energy release, as well as fibre.

one serving = one slice of bread, one small bread roll, two large crackers, 1 oz cereal

Fruit and vegetables

It is recommended that at least five portions should be eaten daily. Fruit and vegetables are high in vitamins, minerals and fibre, and (provided they have not been, for example, fried) are low in fat.

one serving = a medium apple, orange or banana; 100 g cooked/raw vegetables or tinned/fresh/cooked fruit; one wedge of melon; 125 ml fruit or vegetable juice

Meat, fish and alternatives

Current dietary habits in developed countries mean that too much of the daily calorific requirements are met from this group of foods (which includes eggs and nuts) and from high-fat foods. Although these foods are high in protein, and some vitamins and minerals, only 2–3 servings daily are recommended because they have a high fat content.

one serving = one egg, 30 g peanut butter, 80 g lean cooked meat

Dairy products

This group includes milk, cheese and yoghurt, and is high in calcium and vitamins. 2–3 servings per day are recommended. Dairy foods are often high in fat.

1 serving = 250 ml milk or yoghurt; 50 g cheese

Fats, oils and sweets

These foods provide high numbers of calories with little other nutritional value and should be used sparingly, if at all.

Certain groups of individuals may require a diet different from the principles outlined above. For example, pregnant and lactating women have higher energy

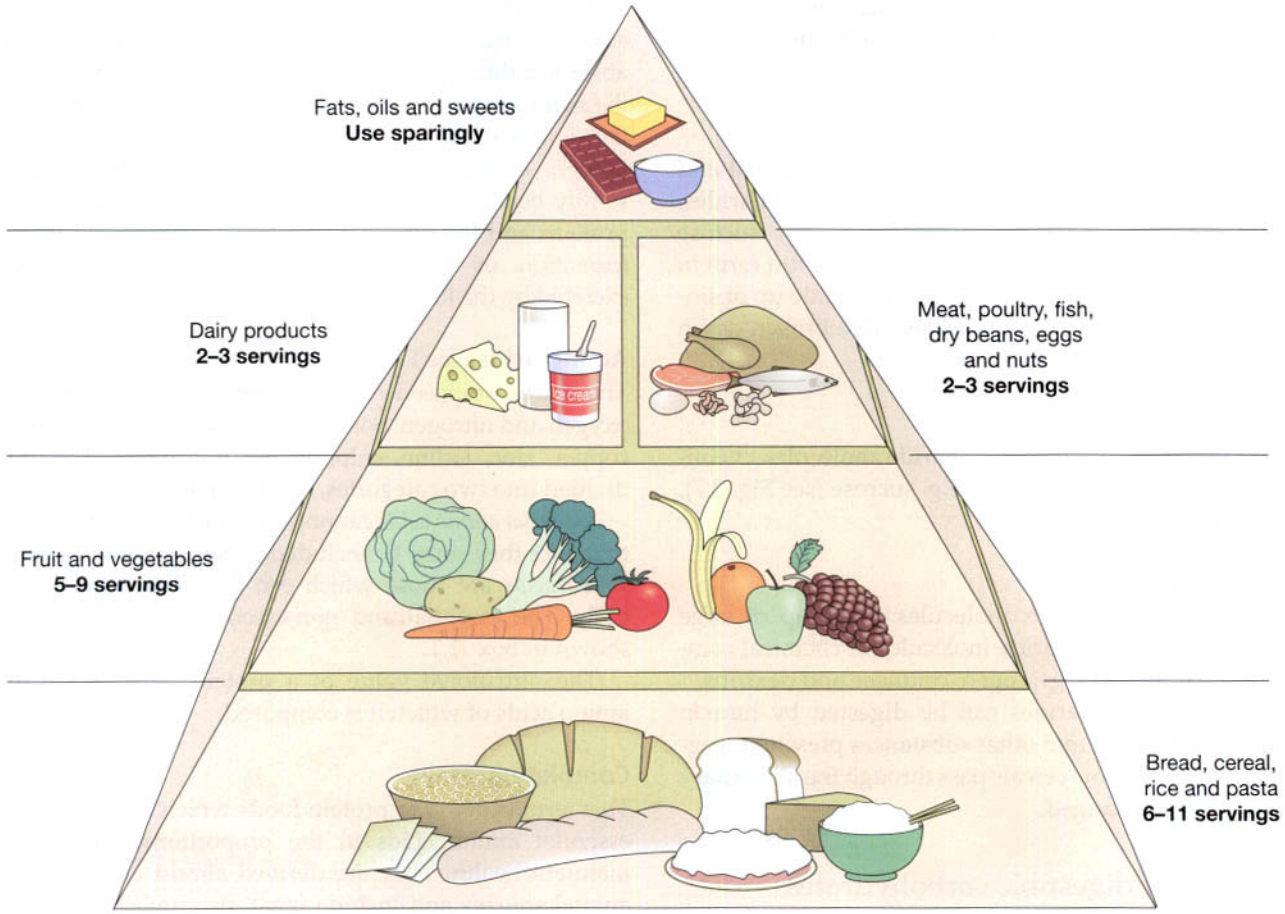


Figure 11.1 The main food groups and their recommended proportions within a balanced diet.

requirements to support the growing baby and milk production. Menstruating women need higher iron levels in their diet than non-menstruating women to compensate for blood loss during menstruation. Babies and growing children have higher fat requirements than adults because they have higher growth and metabolic rates. In some gastrointestinal disorders there is intolerance of certain foods which restricts that person's dietary choices, e.g. coeliac disease (p. 332).

Details of digestion, absorption and utilisation of nutrients are presented in Chapter 12. Structures and chemistry of carbohydrates, proteins and fats are described in Chapter 2.

CARBOHYDRATES

Learning outcomes

After studying this section, you should be able to:

- describe the main mono-, di- and polysaccharides
- list the nutritional function of digestible carbohydrates.

These are found in a wide variety of foods, e.g. sugar, jam, cereals, bread, biscuits, pasta, convenience foods, fruit and vegetables. They consist of carbon, hydrogen and oxygen, the hydrogen and oxygen being in the same

proportion as in water. Carbohydrates are classified according to the complexity of the chemical substances of which they are formed.

Monosaccharides

Carbohydrates are digested in the alimentary canal and when absorbed they are in the form of monosaccharides. Examples include glucose (see Fig. 2.7, p. 23), fructose and galactose. These are, chemically, the simplest form in which a carbohydrate can exist. They are made up of single units or molecules which, if they were broken down further, would cease to be sugars.

Disaccharides

These consist of two monosaccharide molecules chemically combined to form sugars, e.g. sucrose (see Fig. 2.7), maltose and lactose.

Polysaccharides

These consist of complex molecules made up of large numbers of monosaccharide molecules in chemical combination, e.g. starches, glycogen, cellulose and dextrins.

Not all polysaccharides can be digested by human beings; e.g. cellulose and other substances present in vegetables, fruit and some cereals pass through the alimentary canal almost unchanged.

Functions of digestible carbohydrates

These include:

- provision of rapidly available energy and heat
- 'protein sparing'; i.e., when there is an adequate supply of carbohydrate in the diet, protein does not need to be used to provide energy and heat
- provision of a store of energy when carbohydrate is eaten in excess of the body's needs as it is converted to fat and deposited in the fat depots, e.g. under the skin.

PROTEINS OR NITROGENOUS FOODS

Learning outcomes

After studying this section, you should be able to:

- describe the structure of amino acids, including essential and non-essential amino acids
- list the nutritional functions of dietary proteins.

Proteins are broken down into their constituent amino acids by digestion and it is in this form that they are absorbed through the intestinal wall. Dietary protein is the main source of nitrogen that can be used in the body. If it is absent from the diet the body goes into *negative nitrogen balance*. This is because amino acids are constantly being used to form enzymes, hormones and cell proteins and the turnover of cells is accompanied by the formation of nitrogenous waste materials that are excreted by the kidneys.

Amino acids (see Fig. 2.8)

These are composed of the elements carbon, hydrogen, oxygen and nitrogen. Some contain minerals such as iron, copper, zinc, iodine, sulphur and phosphate. They are divided into two categories, *essential* and *non-essential*.

Essential amino acids cannot be synthesised in the body, therefore they must be included in the diet. *Non-essential amino acids* are those which can be synthesised in the body. The essential and non-essential amino acids are shown in Box 11.1.

The nutritional value of a protein depends on the amino acids of which it is composed.

Complete proteins

This term is given to protein foods which contain all the essential amino acids in the proportions required to maintain health. They are derived almost entirely from animal sources and include meat, fish, milk, eggs, soya beans and milk products (excluding butter).

Box 11.1 Essential and non-essential amino acids

Essential amino acids	Non-essential amino acids
Isoleucine	Alanine
Leucine	Arginine
Lysine	Asparagine
Methionine	Aspartic acid
Phenylalanine	Cysteine
Threonine	Cystine
Tryptophan	Glutamic acid
Valine	Glutamine
Histidine	Glycine
	Hydroxyproline
	Proline
	Serine
	Tyrosine

Protein quality

The nutritional value of a protein (its *quality*) is measured by how well it meets the nutritional needs of the body. High-quality protein is usually of animal origin, easily digested and contains all essential amino acids in the proportions required by the body. One way of measuring a protein's quality is to feed it to animals and measure how much is retained in the body for growth and repair; this is called the *biological value* (BV). A balanced diet, containing all the amino acids required, may be achieved by eating a range of foods containing low-quality proteins, provided that deficiencies in amino acid content of any one of the constituent proteins of the diet is supplied by another. A balanced vegetarian diet, which consists primarily of lower-quality protein, e.g. vegetables, cereals and pulses, is based on this principle.

Functions of proteins

Amino acids are used for:

- growth and repair of body cells and tissues
- synthesis of enzymes, plasma proteins, antibodies (immunoglobulins) and some hormones
- provision of energy. Normally a secondary function, this becomes important only when there is not enough carbohydrate in the diet and fat stores are depleted.

When protein is eaten in excess of the body's needs, the nitrogenous part is detached, i.e. it is deaminated, and excreted by the kidneys. The remainder is converted to fat for storage in the fat depots, e.g. in the fat cells of adipose tissue (p. 316).

FATS

Learning outcomes

After studying this section, you should be able to:

- outline the main sources of dietary fat
- list the functions of fats in the body.

Saturated or *animal fat*, containing mainly saturated fatty acids and glycerol, is found in milk, cheese, butter, eggs, meat and oily fish such as herring, cod and halibut. All animal sources of protein contain some saturated fat.

Cholesterol is synthesised in the body and is also obtained in the diet from full fat dairy products, fatty meat and egg yolk.

Unsaturated or *vegetable fat*, containing mainly unsaturated fatty acids and glycerol, is found in some margarine and in most vegetable oils.

Linoleic, linolenic and arachidonic acids are polyunsaturated fatty acids that are essential in the diet because they cannot be synthesised in the body. They are the precursors of prostaglandins, thromboxanes and leukotrienes (p. 226).

Functions of fats

These include:

- provision of a source of chemical energy and heat
- support of certain body organs, e.g. the kidneys, the eyes
- transport and storage of the fat-soluble vitamins: A, D, E, K
- constituent of nerve sheaths and of sebum, the secretion of sebaceous glands in the skin
- formation of cholesterol and steroid hormones
- storage of energy as fat in adipose tissue under the skin and in the mesentery, when eaten in excess of requirements
- insulation—as a subcutaneous layer it reduces heat loss through the skin
- satiety value—when gastric contents (chyme) containing fat enter the duodenum, the emptying time of the stomach is prolonged, postponing the return of hunger.

VITAMINS

Learning outcomes

After studying this section, you should be able to:

- outline the sources and functions of the fat-soluble vitamins: A, D, E and K
- describe the sources and functions of the water-soluble vitamins: the vitamin B complex and C.

Vitamins are chemical compounds required in very small quantities which are essential for normal metabolism and health. They are found widely distributed in food and are divided into two main groups:

- fat-soluble vitamins: A, D, E and K
- water-soluble vitamins: B complex, C.

Fat-soluble vitamins

Vitamin A (retinol)

This vitamin is found in such foods as cream, egg yolk, liver, fish oil, milk, cheese and butter. It is absent from vegetable fats and oils but is added to margarine during manufacture. It can be formed in the body from certain carotenes, the main dietary sources of which are green vegetables, fruit and carrots. Vitamin A and carotene are only absorbed from the small intestine satisfactorily if fat absorption is normal. Although some is synthesised in the body the daily dietary requirement is 600 to 700 µg. The main roles of vitamin A in the body are:

- generation of the light-sensitive pigment rhodopsin (visual purple) in the retina of the eye
- cell growth and differentiation; this is especially important in fast-growing cells, such as the epithelial cells covering both internal and external body surfaces
- promotion of immunity and defence against infection
- promotion of growth, e.g. in bones.

The first sign of vitamin A deficiency is night blindness due to defective retinal pigment. Other consequences include xerophthalmia, which is drying and thickening of the conjunctiva and, ultimately, there is ulceration and destruction of the conjunctiva. This is a common cause of blindness in developing countries. Atrophy and keratinisation of other epithelial tissues leads to increased incidence of infections of the ear, and the respiratory, genitourinary and alimentary tracts. Immunity is compromised and bone development may be slow and faulty.

Vitamin D

Vitamin D_3 is found mainly in animal fats such as eggs, butter, cheese, fish liver oils. Humans and other animals can synthesise vitamin D by the action of the ultraviolet rays of the sun on a form of cholesterol in the skin (7-dehydrocholesterol).

Vitamin D regulates calcium and phosphate metabolism by increasing their absorption in the gut and stimulating their retention by the kidneys. It therefore promotes the calcification of bones and teeth.

Deficiency causes *rickets* in children and *osteomalacia* in adults, due to deficient absorption and utilisation of calcium and phosphate. The daily requirement is 10 µg and stores in fat and muscle are such that deficiency may not be apparent for several years.

Vitamin E

This is a group of eight substances called *tocopherols*. They are found in nuts, egg yolk, wheat germ, whole cereal, milk and butter.

Vitamin E is an antioxidant, which means that it protects body constituents such as membrane lipids from being destroyed in oxidative reactions. Deficiency is rare, because of the widespread occurrence of this vitamin in foods, and is usually seen only in premature babies and in conditions associated with impaired fat absorption, e.g. cystic fibrosis. Haemolytic anaemia occurs, as abnormal red blood cell membranes rupture. White blood cells can likewise be affected, and vitamin E supplements boost immune function. Neurological abnormalities such as ataxia and visual disturbances may occur if the deficiency is severe. Recently, vitamin E has been shown to protect against coronary artery disease. Recommended daily intake is 10 mg for men and 8 mg for women, but this should be increased in high-fat diets.

Vitamin K

The sources of vitamin K are fish, liver, leafy green vegetables and fruit. It is synthesised in the large intestine by microbes and significant amounts are absorbed. Absorption is dependent upon the presence of bile salts in the small intestine. The normal daily requirement is 1 µg/kg body weight and only a small amount is stored in the liver and spleen.

Vitamin K is required by the liver for the production of prothrombin and factors VII, IX and X, all essential for the clotting of blood (p. 67). Deficiency therefore prevents normal blood coagulation. It may occur in adults when there is obstruction to the flow of bile, severe liver damage and in malabsorption conditions, such as *coeliac disease*. Newborn infants may be given vitamin K because their intestines are sterile and require several weeks to become colonised with vitamin K-producing bacteria.

Water-soluble vitamins

Vitamin B complex

This is a group of water-soluble vitamins that promote activity of enzymes at various stages in the chemical breakdown (catabolism) of nutrients to release energy.

Vitamin B_1 (thiamine). This vitamin is present in nuts, yeast, egg yolk, liver, legumes, meat and the germ of cereals. It is rapidly destroyed by heat. The daily requirement

is 0.8 to 1 mg and the body stores only about 30 mg. Thiamine is essential for the complete aerobic release of energy from carbohydrate. When it is absent there is accumulation of lactic and pyruvic acids, which may lead to accumulation of tissue fluid (oedema) and heart failure. Thiamine is also important for nervous system function because of the dependency of these tissues on glucose for fuel.

Deficiency causes *beriberi* which occurs mainly in countries where polished rice is the chief constituent of the diet. In beriberi there is:

- severe muscle wasting
- stunted growth in children
- polyneuritis, causing degeneration of motor, sensory and some autonomic nerves
- susceptibility to infections.

If untreated, death occurs due to cardiac failure or severe microbial infection.

The main cause of thiamine deficiency in developed countries is chronic alcohol abuse, where the diet is usually poor. Neurological symptoms include memory loss, ataxia and visual disturbances; sometimes these are reversed with oral thiamine supplements.

Vitamin B_2 (riboflavine). Riboflavine is found in yeast, green vegetables, milk, liver, eggs, cheese and fish roe. The daily requirement is 1.1 to 1.3 mg and only small amounts are stored in the body. It is concerned with carbohydrate and protein metabolism, especially in the eyes and skin. Deficiency leads to:

- blurred vision, cataract formation and corneal ulceration
- cracking of the skin, commonly around the mouth (angular stomatitis)
- lesions of intestinal mucosa.

Folic acid. This is found in liver, kidney, fresh leafy green vegetables and yeast. It is synthesised by bacteria in the large intestine, and significant amounts derived from this source are believed to be absorbed. The daily requirement is 200 µg, and, as only a small amount is stored in the body, deficiency is evident within a short time. It is essential for DNA synthesis, and when lacking mitosis (cell division) is impaired. This manifests particularly in rapidly dividing tissues such as blood, and folate deficiency therefore leads to a type of megaloblastic anaemia (p. 70), which is reversible with folate supplements. Deficiency at conception and during early pregnancy is linked to an increased incidence of spina bifida (p. 189).

Niacin (nicotinic acid). This is found in liver, cheese, yeast, whole cereals, eggs, fish and nuts; in addition, the body can synthesise it from the amino acid tryptophan. It is associated with energy-releasing reactions in cells. In fat metabolism it inhibits the production of cholesterol and assists in fat breakdown. Deficiency occurs mainly in areas where maize is the chief constituent of the diet because niacin in maize is in an unusable form. The daily requirement is 12 to 17 mg.

Pellagra develops within 6 to 8 weeks of severe deficiency. It is characterised by:

- redness of the skin in parts exposed to light, especially in the neck
- anorexia, nausea, dysphagia and inflammation of the lining of the mouth
- delirium, mental disturbance and dementia.

Vitamin B_6 (pyridoxine). This is found in egg yolk, peas, beans, soya beans, yeast, meat and liver. The daily requirement is about 1.2 to 1.4 mg and dietary deficiency is rare, although certain drugs, e.g. alcohol and antituberculous drugs, antagonise the vitamin and can induce deficiency states. It is associated with amino acid metabolism, including the synthesis of non-essential amino acids and molecules such as haem and nucleic acids.

Vitamin B_{12} (cyanocobalamin). Vitamin B_{12} consists of a number of *cobalamin compounds* (containing cobalt). It is found in liver, meat, eggs, milk and fermented liquors. The normal daily requirement is 1.5 µg.

Like folic acid, vitamin B_{12} is essential for DNA synthesis, and deficiency also leads to a megaloblastic anaemia, which is correctable with supplements. However, vitamin B_{12} is also required for formation and maintenance of myelin, the fatty substance that surrounds and protects some nerves. Deficiency accordingly causes peripheral neuropathy and/or spinal cord degeneration. Such neurological changes are irreversible. The presence of intrinsic factor in the stomach is essential for vitamin B_{12} absorption and deficiency is usually associated with insufficient intrinsic factor (p. 70).

Pantothenic acid. This is found in many foods and is associated with amino acid metabolism. The daily safe intake is 3 to 7 mg and no deficiency diseases have been identified.

Biotin. This is found in yeast, egg yolk, liver, kidney and tomatoes and is synthesised by microbes in the intestine. It is associated with the metabolism of carbohydrates. The daily safe intake is 10 to 200 µg. Deficiency is rare.

Vitamin C (ascorbic acid)

This is found in fresh fruit, especially blackcurrants, oranges, grapefruit and lemons, and also in rosehips and green vegetables. The vitamin is very soluble in water and is easily destroyed by heat, so cooking may be a factor in the development of *scurvy*.

The daily requirement is 40 mg and after 2 to 3 months, deficient intake becomes apparent.

Vitamin C is associated with protein metabolism, especially the laying down of collagen fibres in connective tissue.

Vitamin C, like vitamin E, acts as an antioxidant, protecting body molecules from damaging oxidative reactions. When deficiency occurs, collagen production is affected, leading to fragility of blood vessels, delayed wound healing and poor bone repair. Gums become swollen and spongy and the teeth loosen in their sockets.

Summary of the vitamins

Tables 11.1 and 11.2 summarise the vitamins: their chemical names, sources, stability, functions, deficiency diseases and daily adult requirements.

MINERAL SALTS

Learning outcomes

After studying this section, you should be able to:

- list the commonest mineral salts required by the body
- describe their functions.

Mineral salts (inorganic compounds) are necessary within the body for all body processes, usually in only small quantities.

Calcium

This is found in milk, cheese, eggs, green vegetables and some fish. An adequate supply should be obtained in a normal, well-balanced diet, although requirements are higher in pregnant women and growing children. 99% of body calcium is found in the bones, where it is an essential

Table 11.1 Summary – fat-soluble vitamins (DoH 1991)

Vitamin	Chemical name	Source	Stability	Functions	Effects of deficiency	Daily recommended intake (adults)
A	Retinol (carotene provitamin in plants)	Milk, butter, cheese, egg yolk, fish, liver oils, green and yellow vegetables	Some loss at high temperatures and long exposure to light and air	Maintains healthy epithelial tissues and cornea. Formation of rhodopsin (visual purple)	Keratinisation Xerophthalmia Stunted growth Night blindness	600–700 µg
D	Calciferol	Fish, liver, oils, milk, cheese, egg yolk, irradiated 7-dehydrocholesterol in human skin	Very stable	Facilitates the absorption and use of calcium and phosphate in the maintenance of healthy bones and teeth	Rickets (children) Osteomalacia (adults)	10 µg
E	Tocopherols	Egg yolk, milk, butter, green vegetables, nuts	Stable in heat but oxidised by exposure to air	Antioxidant Promotes immune function	Anaemia Ataxia Visual disturbances	3–4 mg*
K	Phylloquinone	Leafy vegetables, fish, liver, fruit	Destroyed by light, strong acids and alkalis	Formation of prothrombin and factors VII, IX and X in the liver	Slow blood clotting Haemorrhages in the newborn	60–70 µg*

Bile is necessary for the absorption of these vitamins. Mineral oils interfere with absorption.
*Daily safe intake (DoH 1991). Data for recommended intake not available.

Table 11.2 Summary – water-soluble vitamins (DoH 1991)

Vitamin	Chemical name	Source	Stability	Functions	Effects of deficiency	Daily recommended intake (adults)
B_1	Thiamine	Yeast, liver, germ of cereals, nuts, pulses, rice polishings, egg yolk, liver, legumes	Destroyed by heat	Metabolism of carbohydrates and nutrition of nerve cells	General fatigue and loss of muscle tone Ultimately leads to beriberi Stunted growth	0.8–1 mg
B_2	Riboflavine	Liver, yeast, milk, eggs, green vegetables, kidney, fish roe	Destroyed by light and alkalis	Carbohydrate and protein metabolism Healthy skin and eyes	Angular stomatitis Dermatitis Eye lesions	1–1.3 mg
B_6	Pyridoxine	Meat, liver, vegetables, bran of cereals, egg yolk, beans	Stable	Protein metabolism	Very rare	1.2–1.4 mg
B_{12}	Cobalamins	Liver, milk, moulds, fermenting liquors, egg	Destroyed by heat	DNA synthesis	Megaloblastic anaemia Degeneration of nerve fibres of the spinal cord	1.5 μg
B	Folic acid	Dark green vegetables, liver, kidney, eggs Synthesised in colon	Destroyed by heat and moisture	DNA synthesis Normal development of spinal cord in early pregnancy	Anaemia Increased incidence of spina bifida	200 μg
B	Niacin (nicotinic acid)	Yeast, offal, fish, pulses, wholemeal cereals Synthesised in the body from tryptophan	Fairly stable	Necessary for cell respiration Inhibits production of cholesterol	Prolonged deficiency causes pellagra, i.e. dermatitis, diarrhoea, dementia	12–17 mg
B	Pantothenic acid	Liver, yeast, egg yolk, fresh vegetables	Destroyed by excessive heat and freezing	Associated with amino acid metabolism	Unknown	3–7 mg*
B	Biotin	Yeasts, liver, kidney, pulses, nuts	Stable	Carbohydrates and fat metabolism	Dermatitis, conjunctivitis Hypercholesterolaemia	10–200 μg*
C	Ascorbic acid	Citrus fruits, currants, berries, green vegetables, potatoes, liver and glandular tissue in animals	Destroyed by heat, ageing, acids, alkalis, chopping, salting, drying	Formation of collagen Maturation of RBCs Antioxidant	Multiple haemorrhages Slow wound healing Anaemia Gross deficiency causes scurvy	40 mg

*Daily safe intake (DoH 1991). Data for recommended intake not available.

structural component. Calcium is also involved in the coagulation of blood and the mechanism of muscle contraction.

Phosphate

Sources of phosphate include cheese, oatmeal, liver and kidney. If there is sufficient calcium in the diet it is unlikely that there will be a phosphate deficiency.

It is associated with calcium and vitamin D in the hardening of bones and teeth; 85% of body phosphate is found in these sites. Phosphates are an essential part of systems of energy storage inside cells as adenosine triphosphate (ATP, Fig. 2.12, p. 25).

Sodium

Sodium is found in most foods, especially fish, meat, eggs, milk, artificially enriched bread and as cooking and table salt. The normal intake of sodium chloride per day varies from 5 to 20 g and the daily requirement is 1.6 g. Excess is excreted in the urine.

It is the most commonly occurring *extracellular cation* and is associated with:

- contraction of muscles
- transmission of nerve impulses along axons
- maintenance of the electrolyte balance in the body.

Potassium

This substance is to be found widely distributed in all foods, especially fruit and vegetables. The normal intake of potassium chloride is 3.5 g per day and this is in excess of potassium requirements.

It is the most commonly occurring *intracellular cation* and is involved in many chemical activities inside cells including:

- contraction of muscles
- transmission of nerve impulses
- maintenance of the electrolyte balance in the body.

Iron

Iron, as a soluble compound, is found in liver, kidney, beef, egg yolk, wholemeal bread and green vegetables. In normal adults about 1 mg of iron is lost from the body daily. The normal daily diet contains more, i.e. 9 to 15 mg, but only 5–15% of intake is absorbed. Iron is essential for the formation of *haemoglobin* in the red blood cells. It is also necessary for oxidation of carbohydrate and in the synthesis of some hormones and neurotransmitters.

Iron deficiency is a relatively common condition, and causes anaemia if iron stores become sufficiently depleted. Menstruating and pregnant women have increased iron requirements, as do young people experiencing growth spurts. Iron deficiency anaemia may also occur in chronic bleeding, e.g. peptic ulcer disease.

Iodine

Iodine is found in salt-water fish and in vegetables grown in soil containing iodine. In some parts of the world where iodine is deficient in soil very small quantities are added to table salt. The daily requirement of iodine depends upon the individual's metabolic rate. Some people have a higher normal metabolic rate than others and their iodine requirements are greater. The daily requirement is 140 µg.

It is essential for the formation of *thyroxine* and *triiodothyronine*, two hormones secreted by the thyroid gland (p. 220).

FIBRE

Learning outcome

After studying this section, you should be able to:

- describe the sources and functions of dietary fibre.

Fibre is the indigestible part of the diet that comes from plants and meat. It consists of bran, cellulose and other polysaccharides. It is widely distributed in wholemeal flour, the husks of cereals and in vegetables. Dietary fibre is partly digested by microbes in the large intestine with gas (flatus) formation. The daily requirement of fibre is not less than 20 g.

Functions of dietary fibre

Fibre:

- provides bulk to the diet and helps to satisfy the appetite
- stimulates peristalsis (muscular activity) of the alimentary tract
- attracts water, increasing bulk and softness of faeces
- increases frequency of defecation preventing constipation
- prevents some gastrointestinal disorders, e.g. diverticular disease (p. 328).

WATER (see Fig. 2.4, p. 20)

Learning outcomes

After studying this section, you should be able to:

- explain the distribution of water within the body
- describe the functions of water within the body.

Water makes up about 70% of the body weight in men and about 60% in women.

A man weighing 65 kg contains about 40 litres of water, 28 of which are intracellular and 12 extracellular. Extracellular water consists of 2 to 3 litres in plasma and the remainder, interstitial fluid (see Fig. 2.16, p. 28).

A large amount of water is lost each day in faeces, sweat and urine. Under normal circumstances this is balanced by intake in food and to satisfy thirst. Dehydration with serious consequences may occur if intake does not balance loss.

Functions of water

These include:

- provision of the moist internal environment which is required by all living cells in the body, i.e. all the cells except the superficial layers of the skin, the nails, the hair and outer hard layer of the teeth
- participation in all the chemical reactions which occur inside and outside the body cells
- dilution and moistening of food (see saliva, p. 292)
- regulation of body temperature—as a constituent of sweat, which is secreted onto the skin, it evaporates, cooling the body surface (p. 365)
- a major constituent of blood and tissue fluid, it transports some substances in solution and some in suspension round the body
- dilution of waste products and poisonous substances in the body
- providing the medium for the excretion of waste products, e.g. urine and faeces.

DISORDERS OF NUTRITION

Learning outcome

After studying this section, you should be able to:

- describe the main consequences of malnutrition, malabsorption and obesity.

The importance of nutrition is increasingly recognised as essential for health, and illness often alters nutritional requirements.

Malnutrition

This may be due to:

- protein–energy malnutrition (PEM)
- vitamin deficiencies (Tables 11.1 and 11.2)
- both PEM and vitamin deficiencies.

Protein–energy malnutrition (Fig. 11.2)

This is the result of inadequate intake of protein, carbohydrate and fat. Infants and young children are especially susceptible as they need sufficient nutrients to grow and develop normally. If dietary intake is inadequate, it is not uncommon for vitamin deficiency to develop at the same time. Poor nutrition, or malnutrition, reduces the ability to combat other illness and infection.

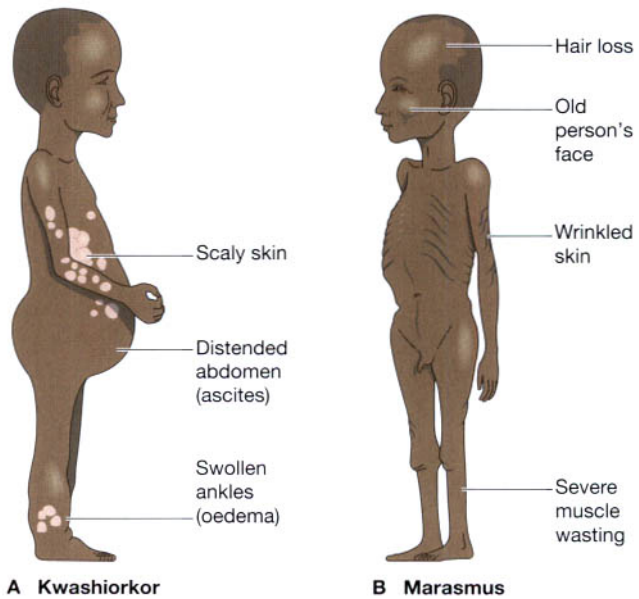


Figure 11.2 Features of protein–energy malnutrition.

Kwashiorkor

This is mainly caused by protein deficiency, and occurs in infants and children in some developing countries and when there has been serious drought and crop failure. Reduced plasma proteins lead to ascites and oedema (p. 118) in the lower limbs that masks emaciation. There is severe liver damage. Growth stops and there is loss of weight and loss of pigmentation of skin and hair accompanied by listlessness, apathy and irritability.

Marasmus

This is caused by deficiency of both protein and carbohydrate. It is characterised by severe emaciation due to breakdown (catabolism) of muscle and fat. Growth is retarded, the skin becomes wrinkled and hair is lost.

Malabsorption

The causes of malabsorption vary widely, from short-term problems such as gastrointestinal infections to chronic conditions such as cystic fibrosis. Malabsorption may be specific for one nutrient, e.g. vitamin B_{12} in pernicious anaemia (p. 70), or it may apply across a spectrum of nutrients, e.g. in tropical sprue (p. 332).

Obesity

This is a very common nutritional disorder in which there is accumulation of excess body fat. Clinically, obesity is present when body weight is 120% of that recommended for the height, age and sex of the individual. It occurs when energy intake exceeds energy expenditure, e.g. in inactive individuals eating more calories than they need for daily energy requirements.

Obesity predisposes to:

- gallstones (p. 336)
- cardiovascular diseases, e.g. ischaemic heart disease (p. 121), hypertension (p. 126)
- hernias (p. 329)
- varicose veins (p. 116)
- osteoarthritis (p. 426)
- type II (non-insulin-dependent) diabetes mellitus
- increased incidence of postoperative complications.

Phenylketonuria

(See p. 185.)

12 The digestive system

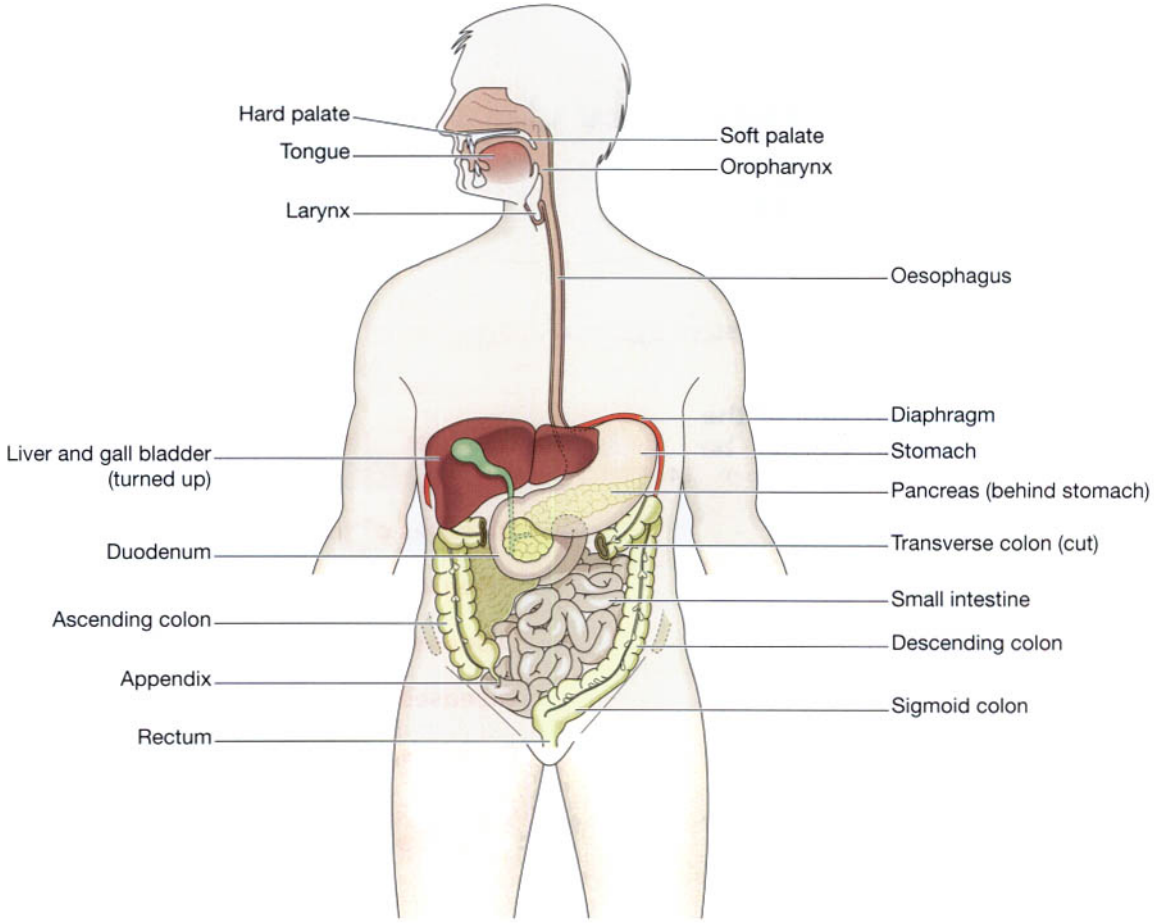


Figure 12.1 The organs of the digestive system.

The digestive system is the collective name used to describe the *alimentary canal*, some *accessory organs* and a variety of *digestive processes* which take place at different levels in the canal to 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 general structure which is modified at different levels to provide for the processes occurring at each level (Fig. 12.2). The complex of digestive processes gradually breaks 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. It therefore goes through a series of changes which release its constituent nutrients: amino acids, mineral salts, fat and vitamins. Chemical substances or *enzymes* (p. 26) which effect 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.

After absorption, nutrients are used to synthesise body constituents. They provide the raw materials for the manufacture of new cells, hormones and enzymes, and the energy needed for these and other processes and for the disposal of waste materials.

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

Ingestion. This is the process of taking food into the alimentary tract.

Propulsion. This moves the contents along the alimentary tract.

Digestion. This consists of:

- *mechanical breakdown* of food by, e.g. mastication (chewing)
- *chemical digestion* of food 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 round the body.

Elimination. Food substances which have been eaten but cannot be digested and absorbed are excreted by the bowel as faeces.

ORGANS OF THE DIGESTIVE SYSTEM (Fig. 12.1)

Learning outcomes

After studying this section, you should be able to:

- list the main organs of the alimentary tract
- list the accessory organs of digestion.

Alimentary tract

This is a long tube through which food passes. It commences at the mouth and terminates at the anus, and the various parts are given separate names, 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:

- 3 pairs of salivary glands
- pancreas
- liver and the 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.

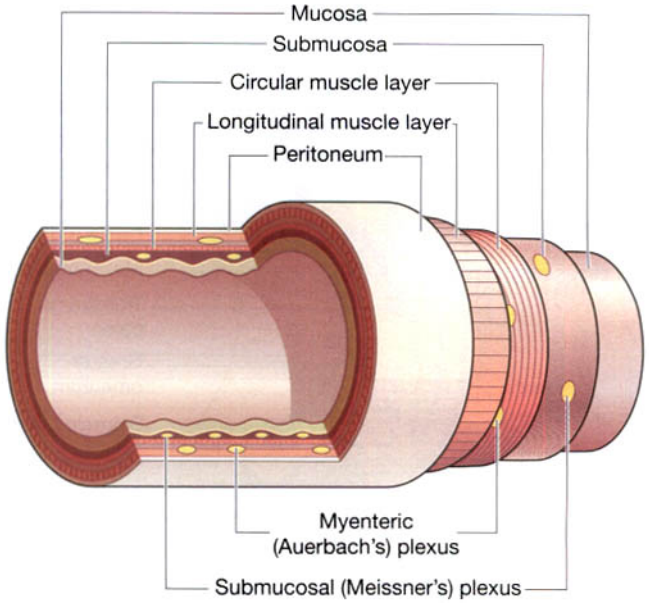


Figure 12.2 General structure of the alimentary canal.

BASIC STRUCTURE OF THE ALIMENTARY CANAL (Fig. 12.2)

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

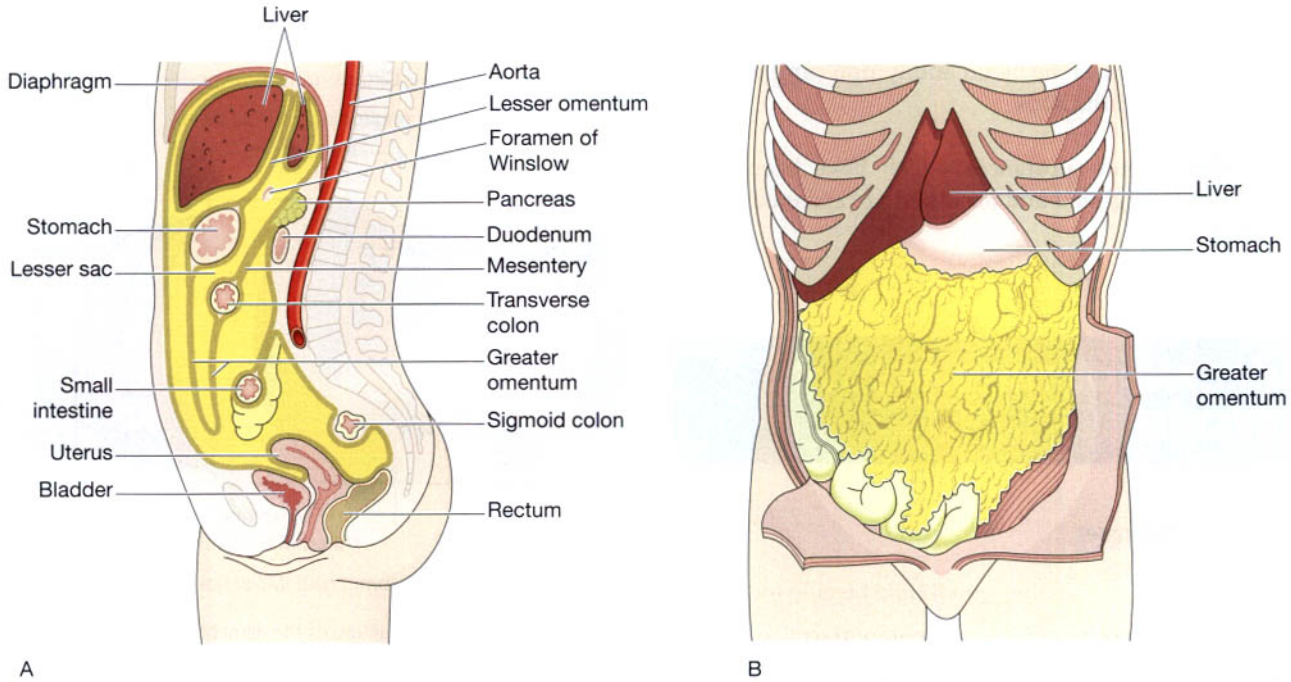


Figure 12.3 A. The peritoneal cavity (gold), the abdominal organs of the digestive system and the pelvic organs. B. The greater omentum.

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

- adventitia or outer covering
- muscle layer
- submucosal layer
- mucosa—lining.

Adventitia (outer covering)

In the thorax this consists of *loose fibrous tissue* and in the abdomen the organs are covered by a serous membrane called *peritoneum*.

Peritoneum

The peritoneum is the largest serous membrane of the body (Fig. 12.3A). It consists of 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 a considerable number of 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 layer*, which lines the abdominal wall
- the *visceral layer*, which covers the organs (viscera) within the abdominal and pelvic cavities.

The arrangement of the peritoneum is such that the organs are invaginated into the closed sac from below, behind and above so that they are at least partly covered by the visceral layer. 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*, and it stores fat, which 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*
- 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.

The parietal peritoneum lines the anterior abdominal wall.

The two layers of peritoneum are actually in contact and friction between them is prevented by the presence

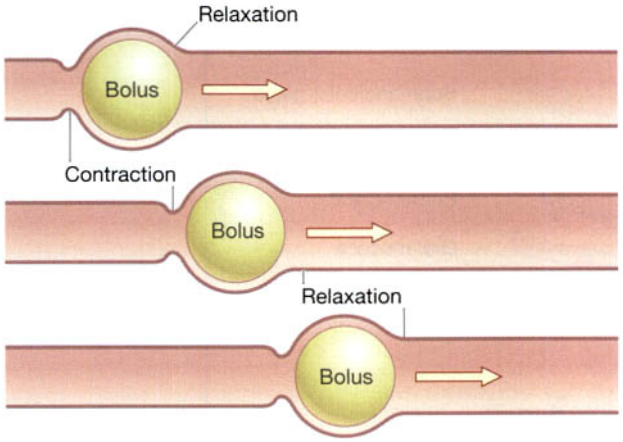


Figure 12.4 Movement of a bolus by peristalsis.

of serous fluid secreted by the peritoneal cells, thus the *peritoneal cavity* is only a *potential cavity*. A similar arrangement is seen with the membranes covering the lungs, the pleura (p. 251). In the male it is completely closed but in the female the uterine tubes open into it and the ovaries are the only structures inside (Ch. 19).

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* or *Auerbach's plexus*. 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). Muscle contraction also mixes food with the digestive juices. Onward movement of the contents of the tract is controlled at various points by *sphincters* consisting of an increased number of circular muscle fibres. They also act as valves preventing backflow in the tract. The control allows time for digestion and absorption to take place.

Submucosa

This layer consists of loose connective tissue with some elastic fibres. Within this layer are plexuses of blood vessels and nerves, lymph vessels and varying amounts of lymphoid tissues. The blood vessels consist of arterioles, venules and capillaries. The nerve plexus is the *submucosal* or *Meissner's plexus*, consisting of sympathetic and parasympathetic nerves which supply the mucosal lining.

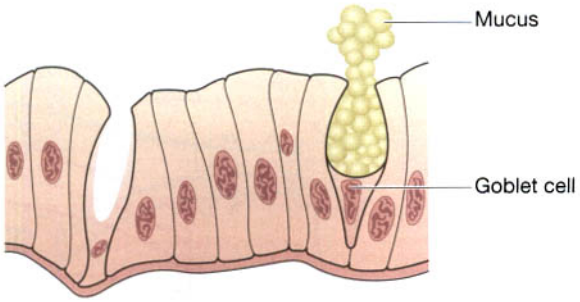


Figure 12.5 Columnar epithelium with goblet cells.

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 has a protective function
- *muscularis mucosa*, a thin outer layer of smooth muscle that provides involutions of the mucosa layer, e.g. gastric glands, villi.

Mucous membrane

In parts of the tract which 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 protects them from digestive enzymes. Below the surface in the regions lined with columnar epithelium are collections of specialised cells, or glands, which pour 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.

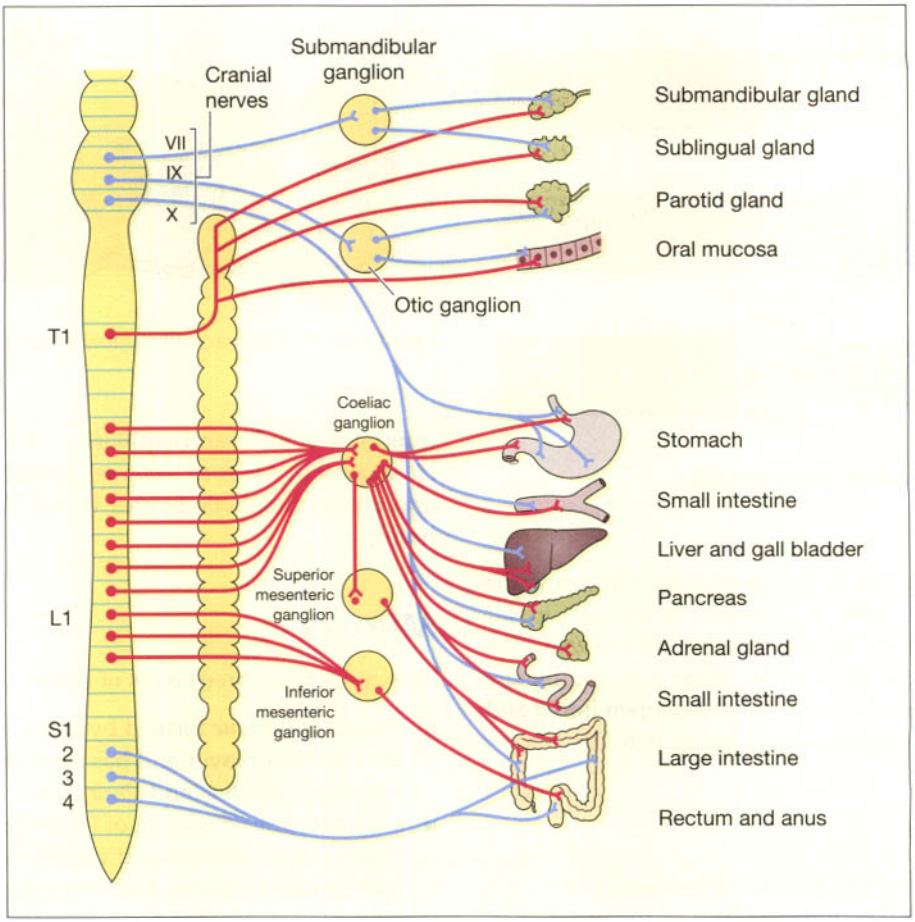


Figure 12.6 Autonomic nerve supply to the digestive system. Parasympathetic – blue; sympathetic – red.

These are *digestive juices* and they contain the enzymes which chemically break down food. Under the epithelial lining are varying amounts of lymphoid tissue.

Nerve supply

The alimentary tract is supplied by nerves from both divisions of the autonomic nervous system, i.e. parasympathetic and sympathetic, and in the main their actions are antagonistic (Fig. 12.6). In the normal healthy state one influence may outweigh the other according to the needs of the body as a whole at a particular time.

The parasympathetic supply. This supply to most of the alimentary tract is provided by one pair of cranial nerves, the *vagus nerves*. Stimulation causes smooth muscle contraction and the secretion of digestive juices. The most distal part of the tract is supplied by sacral nerves.

The sympathetic supply. This is provided by numerous nerves which emerge from the spinal cord in the thoracic and lumbar regions. These form plexuses in the thorax, abdomen and pelvis, from which nerves pass to the organs of the alimentary tract. Their action is to reduce smooth muscle contraction and glandular secretion.

Within the walls of the canal there are two nerve plexuses from which both sympathetic and parasympathetic fibres are distributed (Fig. 12.2).

The myenteric or Auerbach's plexus lies between the two layers of smooth muscle that it supplies, and influences peristalsis.

The submucosal or Meissner's plexus lies in the submucosa and supplies the mucous membrane and secretory glands.

Blood supply

Arterial blood supply

In the thorax. The oesophagus is supplied by paired *oesophageal arteries*, branches from the thoracic aorta.

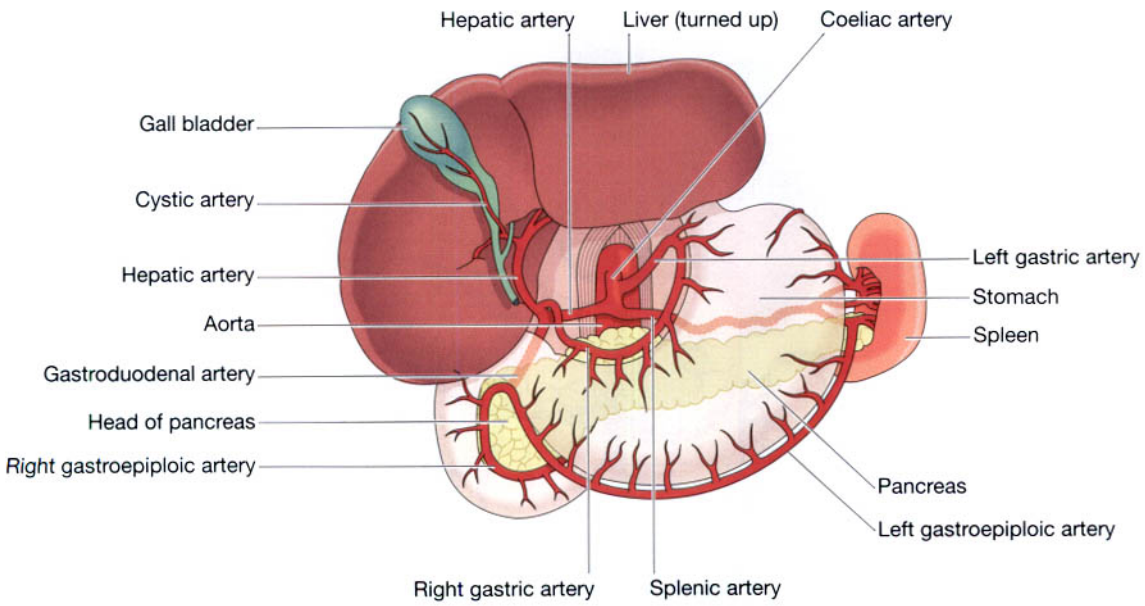


Figure 12.7 Branches of the coeliac artery and the organs they supply. The pancreas is shown behind the stomach.

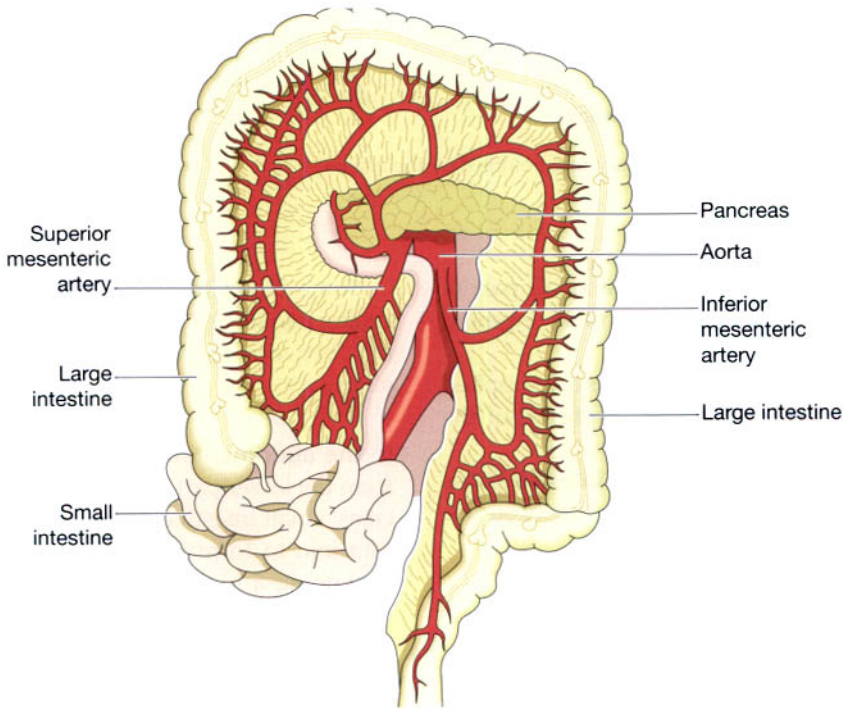


Figure 12.8 Blood supply to the small and large intestines.

In the abdomen and pelvis. The alimentary tract, pancreas, liver and biliary tract are supplied by the unpaired branches from the aorta: the *coeliac artery* and the *superior* and *inferior mesenteric arteries* (Figs 12.7 and 12.8).

The *coeliac artery* divides into three branches which supply the stomach, duodenum, pancreas, spleen, liver, gall bladder and bile ducts. They are:

- left gastric artery
- splenic artery
- hepatic artery.

The *superior mesenteric artery* supplies the whole of the small intestine, the caecum, ascending colon and most of the transverse colon.

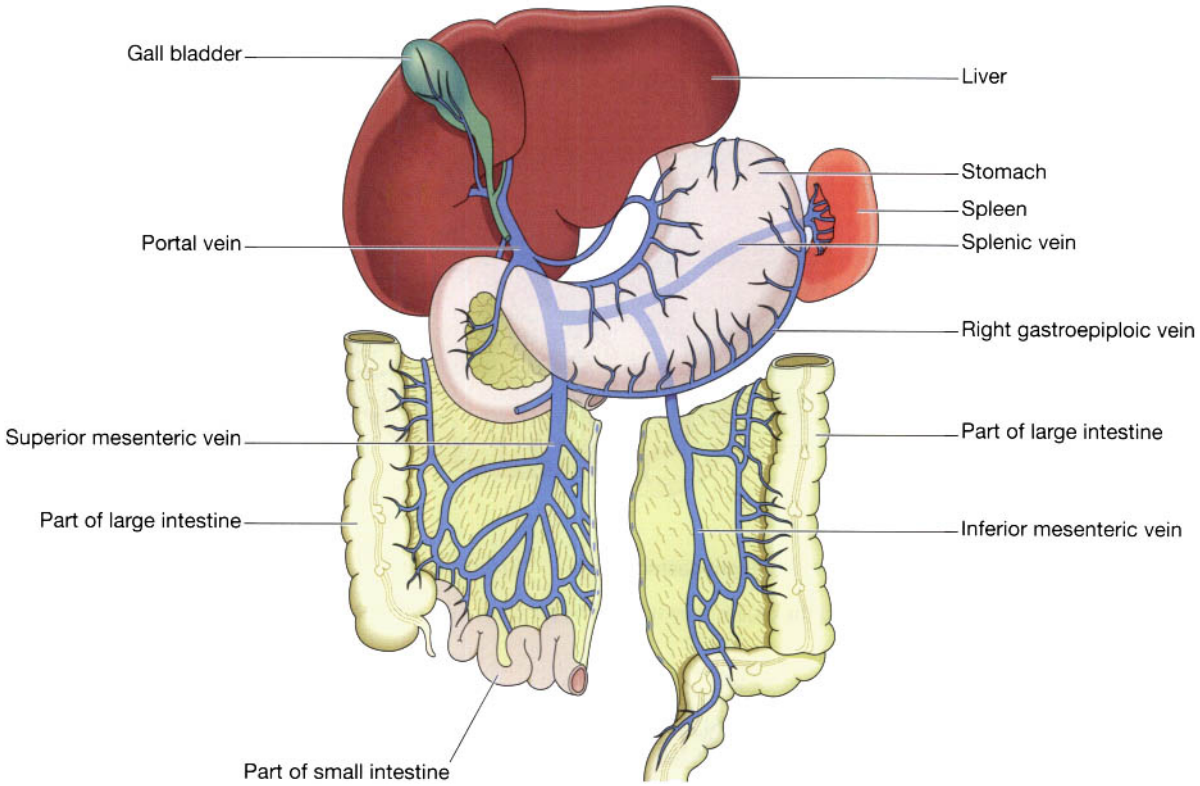


Figure 12.9 Venous drainage from the abdominal organs of the digestive system.

The *inferior mesenteric artery* supplies a small part of the transverse colon, the descending colon, sigmoid colon and most of the rectum.

The distal part of the rectum and the anus are supplied by the *middle* and *inferior rectal arteries*, branches of the internal iliac arteries.

The arteries supplying the stomach and intestines pass between the layers of peritoneum from the posterior abdominal wall to the organs.

Venous drainage

In the thorax. Venous blood from the oesophagus passes in the oesophageal veins to the *azygos* and *hemiazygos veins*. The azygos vein joins the superior vena cava near the heart, and the hemiazygos joins the left brachiocephalic vein.

Some blood from the lower part of the oesophagus drains into the *left gastric vein*. There are anastomotic vessels between the azygos, hemiazygos and left gastric veins.

In the abdomen and pelvis. The veins that drain blood from the lower part of the oesophagus, the stomach, pancreas, small intestine, large intestine and most of the rectum join to form the *portal vein* (Fig. 12.9). This blood, containing a high concentration of absorbed nutritional materials, is conveyed first to the liver then to the inferior vena cava. The circulation of blood in liver lobules is described later (p. 308).

Blood from the lower part of the rectum and the anal canal drains into the *internal iliac veins*. This blood is delivered directly into the inferior vena cava, hence bypassing the hepatic portal circulation.

MOUTH (Fig. 12.10)

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.

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 (alveolar ridges) and the cheeks is the *vestibule* and the remainder of the cavity is the *mouth proper*. The mucous membrane lining of the cheeks and the lips is reflected on to 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 bones forming the hard palate are the maxilla and the palatine bones. The soft palate 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 there 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 a voluntary muscular structure which occupies the floor of the mouth. It is attached by its base to the *hyoid bone* (see Fig. 10.4, p. 242) and by a fold of its mucous membrane covering, called the *frenulum*, to the floor of the mouth (Fig. 12.11). The superior surface consists of stratified squamous epithelium, with numerous *papillae* (little projections), containing nerve endings of the sense of taste, sometimes called the *taste buds*. There are three varieties of papillae (Fig. 12.12).

Vallate papillae, usually between 8 and 12 altogether, are arranged in an inverted V shape towards the base of the tongue. These are the largest of the papillae and are the most easily seen.

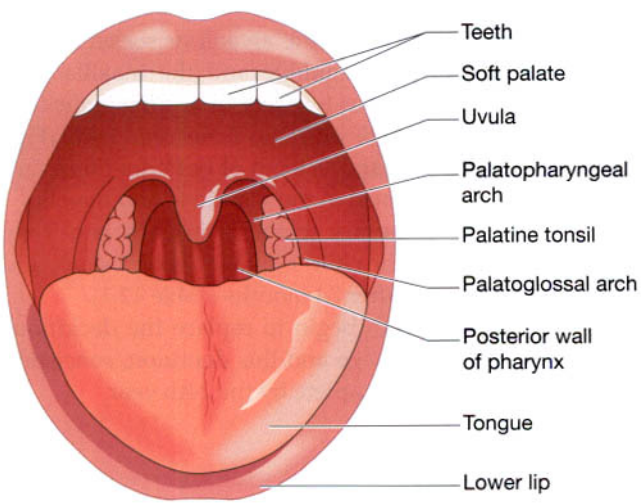


Figure 12.10 Structures seen in the widely open mouth.

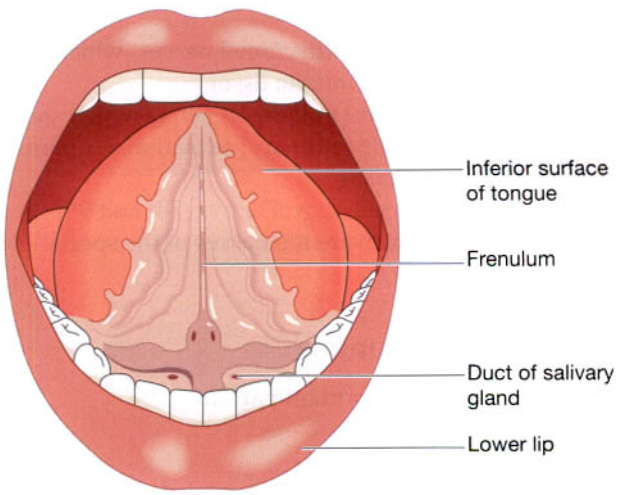


Figure 12.11 The inferior surface of the tongue.

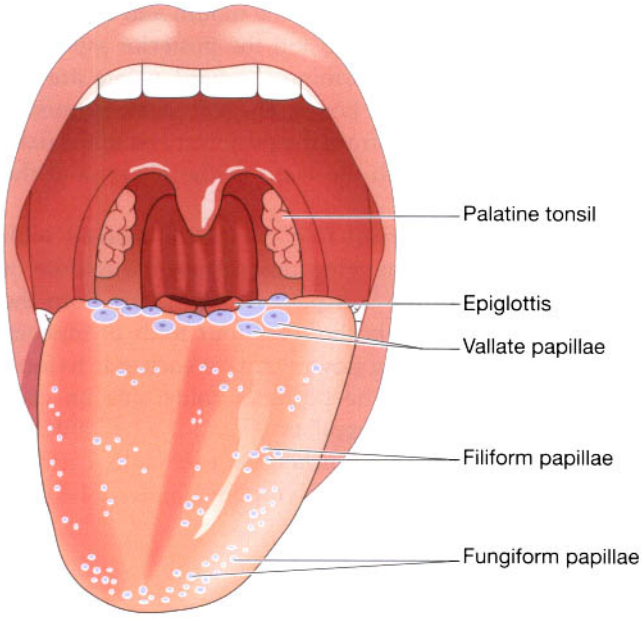


Figure 12.12 Locations of the papillae of the tongue and related structures.

Fungiform papillae are situated mainly at the tip and the edges of the tongue and are more numerous than the vallate papillae.

Filiform papillae are the smallest of the three types. They are most numerous on the surface of the anterior two-thirds of the tongue.

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 tissue
- the *lingual branch of the mandibular nerves* which are the nerves of somatic (ordinary) sensation, i.e. pain, temperature and touch
- the *facial* and *glossopharyngeal nerves* (7th and 9th cranial nerves) which are the nerves of the special sensation of taste.

Functions of the tongue

The tongue plays an important part in:

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

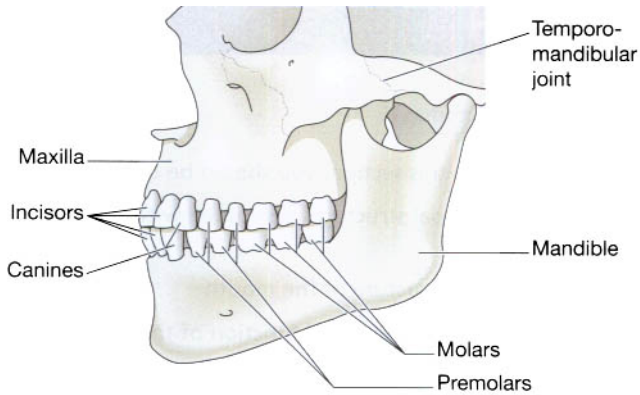


Figure 12.13 The permanent teeth and the jaw bones.

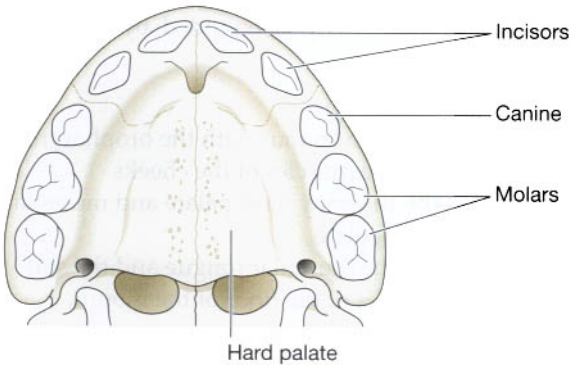


Figure 12.14 The roof of the mouth and the deciduous teeth – viewed from below.

Nerve endings of the sense of taste are present in the papillae and widely distributed in the epithelium of the tongue, soft palate, pharynx and epiglottis.

Teeth

The teeth are embedded in the alveoli or sockets of the alveolar ridges of the mandible and the maxilla (Fig. 12.13). Each individual has two sets, or *dentitions*, the *temporary* or *deciduous teeth* and the *permanent teeth* (Figs 12.14 and 12.15). At birth the teeth of both dentitions are present in immature form in the mandible and maxilla.

There are 20 temporary teeth, 10 in each jaw. They begin to erupt when the child is about 6 months old, and should all be present after 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 24th year.

Functions of the teeth

The *incisor* and *canine* teeth are the cutting teeth and are used for biting off pieces of food, whereas the *premolar*

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

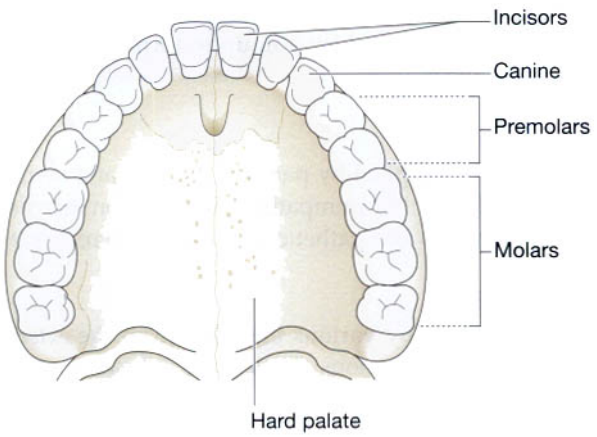


Figure 12.15 The roof of the mouth and the permanent teeth – viewed from below.

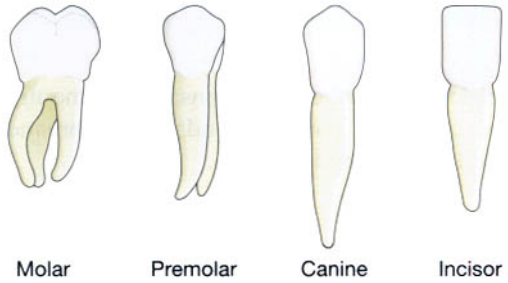


Figure 12.16 The shapes of the permanent teeth.

and *molar* teeth, with broad, flat surfaces, are used for grinding or chewing food (Fig. 12.16).

Structure of a tooth (Fig. 12.17)

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

- *the crown* – the part which protrudes from the gum
- *the root* – the part embedded in the bone
- *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*. Outside the dentine of the crown is a thin layer of very hard substance, the *enamel*. The root of the tooth, on the other hand, is covered with a substance resembling bone, called *cement*, which fixes the tooth in its socket. Blood vessels and nerves pass to the tooth through a small foramen at the apex of each root.

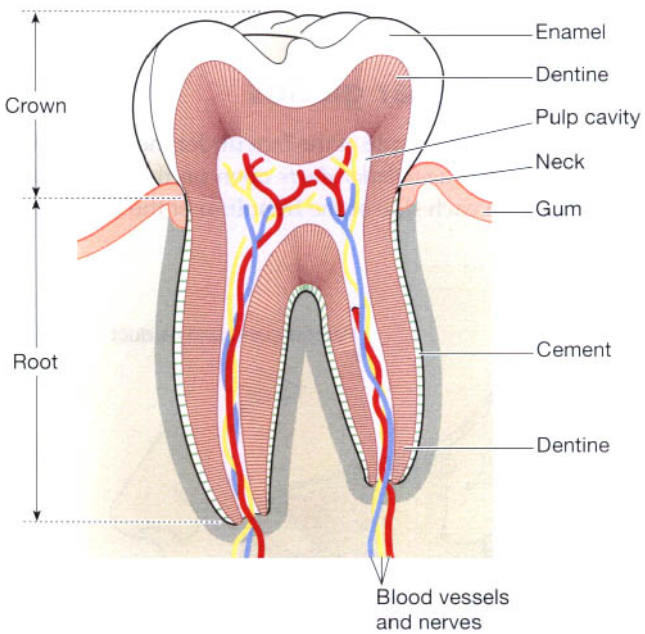


Figure 12.17 A section of a tooth.

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) (see p. 166).

SALIVARY GLANDS (Fig. 12.18)

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 pour their secretions into the mouth. There are three pairs: the parotid glands, the submandibular glands and the sublingual glands.

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. 12.18B). The secretions are poured into ductules which join up to form larger ducts leading into the mouth.

Nerve supply

The glands are supplied by parasympathetic and sympathetic nerve fibres. Parasympathetic stimulation increases secretion, whereas sympathetic stimulation decreases it.

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 lining of the oral cavity. About 1.5 litres of saliva is produced daily and it consists of:

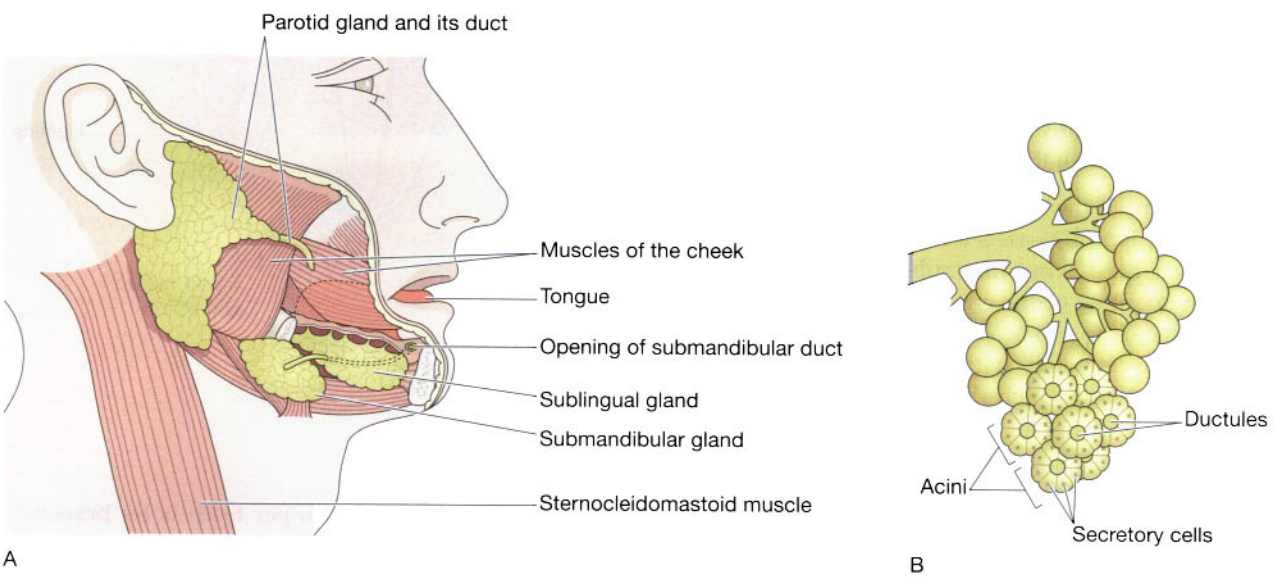


Figure 12.18 A. The position of the salivary glands. B. Enlargement of part of a gland.

- water
- mineral salts
- enzyme: salivary amylase
- mucus
- lysozyme
- immunoglobulins
- blood-clotting factors.

Secretion of saliva

Secretion of saliva is under autonomic nerve control. Parasympathetic stimulation causes vasodilatation and profuse secretion of watery saliva with a relatively low content of enzymes and other organic substances. Sympathetic stimulation causes vasoconstriction and 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, 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 pH (1.5 to 1.8) of the gastric juices, which degrades the amylase.

Lubrication of food. Dry food entering the mouth is moistened and lubricated by saliva before it can be made into a bolus ready for swallowing.

Cleansing and lubricating. An adequate flow of saliva is necessary to cleanse the mouth and keep its tissues soft, moist and pliable. It helps to prevent damage to the mucous membrane by rough or abrasive foodstuffs.

Non-specific defence. Lysozyme, immunoglobulins and clotting factors combat invading microbes.

Taste. The taste buds are stimulated only by chemical substances in solution. Dry foods stimulate the sense of taste only after thorough mixing with saliva. The senses of taste and smell are closely linked in the enjoyment, or otherwise, of food.

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. 243). 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 are built of three layers of tissue.

The lining membrane (mucosa) is stratified squamous epithelium, continuous with the lining of the mouth at one end and with the oesophagus at the other.

The middle layer consists of fibrous 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 *constrictor* muscles which 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. 12.19)

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.

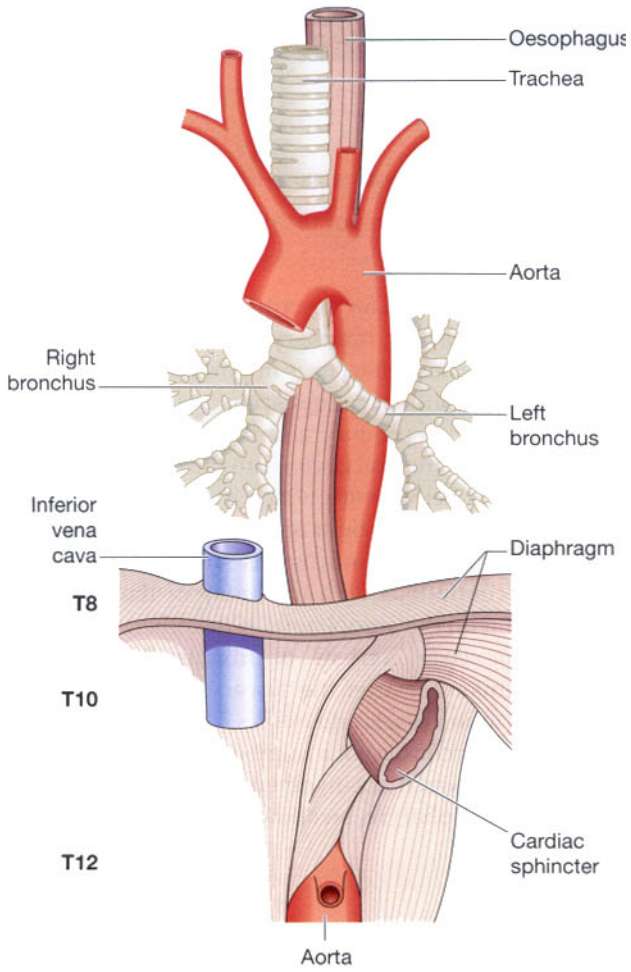


Figure 12.19 The oesophagus and some related structures.

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 which prevents the regurgitation (backward flow) of gastric contents into the oesophagus. The upper and lower ends of the oesophagus are closed by sphincter muscles. The upper *cricopharyngeal 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 sphincter muscle increases. There is an added pinching effect by the contracting muscle fibres of the diaphragm.

Structure

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*. 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 of the oesophagus is supplied mainly by the oesophageal arteries, branches from the 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.

Nerve supply

Sympathetic and parasympathetic nerves terminate in the myenteric and submucosal plexuses. Parasympathetic fibres are branches of the vagus nerves (Fig. 12.6).

Functions of the mouth, pharynx and oesophagus

Formation of a bolus. When food is taken into the mouth it is masticated or chewed by the teeth and moved round the mouth by the tongue and muscles of the cheeks (Fig. 12.20). It is mixed with saliva and formed into a soft mass or *bolus* ready for *deglutition* or swallowing. The length of time that food remains in the mouth depends, to a large extent, on the consistency of the food. Some foods need to the chewed longer than others before the individual feels that the mass is ready for swallowing.

Deglutition or swallowing (Fig. 12.21). This occurs in three stages after mastication is complete and the bolus has been formed. It is initiated voluntarily but completed by a reflex (involuntary) action.

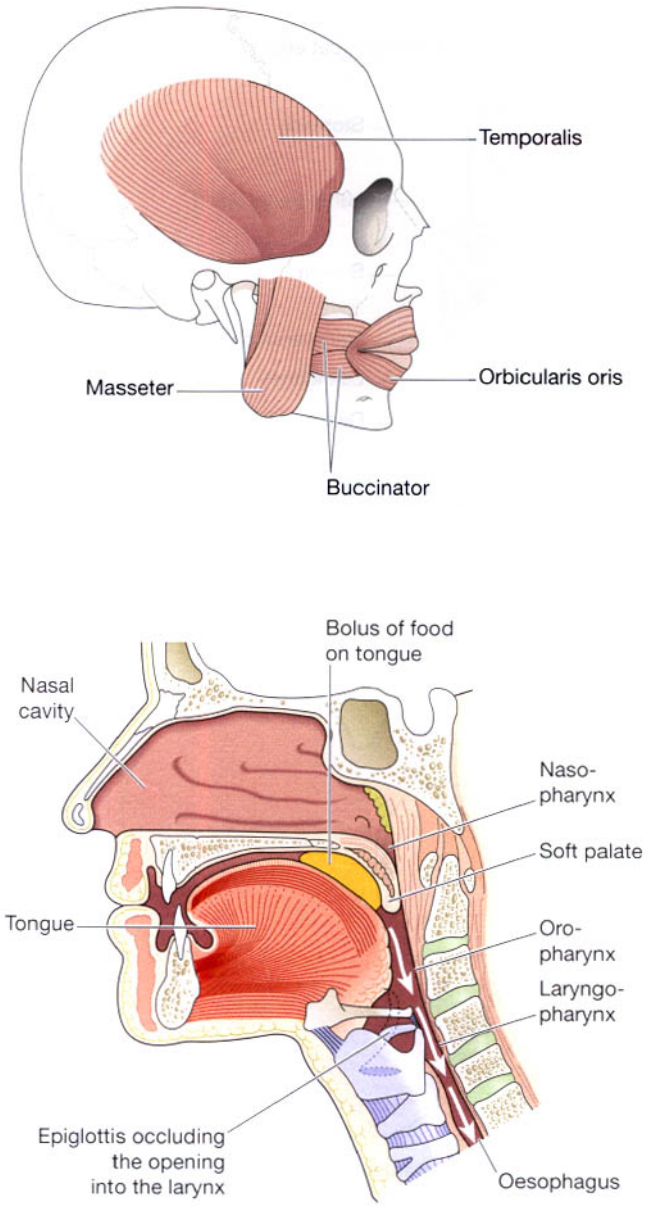


Figure 12.21 Section of the face and neck showing the positions of structures during swallowing.

1. The mouth is closed and the voluntary muscles of the tongue and cheeks push the bolus backwards into the pharynx.
2. The muscles of the pharynx are stimulated by a reflex action initiated in the walls of the oropharynx and coordinated in the medulla and lower pons in the brain stem. Contraction of these muscles propels the bolus down into the oesophagus. All other routes that the bolus could possibly 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.
3. The presence of the bolus in the pharynx stimulates a wave of peristalsis which propels the bolus through the oesophagus to the stomach.

Peristaltic waves pass along the oesophagus only after swallowing (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 maintenance of an acute angle between the oesophagus and the fundus of the stomach, i.e. an acute cardio-oesophageal angle
- 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. 12.22)

Anteriorly – left lobe of liver and anterior abdominal wall

Posteriorly – abdominal aorta, pancreas, spleen, left kidney and adrenal gland

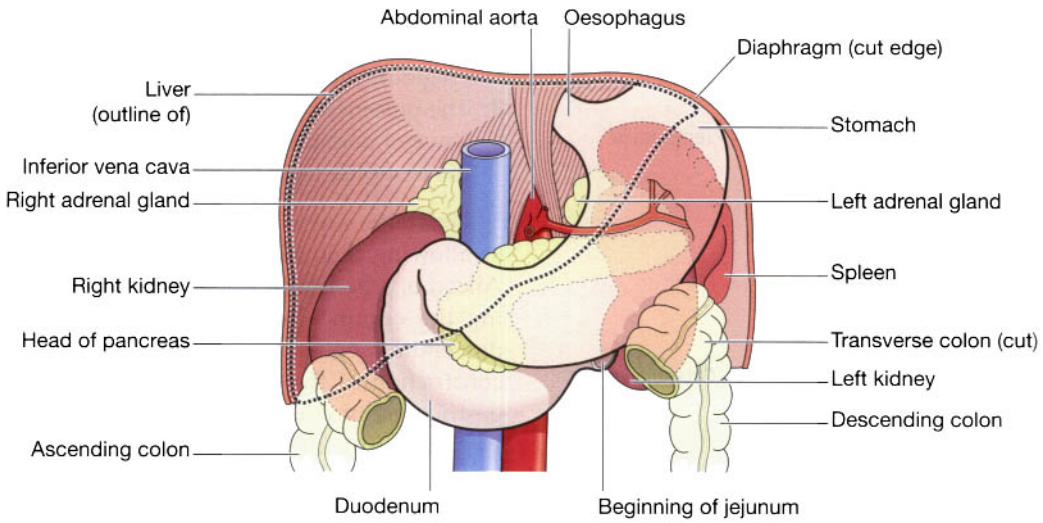


Figure 12.22 The stomach and its associated structures.

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. 12.23)

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 the downwards 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* then slightly upwards towards the pyloric sphincter.

The stomach is divided into three regions: the fundus, the body and the antrum. At the distal end of the pyloric antrum 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.

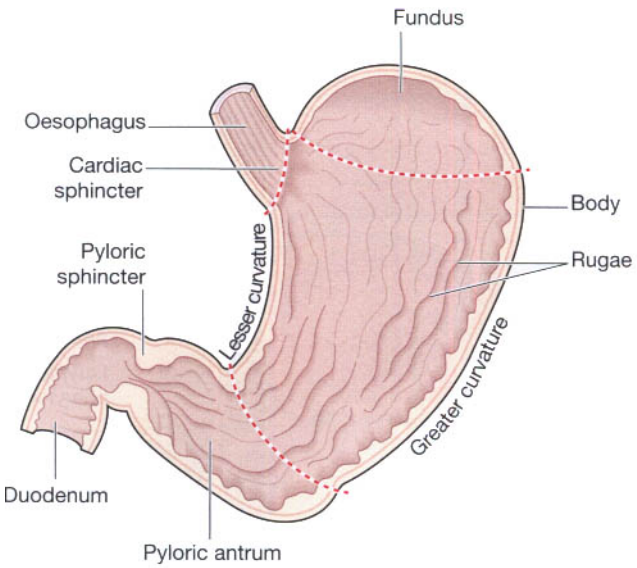


Figure 12.23 Longitudinal section of the stomach.

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. 12.24). 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 (Fig. 12.2).

This arrangement allows for the churning motion characteristic of gastric activity, as well as peristaltic movement. Circular muscle is strongest in the pyloric antrum and sphincter.

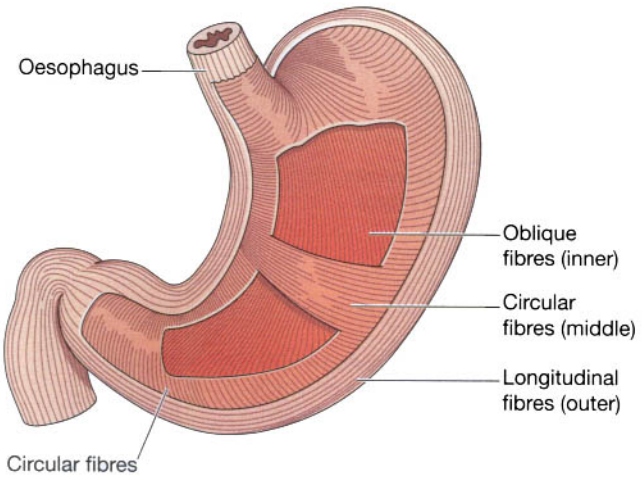


Figure 12.24 The muscle fibres of the stomach wall. Sections have been removed to show the three layers.

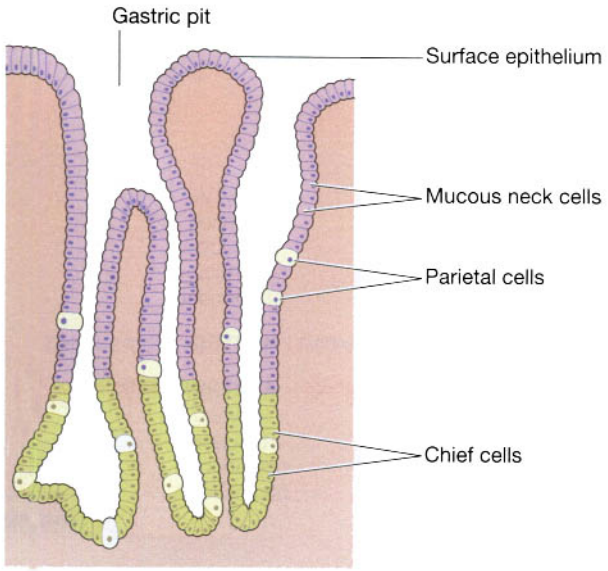


Figure 12.25 Structure of gastric glands.

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' and the surface has a smooth, velvety appearance. Numerous *gastric glands* are situated below the surface in the mucous membrane. They consist of specialised cells that secrete *gastric juice* into the stomach.

Blood supply

Arterial blood is supplied to the stomach by branches of the coeliac artery and venous drainage is into the portal vein. Figures 12.7 and 12.9 give details of the names of these vessels.

Nerve supply

The sympathetic supply to the stomach is mainly from the *coeliac plexus* and the parasympathetic supply is from the *vagus nerves*. Sympathetic stimulation reduces the motility of the stomach and the secretion of gastric juice; vagal stimulation has the opposite effect (Fig. 12.6).

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.

Gastric muscle contraction consists of a churning movement 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 pyloric antrum forces gastric contents, after they are sufficiently liquefied, through the pylorus into the duodenum in small spurts.

Gastric juice

About 2 litres of gastric juice are secreted daily by special secretory glands in the mucosa (Fig. 12.25). It consists of:

- water, mineral salts } secreted by gastric glands
- mucus secreted by goblet cells in the glands and on the stomach surface
- hydrochloric acid, intrinsic factor } secreted by *parietal cells* in the gastric glands
- 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 effective digestion by pepsins.

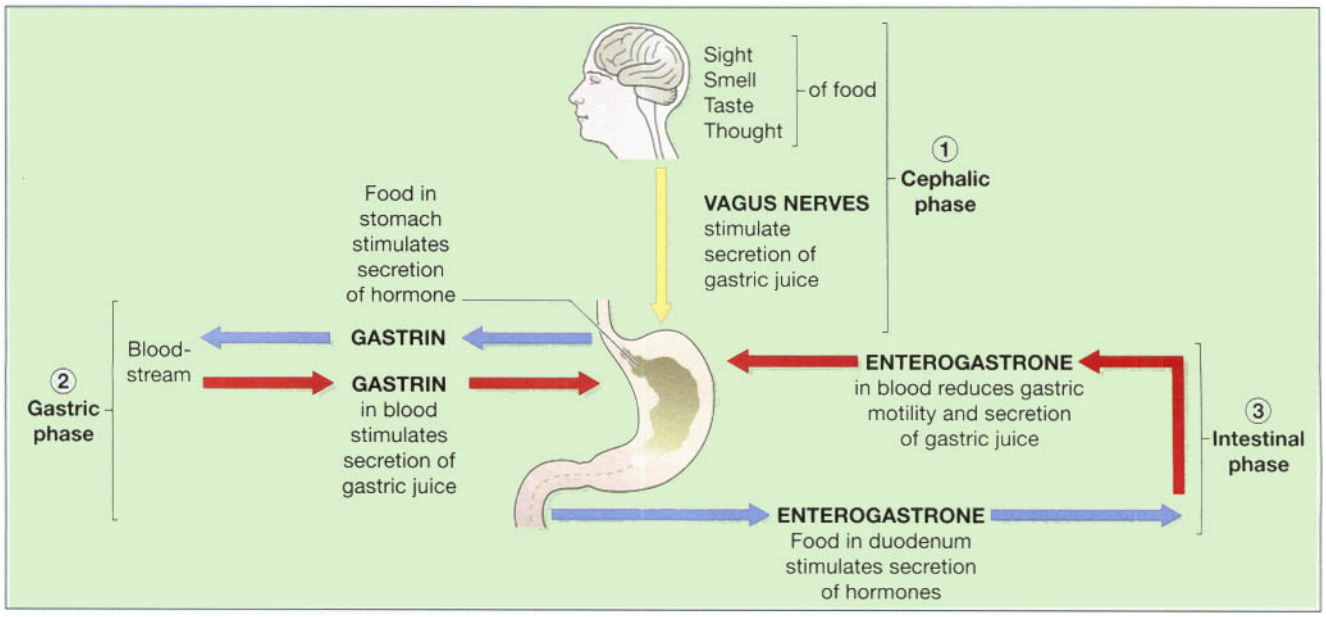


Figure 12.26 The three phases of secretion of gastric juice.

- *Pepsinogens* are activated to *pepsins* by hydrochloric acid and by pepsins already present in the stomach. They begin the digestion of proteins, breaking them into smaller molecules. Pepsins act most effectively at pH 1.5 to 3.5.
- *Intrinsic factor* (a protein) is necessary for the absorption of vitamin B_{12} from the ileum.
- *Mucus* prevents mechanical injury to the stomach wall by lubricating the contents. It 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 digest protein.

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. 12.26).

1. *Cephalic phase*. This flow of juice occurs *before* food reaches the stomach and is due to reflex stimulation of the vagus nerves initiated by the sight, smell or taste of food. When the vagus nerves have been cut (vagotomy) this phase of gastric secretion stops.
2. *Gastric phase*. When stimulated by the presence of food the *enteroendocrine cells* in the pyloric antrum and duodenum secrete *gastrin*, a hormone 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 the secretion of digestive juice is continued after the completion of the meal and the end of the cephalic phase. Gastrin secretion is suppressed when the pH in the pyloric antrum falls to about 1.5.
3. *Intestinal phase*. When the partially digested contents of the stomach reach the small intestine, a hormone complex *enterogastrone** is produced by endocrine cells in the intestinal mucosa, which slows down the secretion of gastric juice and reduces gastric motility. Two of the hormones forming this complex are *secretin* and *cholecystokinin* (CCK).

By slowing the emptying rate of the stomach, the contents of the duodenum become more thoroughly mixed with bile and pancreatic juice. This phase of gastric secretion is most marked when the meal has had a high fat content.

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

* Enterogastrone has been described as any hormone or combination of hormones released by the intestine that inhibits gastric secretion.

Functions of the stomach

These include:

- temporary storage allowing time for the digestive enzymes, pepsins, to act
- chemical digestion – pepsins convert proteins to 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*
- limited absorption of water, alcohol and some lipid-soluble drugs
- non-specific defence against microbes – provided by hydrochloric acid in gastric juice. Vomiting may be a response to ingestion of gastric irritants, e.g. microbes or chemicals
- preparation of iron for absorption further along the tract – the acid environment of the stomach solubilises iron salts, which is required before iron can be absorbed
- production 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 pyloric antrum forces small jets of gastric contents through the pyloric sphincter into the duodenum.

SMALL INTESTINE (Figs 12.27 and 12.28)

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, naming 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 and leads into the large intestine at the *ileocaecal valve*. It is a little over 5 metres long and lies in the abdominal cavity surrounded by the large intestine. In the small intestine the chemical digestion of food is completed and most of the absorption of nutrients takes place.

The small intestine comprises three main sections continuous with each other.

The *duodenum* is about 25 cm long and curves around the head of the pancreas. Secretions from the gall bladder and pancreas are released into the duodenum through a common structure, the hepatopancreatic ampulla, and

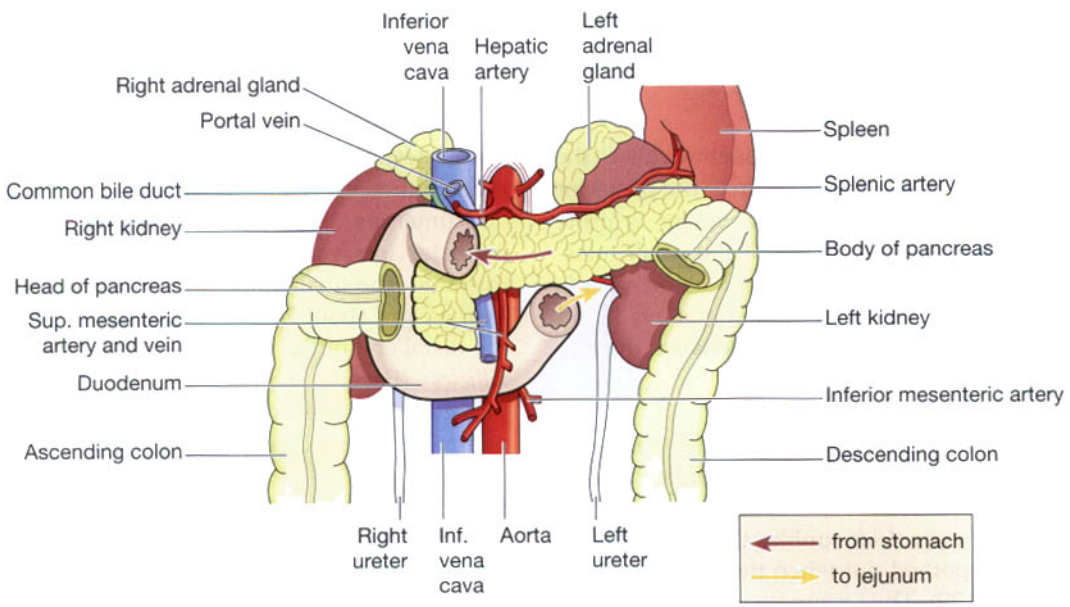


Figure 12.27 The duodenum and its associated structures.

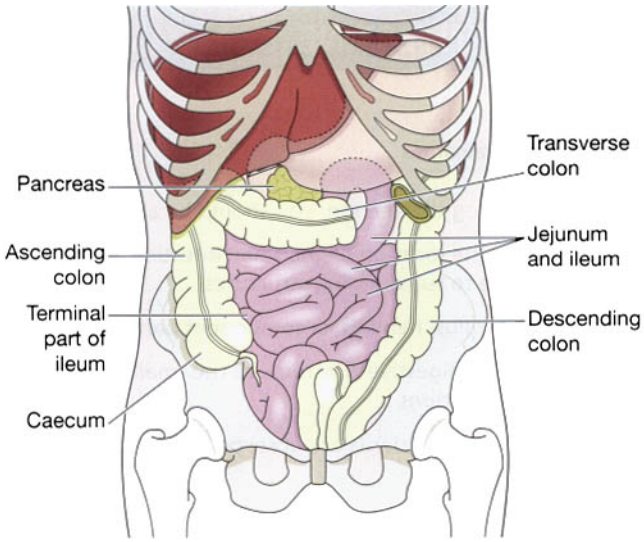


Figure 12.28 The jejunum and ileum and their related structures.

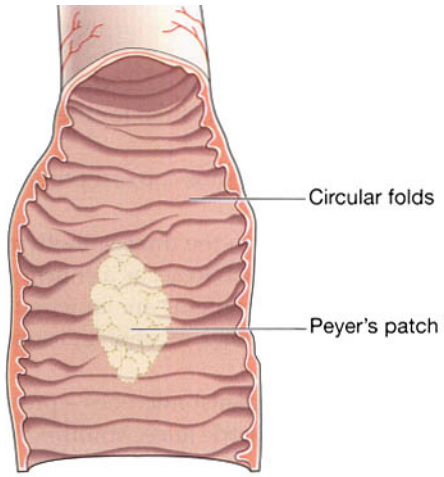


Figure 12.29 Section of a small piece of small intestine (opened out), showing the permanent circular folds.

the opening into the duodenum is guarded by the hepatopancreatic sphincter (of Oddi) (Fig. 12.42).

The *jejunum* is the middle section of the small intestine and is about 2 metres long.

The *ileum*, or 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 regurgitation.

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. A double layer of peritoneum called the *mesentery* attaches the jejunum and ileum to the posterior abdominal wall (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. 12.29). 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 to 1 mm long (Fig. 12.30). Their walls consist of columnar epithelial cells, or *enterocytes*, with tiny *microvilli* (1 μm long) on their free border. *Goblet cells* that secrete mucus are interspersed between the enterocytes. These epithelial cells enclose a network of blood and lymph capillaries. The 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.

The *intestinal glands* are simple tubular glands situated below the surface between the villi. The 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 intestinal contents. The entire epithelium is replaced every 3 to 5 days. During migration the cells form 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 about 20 or 30 larger nodes situated towards the distal end of the ileum are called *aggregated lymphatic follicles* (Peyer's patches). These lymphatic tissues, packed with defensive cells, are strategically placed to neutralise ingested antigens (Ch. 15).

Blood supply (Figs 12.8 and 12.9)

The *superior mesenteric artery* supplies the whole of the small intestine, and venous drainage is by the *superior mesenteric vein* which joins other veins to form the portal vein.

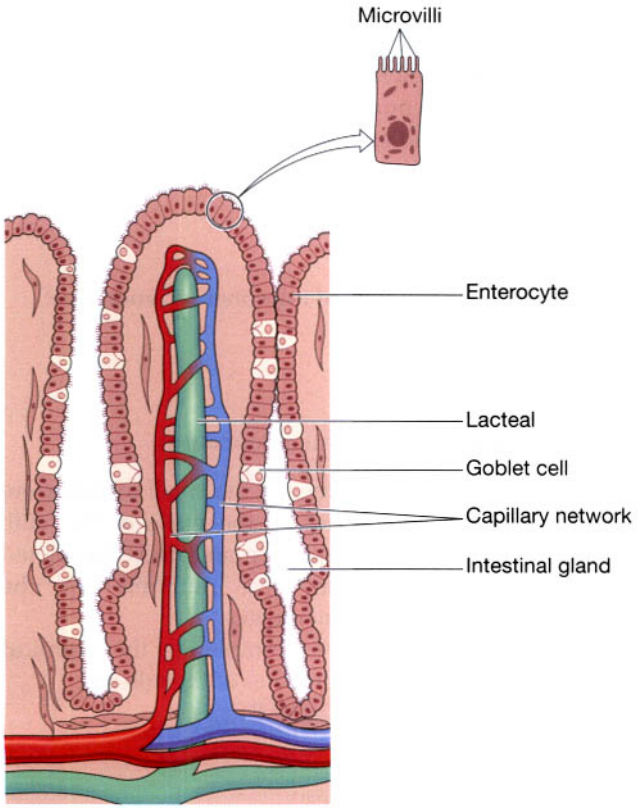


Figure 12.30 A highly magnified view of one complete villus in the small intestine.

Nerve supply

Innervation of the small intestine is both sympathetic and parasympathetic (Fig. 12.6).

Intestinal juice

About 1500 ml of intestinal juice are secreted daily by the glands of the small intestine. It consists of:

- water
- mucus
- mineral salts
- enzyme: enterokinase (enteropeptidases).

The pH of intestinal juice is usually between 7.8 and 8.0.

Functions of the small intestine

The functions are:

- onward movement of its contents which is produced by peristalsis
- secretion of intestinal juice
- 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 the solitary lymph follicles 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. In the small intestine the digestion of all the 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 enters the duodenum at the hepatopancreatic ampulla and consists of:

- water
- mineral salts
- enzymes:
  - —amylase
  - —lipase
- inactive enzyme precursors:
  - —trypsinogen
  - —chymotrypsinogen
  - —procarboxypeptidase.

Pancreatic juice is alkaline (pH 8) because it contains significant quantities of bicarbonate ions, which are 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* (enteropeptidase), 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 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 material from the stomach stimulates the production of these hormones.

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 (Fig. 12.42).

Bile has a pH of 8 and between 500 and 1000 ml are secreted daily. It consists of:

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

Functions

- The bile salts, *sodium taurocholate* and *sodium glycocholate*, emulsify fats in the small intestine.
- The bile pigment, *bilirubin*, is a waste product of the breakdown of erythrocytes and is excreted in the bile rather than in the urine because of its low solubility in water. Bilirubin is altered by microbes in the large intestine. Some of the resultant *urobilinogen*, which is highly water soluble, is reabsorbed and then excreted in the urine, but most is converted to *stercobilin* and excreted in the faeces.
- Fatty acids are insoluble in water, which makes them very difficult to absorb through the intestinal wall. Bile salts make fatty acids soluble, enabling both these and fat-soluble vitamins (e.g. vitamin K) to be readily absorbed.
- Stercobilin colours and deodorises the faeces.

Release from the gall bladder

When a meal has been eaten the hormone CCK is secreted by the duodenum during the intestinal phase of secretion of gastric juice (p. 298). This stimulates contraction of the gall bladder and relaxation of the hepatopancreatic sphincter, enabling the bile and pancreatic juice to pass into the duodenum together. A more marked activity is noted if chyme entering the duodenum contains a high proportion of fat.

Intestinal secretions

The principal constituents of intestinal secretions are:

- water
- mucus
- mineral salts
- enzyme: enterokinase (enteropeptidase).

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

The enzymes involved in completing the chemical digestion of food in the enterocytes of the villi are:

- peptidases
- lipase
- sucrase, maltase and lactase.

Chemical digestion associated with enterocytes

Alkaline intestinal juice (pH 7.8 to 8.0) assists in raising the pH of the intestinal contents to between 6.5 and 7.5.

Enterokinase activates pancreatic peptidases such as trypsin which convert some polypeptides to amino acids and some to smaller peptides. The final stage of breakdown to amino acids of all peptides occurs inside the enterocytes.

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

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

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. 12.31)

Absorption of nutrients occurs by two possible processes:

- *Diffusion*. Monosaccharides, amino acids, fatty acids and glycerol diffuse slowly down their concentration gradients into the enterocytes from the intestinal lumen.
- *Active transport*. Monosaccharides, amino acids, fatty acids and glycerol may be actively transported into the villi; this is faster than diffusion. Disaccharides, dipeptides and tripeptides are also actively transported into the enterocytes where their digestion is completed before transfer into the capillaries of the villi.

Monosaccharides and amino acids pass into the capillaries in the villi and fatty acids and glycerol into the lacteals.

Some proteins are absorbed unchanged, e.g. antibodies present in breast milk and oral vaccines, such as poliomyelitis vaccine. The extent of protein absorption is believed to be limited.

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. It has been calculated that the surface area of the small intestine is about five times that of the whole body.

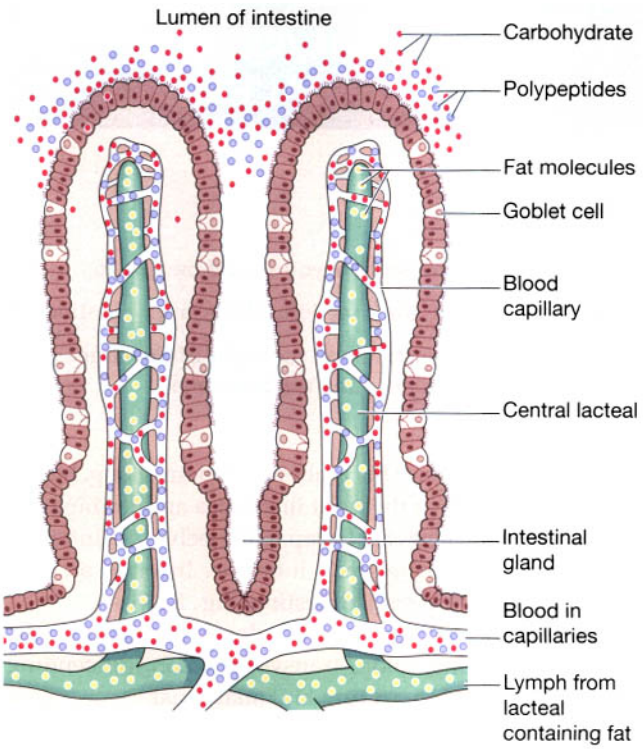


Figure 12.31 The absorption of nutrients.

Large amounts of fluid enter the alimentary tract each day (Fig. 12.32). Of this, only about 500 ml is not absorbed by the small intestine, and passes into the large intestine.

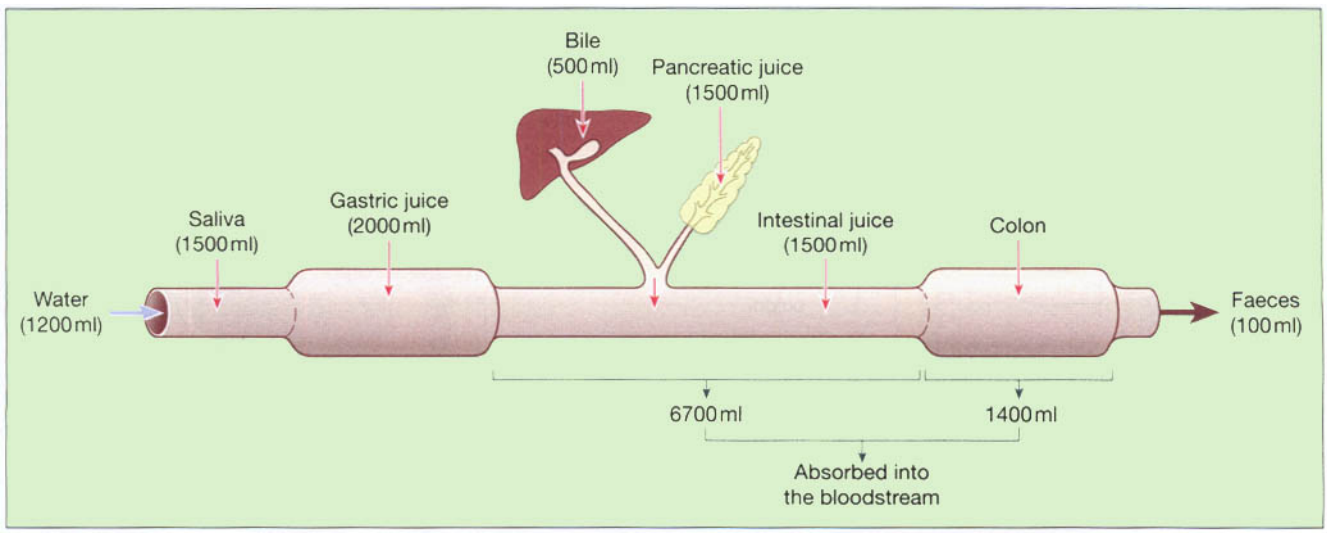


Figure 12.32 Average volumes of fluid ingested, secreted, absorbed and eliminated from the gastrointestinal tract daily.

LARGE INTESTINE (COLON), 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. This is about 1.5 metres long, beginning at the *caecum* in the right iliac fossa and terminating at the *rectum* and *anal canal* deep in the pelvis. Its lumen is larger than that of the small intestine. It forms an arch round the coiled-up small intestine (Fig. 12.33).

For descriptive purposes the colon is divided into the caecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum and anal canal.

The caecum. This is the first part of the colon. 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 usually about 13 cm long and has the same structure as the walls of the colon but contains more lymphoid tissue (Fig. 12.34).

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.

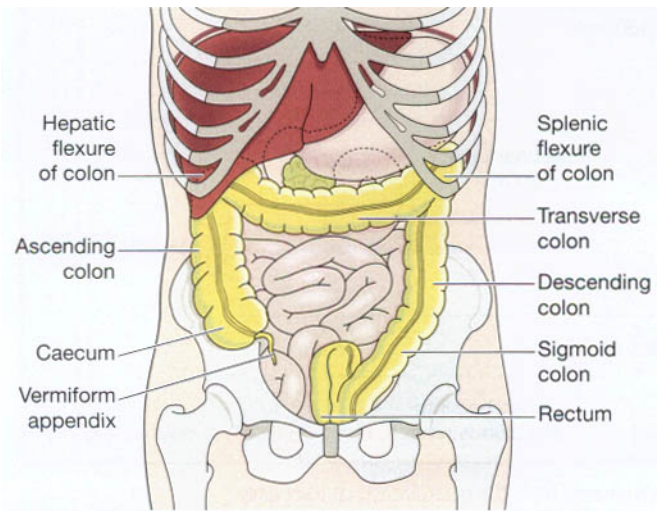


Figure 12.33 The parts of the large intestine (colon) and their positions.

The transverse colon. This is a loop of colon which 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. After it enters the true pelvis it is known as the sigmoid colon.

The sigmoid colon. This part describes an S-shaped curve in the pelvis then continues downwards to become the rectum.

The rectum. This is a slightly dilated section of the colon 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 fibres, is under the control of the autonomic nervous system and the *external sphincter*, formed by skeletal muscle, is under voluntary control (Fig. 12.35).

Structure

The four layers of tissue described in the basic structure of the gastrointestinal tract (Fig. 12.2) are present in the colon, the rectum and the anal canal. The arrangement of the longitudinal muscle fibres is modified in the colon.

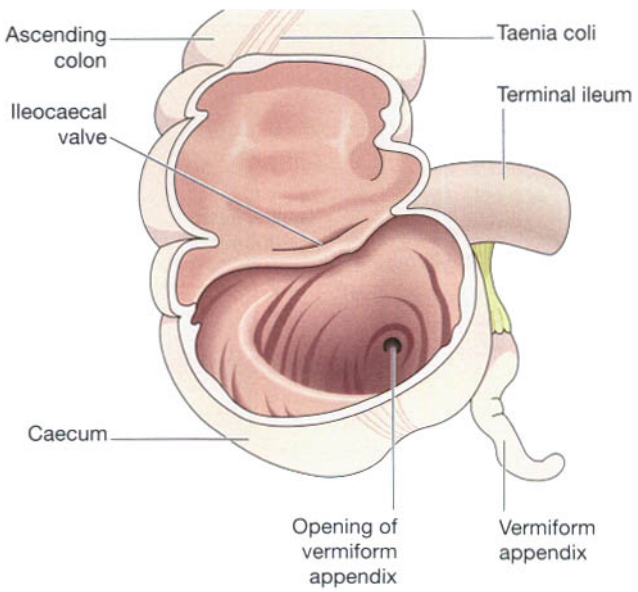


Figure 12.34 Interior of the caecum.

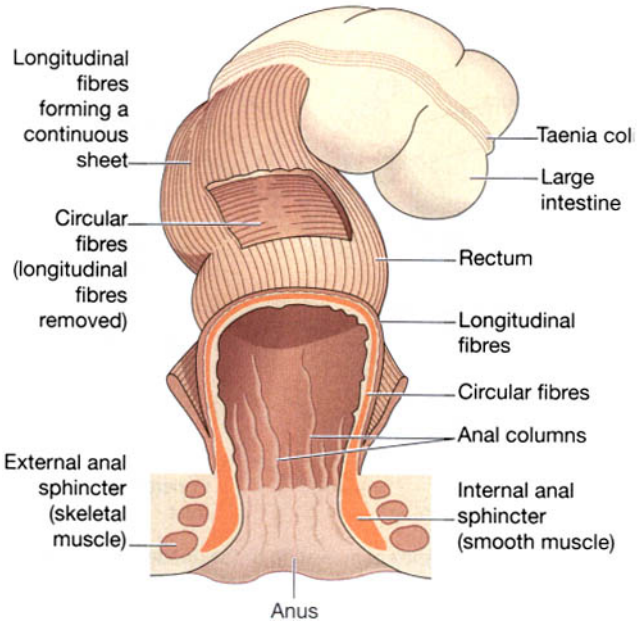


Figure 12.35 Arrangement of muscle fibres in the colon, rectum and anus. Sections have been removed to show the layers.

They do not form a smooth continuous layer of tissue but are collected into three bands, called *taeniae coli*, situated at regular intervals round the 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 colon they give a sacculated or puckered appearance to the organ (Fig. 12.35).

The longitudinal muscle fibres spread out as in the basic structure and completely surround the rectum and the 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 microbes.

In the mucosal lining of the colon and the upper region of the rectum are large numbers of goblet cells forming simple tubular glands, which secrete mucus. They are not present beyond the junction between the rectum and the anus.

The lining membrane of the anus 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 to 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 (Fig. 12.8).

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 distal section of the rectum and the anus are supplied by branches from the *internal iliac arteries*.

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 (Fig. 12.9). Veins draining the distal part of the rectum and the anus join the *internal iliac veins*.

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 some water has been absorbed in the small intestine. In the large intestine absorption of water continues until the familiar semisolid consistency of faeces is achieved. Mineral salts, vitamins and some drugs are also absorbed into the 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 (welchii)*. These microbes are *commensals* in humans. They may become pathogenic if transferred to another part of the body, e.g. *Escherichia 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 and as a feature of some anxiety states. Hydrogen, carbon dioxide and methane are produced by bacterial fermentation of unabsorbed nutrients, especially carbohydrate. Gases pass out of the bowel as *flatus*.

Large numbers of microbes are present in the faeces.

Mass movement

The large intestine does not exhibit peristaltic movement as it is seen 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 the infant defaecation occurs by reflex (involuntary) action. However, sometime in the second or third year of life the ability to override the defaecation reflex is developed. In practical terms this acquired voluntary control means that the brain can inhibit the reflex until such time as 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 the process of defaecation. When defaecation is voluntarily postponed the feeling of fullness and need to defaecate tends to fade until the next mass movement occurs and the reflex is initiated again. Repeated suppression of the reflex may lead to constipation.

Constituents of faeces. The faeces consist of a semi-solid brown mass. The brown colour is due to the presence of stercobilin (p. 310 and Fig. 12.41).

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

- fibre (indigestible cellular plant and animal material)
- dead and live microbes
- epithelial cells 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 roughage in the diet ensures that the contents of the colon are sufficiently bulky to stimulate defaecation.

PANCREAS (Fig. 12.36)

Learning outcome

After studying this section, you should be able to:

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

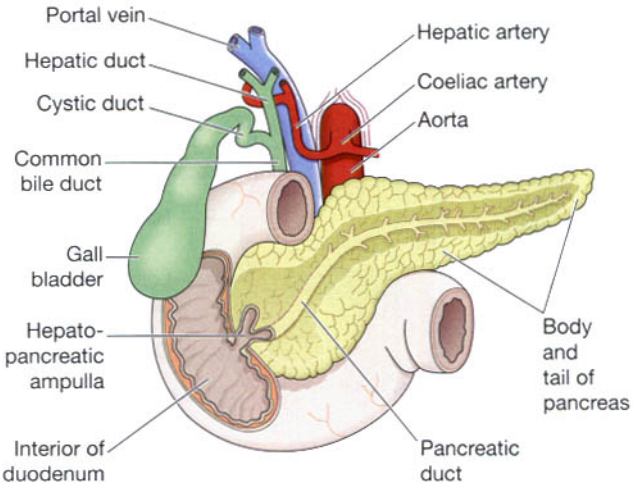


Figure 12.36 The pancreas in relation to the duodenum and biliary tract; part of the anterior wall of the duodenum has been removed.

The pancreas is a pale grey gland weighing about 60 grams. It is about 12 to 15 cm long and is situated in the epigastric and left hypochondriac regions of the abdominal cavity (see Figs 3.36 and 3.37, p. 51). 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 alveoli, 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 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).

The function of the exocrine pancreas is to produce *pancreatic juice* containing enzymes that digest carbohydrates, proteins and fats (p. 301).

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 function of the endocrine pancreas is to secrete the hormones insulin and glucagon, which are principally concerned with control of blood glucose levels.

Blood supply

The splenic and mesenteric arteries supply arterial blood to the pancreas and the venous drainage is by the veins of the same names that join other veins to form the portal vein (Figs 12.7 and 12.9).

Nerve supply

As in the alimentary tract, parasympathetic stimulation increases the secretion of pancreatic juice and sympathetic stimulation depresses it.

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
- list 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.

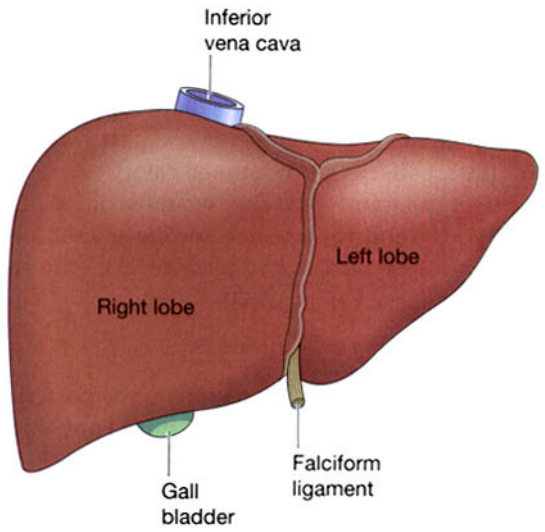


Figure 12.37 The liver: anterior view.

Its upper and anterior surfaces are smooth and curved to fit the under surface of the diaphragm (Fig. 12.37); its posterior surface is irregular in outline (Fig. 12.38).

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

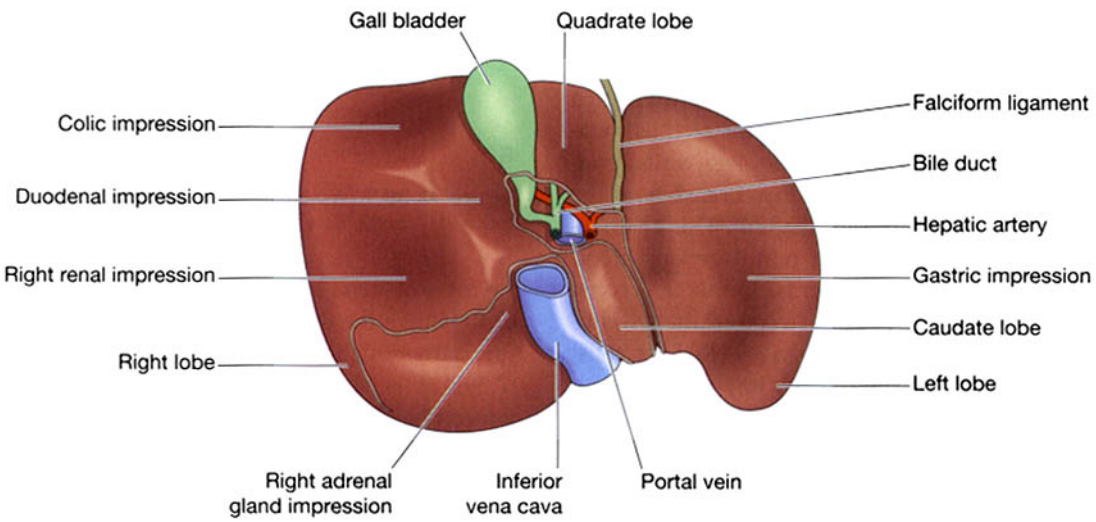


Figure 12.38 The liver, turned up to show the posterior surface.

The liver is enclosed in a thin inelastic capsule and incompletely covered by a layer of peritoneum. Folds of peritoneum form supporting ligaments attaching the liver to 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. 12.38).

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.

The *hepatic artery* enters, carrying arterial blood. It is a branch from the coeliac artery which is a branch 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 some lymph to abdominal and some to thoracic nodes.

Blood supply (Figs 12.7 and 12.9)

The hepatic artery and the portal vein take blood to the liver. Hepatic veins, varying in number, 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 lobules just visible to the naked eye (Fig. 12.39A). These lobules are hexagonal in outline and are formed by cubical-shaped cells, the *hepatocytes*, arranged in pairs of columns radiating from a central vein. Between two pairs of columns of cells there are *sinusoids* (blood vessels with incomplete walls) containing a mixture of blood from the tiny branches of the portal vein and hepatic artery (Fig. 12.39B). 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 any foreign particles present in the blood flowing through the liver.

Blood drains from the sinusoids into *central* or *centrilobular veins*. These then join with veins from other lobules, forming larger veins, until eventually they become the hepatic veins which leave the liver and empty into

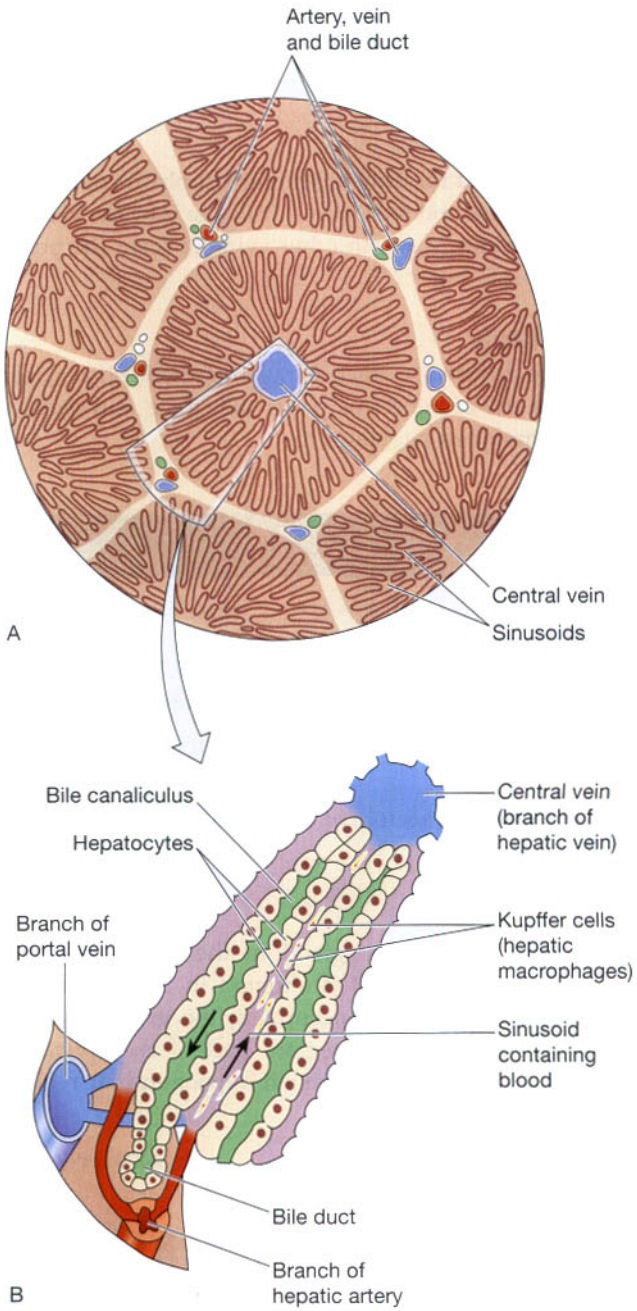


Figure 12.39 A. A magnified transverse section of a liver lobule. B. Direction of the flow of blood and bile in a liver lobule.

the inferior vena cava just below the diaphragm. Figure 12.40 shows the system of blood flow through the liver. One of the functions of the liver is to secrete *bile*. In Figure 12.39B 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.

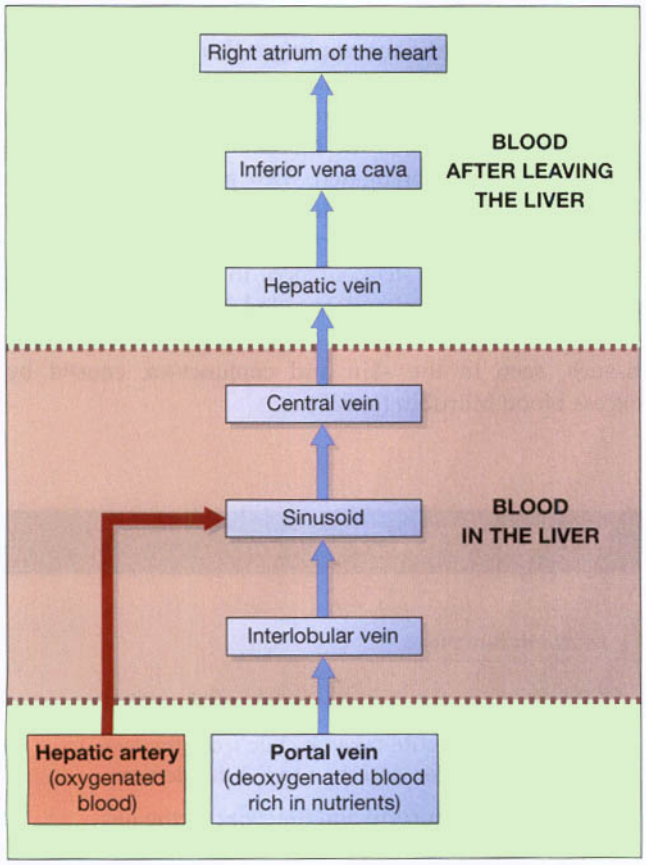


Figure 12.40 Scheme of blood flow through the liver.

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

Functions of the liver

The liver is an extremely active organ. Some of its functions have already been described, and they will only be mentioned here.

Carbohydrate metabolism. *Conversion of glucose to glycogen* in the presence of insulin, and converting liver glycogen back to glucose in the presence of glucagon. These changes are important regulators of the blood glucose level. After a meal the blood in the portal vein has a high glucose content and insulin converts some to glycogen for storage. Glucagon converts this glycogen back to glucose as required, to maintain the blood glucose level within relatively narrow limits.

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

Fat metabolism. *Desaturation of fat*, i.e. converts stored fat to a form in which it can be used by the tissues to provide energy.

Protein metabolism. *Deamination of amino acids*

- removes the nitrogenous portion from the amino acids not required for the formation of new protein; *urea* is formed from this nitrogenous portion which is excreted in urine.
- breaks down genetic material of worn-out cells of the body 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 (Fig. 12.46). *Synthesis of plasma proteins* and most of the *blood clotting factors* from the available amino acids occurs in the liver.

Breakdown of erythrocytes and defence against microbes. This is carried out by phagocytic Kupffer cells (hepatic macrophages) in the sinusoids.

Detoxification of drugs and noxious substances. These include ethanol (alcohol) and toxins produced by microbes.

Metabolism of ethanol. This follows consumption of alcoholic drinks.

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

Synthesis of vitamin A from carotene. Carotene is the provitamin found in some plants, e.g. carrots and green leaves of vegetables.

Production of heat. The liver uses a considerable amount of energy, has a high metabolic rate and 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.

Storage. The substances include:

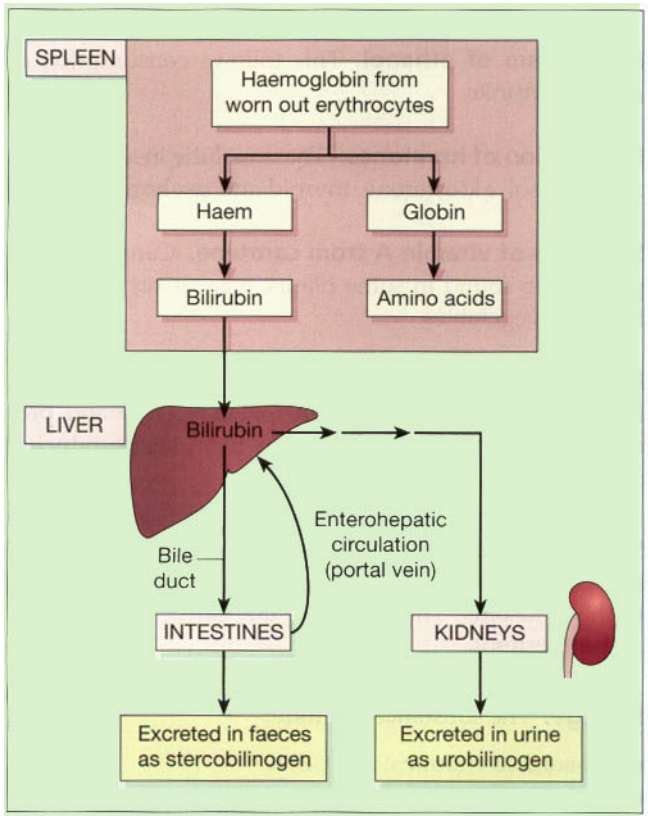
- fat-soluble vitamins: A, D, E, K
- iron, copper
- some water-soluble vitamins, e.g. riboflavine, niacin, pyridoxine, folic acid and vitamin B_{12}.

Composition of bile

About 500 ml of bile are secreted by the liver daily. Bile consists of:

- water
- mineral salts
- mucus
- bile pigments, mainly bilirubin
- bile salts, which are derived from the primary bile acids, cholic acid and chenodeoxycholic acid
- cholesterol.

The bile acids, *cholic* and *chenodeoxycholic acid*, are synthesised by hepatocytes from cholesterol, conjugated (combined) with either glycine or taurine, then secreted into bile as sodium or potassium salts. In the small intestine they emulsify fats, aiding their digestion. 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. 12.41).



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. In its original form bilirubin is insoluble in water and is carried in the blood bound to albumin. In hepatocytes it is conjugated with glucuronic acid and becomes water soluble before being excreted in bile. Bacteria in the intestine change the form of bilirubin and most is excreted as *stercobilinogen* in the faeces. A small amount is reabsorbed and excreted in urine as *urobilinogen* (Fig. 12.41). Jaundice is yellow pigmentation of the tissues, seen in the skin and conjunctiva, caused by excess blood bilirubin (p. 337).

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. 12.42)

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 at an acute angle by the *cystic duct* from the gall bladder. The cystic and hepatic ducts together form the *common bile duct* which passes downwards behind the head of the pancreas to be joined by the main pancreatic duct at the *hepatopancreatic ampulla*. The opening of the combined ducts into the duodenum is controlled by the *hepatopancreatic sphincter* (sphincter of Oddi). The common bile duct is about 7.5 cm long and has a diameter of about 6 mm.

Structure

The walls of the bile ducts have the same layers of tissue as those described in the basic structure of the alimentary canal (Fig. 12.2). In the cystic duct the mucous membrane lining is arranged in irregularly situated 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 to the common bile duct and thence to the duodenum.

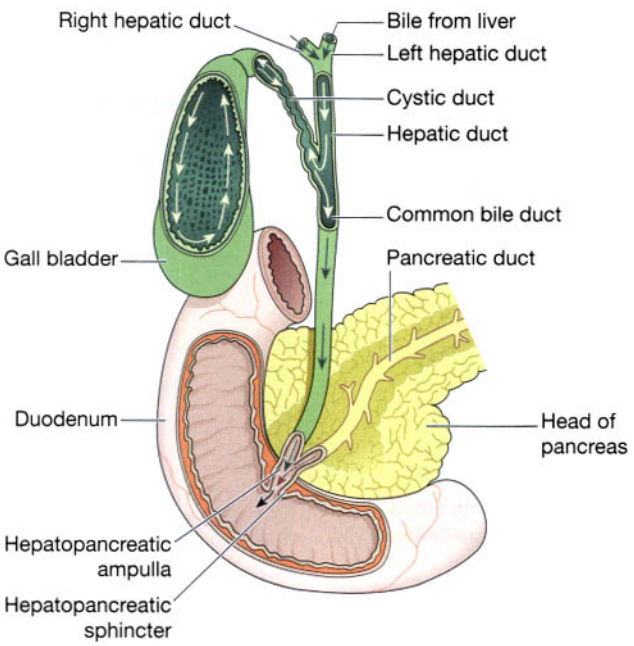


Figure 12.42 Direction of the flow of bile from the liver to the duodenum.

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

Peritoneum covers only the inferior surface. The gall bladder is in contact with the posterior surface of the right lobe of the liver and is held in place by the visceral peritoneum of the liver.

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

Mucous membrane 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 blood to the gall bladder. Blood is drained away by the *cystic vein* which joins the portal vein.

Nerve supply

Nerve impulses are conveyed by sympathetic and parasympathetic nerve fibres. There are the same autonomic plexuses as those described in the basic structure (Fig. 12.2).

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
- 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 to which the principal nutrient groups are subjected, the locations in the gastrointestinal tract where these processes occur and the enzymes responsible for them.

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

	Mouth	Stomach	Small intestine		Large intestine
			Digestion	Absorption	
Carbohydrate	*Salivary amylase*: cooked starches to disaccharides	*Acid* denatures and stops action of salivary amylase	*Pancreatic amylase*: cooked and uncooked starches to disaccharides *Sucrase*, *Maltase*, *Lactase* (in enterocytes): disaccharides to monosaccharides (mainly glucose)	Into blood capillaries of villi	—
Proteins	—	*Acid*: pepsinogen to pepsin *Pepsin*: proteins to polypeptides	*Enterokinase* (in intestinal mucosa): 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

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, Krebs cycle and oxidative phosphorylation.

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

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

Two types of processes are involved.

Catabolism. This process breaks down large molecules into smaller ones releasing *chemical energy* that is stored as adenosine triphosphate (ATP), and *heat*. Heat is used to maintain core body temperature at the optimum level for chemical activity (36.8°C). Excess heat is lost through the skin and excreta (p. 365).

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

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

Both processes occur continually in all cells maintaining an energy balance. Very active tissues, such as muscle or liver, need an adequate 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 *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)

Energy balance

Body weight remains constant when energy intake in the form of nutrients is equal to energy use. When intake exceeds requirement, body weight increases. Conversely, body weight decreases when nutrient intake does not meet energy requirements.

Metabolic rate

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 *post-absorptive 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. The post-absorptive state is important because the intake of food, especially protein, stimulates an increase in metabolic rate, possibly due to increased energy utilisation by the liver. This is called the *specific dynamic action* (SDA) of food. In measuring the BMR, the surface area of the body is taken into account because energy in the form of heat is lost through the skin. Surface area in square metres is calculated from the height and weight of the individual. Some of the wide variety of factors that affect the metabolic rate are shown in Table 12.3.

Most foods contain a mixture of different amounts of carbohydrate, protein, fat, minerals, vitamins, fibre and water. Carbohydrates, proteins and fats are the sources of energy and they are obtained from the variety of food, usually in the following proportions:

protein	10–15%
fat	15–30%
carbohydrate	55–75%

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 small people
Pregnancy, menstruation, lactation	Increased
Ingestion of food	Increased
Muscular activity	Increased
Elevated body temperature	Increased
Excess thyroid hormones	Increased
Starvation	Decreased

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 energy production and carbon dioxide and water (called metabolic water) formation. Much of the energy is stored as ATP, although some is lost as heat. The carbon dioxide is excreted through the lungs.

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 (Fig. 12.48):

- glycolysis
- the citric acid or 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.

Metabolism of carbohydrate

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. 12.43):

- 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 (p. 309).
- Some glucose may remain in the circulating blood to maintain the normal blood glucose of about 2.5 to 5.3 millimoles per litre (mmol/l) (45 to 95 mg/100 ml).
- Some glucose, if in excess of the above requirements, may be converted to the insoluble polysaccharide, *glycogen*, in the liver and in skeletal muscles. *Insulin* is the hormone necessary for this change to take place. 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

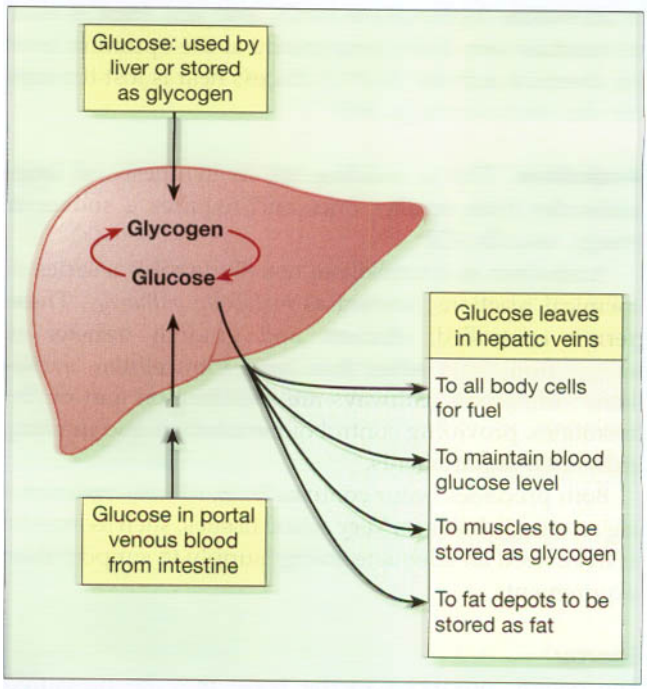


Figure 12.43 Summary of the source, distribution and use of glucose.

glycogen constitutes a store of glucose used for liver activity and to maintain the blood glucose level. Muscle glycogen provides the glucose requirement of muscle activity. *Adrenaline, thyroxine* and *glucagon* are the main hormones associated with the breakdown of glycogen to glucose.

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

All the cells of the body require energy to carry out their metabolic processes including multiplication of cells for replacement of worn out cells, contraction of muscle fibres and synthesis of secretions produced by glandular tissues. 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. 12.44)

Glucose is broken down in the body giving 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 significantly less efficient.

Aerobic respiration (catabolism). Aerobic catabolism of glucose can occur only if 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 the muscle 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 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

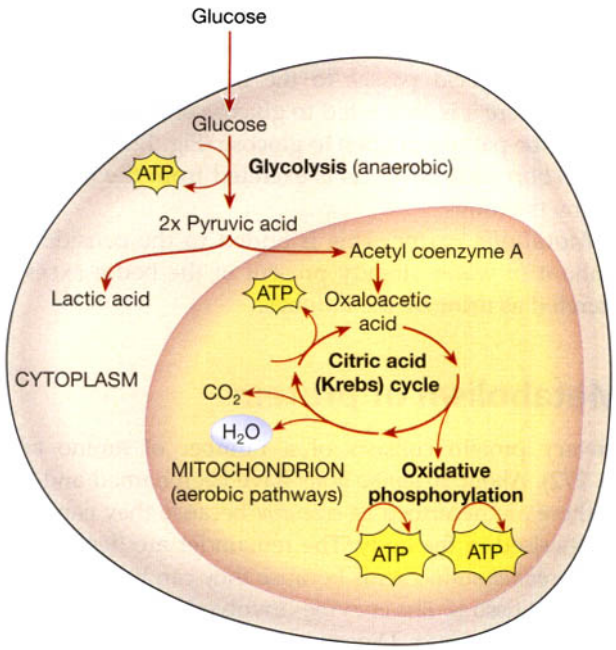


Figure 12.44 Oxidation of glucose.

roundabout called the citric acid cycle (Fig. 12.44). 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. This is far short of the maximum 38 ATP molecules that can be formed. 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. 12.43).

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.

Metabolism of protein

Dietary protein consists of a number of amino acids (p. 272). About *20 amino acids* have been named and nine of these are described as *essential* because they cannot be synthesised in the body. The remainder are described as *non-essential* amino acids because they can be synthesised by many tissues. The enzymes involved in this process are called *transaminases*. Digestion breaks down the protein of the diet to its constituent amino acids in preparation for transfer into the blood capillaries of the villi in the wall of the small intestine. In the portal circulation amino acids are transported to the liver then into the general circulation, thus making them available to all the cells and tissues of the body. 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.

- The *nitrogenous part*, the amino group (NH_2) is converted to ammonia (NH_3) and then combined with carbon dioxide forming *urea* by the process of *deamination* and 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.

Amino acid pool (Fig. 12.45)

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

Sources of amino acids

Exogenous. These are derived from the protein eaten in the diet.

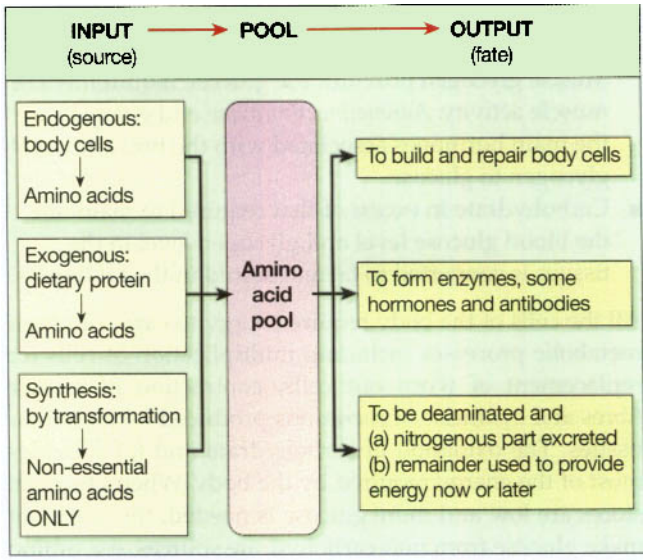


Figure 12.45 Sources and use of amino acids in the body.

Endogenous. These are obtained from the breakdown of body protein. In an adult about 80 to 100 g of protein are broken down and replaced each day. Intestinal mucosa has the most rapid turnover of cells.

Loss of amino acids

Deamination. Amino acids not needed by the body are deaminated, mainly in the liver. The nitrogenous part, or amino group (NH_2) is converted to ammonia (NH_3^+) and then to urea before being excreted by the kidneys. The remainder is used to provide energy and heat.

Excretion. The faeces contain a considerable amount of protein consisting of desquamated cells 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 12.46 depicts what happens to amino acids in the body.

Amino acids and energy release (Fig. 12.48)

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 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

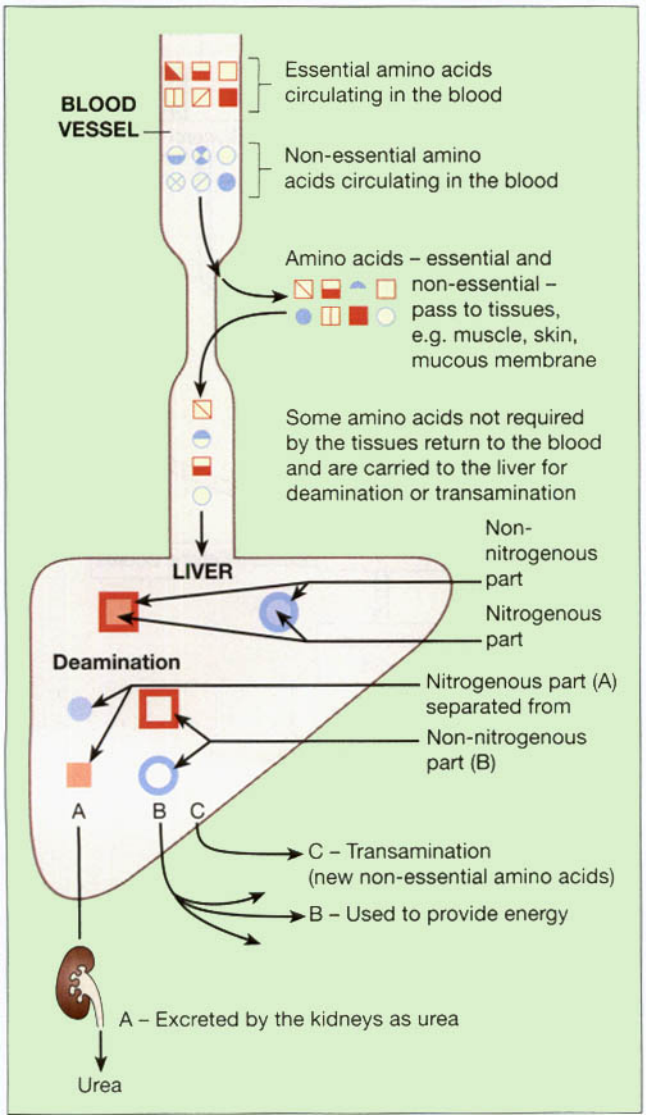


Figure 12.46 The fate of amino acids in the body.

the central metabolic pathways, e.g. acetyl coenzyme A or oxaloacetic acid, and therefore enter the system at a later stage.

Metabolism of fat (Fig. 12.47)

Fat is synthesised from carbohydrates and proteins which are taken into the body in excess of its needs and stored in the fat depots, i.e. under the skin, in the omentum or around the kidneys.

Fats which have been digested and absorbed as fatty acids and glycerol into the *lacteals* are transported via the cisterna chyli and the thoracic duct to the bloodstream and so, by a circuitous route, to the liver. Fatty acids and

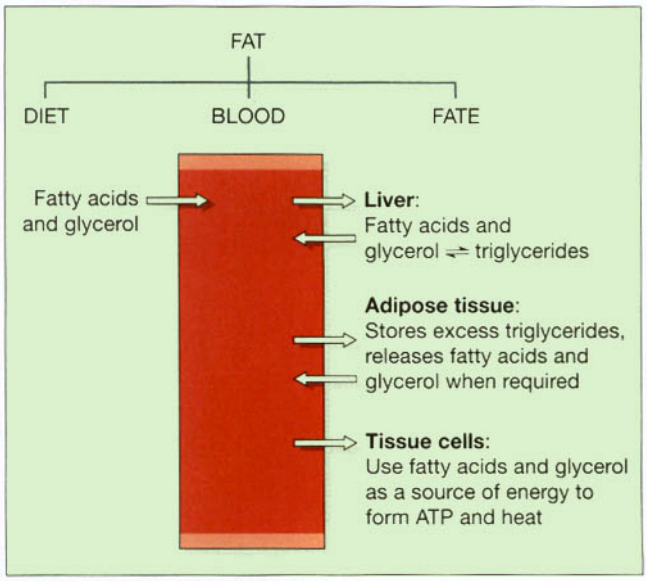


Figure 12.47 Sources, distribution and use of fats in the body.

glycerol circulating in the blood are used by the cells of organs and glands to provide energy and in the synthesis of 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. 24). When required, triglycerides are converted back to fatty acids and glycerol and used to provide energy. The end products of fat metabolism are energy, heat, carbon dioxide and water.

Fatty acids and energy release

When body tissues are deprived of glucose, as occurs in starvation, low-calorie diets or in uncontrolled diabetes mellitus, 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 (Fig. 12.48). 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, ketones are toxic, particularly in the brain. In uncontrolled diabetes mellitus, insulin deficiency results in very high blood sugar levels (hyperglycaemia). Accumulating ketones are excreted by the lungs and give a sweet acetone-like smell to the breath. Ketones are also excreted in the urine (ketonuria).

Glycerol and energy release (Fig. 12.48)

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.

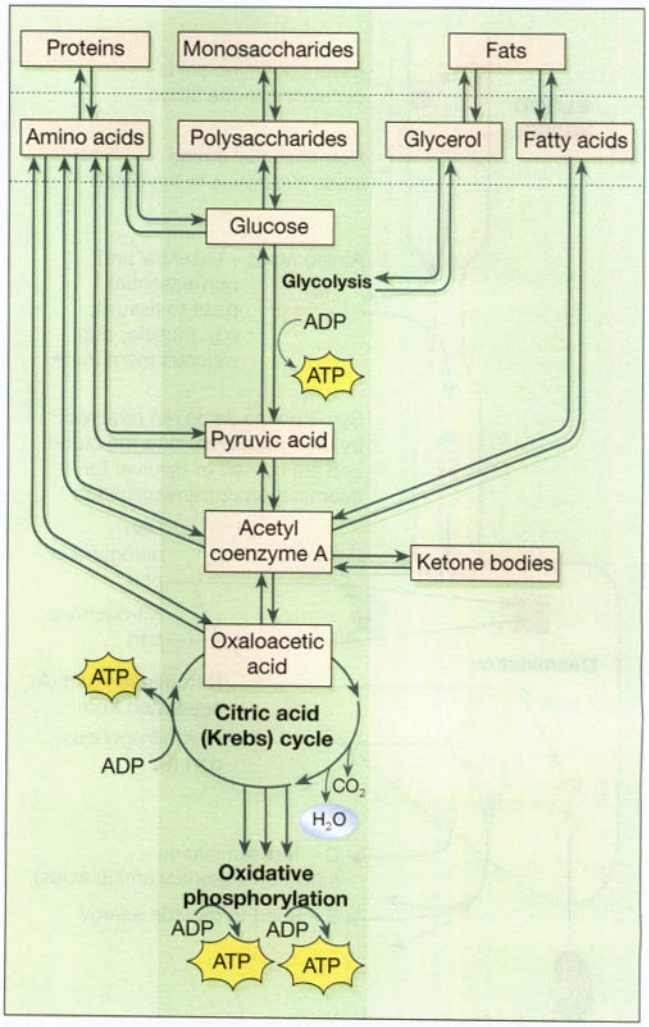


Figure 12.48 Summary of the fates of the three main energy sources in the central metabolic pathways.

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
- describe briefly the site and effects of oral squamous cell carcinoma
- distinguish between cleft lip and cleft palate, including describing the anatomical abnormalities involved.

Inflammatory and infectious conditions

Physical damage

Injury may be caused to tissues in and around the mouth by foods and other substances taken into the mouth, if they are:

- excessively hot or cold
- abrasive
- corrosive.

Corrosive chemicals are the most likely to cause serious tissue damage and acute inflammation. The outcome depends on the extent and depth of the injury.

Thrush (oral candidiasis)

This acute fungal infection of the epithelium of the mouth is caused by the yeast *Candida albicans*. In adults it causes infection mainly in debilitated people and in those whose immunity is suppressed by steroids, antibiotics or cytotoxic drugs. In babies it may be a severe infection, sometimes causing epidemics in nurseries by cross-infection. 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 the fine grooves on the upper surface of the denture and repeatedly reinfects the epithelium.

Angular cheilitis

Painful cracks develop in folds of tissue at the corners of the mouth, usually occurring in elderly debilitated people, especially if they do not wear their dentures and the folds remain moist. The usual causal organisms are *Candida albicans* and *Staphylococcus aureus*.

Dietary deficiency of iron and vitamins in the B group predispose to this condition.

Acute gingivitis (Vincent's infection)

This is an acute infection with severe ulceration of the lips, gums, mouth, throat and the palatine tonsil. It is caused by two commensal organisms acting together, *Borrelia vincenti* and a fusiform bacillus. Both organisms may be present in the mouth and only cause the disease in the presence of:

- malnutrition
- debilitating disease
- poor mouth hygiene
- injury caused by previous infection.

Aphthous stomatitis (recurrent oral ulceration)

Extremely painful ulcers occur singly or in crops inside the mouth. They are often found in association with iron and vitamin B group deficiency but a link has not been established.

Viral infections

Acute herpetic gingivostomatitis

This is caused by *Herpes simplex* virus and is the commonest oral virus infection. It is characterised by extensive and very painful ulceration.

Secondary or recurrent herpes lesions (cold sores)

Lesions, caused by *Herpes simplex* virus, occur round the nose and on the lips. After an outbreak the viruses remain dormant within the cells. Later outbreaks, usually at the same site, are precipitated by a variety of stimuli including failing immune response in old age.

Tumours of the mouth

Squamous cell carcinoma

This is the most common type of malignant tumour in the mouth and carries a poor prognosis. The usual sites are the lower lip and the edge of the tongue. Ulceration occurs frequently and there is early spread to surrounding tissues and cervical lymph nodes.

Developmental defects

Cleft palate and cleft lip (harelip)

During embryonic development, the roof of the mouth (hard palate) develops as two separate (right and left)

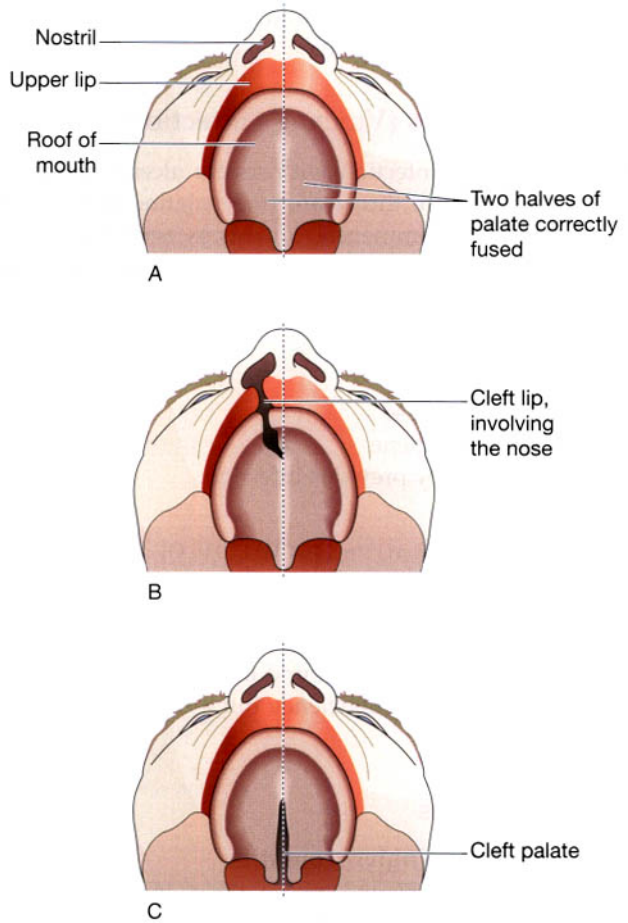


Figure 12.49 Cleft lip and cleft palate: A. Normal hard palate. B. Cleft lip. C. Cleft palate.

halves; this occurs from the lips anteriorly to the uvula posteriorly. Before birth, these two halves fuse along the midline. If fusion is incomplete, a cleft (division) occurs, which may be very minor, or it may be substantial. *Cleft lip* (Fig. 12.49B) may be merely a minor notch in the upper lip, or substantial 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. 12.49C). Factors believed to play a causative part in these conditions include genetic abnormalities, and fetal exposure to detrimental factors such as hypoxia, certain drugs or poor nutrition, between weeks 7 and 10 of pregnancy.

Speech development, and the activities of eating and drinking, cannot take place normally until the defect has been surgically repaired.

DISEASES OF THE PHARYNX

Tonsillitis and diphtheria are described on pages 258 and 259.

DISEASES OF THE SALIVARY GLANDS

Learning outcomes

After studying this section, you should be able to:

- outline the pathophysiology of mumps
- explain the nature of salivary calculi
- describe the commonest 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 inhaled in infected droplets and during the 18- to 21-day incubation period viruses multiply elsewhere in the body before spreading to the salivary glands. The virus is present in saliva for about 7 days before and after symptoms appear so infection may spread to others during this 2-week period. They may also spread to:

- the pancreas, causing pancreatitis
- the testes, causing orchitis after puberty and sometimes atrophy of the glands and sterility
- the brain, causing meningitis or meningoencephalitis.

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

Calculus formation

Calculi (stones) are formed in the salivary glands by the crystallisation of mineral salts in saliva. They may partially or completely block the ducts, leading to swelling of the gland, a predisposition to infection and, in time, atrophy. The causes are not known.

Tumours of the salivary glands

Mixed tumours (pleomorphic salivary adenoma)

This benign tumour consists of epithelial and connective tissue cells and occurs mainly in the parotid gland. A second tumour may develop in the same gland several years after the first has been removed. It rarely undergoes malignant change.

Carcinoma

Malignant tumours may occur in any salivary gland or duct. Some forms have a tendency to infiltrate nerves in the surrounding tissues, causing severe pain. Lymph spread is to the cervical nodes.

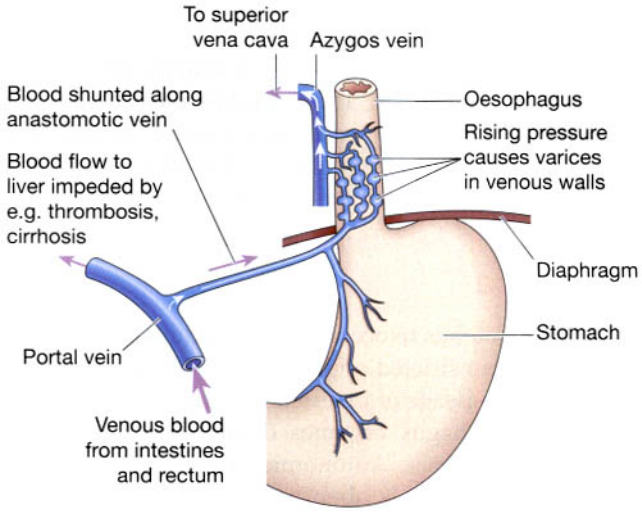


Figure 12.50 Oesophageal varices.

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
- list the likely causes of oesophageal rupture
- describe the main oesophageal tumours
- define oesophageal atresia and tracheo-oesophageal fistula.

Oesophageal varices (Fig. 12.50)

In conditions such as cirrhosis or venous thrombosis, blood flow into the liver via the portal vein is obstructed 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 per cent 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 distal oesophagus, which become distended and weakened by the abnormally high volume of blood. *Varices* develop when 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 by swallowed foodstuffs. Bleeding may be slight, but chronic, leading to iron deficiency anaemia; however, sudden rupture can cause life-threatening haemorrhage.

Inflammatory and infectious conditions

Peptic reflux oesophagitis

This condition, the commonest cause of indigestion, is caused by persistent regurgitation of acid gastric juice into the oesophagus, causing irritation 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 ageing fibrous tissue may cause stricture of the oesophagus. Reflux of gastric contents is associated with:

- increase in the intra-abdominal pressure, e.g. in pregnancy, constipation and obesity
- high acid content of gastric juice
- 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. 330).

Swallowing caustic materials

When swallowed, caustic materials burn the walls of the oesophagus causing an inflammatory reaction. The extent of the damage depends on the concentration and amount swallowed. Following severe injury, healing causes fibrosis, and there is a risk of oesophageal stricture developing later, as the fibrous tissue shrinks.

Microbial infections

Infections are relatively rare and are usually spread from the mouth or pharynx. The microbes most commonly involved are *Candida albicans*, which causes thrush, and herpes viruses. Bottle-fed babies and adults with diminished immunity are most susceptible.

Achalasia

This problem tends to occur in young adults. The cardiac sphincter is constricted and, because of this obstruction blocking the passage of ingested materials into the stomach, the oesophagus becomes dilated and the muscle layer hypertrophies. Autonomic nerve supply to the oesophageal muscle is abnormal, but the cause of the condition is not known.

The condition may lead to dysphagia, regurgitation of gastric contents and possibly aspiration pneumonia.

Oesophageal rupture

This may occur, usually at the distal end, if the oesophagus is suddenly distended:

- during a vomiting attack
- by ingestion of foreign bodies
- by passage of an instrument.

Gastric contents pass into the mediastinum, causing acute inflammation. The cause of weakness in the wall of the oesophagus is not known.

Tumours of the oesophagus

Benign tumours occur rarely.

Malignant tumours

These occur more often in males than females. The most common sites are the distal end of the oesophagus and at the levels of the larynx and bifurcation of the trachea. The tumours are mainly of two types, either of which may eventually lead to oesophageal obstruction.

Scirrhous (fibrous) tumours. These spread round the circumference and along the oesophagus. They cause thickening of the wall and loss of elasticity.

Soft tissue tumours. These grow into the lumen and spread along the wall.

The causes of malignant change are not known but may be associated with diet and regular consumption of very hot food.

Spread of a malignant tumour at the level of the bifurcation of the trachea may ulcerate the wall of the oesophagus, the trachea or a bronchus, leading to aspiration pneumonia. Other local spread may involve adjacent mediastinal structures, such as lymph nodes. Death is usually due to oesophageal obstruction before metastasis occurs.

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 between the oesophagus and the trachea through which milk or regurgitated gastric contents are aspirated.

One or both abnormalities may be present. The causes of these developmental deficiencies are not known.

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

This is a common condition which occurs when an imbalance between the corrosive action of gastric juice and the protective effect of mucus on the gastric mucosa develops. The amount of mucus in the stomach is insufficient to protect the surface epithelium from the destructive effects of hydrochloric acid. It may be acute or chronic.

Acute gastritis

Gastritis occurs with varying degrees of severity. The most severe form is *acute haemorrhagic gastritis.* When the surface epithelium of the stomach is exposed to acid gastric juice the cells absorb hydrogen ions which

increase their internal acidity, disrupt their metabolic processes and trigger the inflammatory reaction. The causes of acute gastritis include:

- regular prolonged use of aspirin and other anti-inflammatory drugs, especially the non-steroids
- regular excessive alcohol consumption
- food poisoning caused by, e.g., *Staphylococcus aureus, Salmonella paratyphi* or viruses
- heavy cigarette smoking
- treatment with cytotoxic drugs and ionising radiation
- ingestion of corrosive poisons, acids and alkalis
- regurgitation of bile into the stomach.

The outcome depends on the extent of the damage. In many cases recovery is uneventful after the cause is removed. In the most severe forms there is ulceration of the mucosa that may be followed by haemorrhage, perforation of the stomach wall and peritonitis. Where there has been extensive tissue damage, healing is by fibrosis causing reduced elasticity and peristalsis.

Chronic gastritis

Chronic gastritis is a milder longer-lasting form. It may follow repeated acute attacks or be an autoimmune disease and is more common in later life.

Helicobacter-associated gastritis

The microbe *Helicobacter pylori* is known to be associated with gastric conditions, especially chronic gastritis and peptic ulcer disease. Antibodies to this microbe develop in early adulthood although lesions of gastritis occur later in life.

Autoimmune chronic gastritis

This is a progressive form of the 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, the secretion of digestive enzymes, hydrochloric acid and intrinsic factor are markedly reduced. The antigens are the gastric parietal cells and the *intrinsic factor* they secrete. When these cells are destroyed as a result of this abnormal autoimmune condition, the inflammation subsides. The initial causes of the autoimmunity are not known but there is a familial predisposition and an association with chronic thyroiditis, thyrotoxicosis and atrophy of the adrenal glands. Secondary effects include:

- pernicious anaemia due to lack of intrinsic factor (p. 70)
- impairment of digestion due to lack of enzymes
- microbial infection due to lack of hydrochloric acid.

Peptic ulceration

Ulceration of the gastrointestinal mucosa is caused by disruption of the normal balance of 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 cell damage 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, following reflux of gastric juice, and round the anastomosis of the stomach and small intestine, following gastrectomy. The underlying causes are not known but, if factors associated with the maintenance of healthy mucosa are defective, acid gastric juice gains access to the epithelium, causing the initial cell damage that leads to ulceration. The main factors are: normal blood supply, mucus secretion and cell replacement.

Blood supply

Reduced blood flow and ischaemia may be caused by excessive cigarette smoking and stress, either physical or mental. In a stressful situation there is an increase in the secretion of the hormones noradrenaline and adrenaline and these cause 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 irradiation and the use of cytotoxic drugs.

In peptic ulcer disease, the alimentary tract is commonly colonised by the bacterium *Helicobacter pylori*, a causative agent in this disorder.

Acute peptic ulcers

These lesions involve tissue to the depth of the submucosa and the lesions may be single or multiple. They are found in many sites in the stomach and in the first few centimetres of the duodenum. The underlying causes are

unknown but their development is often associated with severe stress, e.g. severe illness, shock, burns, severe emotional disturbance and following surgery. Healing without the formation of fibrous tissue usually occurs when the cause of the stress is removed.

Chronic peptic ulcers

These ulcers penetrate through the epithelial and muscle layers of the stomach wall and may include the adjacent pancreas or liver. In the majority of cases they occur singly in the pyloric antrum of the stomach and in the duodenum. Occasionally there are two ulcers facing each other in the duodenum, called kissing ulcers. Healing occurs with the formation of fibrous tissue and subsequent shrinkage may cause:

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

Complications of peptic ulcers

Haemorrhage. Acid gastric juice may cause the development of many tiny ulcers, or *gastric erosions*, leading to multiple capillary bleeding points and possibly iron deficiency anaemia (p. 69).

When a major artery is eroded a serious and possibly life-threatening haemorrhage may occur, causing:

- shock (p. 111)
- haematemesis—vomiting of blood
- melaena—blood in the faeces.

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* and the infection may spread through the diaphragm to the pleural cavity.

Pyloric stenosis. Fibrous tissue formed as an ulcer in the pyloric region heals and may cause narrowing of the pylorus, obstructing outflow from the stomach and resulting in persistent vomiting.

Development of a malignant tumour. This may complicate gastric ulceration.

Tumours of the stomach

Benign tumours of the stomach occur rarely.

Malignant tumours

This is a relatively common form of malignancy and it occurs more frequently in men than women. The local growth of the tumour gradually destroys the normal tissue so that achlorhydria (reduced hydrochloric acid secretion) and pernicious anaemia are frequently secondary features. The causes have not been established but there appears to be:

- a familial predisposition
- an association with diet—high-salt diets and regular consumption of smoked or pickled foods increase the risk
- the presence of other diseases, e.g. chronic gastritis, chronic ulceration and pernicious anaemia.

Spread of gastric carcinoma

Local spread. These tumours spread locally to the remainder of the stomach, to the oesophagus, duodenum, omentum, liver and pancreas. The spleen is seldom affected.

As the tumour grows, the surface may ulcerate and become infected, especially when achlorhydria develops.

Lymphatic spread. This occurs early in the disease. At first the spread is within the lymph channels in the stomach wall, and then to lymph nodes round the stomach, in the mesentery, omentum and walls of the small intestine and colon.

Blood spread. The common sites for blood-spread metastases are the liver, lungs, brain and bones.

Peritoneal spread. When a tumour includes the full thickness of the stomach wall, small groups of cells may break off and spread throughout the peritoneal cavity. Metastases may develop in any tissue in the abdominal or pelvic cavity where the fragments settle.

Congenital pyloric stenosis

In this condition there is spasmodic constriction of the pyloric sphincter, characteristic projective vomiting and failure to put on weight. In an attempt to overcome the spasms, hypertrophy of the muscle of the pyloric antrum develops, causing obstruction of the pylorus 2 to 3 weeks after birth. The reason for the excess stimulation or neuromuscular abnormality of the pylorus is not known but there is a familial tendency and it is more common in males.

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 two commonest forms of inflammatory bowel disease: 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 will be 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, e.g., 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 shifts and is localised to the region above the appendix (the right iliac fossa) (see also p. 174). 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:

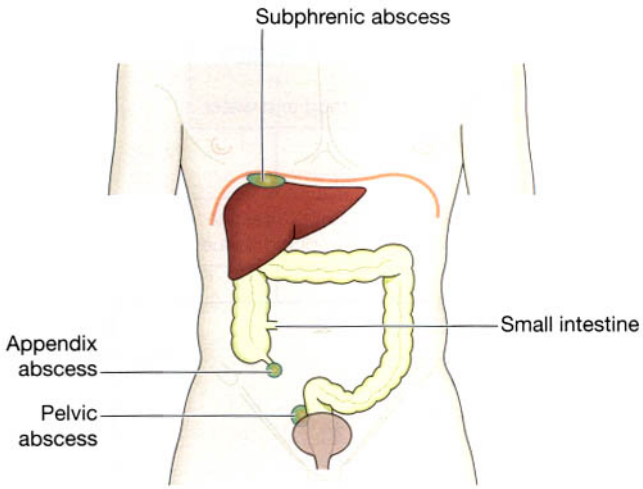


Figure 12.51 Abscess formation; complication of appendicitis.

- microbes spread through the wall of the appendix and infect the peritoneum
- an appendix abscess ruptures and pus enters the peritoneal cavity
- the appendix becomes gangrenous and ruptures, discharging its contents into the peritoneal cavity.

Abscess formation. The most common abscesses are (Fig. 12.51):

- 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.

Fibrous adhesions. When healing takes place fibrous tissue forms 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).

Microbial diseases (Fig. 12.52)

Typhoid fever

This type of enteritis is caused by the microbe *Salmonella typhi*, ingested in food and water. Humans are its only host so the source of contamination is an individual who is either suffering from the disease or is a carrier.

After ingestion of microbes there is an incubation period of about 14 days before signs of the disease

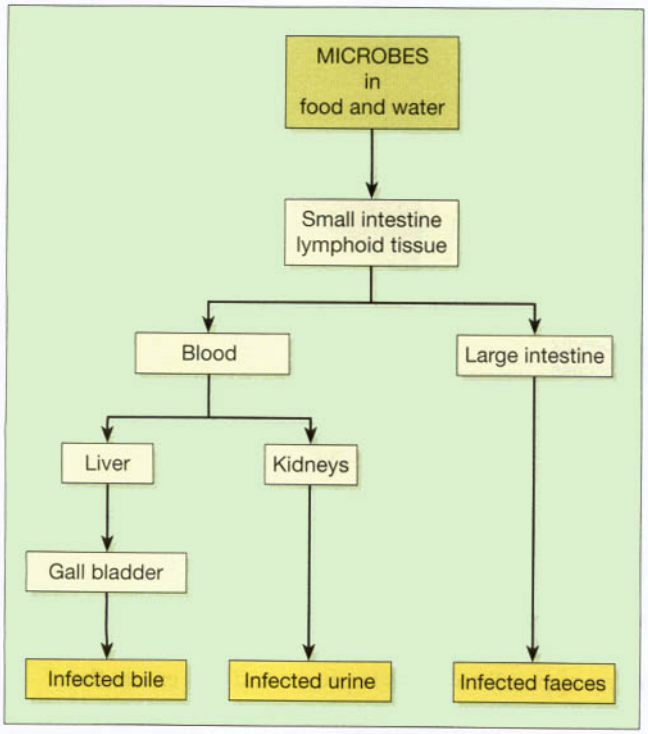


Figure 12.52 The routes of excretion of microbes in enteric fever.

appear. During this period the microbes invade lymphoid tissue in the walls of the small and large intestine, especially the aggregated lymph follicles (Peyer's patches) and solitary lymph nodes. The microbes then enter the blood vessels and spread to the liver, spleen and gall bladder. In the bacteraemic period acute inflammation develops with necrosis of intestinal lymphoid tissue and ulceration of overlying mucosa. Other effects of *Salmonella typhi* or their endotoxins include:

- typhoid cholecystitis in which the microbes multiply in the gall bladder and are excreted in bile, reinfecting the intestine
- red spots on the skin, especially of the chest and abdomen
- enlargement of the spleen
- myocardial damage and endocarditis
- liver and kidney damage
- reduced resistance to other infections, especially of the respiratory tract, e.g. laryngitis, bronchitis, pneumonia.

Uncomplicated recovery takes place in about 5 weeks with healing of intestinal ulcers and very little fibrosis.

Complications

- The ulcers may penetrate a blood vessel, causing haemorrhage, or erode the intestinal wall, leading to acute peritonitis.
- The individual may become a carrier. When this happens the typhoid fever becomes a chronic, asymptomatic infection of the biliary and urinary tracts. Microbes continue to be excreted indefinitely in urine and faeces. Contamination of food and water by carriers is the usual source of infection.

Paratyphoid fever

This disease is caused by *Salmonella paratyphi A* or *B* spread in the same way as typhoid fever, i.e. in food and drink contaminated by infected urine or faeces. The infection, causing inflammation of the intestinal mucosa, is usually confined to the ileum. Other parts of the body are not usually affected but occasionally chronic infection of the urinary and biliary tracts occurs and the individual becomes an asymptomatic carrier, excreting the microbes in urine and faeces.

Other salmonella infections

Salmonella typhimurium and *S. enteritidis* are the most common infecting microbes in this group. 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 infection is usually of short duration but may be accompanied by acute abdominal pain and diarrhoea, causing dehydration and electrolyte imbalance. In children and debilitated elderly people the infection may be severe or even fatal. Chronic infection of the biliary and urinary tracts may develop and the individual becomes a carrier, excreting the organisms in urine and faeces (Fig. 12.52).

Escherichia coli (*E. coli*) food poisoning

Common sources for these organisms include undercooked meat and unpasteurised milk; adequate cooking kills *E. coli*. The severity of the disease depends on the type of *E. coli* responsible; some types are more virulent than others and outbreaks of *E. coli* food poisoning can cause fatalities, particularly in the elderly.

Staphylococcal food poisoning

This is not an infection in the true sense. Acute gastroenteritis is caused by toxins produced by the *Staphylococcus aureus* before ingestion of the contaminated food. The organisms are usually killed by cooking but the toxins can withstand higher temperatures and remain unchanged.

There is usually short-term acute inflammation with violent vomiting and diarrhoea, causing dehydration and electrolyte imbalance. In most cases complete recovery occurs within 24 hours.

Clostridium perfringens (*Cl. welchii*) food poisoning

These microbes, although normally present in the intestines of humans and animals, 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. The spores survive the initial cooking and if the food is cooled slowly they enter the vegetative phase and multipy between the temperatures of 50°C and 20°C. Following refrigeration the microbes multiply if the food is reheated slowly. After being eaten, microbes that remain vegetative die and release endotoxins that cause gastroenteritis.

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 microbes 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.

Cholera

Cholera is caused by *Vibrio cholerae* and is spread by contaminated water, food, hands and fomites. The only known hosts are humans. A very powerful toxin is produced 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. The microbes occasionally spread to the gall bladder where they multiply. They are then excreted in bile and faeces. This carrier state usually lasts for a maximum of about 4 years providing a reservoir for spread of infection.

Dysentery

Bacillary dysentery

This infection of the colon is caused by bacteria of the *Shigella* group. The severity of the condition depends on the organisms involved. In Britain it is usually a relatively mild condition caused by *Shigella sonnei*. Outbreaks may reach epidemic proportions, especially in institutions. Children and elderly 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, containing blood and excess mucus, causes dehydration, electrolyte imbalance and anaemia. When healing occurs the mucous membrane is fully restored. Occasionally a chronic infection develops and the individual becomes a carrier, excreting the microbes in faeces. *Shigella dysenteriae* causes the most severe type of infection. It occurs mainly in tropical countries.

Amoebic dysentery

This disease is caused by *Entamoeba histolytica*. The only known hosts are humans and it is spread by faecal contamination of food, water, hands and fomites. Before ingestion the amoebae are inside resistant cysts. When these reach the colon they grow and divide and invade the mucosal cells, causing inflammation and ulceration. Further development of the disease may result in destruction of the mucosa over a large area and sometimes perforation occurs. Diarrhoea containing mucus and blood is persistent and debilitating.

The disease may progress in a number of ways.

- Healing may produce fibrous adhesions, causing partial or complete obstruction.
- The amoebae may spread to the liver, causing amoebic hepatitis and abscesses.
- Chronic dysentery may develop with intermittent diarrhoea and amoebae in the faeces.

Although most infected people do not develop symptoms they may become carriers.

Inflammatory bowel disease (Table 12.4)

Crohn's disease (regional ileitis)

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 be more widespread. 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 cause of Crohn's

Table 12.4 **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; both sexes affected equally; smokers at higher risk	Usually between 20 and 40 years of age; more women affected than men; 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 inflamed and thickened	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	Surgical removal of entire colon cures the condition

disease is not entirely clear but it may be that immunological abnormality renders the individual susceptible to infection, especially by viruses. 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. 378)
- peri-anal fistula formation
- megaloblastic anaemia due to malabsorption of vitamin B_{12} and folic acid
- cancer of the small or large intestine.

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 and sigmoid colon. From there it may spread to involve a variable proportion of the colon and, sometimes, the entire colon. There are periods of remission lasting weeks, months or years. The cause is not known but there is an association with arthritis, iritis, some skin lesions, haemolytic anaemia and some drug sensitivities. In long-standing cases cancer sometimes develops.

Fulminating ulcerative colitis

This is also called *toxic megacolon*. The colon loses its muscle tone and dilates, the wall becomes thinner and perforation, which may be fatal, may follow. There is a sudden onset of acute diarrhoea, with severe blood loss, leading to dehydration, electrolyte imbalance, perforation, hypovolaemic shock and possibly death.

Diverticular disease

Diverticula are small pouches of mucosa that protrude into the peritoneal cavity through the circular muscle fibres of the colon between the taeniae coli (Fig. 12.53). 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. *Diverticulitis* arises when faeces impact in the diverticula and the walls become inflamed and oedematous as secondary infection develops. This reduces the blood supply causing ischaemic pain. Occasionally, rupture occurs resulting in peritonitis.

The causes of *diverticulosis* (presence of diverticuli) are not known but it is associated with low-residue diet and abnormally active peristalsis. In Western countries diverticulosis is fairly common after the age of 60 but diverticulitis affects only a small proportion.

Tumours of the small and large intestines

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

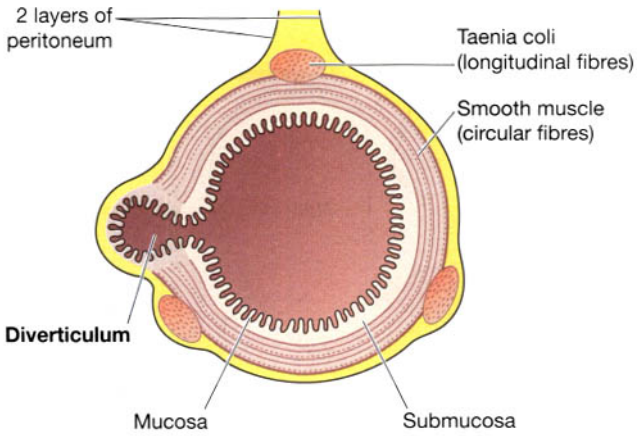


Figure 12.53 Diverticular disease; cross-section of bowel showing one diverticulum.

Benign tumours

Benign neoplasms may form a broad-based mass or develop a pedicle. Occasionally those with pedicles twist upon themselves, causing ischaemia, necrosis and possibly gangrene. Malignant changes may occur.

Malignant tumours

Small intestine. Malignant tumours tend not to obstruct the lumen and may remain unnoticed until symptoms caused by metastases appear. The most common sites of metastases are local lymph nodes, the liver, lungs and brain.

The colon. This is the most common site of malignancy in the alimentary tract in Western countries. The tumour may be:

- a soft friable mass, projecting into the lumen of the colon with a tendency to ulceration, infection and haemorrhage
- a hard fibrous mass encircling the colon, causing reduced elasticity and peristalsis and narrowing of the lumen
- a gelatinous mucoid mass that thickens the wall and tends to ulcerate and become infected.

The most important 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 insufficient fibre are eaten, the disease is much more common. Slow movement of bowel contents may result in the conversion of as yet unknown substances that are present into carcinogenic agents. Predisposing diseases include ulcerative colitis and some benign tumours.

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.

Carcinoid tumours (argentaffinomas)

These tumours are considered, on clinical evidence, to be benign but they spread into the tissues around their original site. They grow very slowly and rarely metastasise. The parent cells are hormone-secreting cells widely dispersed throughout the body, not situated in endocrine glands. Some of these tumours secrete hormones while others do not. They are called APUD cells, an acronym for some of their chemical characteristics. The cells react with silver compounds, hence the name argentaffinomas. Common sites in the intestines for these *apudomas* are the appendix, ileum, stomach, colon and rectum. The tumours are frequently multiple and may spread locally, causing obstruction.

Carcinoid syndrome. This is the name given to the effects of the variety of substances secreted by apudomas in the intestine and elsewhere. The secretions include serotonin (5-hydroxytryptamine), histamine and bradykinin, and the effects include flushing attacks, tachycardia, sweating, anxiety and diarrhoea.

Hernias

A hernia is a protrusion of bowel through a weak point in the musculature of the anterior abdominal wall or an existing opening (Fig. 12.54A). It occurs when there are intermittent increases in intra-abdominal pressure, most commonly in men who lift heavy loads at work. The underlying causes of the abdominal wall weakness are not known. Possible 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 slight pressure over the abdominal swelling
- strangulation, when the venous drainage from the herniated loop of bowel is impaired, causing congestion, ischaemia and gangrene. In addition there is intestinal obstruction.

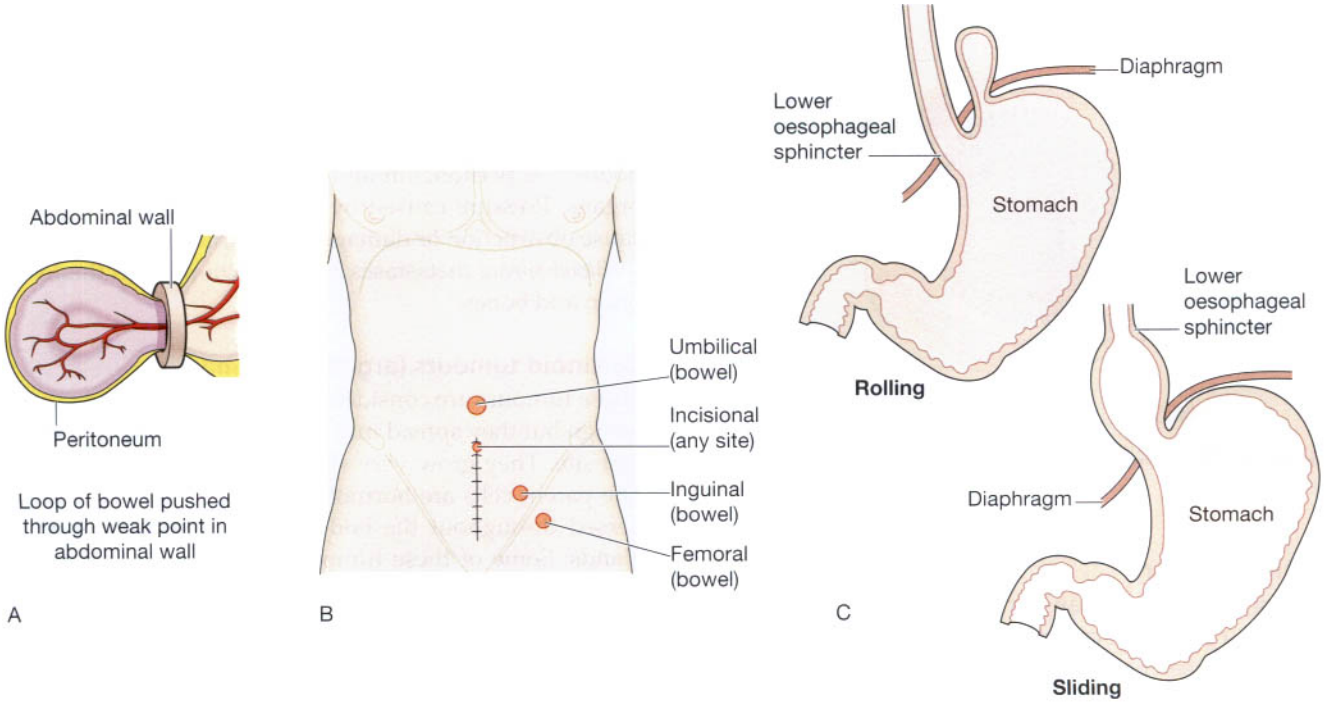


Figure 12.54 Hernias: A. Strangulated hernia formation. B. Common sites of herniation. C. Hiatus hernia.

Sites of hernias (Fig. 12.54B)

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

Incisional hernia. This is caused by repeated stretching of the fibrous tissue formed during the repair of a surgical wound.

Diaphragmatic or hiatus hernia (Fig. 12.54C) This is the protrusion of a part of the fundus of the stomach through the oesophageal opening in the diaphragm. The main complication is irritation caused by 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.

Sliding hiatus hernia. An unusually short oesophagus that ends above the diaphragm pulls a part of the stomach upwards into the thorax. The abnormality may be congenital or 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 normal shortening of the oesophagus by muscular contraction during swallowing.

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.

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

Volvulus

This occurs when a loop of bowel twists through 180°, cutting off its blood supply, causing gangrene and obstruction. It occurs in parts of the intestine that are attached to the posterior abdominal wall by a long double fold of visceral peritoneum, the mesentery. The most common site in adults is the sigmoid colon and in children the small intestine. The causes are unknown but predisposing factors include:

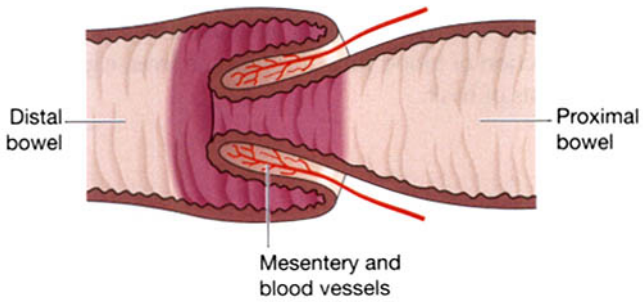


Figure 12.55 Intussusception.

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

Intussusception

In this condition a length of intestine is invaginated into itself (Fig. 12.55). It occurs most commonly in children when a piece of terminal ileum is pushed through the ileocaecal valve. In a child, infection, usually by viruses, causes swelling of the lymphoid tissue in the intestinal wall. 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. polypi, together with the strong peristalsis, may be the cause.

Intestinal obstruction

This is not a disease in itself. The following is a summary of the main causes of obstruction with some examples.

Mechanical causes of obstruction

These include:

- constriction of the intestine by, e.g., strangulated hernia, intussusception, volvulus, peritoneal adhesions; partial obstruction may suddenly become 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
- obstruction by, e.g., a large gallstone or a tumour growing into the lumen
- pressure on the intestine from outside, e.g. a large tumour in any pelvic or abdominal organ, such as a uterine fibroid; this type is most likely to occur inside the confined space of the bony pelvis.

Neurological causes of obstruction

Partial or complete loss of peristaltic activity produces the effects of obstruction. *Paralytic ileus* is the most common form but the paralysis may be more widespread. The cause is either excessive sympathetic stimulation or lack of parasympathetic stimulation. The mechanisms are not clear but there are well-recognised predisposing conditions including:

- general peritonitis, especially when large amounts of exotoxin are released from dead microbes
- following surgery when there has been a considerable amount of handling of the intestines
- severe intestinal infection, especially if there is acute toxaemia, e.g. following ruptured appendix.

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

Vascular causes of obstruction

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

- atheromatous changes in the blood vessel walls, with thrombosis
- embolism
- mechanical obstruction of the bowel, e.g. strangulated hernia.

Malabsorption

Impaired absorption of nutrient materials and water from the intestines is not a disease in itself. It is the result of diseases causing one or more of the following changes:

- atrophy of the villi of the mucosa of the small intestine

- incomplete digestion of food
- interference with the transport of absorbed nutrients from the small intestine to the blood.

Primary malabsorption

Disease of the intestinal mucous membrane

Atrophy of the villi is the main cause, varying in severity from minor abnormality to almost complete loss of function. The most common underlying diseases are coeliac disease and tropical sprue.

Coeliac disease (idiopathic steatorrhoea). This disease is believed to be due to a genetically determined abnormal immunological reaction to the protein *gluten*, present in wheat. When it is removed from the diet, recovery is complete. There is marked villous atrophy and malabsorption characterised by the passage of loose, pale coloured, fatty stools.

There may be abnormal immune reaction to other antigens. Atrophy of the spleen is common and malignant lymphoma of the small intestine may develop. It often presents in infants after weaning but can affect any age.

Tropical sprue. In this disease there is partial villous atrophy with malabsorption, chronic diarrhoea, severe wasting and pernicious anaemia due to deficient absorption of vitamin B_{12} and folic acid. The cause is unknown but it may be that bacterial growth in the small intestine is a factor. The disease is endemic in subtropical and tropical countries except Africa south of the Sahara. After leaving the endemic area most people suffering from sprue recover, but others may not develop symptoms until months or even years later.

Secondary malabsorption

This is associated with incomplete digestion of food, impaired transport of absorbed nutrients and following extensive small bowel resection.

Defective digestion

This occurs in a variety of conditions:

- disease of the liver and pancreas
- following a resection of small intestine
- following surgery if microbes grow in a blind end of intestine.

Impaired transport of nutrients

This occurs when there is:

- lymphatic obstruction by, e.g., lymph node tumours, removal of nodes at surgery, tubercular disease of lymph nodes
- impairment of mesenteric blood flow by, e.g., arterial or venous thrombosis, pressure caused by a tumour
- obstruction of blood flow through the liver, e.g. in cirrhosis of liver.

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
- explain the effects of cystic fibrosis
- outline the main pancreatic tumours and their consequences.

Acute 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. The severity of the disease is directly related to the amount of pancreatic tissue destroyed.

Mild forms may damage only those cells near the ducts.

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 alcoholism. When a gallstone obstructs the hepatopancreatic ampulla there is reflux of bile into the pancreas and the spread of infection from cholangitis. Other associated conditions include:

- cancer of the ampulla or head of pancreas
- virus infections, notably mumps
- chronic renal failure
- renal transplantation
- hyperparathyroidism
- hypothermia
- drugs, e.g. corticosteroids, cytotoxic agents
- diabetes mellitus
- cholecystitis.

Chronic pancreatitis

This is due to repeated attacks of acute pancreatitis or may arise gradually without evidence of pancreatic disease. It is frequently associated with fibrosis and distortion of the main pancreatic duct.

There is obstruction of the tiny acinar ducts by protein material secreted by the acinar cells. This eventually leads to the formation of cysts which may rupture into the peritoneal cavity. Intact cysts may cause obstruction of the:

- common bile duct, causing jaundice
- portal vein, causing venous congestion in the organs drained by its tributaries.

The causes of these changes are not known but they are associated mainly with heavy wine drinking.

Cystic fibrosis (mucoviscidosis)

This is one of the most common genetic diseases, affecting 1 in 2500 babies. It is estimated that almost 20% of people carry the abnormal recessive gene which must be present in *both parents* to cause the disease.

The secretions of all exocrine glands have abnormally high viscosity but the most severely affected are those of the pancreas, intestines, biliary tract, lungs and the reproductive system in the male. Sweat glands secrete abnormally large amounts of salt during excessive sweating. In the pancreas highly viscous mucus is secreted by the walls of the ducts and causes obstruction, parenchymal cell damage, the formation of cysts and defective enzyme secretion. In the newborn, intestinal obstruction may be caused by a plug of meconium and viscid mucus, leading to perforation and meconium peritonitis which is often fatal. In less acute cases there may be impairment of protein and fat digestion resulting in malabsorption, steatorrhoea and failure to thrive in infants. In older children:

- digestion of food and absorption of nutrients is impaired
- there may be obstruction of bile ducts in the liver, causing cirrhosis
- bronchitis, bronchiectasis and pneumonia may develop.

The life span of affected individuals is likely to be less than 40 years; the main treatments offered are aimed at controlling pulmonary infection. Chronic lung disease and *cor pulmonale* are the commonest causes of death.

Tumours of the pancreas

Benign tumours of the pancreas are very rare.

Malignant tumours

These are relatively common and affect men more than women. They occur most frequently in the head of the pancreas, obstructing the flow of bile and pancreatic juice into the duodenum. Jaundice and acute pancreatitis usually develop. Weight loss is the result of impaired digestion and absorption of fat. Tumours in the body and tail of the gland rarely cause symptoms until the disease is advanced. Metastases are often recognised before the primary tumour. The causes of the malignant changes are not known but it is believed that there may be an association with:

- cigarette smoking
- diet high in fats and carbohydrates
- diabetes mellitus.

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.

New liver cells develop only when needed to replace damaged cells. Capacity for regeneration is considerable and 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

Virus infections are the commonest cause of acute liver injury and include Type A, Type B and Type C. 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 by mechanisms not yet understood. 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. 12.40) 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. 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.

Type A virus (infectious hepatitis)

This virus has only one known serological type. It occurs endemically, affecting mainly children, causing a mild illness. Infection is spread by hands, food, water and fomites contaminated by infected faeces. The incubation period is 15 to 40 days and the viruses are excreted in the faeces for 7 to 14 days before clinical symptoms appear and for about 7 days after. Antibodies develop and immunity persists after recovery. Subclinical disease may occur but carriers do not develop.

Type B virus (serum hepatitis)

This virus has a number of serological types. Infection occurs at any age, but mostly in adults. The incubation period is 50 to 180 days. The virus enters the blood and is spread by blood and blood products. People at greatest risk of infection are those who come in contact with blood and blood products in their daily work, e.g. people in the health, ambulance and fire services. The virus is also spread by body fluids, i.e. saliva, semen, vaginal secretions and from mother to fetus. Others at risk include intravenous drug addicts and male homosexuals. Antibodies are formed and immunity persists after recovery. Infection usually leads to severe illness lasting 2 to 6 weeks, often followed by a protracted convalescence. Carriers may, or may not, have had clinical disease. Type B virus may cause massive liver necrosis and death. In less severe cases recovery may be complete. In chronic hepatitis which may develop, live viruses continue to circulate in the blood and other body fluids. The condition may predispose to liver cancer.

Hepatitis C

This virus is spread by blood and blood products. It is prevalent in IV drug users and also occurs as a complication of blood transfusion. The infection can be asymptomatic as a carrier state occurs. When hepatitis develops, it is often recurrent and may result in chronic liver disease, especially cirrhosis.

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 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).

Box 12.1 Some hepatotoxic substances

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

Circulatory disturbances

The intensely active hepatocytes are particularly vulnerable to damage by hypoxia which is usually due to deficient 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.

Chronic hepatitis

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

Chronic persistent hepatitis

This is a mild, persistent inflammation following acute viral hepatitis. There is usually little or no fibrosis.

Chronic active hepatitis

This is a continuing progressive inflammation with cell necrosis and the formation of fibrous tissue that may lead to cirrhosis of the liver. There is distortion of the liver blood vessels and hypoxia, leading to further hepatocyte damage. This condition is commonly associated with Type B virus hepatitis, with some forms of autoimmunity and unpredictable drug reactions.

Non-viral inflammation of the liver

Pyogenic

Ascending cholangitis. Infection, usually by *Escherichia coli*, may spread from the biliary tract. The most common predisposing factor is obstruction of the common bile duct by gallstones.

Liver abscess. Septic emboli from septic foci in the abdomen and pelvis may lodge in branches of the portal vein and cause multiple abscesses or infect the vein, causing *portal pylephlebitis*. Common sources of this type of infection are acute appendicitis, diverticulitis and inflamed haemorrhoids.

Cirrhosis of the liver

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

- alcohol abuse
- hepatitis B and C virus infections
- the effects of bile retained in hepatocytes due to obstruction of bile flow or chronic inflammation
- congenital metabolic abnormalities.

As the inflammation subsides, destroyed liver tissue is replaced by fibrous tissue. There is hyperplasia of hepatocytes adjacent to the damaged area, in an attempt to compensate for the destroyed cells. This leads to the formation of nodules consisting of hepatocytes confined within sheets of fibrous tissue.

As the condition progresses there is the development of portal hypertension, leading to congestion in the organs drained by the tributaries of the portal vein, to ascites and possibly to the development of oesophageal varices (p. 321).

Liver failure may occur when hyperplasia 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 reduced to such an extent that other body activities are impaired. It may 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
- following some medical procedures, e.g. abdominal paracentesis, portacaval shunt operations.

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

Hepatic encephalopathy

The cells affected are the astrocytes in the brain. The condition is characterised by apathy, disorientation, muscular rigidity, delirium and coma. 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 blood
- Other metabolites, normally present 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 substances needed for blood clotting, i.e. prothrombin, fibrinogen and factors II, V, VII, IX and X. Platelet production is impaired but the cause is unknown. Purpura and bleeding may occur.

Oliguria and renal failure

Portal hypertension may cause the development of oesophageal varices. If these rupture, bleeding may lead to a fall in blood pressure sufficient to reduce the renal blood flow, causing progressive oliguria and renal failure.

Oedema and ascites

These may be caused by the combination of two factors.

- Portal hypertension raises the capillary hydrostatic pressure in the organs drained by the tributaries of the portal vein (Fig. 12.9).
- 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*. Eventually free fluid accumulates in the peritoneal cavity and the resultant *ascites* may be severe.

Anaemia

This is usually due to the combined effect of a number of factors:

- upset in the metabolism of folic acid and vitamin B_{12}
- chronic blood loss from oesophageal varices, causing iron deficiency anaemia
- increased breakdown of red blood cells in the congested spleen, causing haemolytic anaemia.

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 of the liver are very rare.

Malignant tumours

In many cases cancer of the liver is 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 other agents is promoted by cirrhotic changes. Malignancy develops in a number of cases of acute hepatitis caused by Type B virus. The most common sites of metastases are the abdominal lymph nodes, the peritoneum and the lungs.

Secondary malignant tumours in the liver are common, especially from primary tumours in the gastrointestinal tract, the lungs and the breast. The metastases 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 large stone may form. The causes are not clear but predisposing factors include:

- changes in the composition of bile that affect the solubility of its constituents
- high levels of blood and dietary cholesterol
- cholecystitis
- diabetes mellitus when associated with high blood cholesterol levels
- haemolytic disease
- female gender
- obesity
- long-term use of oral contraceptives
- several pregnancies in young women especially when accompanied by obesity.

Complications

Biliary colic. If a gallstone gets stuck in the cystic or common bile duct there is strong peristaltic contraction of the

smooth muscle in the wall of the duct (spasm) in an effort to move the stone onwards. The severe pain associated with biliary colic is due to ischaemia of the duct wall over the stone during the smooth muscle spasm.

Inflammation. Gallstones cause irritation and inflammation of the walls of the gall bladder and the cystic and common bile ducts. There may be superimposed microbial infection.

Impaction. Blockage of the cystic duct by a gallstone leads to distension of the gall bladder and *cholecystitis*. This does not cause jaundice because bile from the liver can still pass directly into the duodenum. Obstruction of the common bile duct leads to retention of bile, jaundice and *cholangitis* (infection of the bile ducts).

Acute cholecystitis

This is usually a complication of gallstones or an exacerbation of chronic cholecystitis, especially if there has been partial or intermittent obstruction of the cystic duct. Inflammation develops followed by secondary microbial infections spread from a focus of infection elsewhere in the body, e.g. they may be blood-borne or pass directly from the adjacent colon. Those most commonly involved are *Escherichia coli* and *Streptococcus faecalis*. In severe cases there may be fibrinous exudate into the gall bladder, suppuration, gangrene, perforation, peritonitis, local abscess formation, disruption of gall bladder activity, gallstone formation and the infection may spread to the bile ducts and the liver.

Chronic cholecystitis

The onset is usually insidious, sometimes following repeated acute attacks. Gallstones are usually present and there may be accompanying biliary colic. Pain is due to the spasmodic contraction of muscle, causing ischaemia when the gall bladder is packed with gallstones. There is usually secondary infection with suppuration. Ulceration of the tissues between the gall bladder and the duodenum or colon may occur with fistula formation and, later, fibrous adhesions.

Tumours of the biliary tract

Benign tumours are rare.

Malignant tumours

These are relatively rare but when they do occur the most common sites are:

- the neck of the gall bladder
- the junction of the cystic and bile ducts
- the ampulla of the bile duct.

Local spread to the liver, the pancreas and other adjacent organs is common. Lymph and blood spread lead to widespread metastases. Early sites include the liver, lungs, abdominal lymph nodes and the peritoneum.

Jaundice

This is not a disease in itself. It is a sign of abnormal bilirubin metabolism and excretion. Bilirubin, produced from the breakdown of haemoglobin, is usually conjugated in the liver and excreted in the bile. Conjugation, the process of adding certain groups to the bilirubin molecule, makes it 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, fits and mental handicap. Serum bilirubin may rise to 34 µmol/l before the yellow colouration of jaundice is evident in the skin and conjunctiva (normal 3 to 13 µmol/l).

Jaundice develops when there is an abnormality at some stage in the metabolic sequence caused by one or more factors, e.g.:

- excess haemolysis of red blood cells with the production of more bilirubin than the liver can deal with
- abnormal liver function that may cause:
  - incomplete uptake of unconjugated bilirubin by hepatocytes
  - ineffective conjugation of bilirubin
  - interference with bilirubin secretion into the bile
- obstruction to the flow of bile from the liver to the duodenum.

Types of jaundice

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

Haemolytic jaundice

This is due to increased haemolysis of red blood cells in the spleen. The amount of bilirubin is increased and if hypoxia develops the efficiency of hepatocyte activity is reduced.

Neonatal haemolytic jaundice occurs in many babies, especially in prematurity where the normal high haemolysis is coupled with shortage of conjugating enzymes in the hepatocytes.

Obstructive jaundice

Obstruction to the flow of bile in the biliary tract is caused by, e.g.:

- gallstones
- tumour of the head of the pancreas
- fibrosis of the bile ducts, following inflammation or injury by cholangitis or the passage of gallstones.

Effects include:

- pruritus caused by the irritating effects of bile salts on the skin
- pale faeces due to absence of stercobilin (p. 310)
- dark urine due to the presence of increased amounts of bilirubin.

Hepatocellular jaundice

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

- viral infection
- toxic substances, such as drugs
- amoebiasis (amoebic dysentery)
- cirrhosis of the liver.

The damaged hepatocytes may be unable to remove unconjugated bilirubin from the blood, or conjugate bilirubin, or secrete conjugated bilirubin into bile canaliculi.

13

The urinary system

The urinary system is one of the excretory systems of the body. It consists of the following structures:

- 2 *kidneys*, which secrete urine
- 2 *ureters*, which convey the urine from the kidneys to the urinary bladder
- 1 *urinary bladder* where urine collects and is temporarily stored
- 1 *urethra* through which the urine is discharged from the urinary bladder to the exterior.

Figure 13.1 shows an overview of the urinary system.

The urinary system plays a vital part in maintaining homeostasis of water and electrolyte concentrations within the body. The kidneys produce urine that contains metabolic waste products, including the nitrogenous compounds urea and uric acid, excess ions and some drugs.

The main functions of the kidneys are:

- formation and secretion of urine
- production and secretion of erythropoietin, the hormone responsible for controlling the rate of formation of red blood cells (p. 63)
- production and secretion of renin, an important enzyme in the control of blood pressure (p. 223).

Urine is stored in the bladder and excreted by the process of *micturition*.

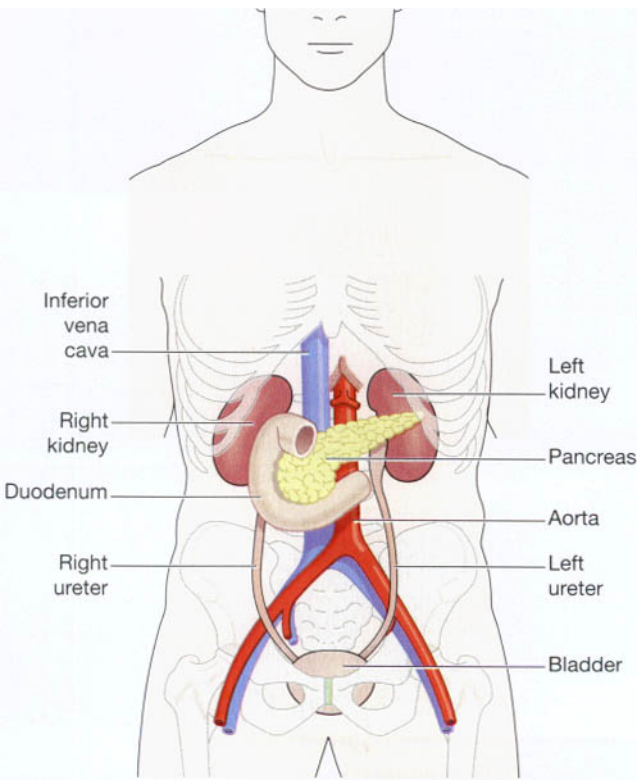


Figure 13.1 The parts of the urinary system (excluding the urethra) and some associated structures.

KIDNEYS

Learning outcomes

After studying this section you should be able to:

- identify the organs associated with the kidneys
- outline the gross structure of the kidneys
- describe the structure of a nephron
- explain the processes involved in the formation of urine
- explain how body water and electrolyte balance is maintained.

The kidneys (Fig. 13.2) lie on the posterior abdominal wall, one on each side of the vertebral column, behind the peritoneum and below the diaphragm. They extend from the level of the 12th thoracic vertebra to the 3rd lumbar vertebra, receiving some protection from the lower rib cage. The right kidney is usually slightly lower than the left, probably because of the considerable space occupied by the liver.

Kidneys are bean-shaped organs, about 11 cm long, 6 cm wide, 3 cm thick and weigh 150 g. They are embedded in, and held in position by, a mass of fat. A sheath of fibroelastic *renal fascia* encloses the kidney and the renal fat.

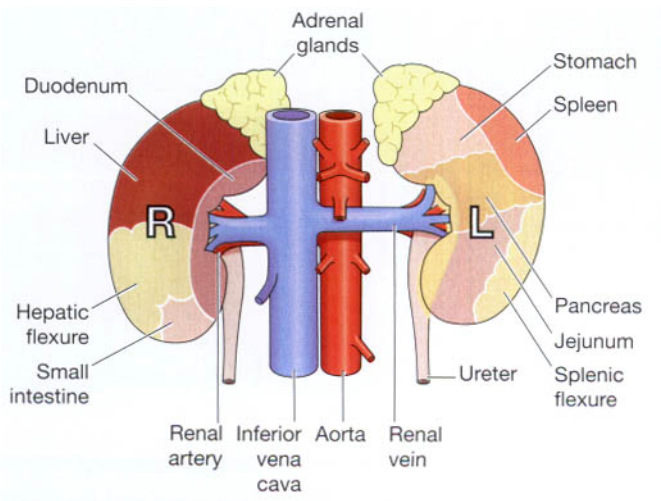


Figure 13.2 Anterior view of the kidneys showing the areas of contact with associated structures.

Organs associated with the kidneys

(Figs 13.1, 13.2 and 13.3)

As the kidneys lie on either side of the vertebral column each is associated with a different group of structures.

Right kidney

Superiorly — the right adrenal gland
Anteriorly — the right lobe of the liver, the duodenum and the hepatic flexure of the colon
Posteriorly — the diaphragm, and muscles of the posterior abdominal wall

Left kidney

Superiorly — the left adrenal gland
Anteriorly — the spleen, stomach, pancreas, jejunum and splenic flexure of the colon
Posteriorly — the diaphragm and muscles of the posterior abdominal wall

Gross structure of the kidney

There are three areas of tissue which can be distinguished when a longitudinal section of the kidney is viewed with the naked eye (Fig. 13.4):

- a *fibrous capsule*, surrounding the kidney
- the *cortex*, a reddish-brown layer of tissue immediately below the capsule and outside the pyramids
- the *medulla*, the innermost layer, consisting of pale conical-shaped striations, the *renal pyramids*.

The hilum is the concave medial border of the kidney where the renal blood and lymph vessels, the ureter and nerves enter.

The renal pelvis is the funnel-shaped structure which acts as a receptacle for the urine formed by the kidney (Fig. 13.4). It has a number of distal branches called *calyces*, each of which surrounds the apex of a renal pyramid. Urine formed in the kidney passes through a *papilla* at the apex of a pyramid into a minor calyx, then into a major calyx before passing through the pelvis into the ureter. The walls of the pelvis contain smooth muscle and are lined with transitional epithelium. Peristalsis of the smooth muscle originating in pacemaker cells in the walls of the calyces propels urine through the pelvis and ureters to the bladder. This is an intrinsic property of the smooth muscle, and is not under nerve control.

Microscopic structure of the kidney

The kidney is composed of about 1 million functional units, the *nephrons*, and a smaller number of *collecting tubules*. The collecting tubules transport urine through the pyramids to the renal pelvis giving them their striped appearance. The tubules are supported by a small amount of connective tissue, containing blood vessels, nerves and lymph vessels.

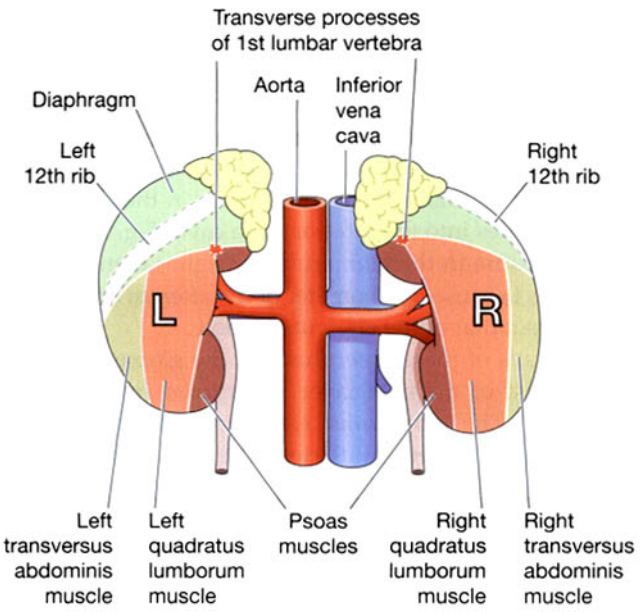


Figure 13.3 Posterior view of the kidneys showing the areas of contact with associated structures.

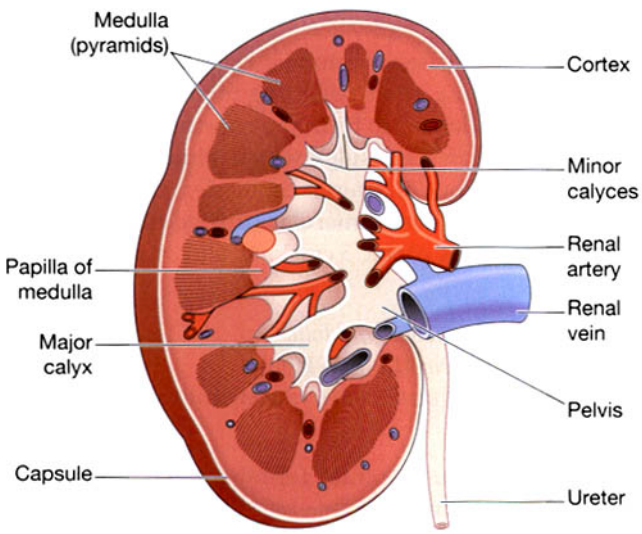


Figure 13.4 A longitudinal section of the right kidney.

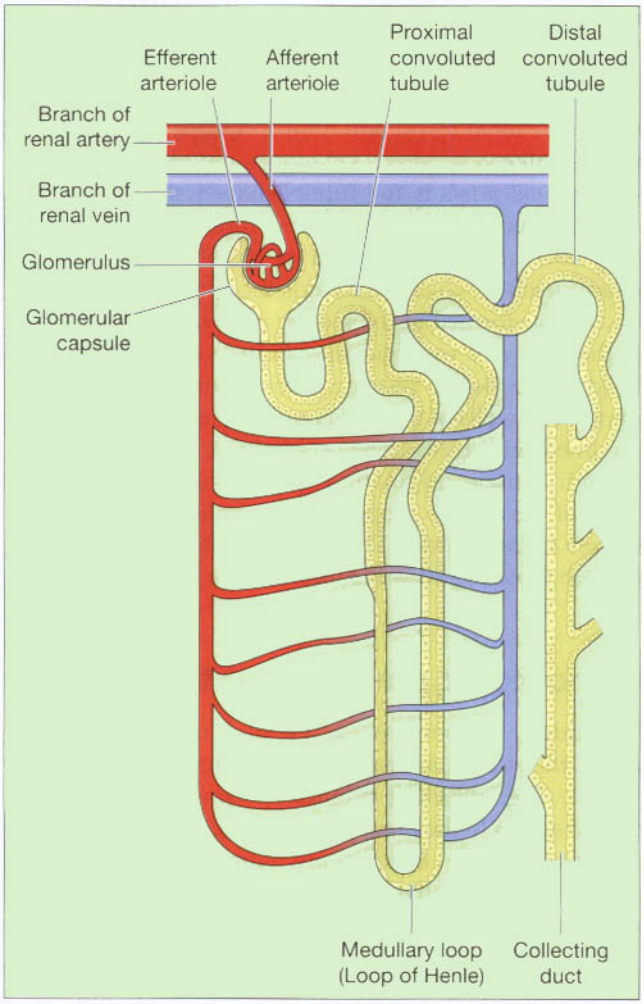


Figure 13.5 A nephron and associated blood vessels.

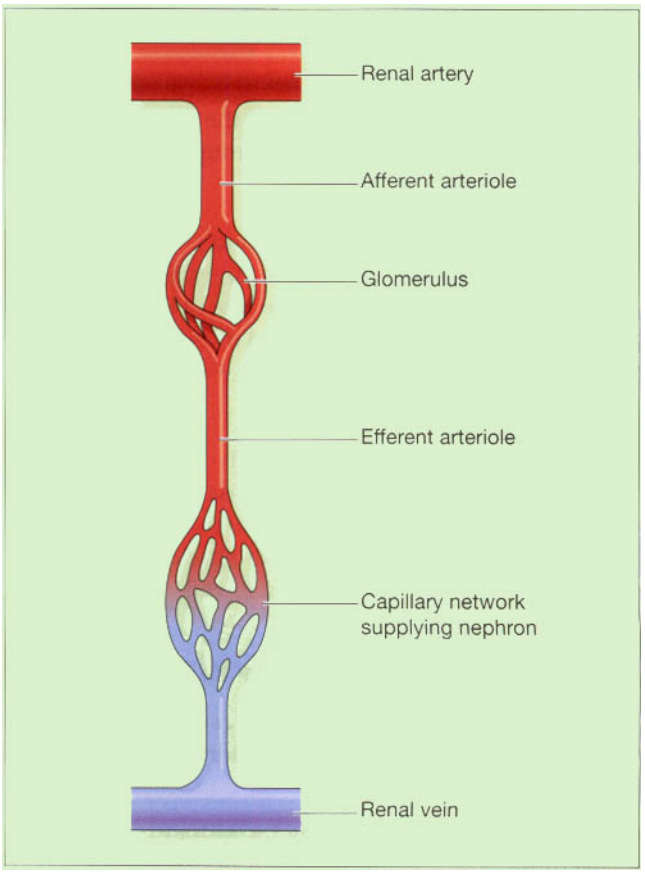


Figure 13.6 The series of blood vessels in the kidney.

The nephron (Fig. 13.5)

The nephron consists of a tubule closed at one end, the other end opening into a collecting tubule. The closed or blind end is indented to form the cup-shaped *glomerular capsule* (Bowman's capsule) which almost completely encloses a network of arterial capillaries, the *glomerulus*. Continuing from the glomerular capsule the remainder of the nephron is about 3 cm long and is described in three parts:

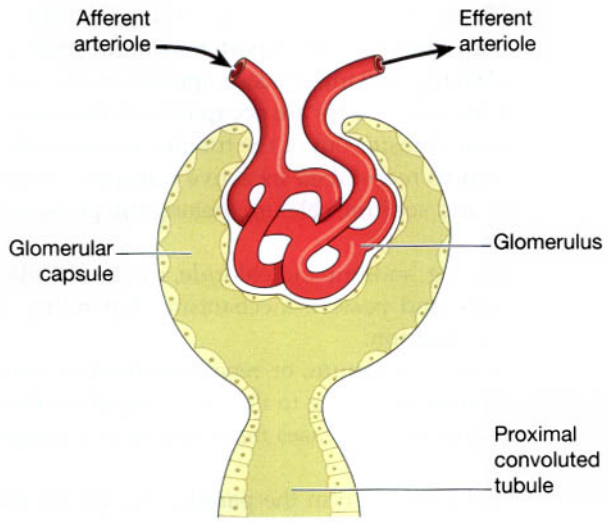
- the *proximal convoluted tubule*
- the *medullary loop* (loop of Henle)
- the *distal convoluted tubule*, leading into a *collecting duct*.

The collecting ducts unite, forming larger ducts that empty into the minor calyces.

After entering the kidney at the hilum the renal artery divides into smaller arteries and arterioles. In the cortex an arteriole, the *afferent arteriole*, enters each glomerular capsule then subdivides into a cluster of capillaries, forming the glomerulus. Between the capillary loops there are connective tissue phagocytic *mesangial cells*, which are part of the reticuloendothelial system (p. 66). The blood vessel leading away from the glomerulus is the *efferent arteriole*; it breaks up into a second capillary network to supply oxygen and nutrients to the remainder of the nephron. Venous blood drained from this capillary bed eventually leaves the kidney in the renal vein which empties into the inferior vena cava (Fig. 13.6). The blood pressure in the glomerulus is higher than in other capillaries because the diameter of the afferent arteriole is greater than that of the efferent arteriole.

The walls of the glomerulus and the glomerular capsule consist of a single layer of *flattened epithelial cells* (Fig. 13.7). The glomerular walls are more permeable than those of other capillaries. The remainder of the nephron and the collecting tubule are formed by a single layer of highly specialised cells.

The nerve supply to the blood vessels of the kidney consists of sympathetic and parasympathetic nerves. The presence of both branches of the autonomic nervous system permits control of renal blood vessel diameter and renal blood flow independently of autoregulation.



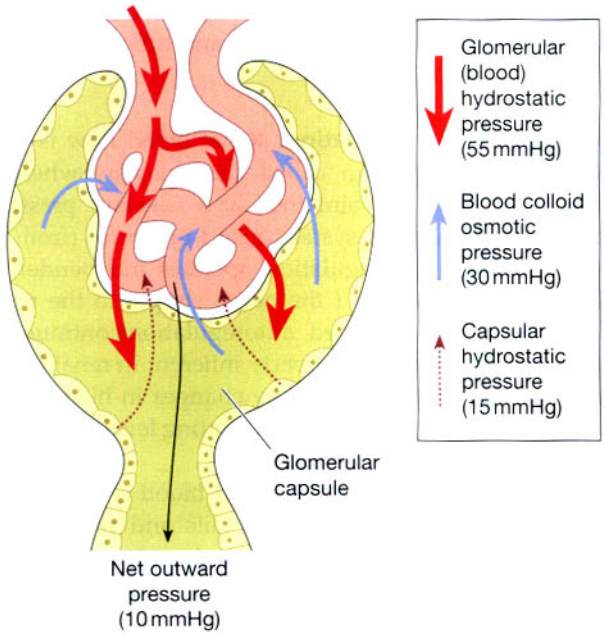


Figure 13.8 Filtration in the nephron.

Functions of the kidney

Formation of urine

The kidneys form urine which passes through the ureters to the bladder for storage prior to excretion. The composition of urine reflects the activities of the nephrons in the maintenance of homeostasis. Waste products of protein metabolism are excreted, electrolyte balance is maintained and the pH (acid–base balance) is maintained by the excretion of hydrogen ions. There are three processes involved in the formation of urine:

- simple filtration
- selective reabsorption
- secretion.

Simple filtration (Fig. 13.8)
Filtration takes place through the semipermeable walls of the glomerulus and glomerular capsule. Water and a large number of small molecules pass through, although some are reabsorbed later. Blood cells, plasma proteins and other large molecules are unable to filter through and remain in the capillaries (see Box 13.1). The filtrate in the glomerulus is very similar in composition to plasma with the important exception of plasma proteins.

Filtration is assisted by the difference between the blood pressure in the glomerulus and the pressure of the filtrate in the glomerular capsule. Because the diameter of the efferent arteriole is less than that of the afferent arteriole, a *capillary hydrostatic pressure* of about 7.3 kPa (55 mmHg) builds up in the glomerulus. This pressure is opposed by the *osmotic pressure* of the blood, about 4 kPa (30 mmHg), and by *filtrate hydrostatic pressure* of about 2 kPa (15 mmHg) in the glomerular capsule. The net *filtration pressure* is, therefore:

7.3 – (4 + 2) = 1.3 kPa, or
55 – (30 + 15) = 10 mmHg.

The volume of filtrate formed by both kidneys each minute is called the *glomerular filtration rate* (GFR). In a healthy adult the GFR is about 125 ml/min; i.e. 180 litres of dilute filtrate are formed each day by the two kidneys. Most of the filtrate is reabsorbed with less than 1%, i.e. 1 to 1.5 litres, excreted as urine. The difference in

Box 13.1 Constituents of glomerular filtrate and glomerular capillaries

Blood constituents in glomerular filtrate	Blood constituents remaining in the glomerulus
Water	Leukocytes
Mineral salts	Erythrocytes
Amino acids	Platelets
Ketoacids	Plasma proteins
Glucose	Some drugs
Hormones	
Creatinine	
Urea	
Uric acid	
Toxins	
Some drugs	

volume and concentration is due to selective reabsorption of some constituents of the filtrate and tubular secretion of others.

Autoregulation of filtration. Renal blood flow is protected by a mechanism called *autoregulation* whereby renal blood flow is maintained at a constant pressure across a wide range of systolic blood pressures (from 80 to 200 mmHg). Autoregulation operates independently of nervous control; i.e. if the nerve supply to the renal blood vessels is interrupted, autoregulation continues to operate. It is therefore a property inherent in renal blood vessels; it may be stimulated by changes in blood pressure in the renal arteries or by fluctuating levels of certain metabolites, e.g. prostaglandins.

In severe shock when the systolic blood pressure falls below 80 mmHg, autoregulation fails and renal blood flow and the hydrostatic pressure decrease, impairing filtration within the nephrons.

Selective reabsorption (Fig. 13.9)

Selective reabsorption is the process by which the composition and volume of the glomerular filtrate are altered during its passage through the convoluted tubules, the medullary loop and the collecting tubule. The general purpose of this process is to reabsorb into the blood those filtrate constituents needed by the body to maintain fluid and electrolyte balance and the pH of the blood. Active transport is carried out at carrier sites in the epithelial membrane using chemical energy to transport substances against their concentration gradients (p. 34).

Some constituents of glomerular filtrate (e.g. glucose, amino acids) do not normally appear in urine because they are completely reabsorbed unless they are present in blood in excessive quantities. The kidneys' maximum capacity for reabsorption of a substance is the *transport maximum*, or renal threshold, e.g. normal blood glucose level is 2.5 to 5.3 mmol/l (45 to 95 mg/100 ml). If the level rises above the transport maximum of about 9 mmol/l (160 mg/100 ml) glucose appears in the urine because all the carrier sites are occupied and the mechanism for active transfer out of the tubules is overloaded. Other substances reabsorbed by active transport include amino acids and sodium, calcium, potassium, phosphate and chloride.

Some ions, e.g. sodium and chloride, can be absorbed by both active and passive mechanisms depending on the site in the nephron.

The transport maximum, or renal threshold, of some substances varies according to the body's need for them at the time, and in some cases reabsorption is regulated by hormones.

Parathyroid hormone from the parathyroid glands and *calcitonin* from the thyroid gland together regulate reabsorption of calcium and phosphate.

Antidiuretic hormone (ADH) from the posterior lobe of the pituitary gland increases the permeability of the distal convoluted tubules and collecting tubules, increasing water reabsorption (Fig. 13.10).

Aldosterone, secreted by the adrenal cortex, increases the reabsorption of sodium and excretion of potassium (Fig. 13.11).

Nitrogenous waste products, such as urea and uric acid, are reabsorbed only to a slight extent.

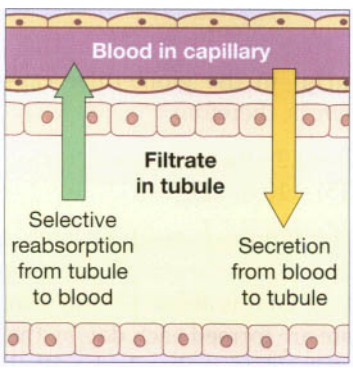


Figure 13.9 Directions of selective reabsorption and secretion in the nephron.

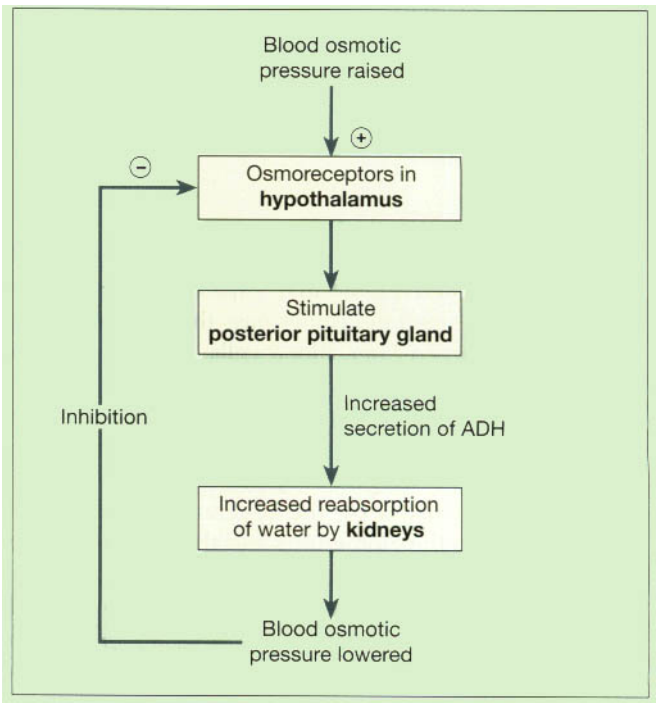


Figure 13.10 Negative feedback regulation of secretion of antidiuretic hormone (ADH).

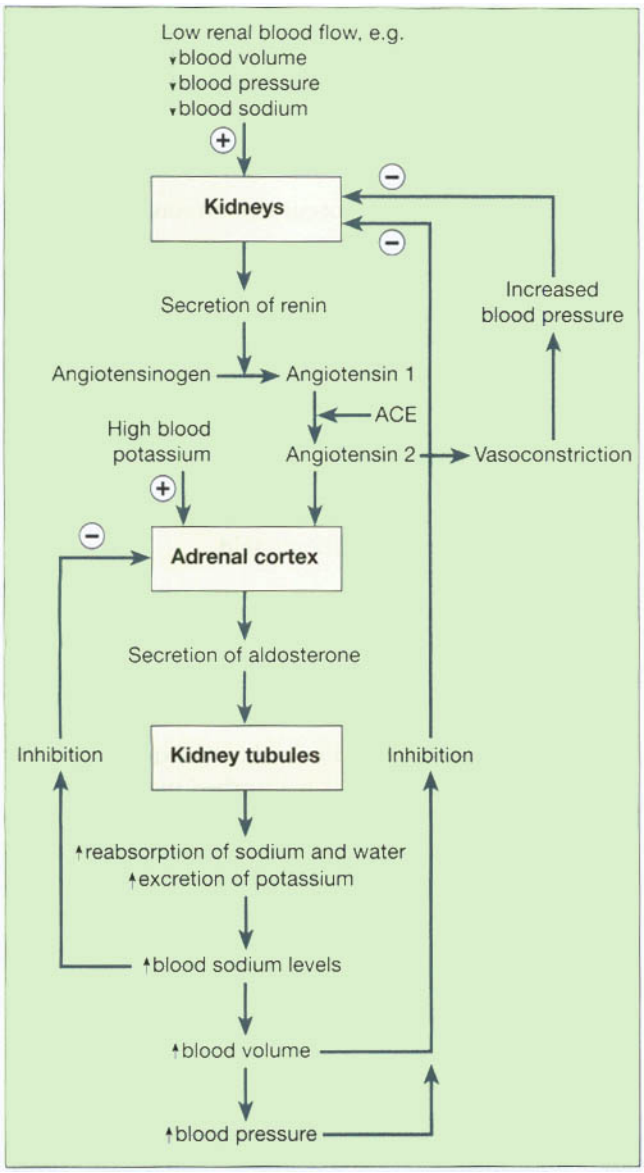


Figure 13.11 Negative feedback regulation of aldosterone secretion. ACE = angiotensin converting enzyme.

Substances that are not normal blood constituents are not reabsorbed. If the blood passes through the glomerulus too quickly for filtration to clear such substances from the blood, the tubules secrete them into the filtrate.

Secretion (Fig. 13.9)

Filtration occurs as the blood flows through the glomerulus. Substances not required and foreign materials, e.g. drugs including penicillin and aspirin, may not be cleared from the blood by filtration because of the short time it remains in the glomerulus. Such substances are cleared by *secretion into the convoluted tubules* and excreted from the body in the urine. Tubular secretion of hydrogen (H^+) ions is important in maintaining homeostasis of blood pH.

Composition of urine

Water	96%
Urea	2%
Uric acid	2%
Creatinine	
Ammonia	
Sodium	
Potassium	
Chlorides	
Phosphates	
Sulphates	
Oxalates	

Urine is clear and amber in colour due to the presence of urobilin, a bile pigment altered in the intestine, reabsorbed then excreted by the kidneys (see Fig. 12.43, p. 314). The specific gravity is between 1020 and 1030, and the pH is around 6 (normal range of 4.5 to 8). A healthy adult passes 1000 to 1500 ml per day. The amount of urine produced and the specific gravity vary according to the fluid intake and the amount of solute excreted. During sleep and muscular exercise urine production is decreased.

Water balance and urine output

Water is taken into the body through the alimentary tract and a small amount (called 'metabolic water') is formed by the metabolic processes. Water is excreted in saturated expired air, as a constituent of the faeces, through the skin as sweat and as the main constituent of urine. The amount lost in expired air and in the faeces is fairly constant and the amount of sweat produced is associated with the maintenance of normal body temperature (p. 365).

The balance between fluid intake and output is therefore controlled by the kidneys. The minimum urinary output, i.e., the smallest volume required to excrete the body's waste products, is about 500 ml per day. The amount produced in excess of this is controlled mainly by *antidiuretic hormone* (ADH) released into the blood by the posterior lobe of the pituitary gland. There is a close link between the posterior pituitary and the hypothalamus in the brain (see Fig. 9.3A and B, p. 216).

Sensory nerve cells in the hypothalamus (*osmoreceptors*) detect changes in the osmotic pressure of the blood. Nerve impulses from the osmoreceptors stimulate the posterior lobe of the pituitary gland to release ADH. When the osmotic pressure is raised, ADH output is increased and as a result, water reabsorption by the cells in distal convoluted tubules and collecting ducts is increased, reducing the blood osmotic pressure and ADH

output. This feedback mechanism maintains the blood osmotic pressure (and therefore sodium and water concentrations) within normal limits (Fig. 13.10).

The feedback mechanism may be opposed when there is an excessive amount of a dissolved substance in the blood. For example, in diabetes mellitus when the blood glucose level is above the transport maximum of the renal tubules, excess water is excreted with the excess glucose. This *polyuria* may lead to dehydration in spite of increased production of ADH but it is usually accompanied by acute thirst and increased water intake.

Electrolyte balance

Changes in the concentration of electrolytes in the body fluids may be due to changes in:

- the body water content, or
- electrolyte levels.

There are several mechanisms that maintain the balance between water and electrolyte concentration.

Sodium and potassium concentration

Sodium is the most common cation (positively charged ion) in extracellular fluid and potassium is the most common intracellular cation.

Sodium is a constituent of almost all foods and it is often added to food during cooking. This means that intake is usually in excess of the body's needs. It is excreted mainly in urine and sweat.

Sodium is a normal constituent of urine and the amount excreted is regulated by the hormone *aldosterone*, secreted by the adrenal cortex. Cells in the afferent arteriole of the nephron are stimulated to produce the enzyme *renin* by sympathetic stimulation, low blood volume or by low arterial blood pressure. Renin converts the plasma protein *angiotensinogen*, produced by the liver, to *angiotensin 1*. *Angiotensin converting enzyme* (ACE), formed in small quantities in the lungs, proximal convoluted tubules and other tissues, converts angiotensin 1 into angiotensin 2 which is a very potent vasoconstrictor and increases blood pressure. Renin and raised blood potassium levels also stimulate the adrenal gland to secrete aldosterone (Fig. 13.11). Water is reabsorbed with sodium and together they increase the blood volume, leading to reduced renin secretion through the negative feedback mechanism (Fig. 13.11). When *sodium reabsorption* is increased *potassium excretion* is increased, indirectly reducing intracellular potassium.

The amount of sodium excreted in sweat is insignificant except when sweating is excessive. This may occur when there is pyrexia, a high environmental temperature or during sustained physical exercise. Normally the renal mechanism described above maintains the concentration of sodium and potassium within physiological limits. When excessive sweating is sustained, e.g. living in a hot climate or working in a hot environment, acclimatisation occurs in about 7 to 10 days and the amount of electrolytes lost in sweat is reduced.

Sodium and potassium occur in high concentrations in digestive juices—sodium in gastric juice and potassium in pancreatic and intestinal juice. Normally these ions are reabsorbed by the colon but following acute and prolonged diarrhoea they may be excreted in large quantities with resultant electrolyte imbalance.

In order to maintain the normal pH (acid–base balance) of the blood, the cells of the proximal convoluted tubules secrete hydrogen ions. In the filtrate they combine with buffers (p. 22):

- bicarbonate, forming carbonic acid ($H^+ + HCO_3^- \rightarrow H_2CO_3$)
- ammonia, forming ammonium ions ($H^+ + NH_3 \rightarrow NH_4^+$)
- hydrogen phosphate, forming dihydrogen phosphate ($H^+ + HPO_3^{2-} \rightarrow H_2PO_3^-$).

Carbonic acid is converted to carbon dioxide (CO_2) and water (H_2O), and the CO_2 is reabsorbed maintaining the buffering capacity of the blood. Hydrogen ions are excreted in the urine as ammonium salts and hydrogen phosphate. The normal pH of urine varies from 4.5 to 7.8 depending on diet, time of day and a number of other factors. Individuals whose diet contains a large amount of animal proteins tend to produce more acidic urine (lower pH) than vegetarians.

URETERS

Learning outcome

After studying this section you should be able to:

- outline the structure and function of the ureters.

The ureters are the tubes that convey urine from the kidneys to the urinary bladder (Fig. 13.12). They are about 25 to 30 cm long with a diameter of about 3 mm.

The ureter is continuous with the funnel-shaped renal pelvis. It passes downwards through the abdominal cavity, behind the peritoneum in front of the psoas muscle into the pelvic cavity, and passes obliquely through the posterior wall of the bladder (Fig. 13.13). Because of this

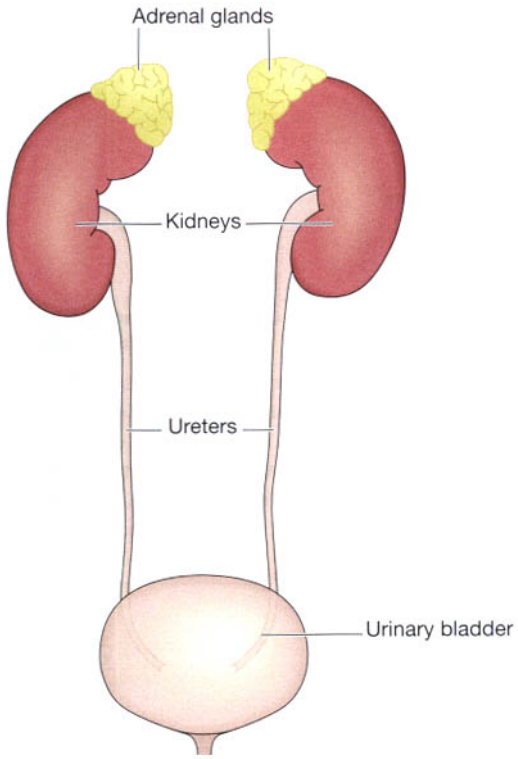


Figure 13.12 The ureters and their relationship to the kidneys and bladder.

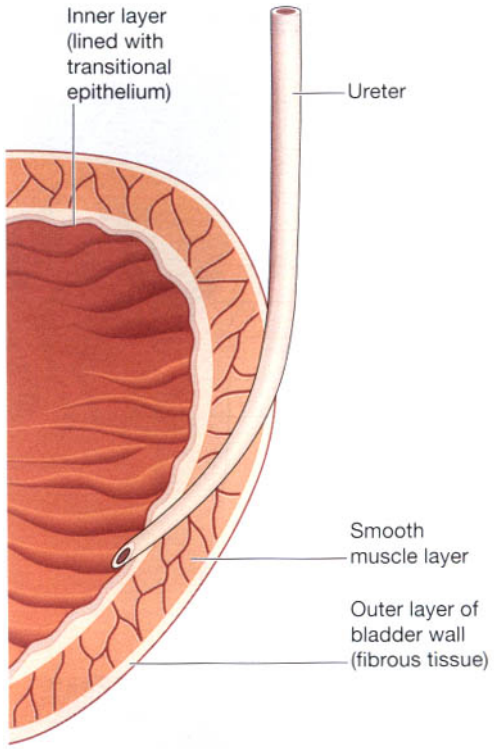


Figure 13.13 The position of the ureter where it passes through the bladder wall.

arrangement, when urine accumulates and the pressure in the bladder rises, the ureters are compressed and the openings occluded. This prevents reflux of urine into the ureters (towards the kidneys) as the bladder fills and during micturition, when pressure increases as the muscular bladder wall contracts.

Structure

The ureters consist of three layers of tissue:

- an outer covering of *fibrous tissue*, continuous with the fibrous capsule of the kidney
- a middle *muscular layer* consisting of interlacing smooth muscle fibres that form a syncytium spiralling round the ureter, some in clockwise and some in anticlockwise directions and an additional outer longitudinal layer in the lower third
- an inner layer, the *mucosa*, lined with transitional epithelium.

Function

The ureters propel the urine from the kidneys into the bladder by peristaltic contraction of the smooth muscle layer. This is an intrinsic property of the smooth muscle and is not under autonomic nerve control. The waves of contraction originate in a pacemaker in the minor calyces. Peristaltic waves occur several times per minute, increasing in frequency with the volume of urine produced, and send little spurts of urine into the bladder.

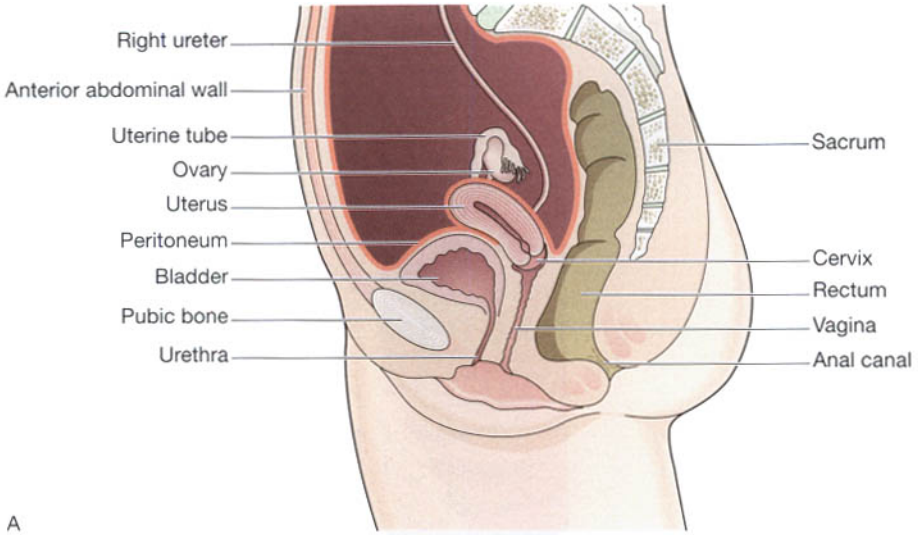
URINARY BLADDER

Learning outcome

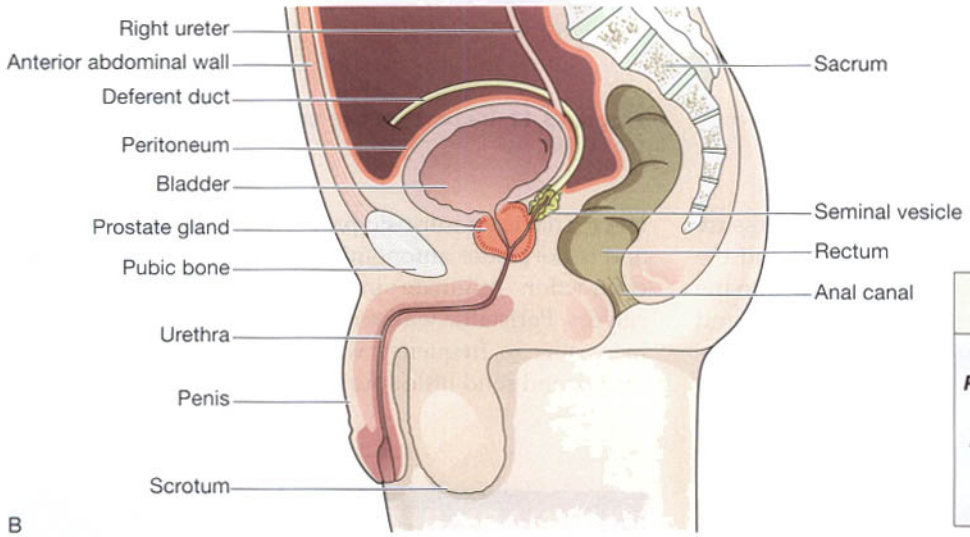
After studying this section you should be able to:

- describe the structure of the bladder.

The urinary bladder is a reservoir for urine. It lies in the pelvic cavity and its size and position vary, depending on the amount of urine it contains. When distended, the bladder rises into the abdominal cavity.



Organs associated with the bladder in the female	
Anteriorly	– the symphysis pubis
Posteriorly	– the uterus and upper part of the vagina
Superiorly	– the small intestine
Inferiorly	– the urethra and the muscles forming the pelvic floor



Organs associated with the bladder in the male	
Anteriorly	– the symphysis pubis
Posteriorly	– the rectum and seminal vesicles
Superiorly	– the small intestine
Inferiorly	– the urethra and prostate gland

Figure 13.14 The pelvic organs associated with the bladder and the urethra in: A. The female. B. The male.

Structure (Fig. 13.15)

The bladder is roughly pear-shaped, but becomes more oval as it fills with urine. It has anterior, superior and posterior surfaces. The posterior surface is the *base*. The bladder opens into the urethra at its lowest point, *the neck*.

The *peritoneum* covers only the superior surface before it turns upwards as the parietal peritoneum, lining the anterior abdominal wall. Posteriorly it surrounds the uterus in the female and the rectum in the male.

The bladder wall is composed of three layers:

- the outer layer of loose connective tissue, containing blood and lymphatic vessels and nerves, covered on the upper surface by the peritoneum
- the middle layer, consisting of a mass of interlacing smooth muscle fibres and elastic tissue loosely arranged in three layers. This is called the *detrusor muscle* and it empties the bladder when it contracts
- the mucosa, lined with transitional epithelium (p. 36).

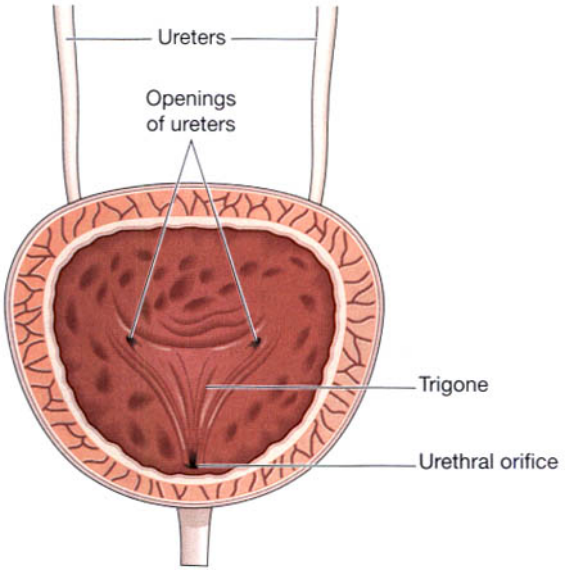


Figure 13.15 Section of the bladder showing the trigone.

When the bladder is empty the inner lining is arranged in folds, or rugae, and these gradually disappear as the bladder fills. The bladder is distensible but when it contains 300 to 400 ml the awareness of the desire to urinate is initiated. The total capacity is rarely more than about 600 ml.

The three orifices in the bladder wall form a triangle or *trigone* (Fig. 13.15). The upper two orifices on the posterior wall are the openings of the ureters. The lower orifice is the point of origin of the urethra. Where the urethra commences is a thickening of the smooth muscle layer forming the *internal urethral sphincter*. This sphincter is not under voluntary control.

URETHRA

Learning outcome

After studying this section you should be able to:

- outline the structure and function of the urethra in males and females.

The urethra is a canal extending from the neck of the bladder to the exterior, at the external urethral orifice. Its length differs in the male and in the female. The male urethra is associated with the urinary and the reproductive systems, and is described in Chapter 19.

The female urethra is approximately 4 cm long. It runs downwards and forwards behind the symphysis pubis and opens at the *external urethral orifice* just in front of the vagina. The external urethral orifice is guarded by the *external urethral sphincter* which is under voluntary control. Except during the passage of urine, the walls of the urethra are in close apposition.

The male urethra is described in detail in Chapter 19, but in both sexes the basic structure is the same. Its walls consist of three layers of tissue.

- the *muscle layer*, continuous with that of the bladder. At its origin there is the *internal urethral sphincter*, consisting mainly of elastic tissue and smooth muscle fibres, under autonomic nerve control. Slow and continuous contraction of this sphincter keeps the urethra closed. In the middle third there is skeletal muscle surrounding the urethra, under voluntary nerve control, that forms the *external urethral sphincter*
- the *submucosa*, a spongy layer containing blood vessels and nerves
- the *mucosa*, which is continuous with that of the bladder in the upper part. In the lower part the lining consists of stratified squamous epithelium, continuous externally with the skin of the vulva.

MICTURITION

Learning outcome

After studying this section you should be able to:

- compare and contrast the process of micturition in babies and adults.

The urinary bladder acts as a reservoir for urine. When 300 to 400 ml of urine have accumulated, afferent autonomic nerve fibres in the bladder wall sensitive to stretch are stimulated. In the infant this initiates a *spinal reflex action* (see p. 159) and micturition occurs (Fig. 13.16). Micturition occurs when autonomic efferent fibres convey impulses to the bladder causing contraction of the detrusor muscle and relaxation of the internal urethral sphincter.

When the nervous system is fully developed the micturition reflex is stimulated but sensory impulses pass upwards to the brain and there is an awareness of the desire to pass urine. By conscious effort, reflex contraction

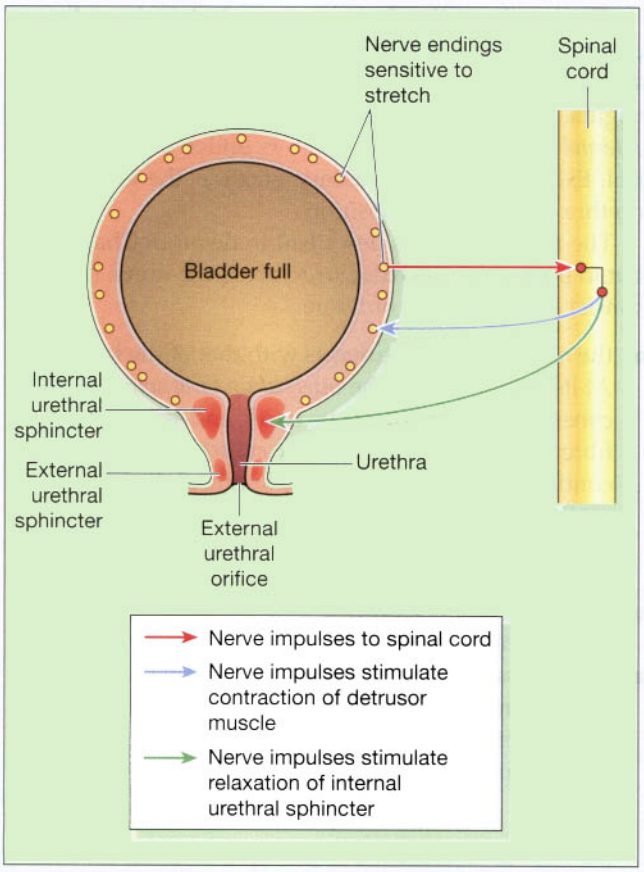


Figure 13.16 Simple reflex control of micturition when conscious effort cannot override the reflex action.

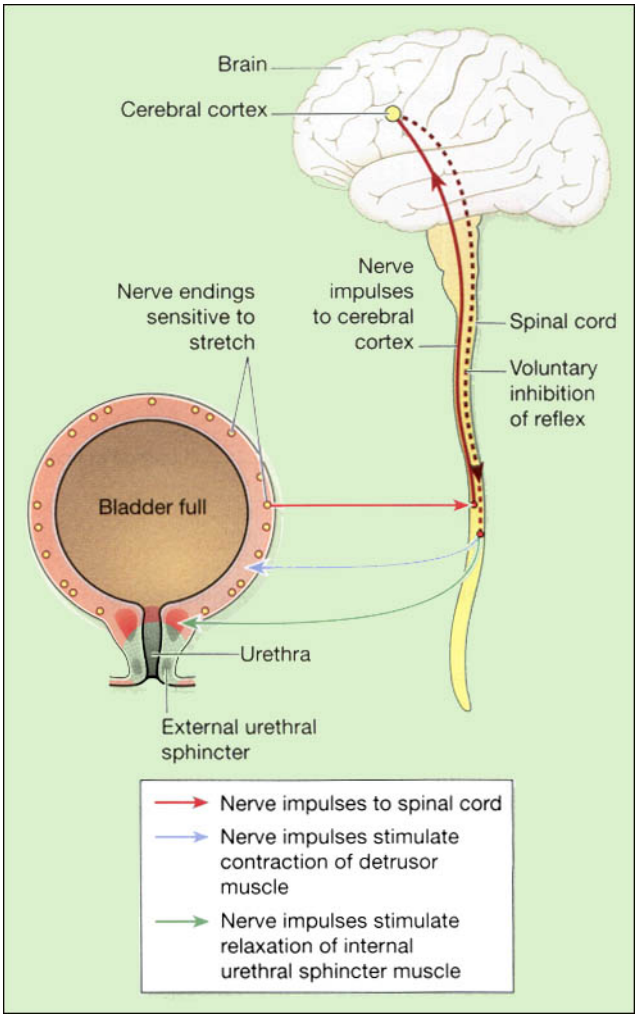


Figure 13.17 Control of micturition when conscious effort overrides the reflex action.

of the bladder wall and relaxation of the internal sphincter can be inhibited for a limited period of time (Fig. 13.17).

In adults, micturition occurs when the detrusor muscle contracts, and there is reflex relaxation of the internal sphincter and voluntary relaxation of the external sphincter. It can be assisted by increasing the pressure within the pelvic cavity, achieved by lowering the diaphragm and contracting the abdominal muscles (Valsalva's manoeuvre). Over-distension of the bladder is extremely painful, and when this stage is reached there is a tendency for involuntary relaxation of the external sphincter to occur and a small amount of urine to escape, provided there is no mechanical obstruction.

DISEASES OF THE KIDNEYS

Learning outcomes

After studying this section you should be able to:

- outline the principal causes and effects of glomerulonephritis
- describe the effects of systemic conditions, e.g. diabetes mellitus and hypertension on kidney function
- discuss the sources and consequences of kidney infections
- explain the causes and implications of acute and chronic renal failure
- describe the pathogenesis of kidney stones
- list common congenital abnormalities of the kidneys
- outline the development and spread of common tumours of the kidney.

Glomerulonephritis (GN)

This term suggests inflammatory conditions of the glomerulus, but there are several types of GN and inflammatory changes are not always present. In many cases immune complexes damage the glomeruli. These are formed when antigens and antibodies combine either within the kidney or elsewhere in the body, and they circulate in the blood. When immune complexes lodge in the walls of the glomeruli they often cause an inflammatory response that impairs glomerular function. Other immune mechanisms are also implicated in GN.

Classification of GN is complex and based on a number of features: the cause, immunological characteristics and findings on microscopy. Microscopic distinction is based on:

- the extent of damage:
  - *diffuse:* affecting all glomeruli
  - *focal:* affecting some glomeruli
- appearance:
  - *proliferative:* increased number of cells in the glomeruli
  - *membranous:* thickening of the glomerular basement membrane.

Examples of some different types of GN and their features are shown in Table 13.1.

Table 13.1 Some types of glomerulonephritis and their features

Type	Presenting features	Other features
Diffuse proliferative GN	Acute nephritis Haematuria Proteinuria	Deposition of immune complexes in all glomeruli stimulates the inflammatory response Often follows 1 to 4 weeks after a β-haemolytic streptococcal infection of the tonsils, pharynx, middle ear or skin; or more rarely by a variety of other microbes Prognosis: good in children, less good in adults, up to 40% develop hypertension or chronic renal failure
Focal proliferative GN	Acute nephritis Haematuria Proteinuria	An inflammatory response develops in parts of some glomeruli Usually accompanied by a systemic disease, e.g. systemic lupus erythematosus (SLE), Henoch–Schönlein purpura, infective endocarditis Prognosis: variable
Membranous GN	Nephrotic syndrome Haematuria Proteinuria	Deposition of immune complexes in the glomerular basement membrane stimulates the inflammatory response Cause is often unknown, but sometimes secondary to infections, tumours, drugs, SLE Prognosis: variable, but most cases progress to chronic renal failure as sclerosis of glomeruli progresses
Minimal change GN	Nephrotic syndrome Haematuria Proteinuria	Immune complexes are not involved Commonest cause of nephrotic syndrome in children, usually occurring between the ages of 1 to 4 years and often following a chest infection Prognosis: good in children, but recurrences are common in adults

Effects of glomerulonephritis

These depend on the type and are listed below.

Haematuria. This is usually painless and not accompanied by other symptoms. When microscopic, it may be found on routine urinalysis when red blood cells have passed from the damaged glomeruli into the filtrate.

Asymptomatic proteinuria. This may also be found on routine urinalysis and when it is of a low level does not cause nephrotic syndrome. It occurs as protein passes through the damaged glomeruli into the filtrate.

Acute nephritis. This is characterised by the presence of:

- anuria or oliguria
- hypertension
- haematuria
- fluid retention
- uraemia.

Loin pain, headache and malaise are also common.

Nephrotic syndrome. (See below.)

Chronic renal failure. This occurs when nephrons are progressively and irreversibly damaged after the renal reserve is lost.

Nephrotic syndrome

This is not a disease in itself but is an important feature of several kidney diseases. The main characteristics are:

- marked proteinuria
- hypoalbuminaemia
- generalised oedema
- hyperlipidaemia.

When glomeruli are damaged, the permeability of the glomerular membrane is increased and plasma proteins pass through in the filtrate. Albumin is the main protein lost because it is the most common and is the smallest of the plasma proteins. When the daily loss exceeds the rate of production by the liver there is a significant fall in the total plasma protein level. The consequent low plasma osmotic pressure leads to widespread oedema and reduced plasma volume (see Fig. 5.57, p. 119). This reduces the renal blood flow and stimulates the renin–angiotensin–aldosterone mechanism, causing increased reabsorption of water and sodium from the renal tubules. The reabsorbed water further reduces the osmotic pressure, increasing the oedema. The key factor is the loss of albumin across the glomerular membrane and as long as this continues the vicious circle is perpetuated

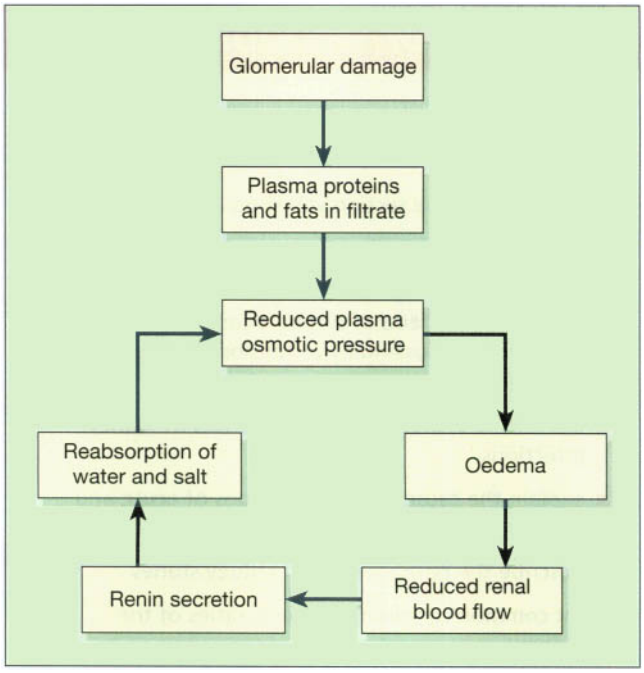


Figure 13.18 Stages of development of nephrotic syndrome.

(Fig. 13.18). Levels of nitrogenous waste products, i.e. uric acid, urea and creatinine, usually remain normal. Hyperlipidaemia, especially hypercholesterolaemia, also occurs but the cause is unknown.

The nephrotic syndrome occurs in a number of diseases. In children the most common cause is minimal-change glomerulonephritis. In adults it may complicate:

- most forms of glomerulonephritis
- diabetes mellitus
- systemic lupus erythematosus
- infections, e.g. malaria, infective endocarditis, syphilis, hepatitis B
- drugs treatment, e.g. penicillamine, gold, captopril, phenytoin.

Diabetic kidney

Renal failure is the cause of death in 10% of all diabetics and up to 50% of cases of the insulin-dependent (type I) diabetes mellitus (p. 236). There is damage to large and small blood vessels in many parts of the body. The effects include:

- progressive glomerulosclerosis followed by atrophy of the tubules
- acute pyelonephritis with papillary necrosis
- atheroma of the renal arteries and their branches, leading to renal ischaemia and hypertension (Ch. 5)
- nephrotic syndrome.

Hypertension and the kidneys

Essential and secondary hypertension (p. 126) both affect the kidneys when there is renal arteriosclerosis and arteriolosclerosis, causing ischaemia. The reduced blood flow stimulates the renin–angiotensin–aldosterone mechanism (Fig. 13.11), raising the blood pressure still further.

Essential hypertension

Benign hypertension. This causes gradual and progressive sclerosis and fibrosis of the glomeruli, leading to renal failure or, more commonly, to malignant hypertension.

Malignant hypertension. This causes rapidly developing arteriolosclerosis which spreads to the glomeruli with subsequent destruction of nephrons, leading to:

- further rise in blood pressure
- reduction in renal blood flow and the amount of filtrate
- increased permeability of the glomeruli, with the passage of plasma proteins and red blood cells into the filtrate resulting in proteinuria and haematuria
- progressive oliguria and renal failure.

Secondary hypertension

This is caused by long-standing kidney diseases such as chronic glomerulonephritis and pyelonephritis and leads to chronic renal ischaemia, further hypertension and renal failure.

Acute pyelonephritis

This is an acute microbial infection of the renal pelvis and calyces, spreading to the kidney substance causing formation of small abscesses. The infection may travel up the urinary tract from the perineum or be blood-borne. It is accompanied by fever, malaise and loin pain.

Ascending infection

Upward spread of microbes from the bladder (see cystitis, p. 357) is the most common cause of this condition. Reflux of infected urine into the ureters when the bladder contracts during micturition predisposes to upward spread of infection to the renal pelves and kidney substance.

Blood-borne infection

The source of microbes may be from septicaemia or elsewhere in the body, e.g. respiratory tract infections, infected wounds or abscesses.

When the infection spreads into the kidney tissue it causes suppuration and destruction of nephrons. The prognosis depends on the amount of healthy kidney remaining after the infection subsides. Necrotic tissue is eventually replaced by fibrous tissue but there may be some hypertrophy of healthy nephrons. There are a number of outcomes: healing, recurrence, especially if there is a structural abnormality of the urinary tract, and chronic pyelonephritis. Perinephric abscess and papillary necrosis are complications, usually if the condition is untreated.

Chronic pyelonephritis

This usually follows repeated attacks of acute pyelonephritis with scar tissue formation. It is usually associated with reflux of urine from the bladder to the ureter enabling microbes to gain access to the kidneys. A congenital abnormality of the angle of insertion of the ureter into the bladder often predisposes to the reflux of urine but it is sometimes caused by an obstruction that develops later in life. The progressive loss of functioning nephrons leads to chronic renal failure and uraemia. Concurrent hypertension is common.

Acute renal failure

There is a sudden and severe reduction in the glomerular filtration rate and kidney function that is usually reversible over days or weeks when treated. This occurs as a complication of a variety of conditions not necessarily associated with the kidneys. The causes of acute renal failure are classified as:

- *prerenal*: the result of reduced renal blood flow, especially severe and prolonged shock
- *renal*, or parenchymal: damage to the kidney itself due to, e.g., acute tubular necrosis, glomerulonephritis
- *post-renal*: obstruction to the outflow of urine, e.g. tumour of the bladder, uterus or cervix, large calculus in the renal pelvis.

Acute tubular necrosis (ATN)

This is the most common cause of acute renal failure. There is severe damage to the tubular epithelial cells caused by ischaemia or nephrotoxicity.

Ischaemic ATN

This is caused by severe and prolonged shock due to, e.g., haemorrhage, severe trauma, marked dehydration, acute intestinal obstruction, prolonged and complicated surgical procedures, extensive burns.

Nephrotoxic ATN

This is caused by:

- toxic chemicals, e.g. carbon tetrachloride (used in dry cleaning), chromic acid, ethylene glycol (antifreeze), mercurial compounds, ionising radiation
- drugs, e.g. trilene, aminoglycosides, paracetamol overdose
- endogenous substances, e.g. myoglobin (from damaged muscle), haemoglobin (from incompatible blood transfusion).

Oliguria (less than 400 ml of urine per day in adults), *severe oliguria* (less than 100 ml of urine per day in adults) or *anuria* (absence of urine) may last for a few weeks, followed by diuresis. There is reduced glomerular filtration and tubular selective reabsorption and secretion, leading to:

- generalised and pulmonary oedema
- accumulation of urea (uraemia) and other metabolic waste products
- electrolyte imbalance which may be exacerbated by the retention of potassium (hyperkalaemia) released from cells following severe injury and extensive tissue damage elsewhere in the body
- acidosis due to disrupted excretion of hydrogen ions.

Profound diuresis (the diuretic phase) occurs during the healing process when the epithelial cells of the tubules have regenerated but are still incapable of selective reabsorption and secretion. Diuresis may lead to acute dehydration, complicating the existing high plasma urea, acidosis and electrolyte imbalance. If the patient survives the initial acute phase, a considerable degree of renal function is usually restored over a period of months.

Chronic renal failure

This is reached when irreversible damage to nephrons is so severe that 75% of renal function has been lost and the kidneys cannot function effectively. The main causes are glomerulonephritis, diabetes mellitus, chronic pyelonephritis and hypertension. The effects are reduced glomerular filtration rate, selective reabsorption and secretion, and glomerular fibrosis, which interferes with blood flow. These changes have a number of effects on the body.

- *Uraemia* develops after about 7 days of anuria because of the reduced glomerular filtration rate and impaired tubular secretion of urea. Increased blood urea usually leads to confusion and mental disorientation.
- *Polyuria* is caused by defective reabsorption of water in spite of the reduced glomerular filtration rate (GFR) (Table 13.2). This may cause nocturia, thirst and polydipsia.
- *Fixed specific gravity.* The specific gravity of the urine is similar to that of glomerular filtrate, i.e. about 1.010 (normal = 1.020 to 1.030). It remains low and fixed because of defective tubular reabsorption of water.
- *Acidosis.* Control of the pH of body fluids is lost mainly because the tubules fail to remove hydrogen ions by forming ammonia and hydrogen phosphates.
- *Electrolyte imbalance* occurs as tubular reabsorption and secretion are impaired.
- *Anaemia* caused by deficiency of the hormone erythropoietin occurs when the chronic state extends over a period of months and is usually exacerbated by dialysis. It results in fatigue, dyspnoea and cardiac failure.
- *Hypertension* is often a consequence if not the cause of renal failure.

Anorexia, nausea and very deep (Kussmaul's) respirations occur as uraemia progresses. In the later stages there may also be hiccoughs, vomiting, muscle twitching, confusion, drowsiness and coma.

Renal calculi

Calculi (stones) form in the kidneys and bladder when urinary constituents normally in solution are precipitated. The solutes involved are oxalates, phosphates, urates and uric acid, and stones usually consist of more than one substance, deposited in layers. They are more

Table 13.2 Polyuria in chronic renal failure

	Normal kidney	End-stage kidney
GFR	125 ml/min or 180 l/day	10 ml/min or 14 l/day
Reabsorption of water	>99%	Approx. 30%
Urine output	<1 ml/min or 1.5 l/day	Approx. 7 ml/min or 10 l/day

common in males and after 30 years of age. Most originate in collecting tubules or in renal papillae. They then pass into the renal pelvis where they may increase in size. Some become too large to pass through the ureter and may obstruct the outflow of urine causing renal failure. Others pass to the bladder and are either excreted or increase in size and obstruct the urethra. Sometimes stones originate in the bladder, usually in developing countries and often in children. Predisposing factors include:

- *Dehydration*. This leads to increased reabsorption of water from the tubules but does not change solute reabsorption, resulting in a reduced volume of highly concentrated filtrate in the collecting tubules.
- *pH of urine*. When the normally acid filtrate becomes alkaline some substances may be precipitated, e.g. phosphates. This occurs when the kidney buffering system is defective, and in some infections.
- *Infection*. Necrotic material and pus provide foci upon which solutes in the filtrate may be deposited and the products of infection may alter the pH of the urine. Infection sometimes leads to alkaline urine (see above).
- *Metabolic conditions*. These include hyperparathyroidism and gout.

Small calculi

These may pass through or become impacted in a ureter and damage the epithelium, leading to haematuria then fibrosis and stricture. In ureteric obstruction, usually unilateral, there is spasmodic contraction of the ureter, causing acute intermittent ischaemic pain (*renal colic*) as the ureter contracts over the stone. Stones reaching the bladder may be passed in urine or increase in size and eventually obstruct the urethra. Consequences include retention of urine and bilateral hydronephrosis, infection proximal to the blockage, pyelonephritis and severe kidney damage.

Large calculi (staghorn calculus)

One large stone may form, filling the renal pelvis and the calyces (Fig. 13.19). It causes stagnation of urine, predisposing to infection, hydronephrosis and occasionally kidney tumours. It may cause chronic renal failure.

Congenital abnormalities of the kidneys

Misplaced (ectopic) kidney

One or both kidneys may develop in abnormally low positions. Misplaced kidneys function normally if the blood vessels are long enough to provide an adequate blood supply but a kidney in the pelvis may cause problems during pregnancy as the expanding uterus compresses renal blood vessels or the ureters. If the ureters become kinked there is increased risk of infection as there is a tendency for reflux and backflow to the kidney. There may also be difficulties during parturition (childbirth).

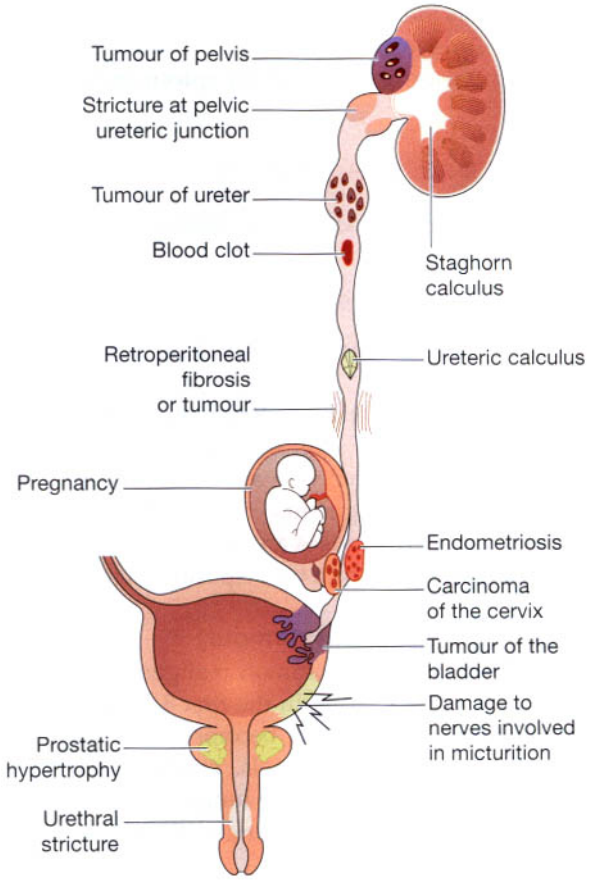


Figure 13.19 Summary of obstructions of the urinary tract.

Polycystic disease

This disease, caused by genetic abnormality, occurs in infantile and adult forms. The *infantile form* is very rare and the child usually dies soon after birth.

Adult polycystic kidney disease. This inherited condition usually becomes apparent at between 30 and 50 years of age. Both kidneys are affected. Dilatations (cysts) form at the junction of the distal convoluted and collecting tubules. The cysts slowly enlarge and pressure causes ischaemia and necrosis of nephrons, resulting in their destruction. The disease is progressive and secondary hypertension and chronic renal failure usually develop. Death may be due to chronic renal failure, cardiac failure, cerebral haemorrhage or subarachnoid haemorrhage due

to increased incidence of berry aneurysms of the circulus arteriosus. Other associated abnormalities include polycystic liver disease and cysts in the spleen and pancreas.

Tumours of the kidney

Benign tumours of the kidney are relatively uncommon.

Malignant tumours

Renal clear cell carcinoma (Grawitz's tumour or hypernephroma)

This is a tumour of tubular epithelium and is more common after 50 years of age, especially in males. Local spread involves the renal vein and leads to early blood-spread of tumour fragments, most commonly to the lungs and bones. The causes are not known but cigarette smoking is believed to be a predisposing factor.

Nephroblastoma (Wilms' tumour)

This is one of the most common malignant tumours in children, usually occurring in the first 3 years. It is usually unilateral but rapidly becomes very large and invades the renal blood vessels, causing early blood-spread of the malignancy to the lungs. It is believed that the cell abnormalities occur before birth but the cause is not known.

DISEASES OF THE RENAL PELVIS, URETERS, BLADDER AND URETHRA

Learning outcomes

After studying this section you should be able to:

- describe the causes and implications of urinary obstruction
- explain the pathological features of urinary tract infections
- outline the characteristics of the main bladder tumours
- discuss the principal causes of urinary incontinence.

These structures are considered together because their combined functions are to collect and store urine prior to excretion from the body. Obstruction and infection are the main causes of dysfunction.

Obstruction to the outflow of urine

Hydronephrosis

This is dilatation of the renal pelvis and calyces caused by accumulation of urine. It leads to destruction of the nephrons, fibrosis and atrophy of the kidney. One or both kidneys may be involved, depending on the cause and site. When there is an abnormality of the bladder or urethra both kidneys are affected whereas an obstruction above the bladder is more common and affects only one kidney (Fig. 13.19).

Complete sustained obstruction

In this condition hydronephrosis develops quickly, pressure in the nephrons rises and urine production stops. The most common causes are a large calculus or tumour. The outcome depends on whether one or both kidneys are involved (homeostasis can be maintained by one kidney).

Partial or intermittent obstruction

This may lead to progressive hydronephrosis caused by, e.g.:

- a succession of renal calculi in a ureter, eventually moved onwards by peristalsis
- a calculus that partially blocks the ureter
- constriction of a ureter or the urethra by fibrous tissue, following epithelial inflammation caused by the passage of a stone or by infection
- a tumour in the urinary tract or in the abdominal or pelvic cavity
- enlarged prostate gland in the male.

Spinal lesions

The immediate effect of transverse spinal cord lesions that damage the nerve supply to the bladder is that micturition does not occur. When the bladder fills the rise in pressure causes overflow incontinence, back pressure into the ureters and hydronephrosis. Reflex micturition is usually re-established after a time, but loss of voluntary control may be irreversible. Pressure on the spinal cord and other abnormalities, e.g. spina bifida, can also impair micturition.

Complications of urinary tract obstruction

Infection. Stasis of urine predisposes to infection and pyelonephritis. The microbes usually spread upwards in the urinary tract or are sometimes bloodborne.

Calculus formation. Infection and urinary stasis predispose to calculus formation when:

- the pH of urine changes from acid to alkaline, promoting the precipitation of some solutes, e.g. phosphates
- cell debris and pus provide foci upon which solutes in the urine may be deposited.

Infections of the urinary tract

Infection of any part of the tract may spread upwards causing pyelonephritis (p. 353) and severe kidney damage.

Ureteritis

Inflammation of a ureter is usually due to the upward spread of infection in cystitis.

Acute cystitis

This is inflammation of the bladder and may be due to:

- spread of microbes that are commensals of the bowel (*Escherichia coli* and *Streptococcus faecalis*) from the perineum, especially in women because of the short wide urethra, its proximity to the anus and the moist perineal conditions
- a mixed infection of coliform and other organisms which may follow the passage of a urinary catheter or other instrument
- inflammation in the absence of microbes, e.g. following radiotherapy or passage of a catheter or other instrument.

The effects are inflammation, with oedema and small haemorrhages of the mucosa, which may be accompanied by *haematuria*. There is hypersensitivity of the sensory nerve endings in the bladder wall, which are stimulated before the bladder has filled leading to *frequency of micturition* and *dysuria* (a burning sensation on micturition). The urine may appear cloudy and have an unpleasant smell. Lower abdominal pain often accompanies cystitis.

Predisposing factors. The most important predisposing factors are coliform microbes in the perineal region and stasis of urine in the bladder. During sexual intercourse there may be trauma to the urethra and transfer of microbes from the perineum, especially in the female. Hormones associated with pregnancy cause relaxation of perineal muscle and relaxation and kinking of the ureters. Towards the end of pregnancy pressure caused by the fetus may obstruct the outflow of urine. In the male, prostatitis provides a focus of local infection or an enlarged prostate gland may cause progressive urethral obstruction.

Chronic cystitis

This may follow repeated attacks of acute cystitis. It occurs most commonly in males over 60 years of age when compression of the urethra by an enlarged prostate gland prevents the bladder from emptying completely. Calculus formation is common, especially if the normally acid urine becomes alkaline due to microbial action or kidney damage.

Urethritis

This is inflammation of the urethra. A common cause is *Neisseria gonorrhoeae* (gonococcus) spread by sexual intercourse directly to the urethra in the male and indirectly from the perineum in the female. Many cases of urethritis have no known cause, i.e. *non-specific urethritis* (Ch. 19).

Tumours of the bladder

It is not always clear whether bladder tumours are benign or malignant. Tumours are often multiple and recurrence is common. The causes of both types are not known but predisposing factors include cigarette smoking, taking high doses of analgesics over a long period and exposure to chemicals used in some industries, e.g. manufacture of aniline dyes, rubber industry, benzidine-based industries.

Papillomas

These tumours arise from transitional epithelium and are usually benign. They consist of a stalk with fine-branching fronds which tend to break off, causing painless bleeding and haematuria. Papillomas commonly recur, even when they are benign. Although the cells are well differentiated some papillomas behave as carcinomas and invade surrounding blood and lymph vessels.

Solid tumours

These are all malignant to some degree. At an early stage the more malignant and solid tumours rapidly invade the bladder wall and spread in lymph and blood to other parts of the body. If the surface ulcerates there may be haemorrhage and necrosis.

Urinary incontinence

In this condition there is involuntary passage of urine due to defective voluntary control of the external urethral sphincter.

Stress incontinence

This is leakage of urine when intra-abdominal pressure is raised, e.g. on coughing, laughing, sneezing or lifting. It usually affects women when there is weakness of the muscles of the pelvic floor or pelvic ligaments, e.g. after childbirth or as part of the ageing process.

Retention and overflow incontinence

This occurs when there is:

- retention of urine due to obstruction of urinary outflow, e.g. enlarged prostate or urethral stricture
- a neurological abnormality affecting the nerves involved in micturition, e.g. stroke, spinal cord injury or multiple sclerosis.

The bladder becomes distended and when the pressure inside overcomes the resistance of the urethral sphincter, urine dribbles from the urethra. The individual may be unable to initiate and/or maintain micturition.

Urge incontinence

Leakage of urine follows a sudden and intense urge to void and may be due to a urinary tract infection, calculus, tumour or sudden stress.

4

Protection and survival

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14

The skin

The skin completely covers the body and is continuous with the membranes lining the body orifices. It:

- protects the underlying structures from injury and from invasion by microbes
- contains sensory (*somatic*) nerve endings of pain, temperature and touch
- is involved in the regulation of body temperature.

Structure of the skin

Learning outcome

After studying this section you should be able to:

- describe the structure of the skin.

The skin has a surface area of about 1.5 to 2 m^2 in adults and it contains glands, hair and nails. There are two main layers:

- epidermis
- dermis.

Between the skin and underlying structures there is a layer of subcutaneous fat.

Epidermis (Fig. 14.1)

The epidermis is the most superficial layer of the skin and is composed of *stratified keratinised squamous epithelium* (see Fig. 3.12, p. 36) which varies in thickness in different parts of the body. It is thickest on the palms of the hands and soles of the feet. There are no blood vessels or nerve endings in the epidermis, but its deeper layers are bathed in interstitial fluid from the dermis, which provides oxygen and nutrients, and is drained away as lymph.

There are several layers (strata) of cells in the epidermis which extend from the deepest *germinative layer* to the surface *stratum corneum* (a thick horny layer). The cells on the surface are flat, thin, non-nucleated, dead cells, or *squames*, in which the cytoplasm has been replaced by the fibrous protein *keratin*. These cells are constantly being rubbed off and replaced by cells which originated in the germinative layer and have undergone gradual change as they progressed towards the surface. Complete replacement of the epidermis takes about 40 days.

The maintenance of healthy epidermis depends upon three processes being synchronised:

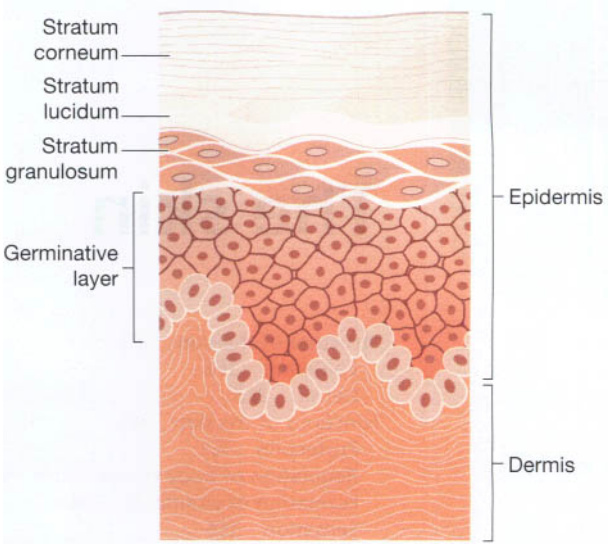

Figure 14.1 The skin showing the main layers of the epidermis.

- desquamation (shedding) of the keratinised cells from the surface
- effective keratinisation of the cells approaching the surface
- continual cell division in the deeper layers with newly formed cells being pushed to the surface.

Hairs, secretions from sebaceous glands and ducts of sweat glands pass through the epidermis to reach the surface.

The surface of the epidermis is ridged by projections of cells in the dermis called the *papillae*. The pattern of ridges is different in every individual and the impression made by them is the 'fingerprint'. The downward projections of the germinative layer between the papillae are believed to aid nutrition of epidermal cells and stabilise the two layers, preventing damage due to shearing forces. *Blisters* develop when acute trauma causes separation of the dermis and epidermis and serous fluid collects between the two layers.

The colour of the skin is affected by three main factors.

- *Melanin*, a dark pigment derived from the amino acid tyrosine and secreted by *melanocytes* in the deep germinative layer, is absorbed by surrounding epithelial cells. The amount is genetically determined and varies between different parts of the body, between members of the same race and between races. The number of melanocytes is fairly constant so the differences in colour depend on the amount of melanin secreted. It protects the skin from the harmful effects of sunlight. Exposure to sunlight promotes synthesis of increased amounts of melanin.

- *The level of oxygenation of haemoglobin* and the amount of blood circulating in the dermis give the skin its pink colour.
- *Bile pigments* in blood and *carotenes* in subcutaneous fat give the skin a yellowish colour.

Dermis (Fig. 14.2)

The dermis is tough and elastic. It is formed from connective tissue and the matrix contains *collagen fibres* interlaced with *elastic fibres*. Rupture of elastic fibres occurs when the skin is overstretched, resulting in permanent *striae*, or stretch marks, that may be found in pregnancy and obesity. Collagen fibres bind water and give the skin its tensile strength, but as this ability declines with age, wrinkles develop. Fibroblasts, macrophages and mast cells are the main cells found in the dermis. Underlying its deepest layer there is areolar tissue and varying amounts of adipose tissue (fat). The structures in the dermis are:

- blood vessels
- lymph vessels
- sensory (somatic) nerve endings
- sweat glands and their ducts
- hairs, arrector pili muscles and sebaceous glands.

Blood vessels. Arterioles form a fine network with capillary branches supplying sweat glands, sebaceous glands, hair follicles and the dermis. The epidermis has no blood supply. It obtains nutrients and oxygen from interstitial fluid derived from blood vessels in the papillae of the dermis.

Lymph vessels. These form a network throughout the dermis.

Sensory nerve endings. Sensory receptors (specialised nerve endings) which are sensitive to *touch, change in temperature, pressure* and *pain* are widely distributed in the dermis. Incoming stimuli activate different types of sensory receptors shown in Figure 14.2 and Box 14.1. The skin is an important sensory organ through which individuals receive information about their environment. Nerve impulses, generated in the sensory receptors in the dermis, are conveyed to the spinal cord by sensory *(somatic cutaneous)* nerves, then to the sensory area of the cerebrum where the sensations are perceived.

Sweat glands

Sweat glands are found widely distributed throughout the skin and are most numerous in the palms of the hands, soles of the feet, axillae and groins. They are composed of epithelial cells. The bodies of the glands lie coiled in the subcutaneous tissue. Some ducts open onto the skin surface at tiny depressions, or pores, and others open into hair follicles. Glands opening into hair follicles

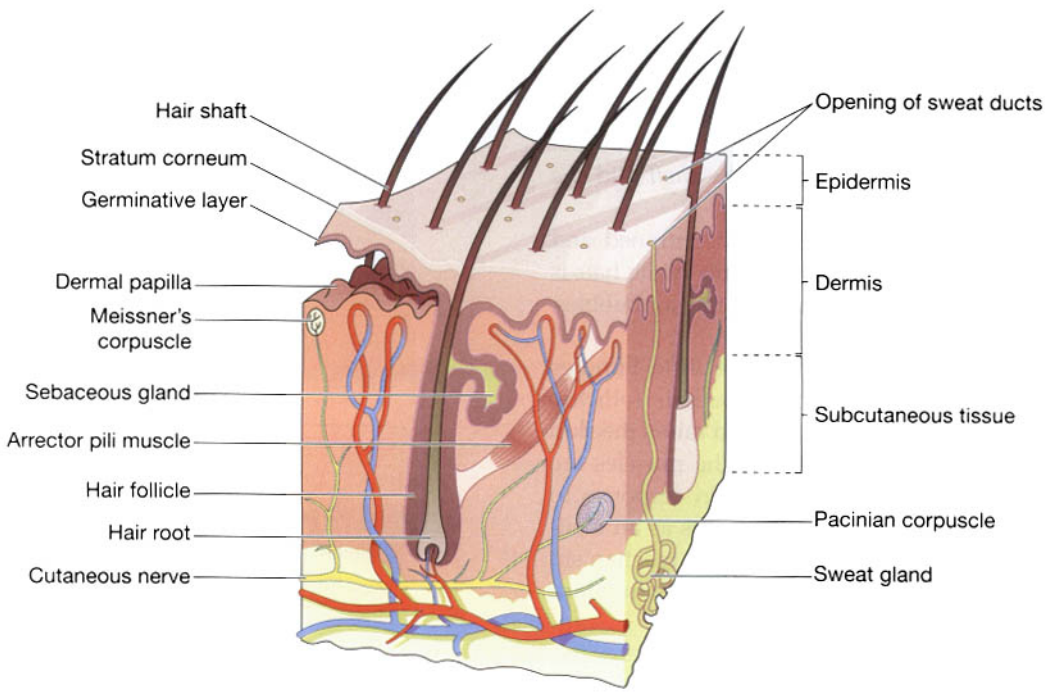

Figure 14.2 The skin showing the main structures in the dermis.

Box 14.1. Sensory receptors in the skin

Sensory receptor	Stimulus
Meissner's corpuscle	Light pressure
Pacinian corpuscle	Deep pressure
Free nerve ending	Pain

do not become active until puberty. In the axilla they secrete an odourless milky fluid which, if decomposed by surface microbes, causes an unpleasant odour. The functions of this secretion are not known. Sweat glands are stimulated by sympathetic nerves in response to raised body temperature and fear.

The most important function of sweat secreted by glands opening on to the skin surface is in the regulation of body temperature. Evaporation of sweat from body surfaces takes heat from the body and the amount of sweat produced is governed by the temperature-regulating centre in the hypothalamus. Excessive sweating may lead to dehydration and serious depletion of body sodium chloride unless intake of water and salt is appropriately increased. After 7 to 10 days' exposure to high environmental temperatures the amount of salt lost is substantially reduced but water loss remains high.

Hairs

These are formed by a down-growth of epidermal cells into the dermis or subcutaneous tissue, called *hair follicles*. At the base of the follicle is a cluster of cells called the *bulb*. The hair is formed by multiplication of cells of the bulb and as they are pushed upwards, away from their source of nutrition, the cells die and become keratinised. The part of the hair above the skin is the *shaft* and the remainder, the *root* (Fig. 14.2).

The colour of the hair is genetically determined and depends on the amount of melanin present. White hair is the result of the replacement of melanin by tiny air bubbles.

The arrector pili (Fig. 14.2). These are little bundles of smooth muscle fibres attached to the hair follicles. Contraction makes the hair stand erect and raises the skin around the hair, causing 'goose flesh'. The muscles are stimulated by sympathetic nerve fibres in response to fear and cold. Erect hairs trap air, which acts as an insulating layer. This is an efficient warming mechanism especially when accompanied by shivering, i.e. involuntary contraction of the skeletal muscles.

The sebaceous glands (Fig. 14.2). These consist of secretory epithelial cells derived from the same tissue as the hair follicles. They secrete an oily substance, *sebum*, into the hair follicles and are therefore present in the skin of all parts of the body except the palms of the hands and the soles of the feet. They are most numerous in the skin of the scalp, face, axillae and groins. In regions of transition from one type of superficial epithelium to another, such as lips, eyelids, nipple, labia minora and glans penis, there are sebaceous glands that are independent of hair follicles, secreting sebum directly on to the surface.

Sebum keeps the hair soft and pliable and gives it a shiny appearance. On the skin it provides some waterproofing and acts as a bactericidal and fungicidal agent, preventing the successful invasion of microbes. It also prevents drying and cracking of skin, especially on exposure to heat and sunshine. The activity of these glands increases at puberty and is less at the extremes of age, rendering infants and the elderly prone to the effects of excessive moisture, e.g. nappy rash in infants.

Nails (Fig. 14.3)

The nails in human beings are equivalent to the claws, horns and hoofs of animals. They are derived from the same cells as epidermis and hair and consist of a hard, horny keratin plate. They protect the tips of the fingers and toes.

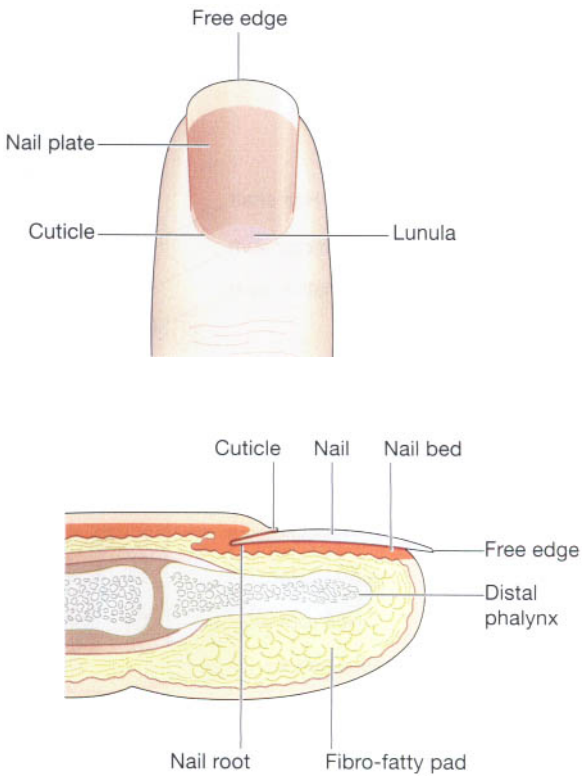

Figure 14.3 The nail and related skin.

The *root* of the nail is embedded in the skin, is covered by the *cuticle* and forms the hemispherical pale area called the *lunula*.

The *nail plate* of the nail is the exposed part that has grown out from the germinative zone of the epidermis called the *nail bed*.

Finger nails grow more quickly than toe nails and growth is quicker when the environmental temperature is high.

Functions of the skin

Learning outcome

After studying this section you should be able to:

- explain the following functions of the skin: protection, regulation of body temperature, formation of vitamin D, sensation, absorption and excretion.

Protection

The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. As an important non-specific defence mechanism it acts as a barrier against:

- invasion by microbes
- chemicals
- physical agents, e.g. mild trauma, ultraviolet light
- dehydration.

The dermis contains specialised immune cells called Langerhans cells. They phagocytose intruding antigens and travel to lymphoid tissue, where they present antigen to T-lymphocytes, thus stimulating an immune response (p. 379).

Due to the presence of the sensory nerve endings in the skin the body reacts by reflex action to unpleasant or painful stimuli, protecting it from further injury (p. 159).

Regulation of body temperature

The temperature of the body remains fairly constant at about 36.8°C (98.4°F) across a wide range of environmental temperatures. In health, variations are usually limited to between 0.5 and 0.75°C, although it is raised slightly in the evening, during exercise and in women just after ovulation. When metabolic rate increases body temperature rises and when it decreases body temperature falls.

To ensure this constant temperature a balance is maintained between heat produced in the body and heat lost to the environment.

Heat production

Some of the energy released in the cells during metabolic activity is in the form of heat and the most active organs, chemically and physically, produce the most heat. The principal organs involved are as follows.

- *The muscles*. Contraction of skeletal muscles produces a large amount of heat and the more strenuous the muscular exercise the greater the heat produced. Shivering involves muscle contraction and produces heat when there is the risk of the body temperature falling below normal.
- *The liver* is very chemically active, and heat is produced as a by-product. Metabolic rate and heat production are increased after eating.
- *The digestive organs* produce heat during peristalsis and by the chemical reactions involved in digestion.

Heat loss

Most of the heat loss from the body occurs through the skin. Small amounts are lost in expired air, urine and faeces.

Only the heat lost through the skin can be regulated to maintain a constant body temperature. There is no control over heat lost by the other routes.

Heat loss through the skin is affected by the difference between body and environmental temperatures, the amount of the body surface exposed to the air and the type of clothes worn. Air is a poor conductor of heat and when layers of air are trapped in clothing and between the skin and clothing they act as effective insulators against excessive heat loss. For this reason several layers of lightweight clothes provide more effective insulation against a low environmental temperature than one heavy garment. A balance is maintained between heat production and heat loss. Control is achieved mainly by thermoreceptors in the hypothalamus.

Mechanisms of heat loss. In *evaporation*, the body is cooled when heat is used to convert the water in sweat to water vapour.

In *radiation*, exposed parts of the body radiate heat away from the body.

In *conduction*, clothes and other objects in contact with the skin take up heat.

In *convection*, air passing over the exposed parts of the body is heated and rises, cool air replaces it and convection currents are set up. Heat is also lost from the clothes by convection.

Control of body temperature

Nervous control. The *temperature regulating centre* in the hypothalamus is responsive to the temperature of circulating blood. This centre controls body temperature through autonomic nerve stimulation of the sweat glands when body temperature rises.

The *vasomotor centre* in the medulla oblongata controls the diameter of the small arteries and arterioles, and therefore the amount of blood which circulates in the capillaries in the dermis. The vasomotor centre is influenced by the temperature of its blood supply and by nerve impulses from the hypothalamus. When body temperature rises the skin capillaries dilate and the extra blood near the surface increases heat loss by radiation, conduction and convection. The skin is warm and pink in colour. When body temperature falls arteriolar constriction conserves heat and the skin is whiter and feels cool.

Activity of the sweat glands. When the temperature of the body is increased by 0.25 to 0.5°C the sweat glands are stimulated to secrete sweat, which is conveyed to the surface of the body by ducts. When sweat droplets can be seen on the skin the rate of production is exceeding the rate of evaporation. This is most likely to happen when the environmental air is humid and the temperature high.

Loss of heat from the body by unnoticeable evaporation of water through the skin and expired air occurs even when the environmental temperature is low. This is called *insensible water loss* (around 500 ml per day) and is accompanied by insensible heat loss.

Effects of vasodilatation. The amount of heat lost from the skin depends to a great extent on the amount of blood in the vessels in the dermis. As heat production increases, the arterioles become dilated and more blood pours into the capillary network in the skin. In addition to increasing the amount of sweat produced the temperature of the skin is raised and there is an increase in the amount of heat lost by radiation, conduction and convection.

If the external environmental temperature is low or if heat production is decreased, vasoconstriction is stimulated by sympathetic nerves. This decreases the blood flow near the body surface, conserving heat.

Fever. This is often the result of infection and is caused by release of chemicals (*pyrogens*) from damaged tissue and the cells involved in inflammation. Pyrogens act on the hypothalamus, which releases prostaglandins that reset the hypothalamic thermostat to a higher temperature. The body responds by activating heat-promoting mechanisms, e.g. shivering and vasoconstriction until the new higher temperature is reached. When the thermostat is reset to the normal level, heat-loss mechanisms are activated. There is profuse sweating and vasodilatation accompanied by warm, pink (flushed) skin until body temperature falls to the normal range again.

Hypothermia. This is present when core temperature, e.g. the rectal temperature, is below 35°C (95°F). At a rectal temperature below 32°C (89.6°F), compensatory mechanisms to restore body temperature usually fail, e.g. shivering is replaced by muscle rigidity and cramps, vasoconstriction fails to occur and there is lowered blood pressure, pulse and respiration rates. Mental confusion and disorientation occur. Death usually occurs when the temperature falls below 25°C (77°F).

Individuals at the extremes of age are prone to hypothermia.

Formation of vitamin D

7-dehydrocholesterol is a lipid-based substance in the skin and ultraviolet light from the sun converts it to vitamin D. This circulates in the blood and is used, with calcium and phosphate, in the formation and maintenance of bone. Any vitamin D in excess of immediate requirements is stored in the liver.

Sensation

Sensory receptors consist of nerve endings in the dermis that are sensitive to touch, pressure, temperature or pain. Stimulation generates nerve impulses in sensory nerves that are transmitted to the cerebral cortex (see Fig. 7.20B, p. 153). Some areas have more sensory receptors than others causing them to be especially sensitive, e.g. the lips and fingertips.

Absorption

This property is limited but substances that can be absorbed include:

- some drugs, in transdermal patches, e.g. hormones used as replacement therapy in postmenopausal women, nicotine as an aid to stopping smoking
- some toxic chemicals, e.g. mercury.

Excretion

The skin is a minor excretory organ for some substances including:

- sodium chloride in sweat and excess sweating may lead to abnormally low blood sodium levels
- urea, especially when kidney function is impaired
- aromatic substances, e.g. garlic and other spices.

Wound healing

Learning outcome

After studying this section you should be able to:

- compare and contrast the processes of primary and secondary wound healing.

Conditions required for wound healing

Systemic factors. These include good nutritional status and general health. Infection, impaired immunity, poor blood supply and systemic conditions, e.g. diabetes mellitus and cancer, reduce the rate of wound healing.

Local factors. Local factors that facilitate wound healing include:

- good blood supply providing oxygen and nutrients and removing waste products
- freedom from contamination by, e.g., microbes, foreign bodies, toxic chemicals.

Primary healing (healing by first intention)

This method of healing follows minimal destruction of tissue when the damaged edges of a wound are in close apposition (Fig. 14.4). There are several overlapping stages in the repair process.

Inflammation. The cut surfaces become inflamed and blood clot and cell debris fill the gap between them in the first few hours. Phagocytes and fibroblasts migrate into the blood clot:

- phagocytes begin to remove the clot and cell debris stimulating fibroblast activity
- fibroblasts secrete collagen fibres which begin to bind the surfaces together.

Proliferation. There is proliferation of epithelial cells across the wound, through the clot. The epidermis meets and grows upwards until the full thickness is restored. The clot above the new tissue becomes the scab and separates after 3 to 10 days. *Granulation tissue*, consisting of new capillary buds, phagocytes and fibroblasts, develops, invading the clot and restoring the blood supply to the wound. Fibroblasts continue to secrete collagen fibres as the clot and any bacteria are removed by phagocytosis.

Maturation. The granulation tissue is replaced by fibrous scar tissue. Rearrangement of collagen fibres occurs and the strength of the wound increases. In time the scar becomes less vascular, appearing after a few months as a fine line.

The channels left when stitches are removed heal by the same process.

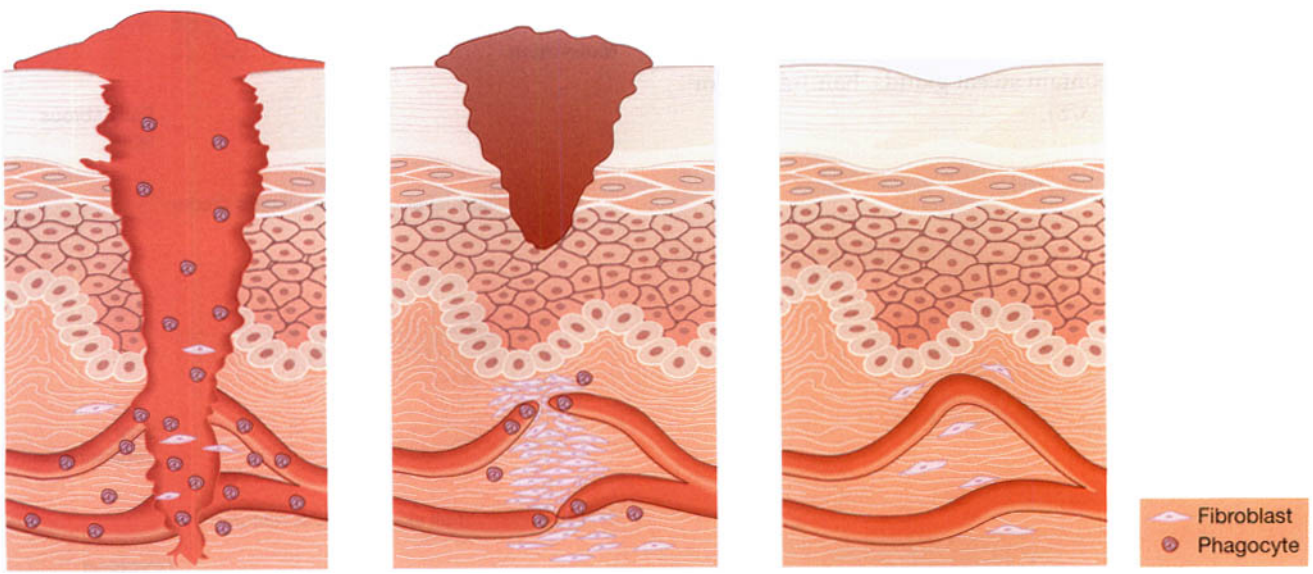

Figure 14.4 Stages in primary wound healing.

Secondary healing (healing by second intention)

This method of healing follows destruction of a large amount of tissue or when the edges of a wound cannot be brought into apposition, e.g. varicose ulcers and pressure sores (decubitus ulcers). The stages of secondary healing are the same as in primary healing and the time taken for healing depends on the effective removal of the cause and on the size of the wound. There are several recognised stages in the repair process, e.g. of decubitus ulcers (Fig. 14.5):

Inflammation. This develops on the surface of the healthy tissue and separation of necrotic tissue (*slough*) begins, due mainly to the action of phagocytes in the inflammatory exudate.

Proliferation. This begins as granulation tissue, consisting of capillary buds, phagocytes and fibroblasts, develops at the base of the cavity. It grows towards the surface, probably stimulated by macrophages. Phagocytes in the plentiful blood supply tend to prevent infection of the wound by ingestion of bacteria after separation of the slough. Some fibroblasts in the wound develop a limited ability to contract, reducing the size of the wound and healing time. When granulation tissue reaches the level of the dermis, epithelial cells at the edges proliferate and grow towards the centre.

Maturation. This occurs as scar tissue replaces granulation tissue, usually over several months until the full thickness of the skin is restored. The fibrous scar tissue is shiny and does not contain sweat glands, hair follicles or sebaceous glands (p. 378).

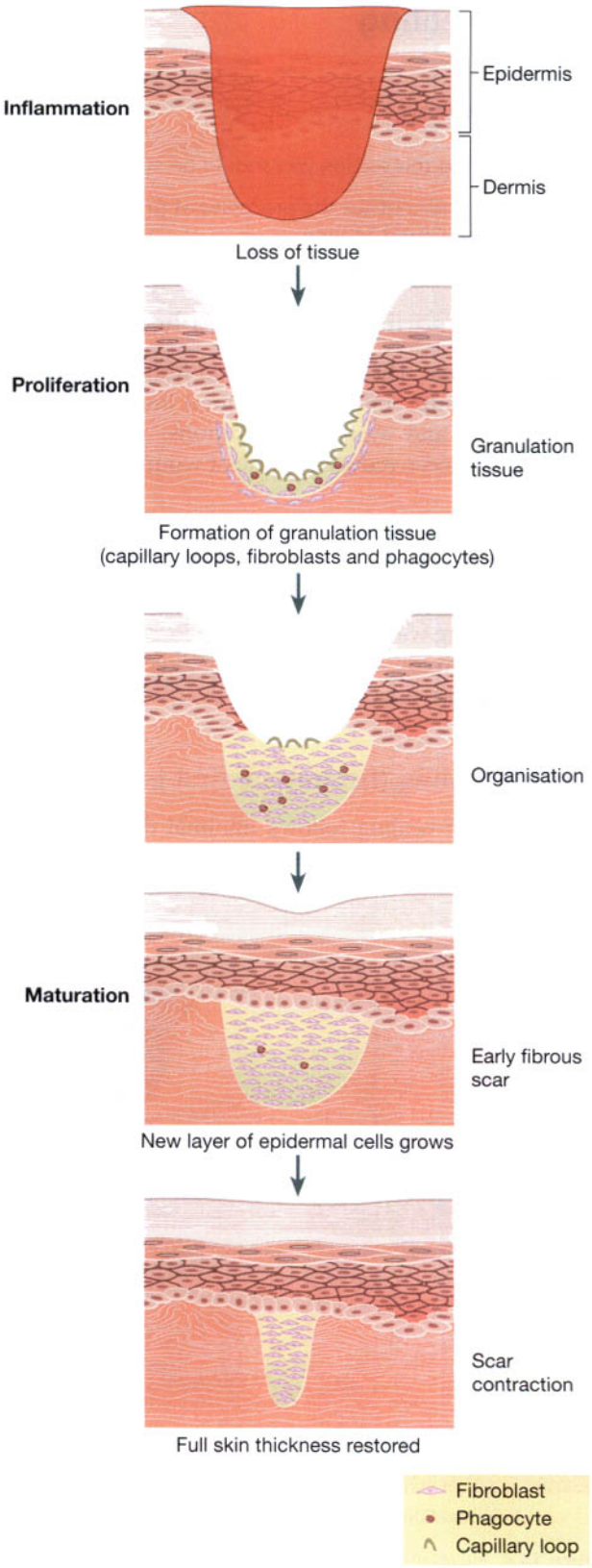

Figure 14.5 Stages in secondary wound healing.

DISORDERS OF THE SKIN

Learning outcomes

After studying this section you should be able to:

- list the causes of diseases in this section
- explain the pathological features and effects of common conditions affecting the skin: infections, non-infective inflammatory conditions, pressure sores, burns and tumours.

Infections

Viral infections

Human papilloma virus (HPV)

This causes *warts* or *veruccas* that are spread by direct contact, e.g. from another lesion, or another infected individual. There is proliferation of the epidermis and development of a small firm growth. Common sites are the hands, the face and soles of the feet.

Herpes viruses

Chicken pox and shingles (p. 183) are caused by the herpes zoster virus. Other herpes viruses cause *cold sores* (HSV1) and *genital herpes* (HSV2). The latter cause genital warts affecting the genitalia and/or anus and are spread by direct contact during sexual intercourse.

Bacterial infections

Impetigo

This is a highly infectious condition commonly caused by *Staphylococcus aureus*. Superficial pustules develop, usually round the nose and mouth. It is spread by direct contact and affects mainly children and immunosuppressed individuals. When caused by *Streptococcus pyogenes* (group A β-haemolytic streptococcus) the infection may be complicated, a few weeks later, by an immune reaction causing glomerulonephritis (p. 351).

Cellulitis

This is a spreading infection caused by some anaerobic microbes or by *Streptococcus pyogenes* or *Clostridium perfringens*. The spread of infection is facilitated by the formation of enzymes that break down the connective tissue that normally isolates an area of inflammation. The microbes enter the body through a break in the skin. If untreated, the products of inflammation may enter the blood causing septicaemia. In severe cases *necrotising fasciitis* may occur, there is oedema and necrosis of subcutaneous tissue that usually includes the fascia in the affected area.

Fungal infections

Ringworm and tinea pedis

These are superficial infections of the skin. In ringworm there is an outward spreading ring of inflammation. It most commonly affects the scalp and is found in cattle from which infection is spread.

Tinea pedis (athlete's foot) affects the area between the toes. Both infections are spread by direct contact.

Non-infective inflammatory conditions

Eczema and dermatitis

These two terms are synonymous and describe inflammatory conditions which can be acute or chronic. In acute dermatitis there is redness, swelling and exudation of serous fluid usually accompanied by itching. This is often followed by crusting and scaling. If the condition becomes chronic, the skin thickens and may become leathery due to long-term scratching. Infection may complicate scratching.

Atopic dermatitis is caused by allergens and commonly affects atopic individuals. Children who may also suffer from hay fever or asthma (pp. 259 and 260) are often affected.

Contact dermatitis may be caused by:

- direct contact with irritants, e.g. cosmetics, soap, detergent, strong acids or alkalis, industrial chemicals
- a hypersensitivity reaction (see Fig. 15.9, p. 384) to, e.g., synthetic rubber, nickel, dyes and other chemicals.

Psoriasis

This condition is genetically determined and characterised by exacerbations and periods of remission of varying duration. It is a common condition, especially between the ages of 15 and 40 years. There is proliferation of the cells of the basal layers of the epidermis and the more rapid upward progress of these cells through the epidermis results in incomplete maturation of the upper layer. The skin is shiny, silver coloured and scaly. Bleeding may occur when scales are scratched or rubbed off. The elbows, knees and scalp are common sites but other parts can be affected. Triggering factors that lead to exacerbation of the condition include trauma, infection and sunburn. Sometimes psoriasis is associated with arthritis.

Acne vulgaris

This is a common condition in adolescents that is thought to be caused by increased levels of male sex hormones after puberty. It occurs when sebaceous glands in hair follicles become blocked and then infected leading to inflammation and pustule formation. In severe cases permanent scarring may result. The most common sites are the face, chest and upper back.

Pressure sores

Also known as *decubitus ulcers*, these occur over 'pressure points', areas where the skin is compressed for long periods between a bony prominence and a hard surface, e.g. a bed or chair. When this occurs, blood flow to the affected area is impaired and ischaemia develops. Initially the skin reddens, and later as ischaemia and necrosis occur the skin sloughs and an ulcer forms that may then enlarge into a cavity. If infection occurs, this can result in septicaemia. Healing takes place by second intention (p. 368).

Predisposing factors

These may be:

- extrinsic, e.g. pressure, shearing forces, trauma, immobility, moisture, infection
- intrinsic, e.g. poor nutritional status, emaciation, incontinence, infection, concurrent illness, sensory impairment, poor circulation, old age.

Burns

These may be caused by many types of trauma including: heat, cold, electricity, ionising radiation and chemicals, including strong acids or alkalis.

Local damage occurs disrupting the structure and functions of the skin. Infection is a common complication of any burn as the outer barrier formed by the epidermis is lost.

Burns are classified according to their depth:

- *partial thickness* (superficial) when only the epidermis is involved.
- *full thickness* (deep) when the epidermis and dermis are destroyed. These burns are usually relatively painless as the sensory nerve endings in the dermis are destroyed. After a few days the destroyed tissue coagulates and forms an *eschar*, or thick scab, which sloughs off after 2 to 3 weeks. In *circumferential burns* which encircle any area of the body complications may arise from constriction of the part by eschar, e.g. respiratory impairment may follow circumferential burns of the chest, or the circulation to the distal part of an affected limb may be seriously impaired. Skin grafting is required except for small injuries. Otherwise, healing, which is prolonged, occurs by second intention (p. 368) and there is no regeneration of sweat glands, hair follicles or sebaceous glands. Resultant scar tissue often limits movement of affected joints.

The extent of burns in adults is roughly estimated using the 'rule of nines' (Fig. 14.6). In adults, hypovolaemic shock usually develops when 15% of the surface area is affected. Fatality is likely in adults with full thickness burns if the surface area affected is added to the patient's age and the total is greater than 80.

Complications of burns

Dehydration and hypovolaemia. These may occur in extensive burns due to excessive leakage of water and plasma proteins from the surface of the damaged skin.

Shock. This may accompany severe hypovolaemia.

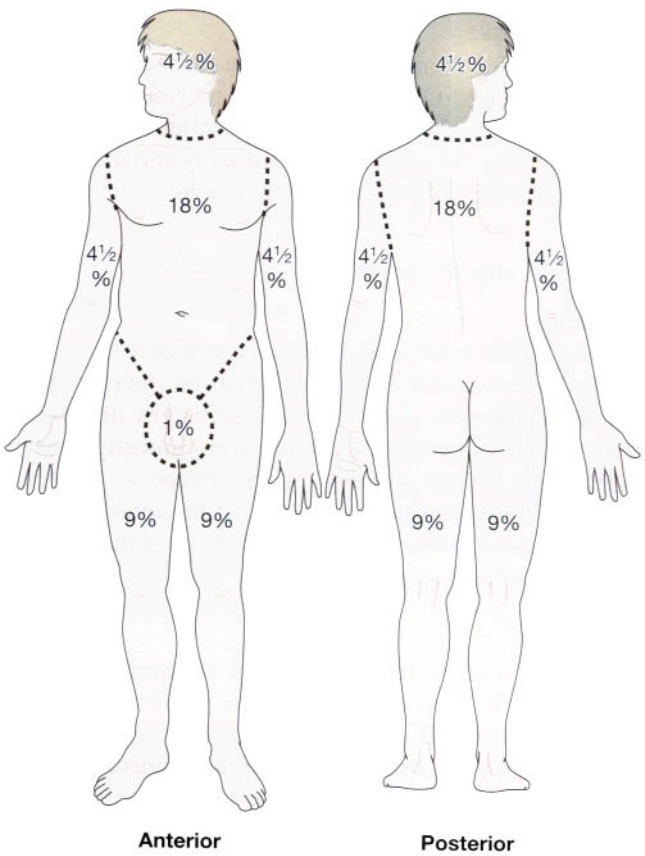

Figure 14.6 The 'rule of nines' for estimating the extent of burns.

Hypothermia. This develops when thermoregulation is impaired and excessive heat is lost.

Infection. Infection of the surface of a burn may result in septicaemia.

Renal failure. This occurs when the kidney tubules cannot deal with the amount of waste from haemolysed erythrocytes and damaged tissue.

Contractures. These may develop later as fibrous scar tissue contracts distorting the limbs, e.g. the hands, and impairing function.

Malignant tumours

Basal cell carcinoma

This is the least malignant and most common type of skin cancer. It is associated with long-term exposure to sunlight and is therefore most likely to occur on sun-exposed sites, usually the head or neck. It appears as a shiny nodule and later this breaks down, becoming an ulcer, commonly called a *rodent ulcer*. This is locally invasive but seldom metastasises.

Malignant melanoma

This is malignant proliferation of melanocytes, usually originating in a mole that may have an irregular outline. It may ulcerate and bleed and most commonly affects young and middle-aged adults. Predisposing factors are believed to be a fair skin and recurrent episodes of intensive exposure to sunlight including repeated episodes of sunburn in childhood. Likely sites for this tumour show a strong gender bias, with the lower leg being the commonest site in females and the torso being a common site in males. Metastases develop early and are frequently found in lymph nodes. The most common sites of blood-spread metastases are the liver, brain, lungs, bowel and bone marrow.

Kaposi's sarcoma

In this rare condition, a malignant tumour arises in the walls of lymphatic vessels. A small red-blue patch or nodule develops usually on the lower limbs.

It is also an AIDS-related disease and has thus become more common. In such cases, multiple lesions affect many sites of the body.

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15

Resistance and immunity

An individual is under constant attack from an enormous range of potentially harmful invaders, from the months spent in the womb to the end of his life. These invaders include such diverse entities as bacteria, viruses, cancer cells, parasites and foreign (non-self) cells, e.g. in tissue transplant. The body therefore has developed a wide selection of protective measures, which can be divided into two categories.

Non-specific defence mechanisms. These protect against any of an enormous range of possible dangers.

Specific defence mechanisms. These are grouped together under the term *immunity*. Resistance is directed against only one particular invader. In addition, *immunological memory* develops, which confers long-term immunity to specific infections. An *antigen* is anything that stimulates an immune response.

NON-SPECIFIC DEFENCE MECHANISMS

Learning outcomes

After studying this section, you should be able to:

- describe the functions and features of the inflammatory response
- discuss the process of phagocytosis
- list the main antimicrobial substances of the body.

These are the first lines of general defence; they prevent entry and minimise further passage of microbes and other foreign material into the body.

There are four main non-specific defence mechanisms:

- defence at body surfaces
- phagocytosis
- natural antimicrobial substances
- the inflammatory response.

Defence at body surfaces

When skin and mucous membrane are intact and healthy they provide an efficient physical barrier to invading microbes. The outer layer of skin can be penetrated by only a few microbes and the mucus secreted by mucous membranes traps microbes and other foreign material on its sticky surface. Sebum and sweat secreted on to the skin surface contain antibacterial and antifungal substances.

Hairs in the nose act as a coarse filter and the sweeping action of cilia in the respiratory tract moves mucus and inhaled foreign materials towards the throat. Then it is expectorated or swallowed.

The one-way flow of urine from the bladder minimises the risk of microbes ascending through the urethra into the bladder.

Phagocytosis

The process of phagocytosis (cell eating) is shown in Figure 4.10, page 68. Phagocytic defence cells such as macrophages and neutrophils are attracted to sites of inflammation and infection by chemotaxis, when chemoattractants are released by injured cells and invading microbes. Phagocytes trap particles either by engulfing them with their body mass or by extending long pseudopodia towards them, which grasp them and reel them in (Fig. 15.1). These cells are non-selective in their targets; they will bind, engulf and digest foreign cells or particles.

Macrophages have an important role as a link between the non-specific and specific defence mechanisms. After ingestion and digestion of an antigen, they act as *antigen-presenting cells*, displaying their antigen on their own cell surface to stimulate T-lymphocytes and activate the immune response (p. 379).

Natural antimicrobial substances

Hydrochloric acid. This is present in high concentrations in gastric juice, and kills the majority of ingested microbes.

Lysozyme. This is a small molecule protein with antibacterial properties present in granulocytes, tears, and other body secretions. It is not present in sweat, urine and cerebrospinal fluid.

Antibodies. These are present in nasal secretions and saliva and are able to inactivate some microbes.

Saliva. This is secreted into the mouth and washes away food debris that may serve as culture medium for microbes. Its slightly acid reaction inhibits the growth of some microbes.

Interferons. These are substances produced by T-lymphocytes and by cells that have been invaded by viruses. They prevent viral replication within cells and spread of viruses to other cells.

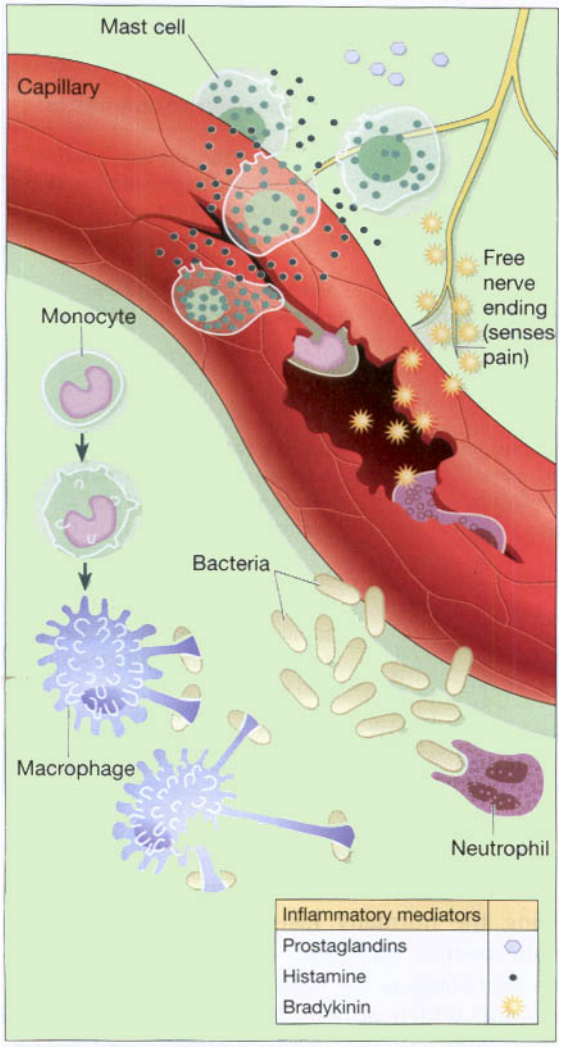


Figure 15.1 The inflammatory response.

Complement. Complement is a system of about 20 proteins found in the blood and tissues. It is activated by the presence of *immune complexes* (an antigen and antibody bound together) and by foreign sugars on bacterial cell walls. Complement:

- binds to, and makes holes in, bacterial cell walls, thus destroying the microbe
- binds to bacterial cell walls, stimulating phagocytosis by neutrophils and macrophages
- attracts phagocytic cells such as neutrophils into an area of infection.

The inflammatory response

This is the physiological response to tissue damage and is accompanied by a characteristic series of local changes (Fig. 15.1). It most commonly takes place when microbes have overcome the non-specific defence mechanisms. Its purpose is protective: to isolate, inactivate and remove both the causative agent and damaged tissue so that healing can take place.

Inflammatory conditions are recognised by their Latin suffix '-itis'; for example, appendicitis is inflammation of the appendix and laryngitis is inflammation of the larynx.

Causes of inflammation

The numerous causes of inflammation may be classified as follows:

- microbes, e.g. bacteria, viruses, protozoa, fungi
- physical agents, e.g. heat, cold, mechanical injury, ultraviolet and ionising radiation
- chemical agents
  - organic, e.g. microbial toxins and organic poisons, such as weedkillers
  - inorganic, e.g. acids, alkalis
- antigens that stimulate immunological responses.

Acute inflammation

Episodes of acute inflammation are usually of short duration, e.g. days to a few weeks, and may range from mild to very severe. The cardinal signs of inflammation are:

- redness
- heat
- pain
- swelling
- loss of function.

The acute inflammatory response is described in a series of overlapping stages: increased blood flow, increased formation of tissue fluid and migration of leukocytes. Some of the most important substances released in inflammation are summarised in Table 15.1.

Increased blood flow

Following injury, both the arterioles supplying the damaged area and the local capillaries dilate, increasing blood flow to the site.

This is caused mainly by the local release of a number of chemical mediators from damaged cells, e.g. histamine and serotonin. Increased blood flow to the area of tissue damage provides more oxygen and nutrients for the increased cellular activity that accompanies inflammation. Increased blood flow causes the increased temperature and reddening of an inflamed area.

Increased formation of tissue fluid

One of the cardinal signs of inflammation is swelling (oedema) of the tissues involved, which is caused by

Table 15.1 Summary of the principal substances released in inflammation

Substance	Made by	Trigger for release	Main pro-inflammatory actions
Histamine	Mast cells (in most tissues), basophils (blood); stored in cytoplasmic granules	Binding of antibody to mast cells and basophils	Vasodilatation, itching, ↑vascular permeability, degranulation, smooth muscle contraction (e.g. bronchoconstriction)
Serotonin (5-HT)	Platelets Mast cells and basophils (stored in granules) Also in CNS (acts as neurotransmitter)	When platelets are activated, and when mast cells/basophils degranulate	Vasoconstriction, ↑vascular permeability
Prostaglandins (PGs)	Nearly all cells; not stored, but made from cell membranes as required	Many different stimuli, e.g. drugs, toxins, other inflammatory mediators, hormones, trauma	Diverse, sometimes opposing, e.g. fever, pain, vasodilatation or vasoconstriction, ↑vascular permeability
Heparin	Liver, mast cells, basophils (stored in cytoplasmic granules)	Released when cells degranulate	Anticoagulant (prevents blood clotting), which maintains blood supply (nutrients, O_2) to injured tissue and washes away microbes and wastes
Bradykinin	Tissues and blood	When blood clots, in trauma and inflammation	Pain Vasodilatation

fluid leaving local blood vessels and entering the interstitial spaces. There are two main causes of oedema.

Increased permeability of small blood vessel walls. This is caused by inflammatory mediators, e.g. prostaglandins, histamine and serotonin, which are released by injured cells and cause the cells that form the single-layered venule wall to pull apart from one another. This opens channels that allow the movement of:

- excess fluid, which leaves the blood and enters the tissues, and
- plasma proteins, which are normally retained within the bloodstream and contribute to the osmotic pressure of the blood. When plasma proteins leave the blood, as in inflammation, the osmotic pressure of the blood falls and water moves from the bloodstream into the tissues.

Increased hydrostatic pressure. The increased blood flow into the capillary bed forces fluid out of the vessels and into the tissues.

Some interstitial fluid returns to the capillaries but most of the inflammatory exudate, phagocytes and cell debris are removed in lymph vessels because the pores of lymph vessels are larger, and the pressure inside is lower, than in blood capillaries.

Migration of leukocytes

Loss of fluid from the blood thickens it, slowing flow and allowing the normally fast-flowing white blood cells to make contact with, and adhere to, the vessel wall. In the acute stages, the most important leukocyte is the neutrophil, which adheres to the blood vessel lining, squeezes between the endothelial cells and enters the tissues, where its main function is in phagocytosis of antigens.

Later in the inflammatory response, after about 24 hours, macrophages become the predominant cell type at the inflamed site, and they persist in the tissues if the situation is not resolved, leading to chronic inflammation. Macrophages are larger and longer lived than the neutrophils. They phagocytose dead/dying tissue, microbes and other antigenic material, and dead/dying neutrophils.

Chemotaxis. This is the chemical attraction of leukocytes to an area of inflammation. The role of chemoattractants and the way in which they work is not fully understood.

It may be that chemoattractants act to retain passing leukocytes in the inflamed area, rather than actively attracting them from distant areas of the body. Known chemoattractants include microbial toxins, chemicals released from leukocytes, prostaglandins from damaged cells and complement proteins.

Benefits of acute inflammation

Most aspects of the inflammatory response are hugely beneficial, promoting removal of the harmful agent and setting the scene for healing to follow.

Promotion of phagocytosis (see Fig. 4.8). Neutrophils and macrophages in the tissues are actively recruited into inflamed areas. They engulf particles of biological and non-biological origin. Biological material includes dead and damaged cells, microbes, and damaged connective tissue fibres. Most biological material is digested by enzymes inside phagocytes. Phagocyte activity is promoted by the raised temperatures (local and systemic) associated with inflammation. Some microbes resist digestion and provide a possible source of future infection, e.g. *Mycobacterium tuberculosis*. Non-biological materials which cannot be digested include inhaled dust particles and chemical substances. Many phagocytes may die in an inflamed area if the material they ingest resists digestion, or if the number of particles is excessive. When this happens the phagocytes disintegrate and release material that may become fibrosed or cause further damage.

Promotion of the immune response. Formation of tissue exudate allows protective proteins such as antibodies to leave the bloodstream easily and collect at the site. The antibodies may promote phagocytosis of the microbes and neutralise their toxins.

Toxin dilution. Inflammatory exudate dilutes damaging and waste materials in the area, and assists their removal from the site. This is of particular importance when injurious chemicals and bacterial toxins are involved.

Increased core temperature. Body temperature rises when an endogenous pyrogen (interleukin 1) is released from macrophages and granulocytes in response to microbial toxins or immune complexes. Interleukin 1 is a chemical mediator that resets the temperature thermostat in the hypothalamus at a higher level, causing pyrexia and other symptoms that may also accompany inflammation, e.g. fatigue and loss of appetite. Pyrexia increases the metabolic rate of cells in the inflamed area and, consequently, there is an increased need for oxygen and nutrients. The increased temperature of inflamed tissues has the twin benefits of inhibiting the growth and division of microbes, whilst promoting the activity of phagocytes.

Fibrin formation. Fibrinogen, secreted by fibroblasts present in inflammatory exudate, is acted upon by thromboplastin released from damaged cells and forms an insoluble fibrin network. This may:

- wall off the inflamed area, preventing the spread of the cause
- bind together the cut edges of a wound during primary healing.

Some microbes such as *Streptococcus pyogenes*, which causes tonsillitis, pharyngitis and some skin infections, secrete toxins that break down fibrin, enabling infection to spread.

Harmful effects of acute inflammation

Tissue swelling. This is the result of the increased blood flow and exudation and is often accompanied by loss of function. The effects can be harmful, depending on the site:

- in a joint—limitation of movement
- in the larynx—interference with breathing
- in a confined space, such as inside the skull or under the periosteum of bone—severe pain due to pressure on nerves.

Pain. This occurs when local swelling compresses sensory nerve endings. It is exacerbated by chemical mediators of the inflammatory process, e.g. bradykinin, prostaglandins that potentiate the sensitivity of the sensory nerve endings to painful stimuli.

Suppuration (pus formation)

Pus consists of dead phagocytes, dead cells, cell debris, fibrin, inflammatory exudate and living and dead microbes. It is contained within a membrane of new blood capillaries, phagocytes and fibroblasts. The most common causative pyogenic microbes are *Staphylococcus aureus* and *Streptococcus pyogenes*. Small amounts of pus form *boils* and larger amounts form *abscesses*. *Staphylococcus aureus* produces the enzyme coagulase which converts fibrinogen to fibrin, localising the pus. *Streptococcus pyogenes* produces streptolysins that promote the breakdown of connective tissue, causing spreading infection. Healing, following pus formation, is by granulation and fibrosis (see Ch. 14).

Superficial abscesses tend to rupture through the skin and discharge pus. Healing is usually complete unless there is extensive tissue damage.

Deep-seated abscesses may have a variety of outcomes. There may be:

- early rupture with complete discharge of pus on to the surface, followed by healing
- rupture and limited discharge of pus on to the surface, followed by the development of a chronic abscess with an infected open channel or *sinus* (Fig. 15.2)

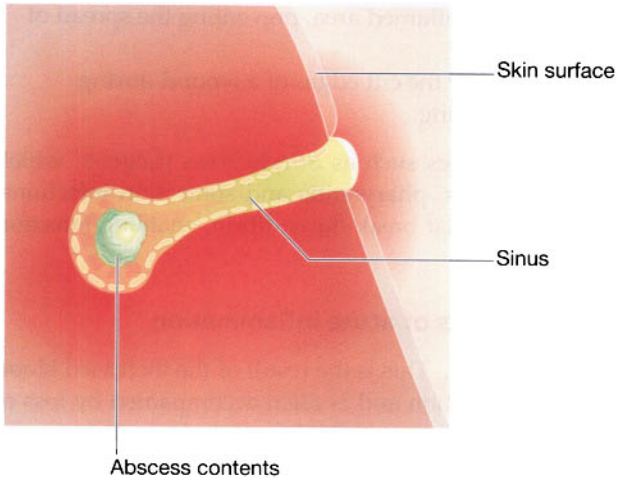


Figure 15.2 Sinus between an abscess and the surface of the body.

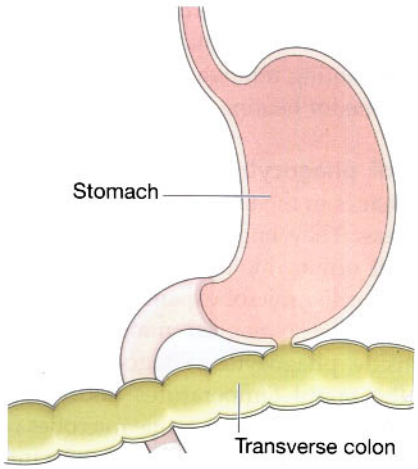


Figure 15.3 Fistula between the stomach and the colon.

- rupture and discharge of pus into an adjacent organ or cavity, forming an infected channel open at both ends or *fistula* (Fig. 15.3)
- eventual removal of pus by phagocytes, followed by healing
- enclosure of pus by fibrous tissue that may become calcified, harbouring live organisms which may become a source of future infection
- formation of fibrous adhesions between adjacent membranes, e.g. pleura, peritoneum
- shrinkage of fibrous tissue as it ages that may reduce the lumen or obstruct a tube, e.g. oesophagus, bowel, blood vessel.

Outcomes of acute inflammation

Resolution. This occurs when the cause has been successfully overcome. The inflammatory process is reversed and:

- damaged cells are phagocytosed
- fibrin strands are broken down by fibrinolytic enzymes
- waste material is removed in lymph and blood vessels
- repair is complete leaving only a small scar.

Development of chronic inflammation. (See below.) Any form of acute inflammation may develop into the chronic form if resolution is not complete, e.g. if live microbes remain at the site, as in some deep-seated abscesses, wound infections and bone infections.

Chronic inflammation

The processes involved are very similar to those of acute inflammation but, because the process is of longer duration, considerably more tissue is likely to be destroyed. The inflammatory cell types are mainly lymphocytes instead of neutrophils, and fibroblasts are activated, leading to the laying down of collagen, and *fibrosis*. If the body defences are unable to clear the infection, they may try to wall it off instead, forming nodules called *granulomas*, within which are collections of defensive cells. Tuberculosis is an example of an infection which frequently becomes chronic, leading to granuloma formation. The causative bacterium, *Mycobacterium tuberculosis*, is resistant to body defences and so pockets of organisms are sealed up in granulomas within the lungs.

Chronic inflammation may either be a complication of acute inflammation (see above) or a primary condition of slow onset.

Slow onset of inflammation

This may have several causes.

- There may be infection by low-virulence organisms in an area with a poor blood supply, e.g. endocarditis caused by non-haemolytic streptococci.
- Inorganic materials may be involved, for instance when:
  - an internal stitch has not dissolved
  - toxic silicic acid is formed when silicon, inhaled in dust, is dissolved.
- Hypersensitivity may develop following repeated exposure to some chemicals, e.g. in contact dermatitis skin proteins are altered when some chemicals are absorbed, the altered proteins act as antigens, stimulating the production of antibodies and initiating the inflammatory process.

Fibrosis (scar formation)

Fibrous tissue is formed during healing when there is loss of tissue or the cells destroyed do not regenerate,

e.g. following chronic inflammation, persistent ischaemia, suppuration or large-scale trauma. The process begins with formation of granulation tissue, then, over time, the new capillaries and inflammatory material are removed leaving only the collagen fibres secreted by the fibroblasts. Fibrous tissue may have long-lasting damaging effects.

Adhesions consisting of fibrous tissue may limit movement, e.g. between the layers of pleura, preventing inflation of the lungs; between loops of bowel, interfering with peristalsis.

Fibrosis of infarcts. Blockage of an end-vessel by a thrombus or an embolus causes an infarct (area of dead tissue). Fibrosis of one large infarct or of numerous small infarcts may follow, leading to varying degrees of organ dysfunction, e.g. in heart, brain, kidneys, liver.

Tissue shrinkage occurs as fibrous tissue ages. The effects depend on the site and extent of the fibrosis, e.g.:

- Small tubes, such as blood vessels, air passages, ureters, the urethra and ducts of glands may become narrow or obstructed and lose their elasticity
- Contractures (bands of shrunken fibrous tissue) may extend across joints, e.g. in a limb or digit there may be limitation of movement or, following burns of the neck, the head may be pulled to one side.

IMMUNITY

Learning outcomes

After studying this section, you should be able to:

- discuss the roles of the different types of T-lymphocyte in providing cell-mediated immunity
- describe the process of antibody-mediated immunity
- distinguish between artificially and naturally acquired immunity, giving examples of each
- distinguish between active and passive immunity, giving examples of each.

The cell type involved in immunity is the lymphocyte (p. 67). This white blood cell is manufactured in the bone marrow, and has a characteristically large, single nucleus. Once released into the bloodstream from the bone marrow, lymphocytes are further processed to make two functionally distinct types: the T-lymphocyte and the B-lymphocyte.

T-lymphocytes. These are processed by the thymus gland, which lies between the heart and the sternum. The hormone thymosin, produced by the thymus, is responsible for promoting the processing, which leads to the formation of fully specialised (differentiated), mature, functional T-lymphocytes. It is important to recognise that a mature T-lymphocyte has been programmed to recognise only one type of antigen, and during its subsequent travels through the body will react to no other antigen, however dangerous it might be. Thus, a T-lymphocyte manufactured to recognise the chickenpox virus will not react to a measles virus, a cancer cell, or a tuberculosis bacterium.

T-lymphocytes provide *cell-mediated immunity*, discussed below.

B-lymphocytes. These are processed in the bone marrow. Their role is in production of *antibodies* (immunoglobulins), which are proteins designed to bind to, and cause the destruction of, an antigen. As with T-lymphocytes, each B-lymphocyte targets one specific antigen; the antibody released reacts with one type of antigen and no other. B-lymphocytes provide *antibody-mediated immunity*, discussed below.

From this description of T- and B-lymphocytes, it is clear that for every one of the millions of possible antigens that might be encountered in life there is one corresponding T- and B-lymphocyte. There is therefore a vast number of different T- and B-lymphocytes in the body, each capable of responding to only one antigen.

Cell-mediated immunity

T-lymphocytes that have been activated in the thymus gland are released into the circulation. When they encounter their antigen for the first time, they become sensitised to it. If the antigen has come from outside the body, it needs to be 'presented' to the T-lymphocyte on the surface of an antigen-presenting cell. There are different types of antigen-presenting cell, including macrophages. Macrophages are part of the non-specific defences, because they engulf and digest antigens indiscriminately, but they also participate in immune responses. To do this, after digesting the antigen they transport the most antigenic fragment to their own cell membrane and display it on their surface (Fig. 15.4). On their movement around the body, still displaying the antigen fragment, they eventually come into contact with

the T-lymphocyte that has been processed to target that particular antigen.

If the antigen is an abnormal body cell, such as a cancer cell, it too will be displaying foreign (non-self) material on its cell membrane that will stimulate the T-lymphocyte. Whichever way the antigen is presented to the T-lymphocyte, it stimulates the division and proliferation (*clonal expansion*) of the T-lymphocyte (Fig. 15.4). Three main types of specialised T-lymphocyte are produced, each of which is still directed against the original antigen, but which will tackle it in different ways.

Memory T-cells

These provide *cell-mediated immunity* by responding rapidly to another encounter with the same antigen.

Cytotoxic T-cells

These directly inactivate any cells carrying antigens. They attach themselves to the target cell and release powerful toxins, which are very effective because the two cells are so close together. The main role of cytotoxic T-lymphocytes is in destruction of abnormal body cells, e.g. infected cells and cancer cells.

Helper T-cells

These are essential for correct functioning of not only cell-mediated immunity, but also antibody-mediated immunity. Their central role in immunity is emphasised in situations where they are destroyed, as by the human immunodeficiency virus (HIV). When helper T-lymphocyte numbers fall significantly, the whole immune system is compromised. T-helpers are the commonest of the T-lymphocytes; their main functions include:

- production of special chemicals called *cytokines*, e.g. interleukins and interferons, which support and promote cytotoxic T-lymphocytes and macrophages
- cooperating with B-lymphocytes to produce antibodies; although B-lymphocytes are responsible for antibody manufacture, they require to be stimulated by a helper T-lymphocyte first.

Antibody-mediated (humoral) immunity

B-lymphocytes, unlike T-lymphocytes, which are free to circulate around the body, are fixed in lymphoid tissue (e.g. the spleen and lymph nodes). B-lymphocytes, unlike T-lymphocytes, recognise and bind antigen particles without having to be presented with them by an antigen-presenting cell. Once its antigen has been detected and bound, and with the help of a helper T-lymphocyte, the

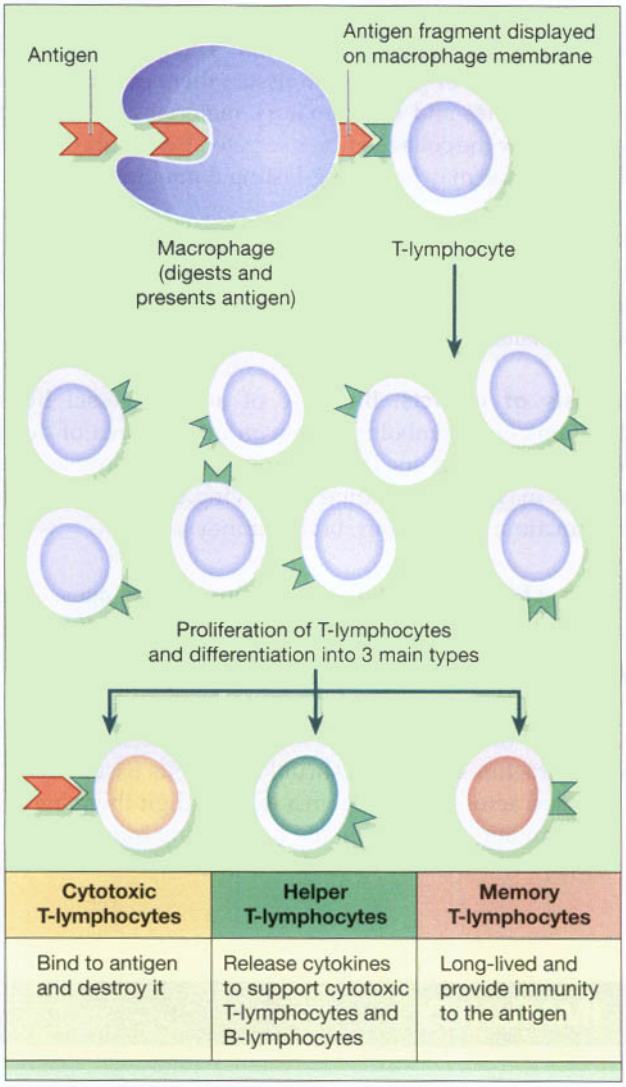


Figure 15.4 Clonal expansion of T-lymphocytes.

B-lymphocyte enlarges and begins to divide (clonal expansion, Fig. 15.5). It produces two functionally distinct types of cell, plasma cells and memory B-cells.

Plasma cells

These secrete antibodies into the blood. Antibodies are carried throughout the tissues, while the B-lymphocytes themselves remain fixed in lymphoid tissue. Plasma cells live no longer than a day, and produce only one type of antibody, which targets the specific antigen that originally bound to the B-lymphocyte. Antibodies:

- bind to antigens, labelling them as targets for other defence cells such as cytotoxic T-lymphocytes and macrophages
- bind to bacterial toxins, neutralising them
- activate complement (p. 375).

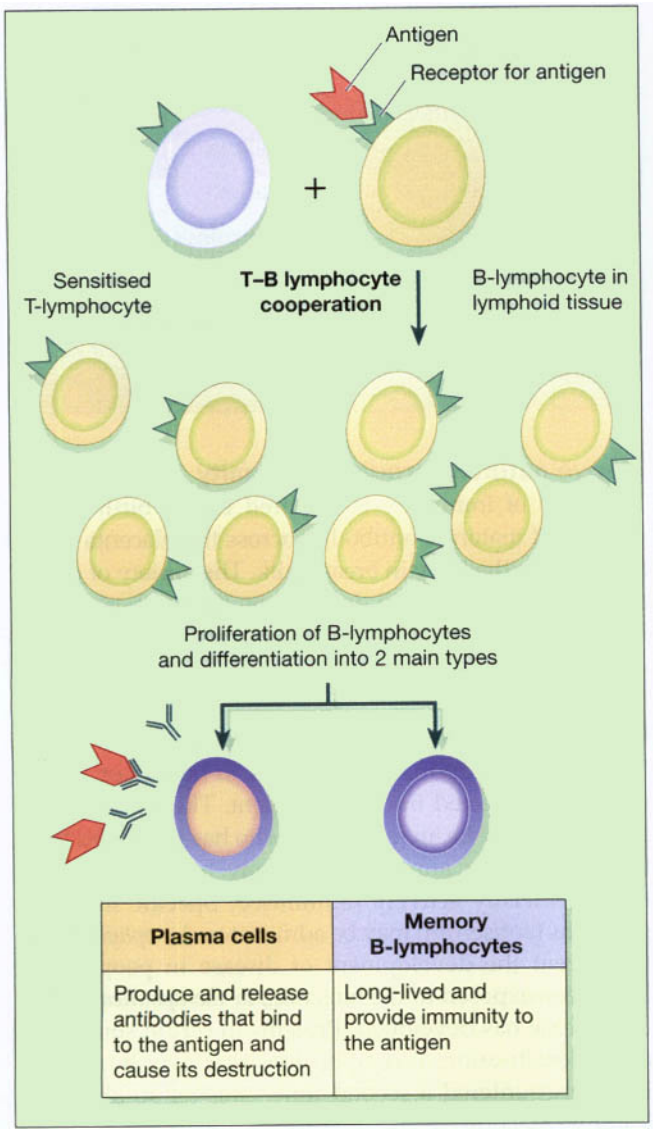


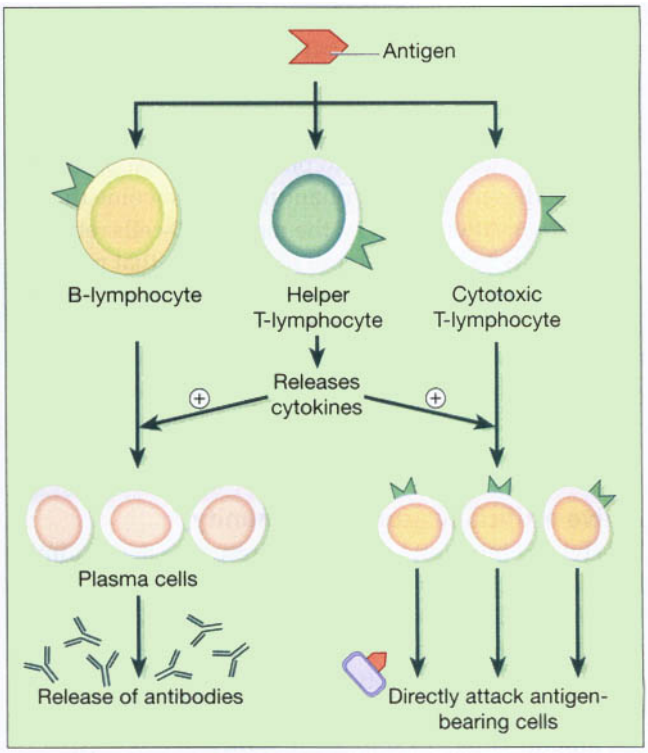
Figure 15.5 Clonal expansion of B-lymphocytes.

Memory B-cells

These cells remain in the body long after the initial episode has been dealt with, and rapidly respond to another encounter with the same antigen by stimulating the production of antibody-secreting plasma cells.

The interdependence of the two parts of the immune system is summarised in Figure 15.6.

The fact that the body does not normally develop immunity to its own cells is due to the fine balance that exists between the immune reaction and its suppression. *Autoimmune diseases* are due to the disturbance of this balance.



Acquired immunity

When antigens, e.g. microbes, are encountered for the first time there is a *primary response* in which a low level of antibodies can be detected in the blood after about 2 weeks. Although the response may be sufficient to combat the antigen, the antibody levels then fall unless there is another encounter with the same antigen within a short period of time (2 to 4 weeks). The second encounter produces a *secondary response* in which there is a rapid response by memory B-cells resulting in a marked increase in antibody production (Fig. 15.7). Further increases can be achieved by later encounters but eventually a maximum is reached. This principle is used in active immunisation against infectious diseases.

Immunity may be acquired *naturally* or *artificially* and both forms may be *active* or *passive* (Fig. 15.8). Active immunity means that the individual has responded to an antigen and produced his own antibodies, lymphocytes are activated and the memory cells formed provide long-lasting resistance. In passive immunity the individual is given antibodies produced by someone else. The antibodies are then destroyed and unless lymphocytes are stimulated, passive immunity is short lasting.

Active naturally acquired immunity

The body may be stimulated to produce its own antibodies by:

- *Having the disease.* During the course of the illness, B-lymphocytes develop into plasma cells that produce antibodies in sufficient quantities to overcome the infection. After recovery, the memory B-cells retain the ability to produce more plasma cells that produce the specific antibodies, conferring immunity to future infection by the same microbe or strain of microbe.
- *Having a subclinical (subliminal) infection.* In this case the microbial infection is not sufficiently severe to cause clinical disease but stimulates sufficient memory B-cells to establish immunity.

Active artificially acquired immunity

This type of immunity develops in response to the administration of dead or live artificially weakened microbes (*vaccines*) or deactivated toxins (*toxoids*). The vaccines and toxoids retain the antigenic properties that stimulate the development of immunity but they cannot cause the disease. Many microbial diseases can be prevented by artificial immunisation. Examples are shown in Box 15.1.

Active immunisation against some infectious disorders confers lifelong immunity, e.g. diphtheria, whooping cough or mumps. In other infections the immunity may last for a number of years or for only a few weeks before revaccination is necessary. Apparent loss of immunity may be due to infection with a different strain of the same microbe, which has different antigenic properties but causes the same clinical illness, e.g. viruses that cause the common cold and influenza. In the elderly and when nutrition is poor the production of lymphocytes, especially B-lymphocytes, is reduced and the primary and secondary response may be inadequate.

Box 15.1. Diseases preventable by vaccination

- Anthrax
- Cholera
- Diphtheria
- Hepatitis B
- Measles
- Mumps
- Poliomyelitis
- Rubella
- Smallpox
- Tetanus
- Tuberculosis
- Typhoid
- Whooping cough

Passive naturally acquired immunity

This type of immunity is acquired before birth by the passage of maternal antibodies across the placenta to the fetus and to the baby in breast milk. The variety of different antibodies provided depends on the mother's active immunity. The baby's lymphocytes are not stimulated and the immunity is short lived.

Passive artificially acquired immunity

In this type, ready-made antibodies, in human or animal serum, are injected into the recipient. The source of the antibodies may be an individual who has recovered from the infection, or animals, commonly horses, that have been artificially actively immunised. Specific immunoglobulins (antiserum) may be administered *prophylactically* to prevent the development of disease in people who have been exposed to the infection, or *therapeutically* after the disease has developed. Proteins in serum sometimes cause sensitisation of lymphocytes that may be damaging if encountered a second time, causing an abnormal immune reaction.

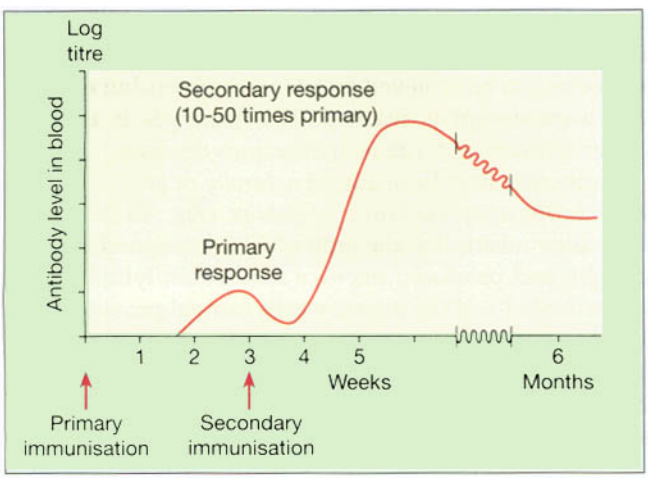


Figure 15.7 The antibody responses to immunisation.

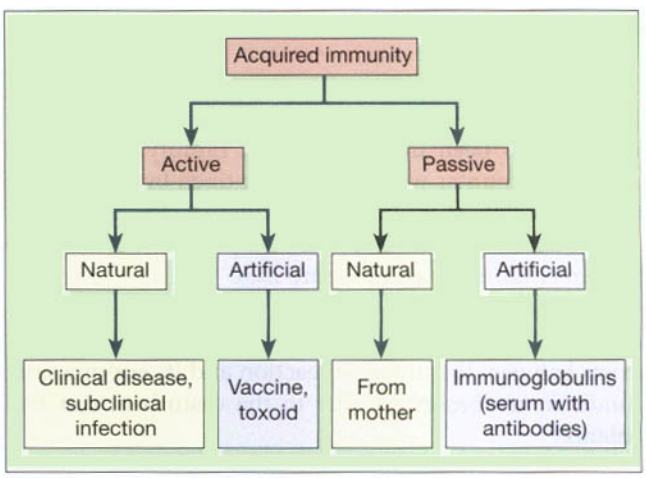


Figure 15.8 Summary of the types of acquired immunity.

HYPERSENSITIVITY (ALLERGY)

Learning outcome

After studying this section, you should be able to:

- describe, with examples, the four types of allergic response.

Allergy is powerful immune response to an antigen (allergen). The allergen itself is usually harmless (e.g. house dust, animal dander, grass pollen). It is therefore usually the immune response that causes the damage to the body, not the allergen itself. Upon initial exposure to the allergen the individual becomes sensitised to it, and on second and subsequent exposures the immune system mounts a response entirely out of proportion to the perceived threat. It should be noted that these responses are exaggerated versions of normal immune function. Sometimes symptoms are mild, if annoying, e.g. the running nose and streaming eyes of hay fever. Occasionally the reaction can be extreme, overwhelming body systems and causing death (e.g. anaphylactic shock, p. 111).

There are four mechanisms of hypersensitivity, which are classified according to what parts of the immune system are involved. They are summarised in Figure 15.9.

Type I, anaphylactic hypersensitivity

This occurs in individuals who have inherited very high levels of a type of antibody called immunoglobulin E (IgE). When exposed to an allergen, e.g. house dust, these high levels of antibody activate mast cells and basophils (p. 66), which release their granular contents. The most important substance released is histamine, which constricts some smooth muscle (e.g. airway smooth muscle), causes vasodilatation and increases vascular permeability (leading to exudation of fluid and proteins into the tissues). Examples of type I reactions include the serious situation of anaphylaxis. There is profound bronchoconstriction and shock due to extensive vasodilatation. The condition can lead to death.

Type II, cytotoxic hypersensitivity

When an antibody reacts with an antigen on a cell surface, that cell is marked for destruction by a number of mechanisms, e.g. phagocytosis, or destruction by lytic enzymes. This is the usual procedure in the elimination of, for example, bacteria, but if the antibodies are directed against self-antigens the result is destruction of the body's own tissues (autoimmune disease). Type II mechanisms cause other conditions, e.g. haemolytic disease of the newborn (p. 71) and transfusion reactions (p. 72).

Type III, immune-complex-mediated hypersensitivity

Antibody–antigen complexes (immune complexes) are usually cleared efficiently from the blood by phagocytosis. If they are not, for example when there is phagocyte failure or an excessive production of immune complexes (e.g. in chronic infections), they can be deposited in tissues, e.g. kidneys, skin, joints and the eye, where they set up an inflammatory reaction. The kidney is a common site of deposition since it receives a large proportion of the cardiac output and filters the blood. Immune complexes collecting here lodge in and block the glomeruli (p. 351), impairing kidney function (glomerulonephritis). Sensitivity to penicillin is also a type III reaction; antibodies bind to penicillin (the antigen), and the symptoms are the result of deposition of immune complexes in tissues – rashes, joint pains and sometimes haematuria.

Type IV, delayed type hypersensitivity

Unlike types I–III, type IV hypersensitivity does not involve antibodies, but is an overreaction of T-lymphocytes to an antigen. When an antigen is detected by memory T-lymphocytes, it provokes clonal expansion of the T-lymphocyte (Fig. 15.4), and large numbers of cytotoxic T-lymphocytes are released to eliminate the antigen. Usually this system is controlled and the T-lymphocyte response is appropriate. If not, the actively aggressive cytotoxic T-lymphocytes damage normal tissues.

An example of this is contact dermatitis (p. 369). Graft rejection is also caused by T-lymphocytes; an incompatible skin graft, for instance, will become necrotic and slough off in the days following application of the graft.

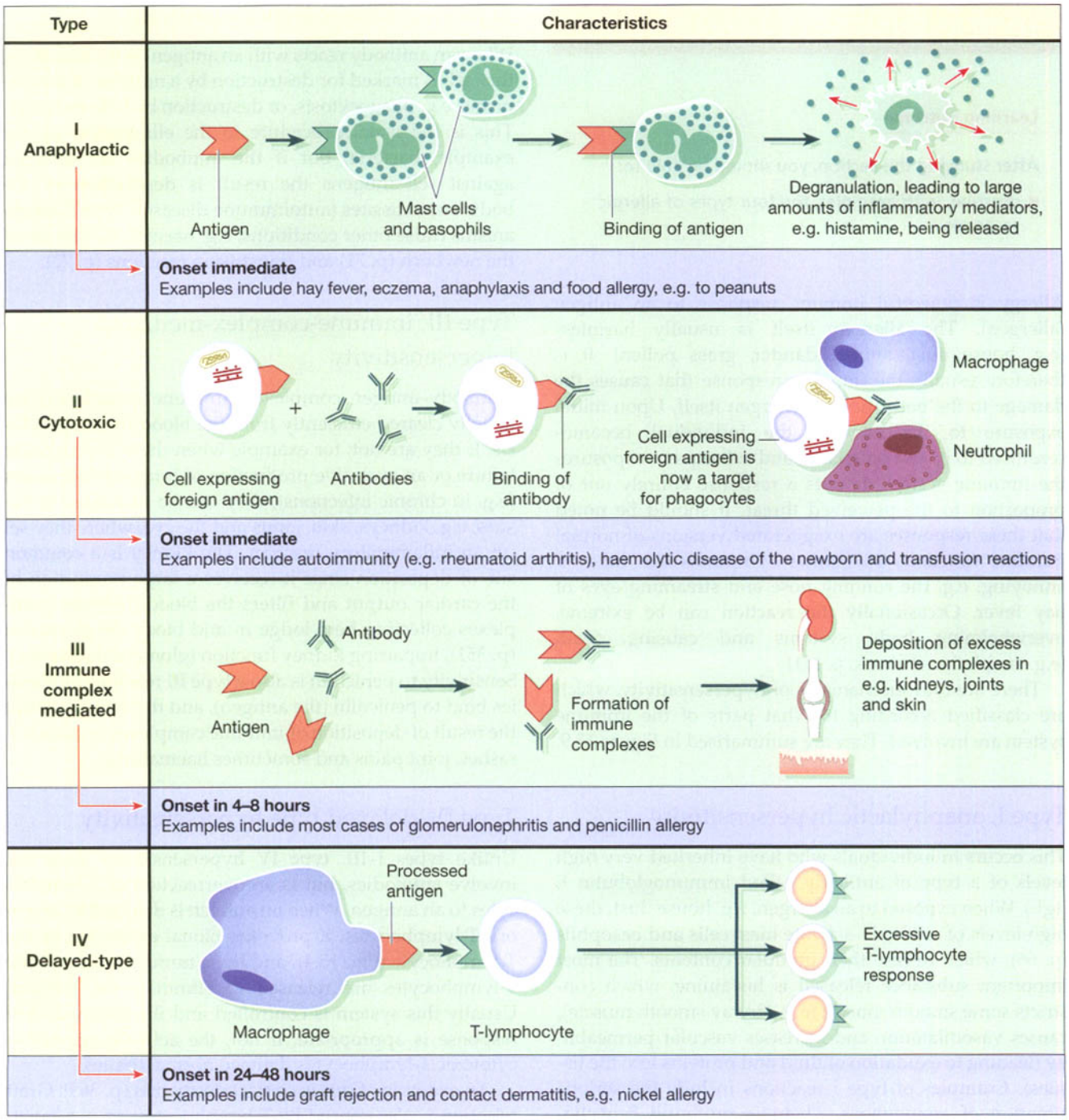


Figure 15.9 The four types of hypersensitivity.

AUTOIMMUNE DISEASES

Learning outcomes

After studying this section, you should be able to:

- describe the basis of autoimmune disease
- discuss the specific examples of autoimmune disease.

Normally, an immune response is mounted only against foreign (non-self) antigens, but occasionally the body fails to recognise its own tissues and attacks itself. The resulting autoimmune disorders, examples of type II hypersensitivity, include a number of relatively common conditions.

Rheumatoid arthritis (p. 425)
The body produces antibodies to the membrane lining the joints, the synovial membrane. In most sufferers, the antibody can be detected in the blood; it is called *rheumatoid factor*. The antibodies bind to the synovial membrane, leading to chronically inflamed joints that are stiff, painful and swollen.

Hashimoto's disease (p. 230)
The body makes antibodies to thyroglobulin, leading to destruction of thyroid hormone, and hyposecretion of the thyroid.

Graves' disease
The body makes antibodies to the thyroid cells. Unlike Hashimoto's disease, however, the effect of the antibodies is to stimulate the gland, with a resultant hyperthyroidism (p.229).

Autoimmune haemolytic anaemia (p. 72)
In this, individuals make antibodies to their own red blood cells, leading to haemolytic anaemia.

Myasthenia gravis
This autoimmune condition of unknown origin affects more women than men, and usually those between 20 and 40 years. Antibodies are produced that bind to and block the acetylcholine receptors of neuromuscular junctions. The transmission of nerve impulses to muscle fibres is therefore blocked. This causes progressive and extensive muscle weakness, although the muscles are normal. Extraocular and eyelid muscles are affected first, causing *ptosis* (drooping of the eyelid) or *diplopia* (double vision), followed by those of the neck (possibly affecting chewing, swallowing and speech) and limbs. There are periods of remission, relapses being precipitated by, for example, strenuous exercise, infections or pregnancy.

IMMUNODEFICIENCY

Learning outcome

After studying this section, you should be able to:

- discuss the causes and effects of acquired immune deficiency syndrome (AIDS).

When the immune system is compromised, there is a tendency to recurrent infections, often by microbes not normally pathogenic in humans (*opportunistic infections*). Immunodeficiency is classified as primary (usually occurring in infancy and genetically mediated) or secondary, that is, acquired in later life as the result of another disease, e.g. protein deficiency, acute infection, chronic renal failure, bone marrow diseases, following splenectomy or acquired immune deficiency syndrome (AIDS).

Acquired immune deficiency syndrome (AIDS)

This condition is caused by the human immunodeficiency virus (HIV), an RNA retrovirus which produces the enzyme *reverse transcriptase* inside the cells of the infected person (host cells). This enzyme transforms viral RNA to DNA and this new DNA, called the provirus, is incorporated into the host cell DNA. The host cell then produces new copies of the virus that pass out into tissue fluid and blood and infect other host cells. When infected host cells divide, copies of the provirus are integrated into the DNA of daughter cells, spreading the disease within the body.

HIV has an affinity for cells that have a protein receptor called CD_4 in their membrane, including T-lymphocytes, monocytes, macrophages, some B-lymphocytes and, possibly, cells in the gastrointestinal tract and neuroglial cells in the brain. Helper T-cells (Fig. 15.4) are the main cells involved. When infected their number is reduced, causing suppression of both antibody-mediated and cell-mediated immunity with the consequent development of widespread opportunistic infections, often by microbes of relatively low pathogenicity.

HIV has been isolated from semen, cervical secretions, lymphocytes, plasma, cerebrospinal fluid, tears, saliva, urine and breast milk. The secretions known to be especially infectious are semen, cervical secretions, blood and blood products.

Infection is spread by:

- sexual intercourse, vaginal and anal
- contaminated needles used:
  - during treatment of patients
  - when drug abusers share needles.
- an infected mother to her child:
  - across the placenta before birth
  - while the baby is passing through the birth canal
  - possibly by breast milk.

The presence of antibodies to HIV indicates that the individual has been exposed to the virus but *not* that a naturally acquired immunity has developed. Not all those who have antibodies in their blood develop AIDS although they may act as carriers and spread the infection to others.

A few weeks after infection there may be an acute influenza-like illness with no special features, followed by a period of two or more years without symptoms.

Chronic HIV infection may cause persistent generalised lymphadenopathy (PGL). Some patients may then develop AIDS-related complex (ARC) and experience chronic low-grade fever, diarrhoea, weight loss, anaemia and leukopenia.

When AIDS develops the main complications are widespread recurrent opportunistic infections and tumours. Outstanding features include the following.

- Pneumonia may be present, commonly caused by *Pneumocystis carinii*, but many other microbes may be involved.
- There may be persistent nausea, diarrhoea and loss of weight due to recurrent infections of the alimentary tract by a wide variety of microbes.
- Meningitis, encephalitis and brain abscesses may be recurrent, either caused by opportunistic microbes or possibly by HIV.
- There may be deterioration in neurological function characterised by forgetfulness, loss of concentration, confusion, apathy, dementia, limb weakness, ataxia and incontinence.
- Skin eruptions, often widespread, may be seen, e.g. eczema, psoriasis, cellulitis, impetigo, warts, shingles and 'cold sores'.
- Generalised lymphadenopathy may occur, i.e. non-infective enlargement of lymph nodes.
- There may be malignant tumours:
  - lymphomas, i.e. tumours of lymph nodes
  - Kaposi's sarcoma, consisting of tumours under the skin and in internal organs (p. 371).