**Digestive System**

The digestive system describes the alimentary canal, its accessory organs and a variety of digestive processes that prepare food eaten in the diet for absorption. The alimentary canal begins at the mouth, passes through the thorax, abdomen and pelvis and ends at the anus. It has a basic structure which is modified at different levels to provide for the processes occurring at each level. The digestive processes gradually break down the foods eaten until they are in a form suitable for absorption.

For example, meat, even when cooked, is chemically too complex to be absorbed from the alimentary canal. Digestion releases its constituents: amino acids, mineral salts, fat and vitamins. Digestive enzymes responsible for these changes are secreted into the canal by specialised glands, some of which are in the walls of the canal and some outside the canal, but with ducts leading into it.

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

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

- **Ingestion.** This is the taking of food into the alimentary tract, i.e. eating and drinking.
- **Propulsion.** This mixes and moves the contents along the alimentary tract.
- **Digestion.** This consists of:
  - a. mechanical breakdown of food by, e.g. mastication (chewing)
  - b. chemical digestion of food into small molecules by enzymes present in secretions produced by glands and accessory organs of the digestive system.
- **Absorption.** This is the process by which digested food substances pass through the walls of some organs of the alimentary canal into the blood and lymph capillaries for circulation and use by body cells.
- **Elimination.** Food substances that have been eaten but cannot be digested and absorbed are excreted from the alimentary canal as faeces by the process of defaecation.

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

Alimentary canal

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

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

Accessory organs

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

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

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

Basic structure of the alimentary canal

The layers of the walls of the alimentary canal follow a consistent pattern from the oesophagus onwards.

In the organs from the oesophagus onwards, modifications of structure are found which are associated with specific functions.

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

- adventitia or serosa – outer covering
- muscle layer
Adventitia or serosa
This is the outermost layer. In the thorax it consists of loose fibrous tissue and in the abdomen the organs are covered by a serous membrane (serosa) called peritoneum.

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

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

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

Mucosa
This consists of three layers of tissue:

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

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

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

The oral cavity is lined throughout with mucous membrane, consisting of stratified squamous epithelium containing small mucus-secreting glands. The part of the mouth between the gums and the cheeks is the vestibule and the remainder of its interior is the oral cavity. The mucous membrane lining of the cheeks and the lips is reflected onto the gums or alveolar ridges and is continuous with the skin of the face.

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

The uvula is a curved fold of muscle covered with mucous membrane, hanging down from the middle of the free border of the soft palate. Originating from the upper end of the uvula are four folds of mucous membrane, two passing downwards at each side to form membranous arches. The posterior folds, one on each side, are the palatopharyngeal arches and the two anterior folds are the palatoglossal arches. On each side, between the arches, is a collection of lymphoid tissue called the palatine tonsil.

**Tongue**

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

Functions of the tongue

The tongue plays an important part in:

- chewing (mastication)
- swallowing (deglutition)
Digestive system

➢ speech
➢ taste

Teeth
The teeth are embedded in the alveoli or sockets of the alveolar ridges of the mandible and the maxilla. Babies are born with two sets, or dentitions, the temporary or deciduous teeth and the permanent teeth. 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 at about 6 months of age, and should all be present by 24 months.
The permanent teeth begin to replace the deciduous teeth in the 6th year of age and this dentition, consisting of 32 teeth, is usually complete by the 21st year.
Functions of the teeth
Teeth have different shapes depending on their functions. Incisors and canine teeth are the cutting teeth and are used for biting off pieces of food, whereas the premolar and molar teeth, with broad, flat surfaces, are used for grinding or chewing food.

Salivary glands
Salivary glands release their secretions into ducts that lead to the mouth. There are three main pairs: the parotid glands, the submandibular glands and the sublingual glands.
There are also numerous smaller salivary glands scattered around the mouth.
Parotid glands
These are situated one on each side of the face just below the external acoustic meatus. 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.

Composition of saliva

Delivered by: Mr. Yogesh Sharma, Asso. Professor, JCP, Jaipur
Saliva is the combined secretions from the salivary glands and the small mucus-secreting glands of the oral mucosa. About 1.5 litres of saliva is produced daily and it consists of:

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

Functions of saliva

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

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

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

Non-specific defence
Lysozyme and immunoglobulins present in saliva combat invading microbes.

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

Pharynx
The pharynx is divided for descriptive purpose into three parts, the nasopharynx, oropharynx and laryngopharynx. The nasopharynx is important in respiration.
The oropharynx and laryngopharynx are passages common to both the respiratory and the digestive systems. Food passes from the oral cavity into the pharynx then to the oesophagus below, with which it is continuous. The walls of the pharynx consist of three layers of tissue. The lining membrane (mucosa) is stratified squamous epithelium, continuous with the lining of the mouth at one end and the oesophagus at the other. Stratified epithelial tissue provides a lining well suited to the wear and tear of swallowing ingested food. The middle layer consists of connective tissue, which becomes thinner towards the lower end and contains blood and lymph vessels and nerves. The outer layer consists of a number of involuntary muscles that are involved in swallowing. When food reaches the pharynx, swallowing is no longer under voluntary control.

**Oesophagus**

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

**Functions of the mouth, pharynx and oesophagus**

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

**Swallowing (deglutition)**

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

**Peristalsis**

Peristaltic waves pass along the oesophagus only after swallowing begins. 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.

**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**

Anteriorly  
left lobe of liver and anterior abdominal wall

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

Superiorly  
diaphragm, oesophagus and left lobe of liver

Inferiorly  
transverse colon and small intestine

To the left  
diaphragm and spleen

To the right  
liver and duodenum.

**Structure of the stomach**

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

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

Longitudinal section of the stomach

**Gastric juice and functions of the stomach**

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

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

**Gastric juice**

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

- water
- mineral salts
- mucus secreted by mucous neck cells in the glands and surface mucous cells on the stomach surface
- hydrochloric acid and
- intrinsic factor secreted by parietal cells in 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 the action of pepsins.
- Pepsinogens are activated to pepsins by hydrochloric acid and by pepsins already present in the stomach. These enzymes begin the digestion of proteins, breaking them into smaller molecules. Pepsins have evolved to act most effectively at a very low pH, between 1.5 and 3.5.
- Intrinsic factor (a protein) is necessary for the absorption of vitamin B12 from the ileum. (Deficiency leads to pernicious anemia.)
- Mucus prevents mechanical injury to the stomach wall by lubricating the contents. It also prevents chemical injury by acting as a barrier between the stomach wall and the corrosive gastric juice – hydrochloric acid is present in potentially damaging concentrations and pepsins would digest the gastric tissues.

**Secretion of gastric juice**

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

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

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

3. **Intestinal phase.** When the partially digested contents of the stomach reach the small intestine, two hormones, secretin and cholecystokinin, are produced by endocrine cells in the intestinal mucosa. They slow down the secretion of gastric juice and reduce gastric motility. By slowing the emptying rate of the stomach, the chyme in the duodenum becomes more thoroughly mixed with bile and pancreatic juice. This phase of gastric secretion is most marked following a meal with a high fat content. The rate at which the stomach empties depends largely on the type of food eaten. A carbohydrate meal leaves the stomach in 2–3 hours, a protein meal remains longer and a fatty meal remains in the stomach longest.

**Functions of the stomach**

These include:
- temporary storage allowing time for the digestive enzymes, pepsins, to act
- chemical digestion – pepsins break proteins into polypeptides
- mechanical breakdown – the three smooth muscle layers enable the stomach to act as a churn, gastric juice is added and the contents are liquefied to chyme. Gastric motility and secretion are increased by parasympathetic nerve stimulation
- limited absorption – water, alcohol and some lipidsoluble drugs
- non-specific defence against microbes – provided by hydrochloric acid in gastric juice. Vomiting may occur in response to ingestion of gastric irritants, e.g. microbes or chemicals
- preparation of iron for absorption – the acid environment of the stomach solubilises iron salts, essential for iron absorption in the small intestine
- production and secretion of intrinsic factor needed for absorption of vitamin B12 in the terminal ileum
- regulation of the passage of gastric contents into the duodenum. When the chyme is sufficiently acidified and liquefied, the pylorus forces small jets of gastric contents through the pyloric sphincter into the duodenum. The sphincter is normally closed, preventing backflow of chyme into the stomach
- secretion of the hormone gastrin
Small intestine

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

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

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

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

Intestinal juice

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

Functions of the small intestine

The functions are:

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

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

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

Pancreatic juice

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

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

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

Functions

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

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

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

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

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

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

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

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

Intestinal secretions

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The principal constituents of intestinal secretions are water, mucus and mineral salts. Most of the digestive enzymes in the small intestine are contained in the enterocytes of the epithelium that covers the villi. Digestion of carbohydrate, protein and fat is completed by direct contact between these nutrients and the microvilli and within the enterocytes.

**Chemical digestion associated with enterocytes**

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

- peptidases
- lipase
- sucrase, maltase and lactase.

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

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

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

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

**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**

Absorption of nutrients from the small intestine through the enterocytes occurs by several processes, including diffusion, osmosis, facilitated diffusion and active transport.

Water moves by osmosis; small fat-soluble substances, e.g. fatty acids and glycerol, are able to diffuse through cell membranes; while others are generally transported inside the villi by other mechanisms.

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

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

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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 B12 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 surface. Large amounts of fluid enter the alimentary tract each day. Of this, only about 1500 mL is not absorbed by the small intestine, and passes into the large intestine.

**Large intestine, rectum and anal canal**

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

**The caecum**

This is the first part of the large intestine. 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 ileocecal valve opens from the ileum. The vermiform appendix is a fine tube, closed at one end, which leads from the caecum. It is about 8–9 cm long and has the same structure as the walls of the large intestine but contains more lymphoid tissue.

The appendix has no digestive function but can cause significant problems when it becomes inflamed (appendicitis).

**The colon**

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

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

**The transverse colon:** This part extends across the abdominal cavity in front of the duodenum and the stomach to the area of the spleen where it forms the splenic flexure and curves acutely downwards to become the descending colon.
The descending colon: This passes down the left side of the abdominal cavity then curves towards the midline. At the level of the iliac crest it is known as the sigmoid colon.

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

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

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

Functions of the large intestine, rectum and anal canal

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

Microbial activity
The large intestine is heavily colonised by certain types of bacteria, which synthesise vitamin K and folic acid. They include Escherichia coli, Enterobacter aerogenes, Streptococcus faecalis and Clostridium perfringens. These microbes are commensals, i.e. normally harmless, in humans. However, they may become pathogenic if transferred to another part of the body, e.g. E. coli may cause cystitis if it gains access to the urinary bladder. Gases in the bowel consist of some of the constituents of air, mainly nitrogen, swallowed with food and drink. Hydrogen, carbon dioxide and methane are produced by bacterial fermentation of unabsorbed nutrients, especially carbohydrate. Gases pass out of the bowel as flatus (wind).

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

**Defaecation**

Usually the rectum is empty, but when a mass movement forces the contents of the sigmoid colon into the rectum the nerve endings in its walls are stimulated by stretch. In infants, defaecation occurs by reflex (involuntary) action. However, during the second or third year of life children develop voluntary control of bowel function.

**Constituents of faeces:** The faeces consist of a semisolid brown mass. The brown colour is due to the presence of stercobilin.

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

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

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

**Pancreas**

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

The pancreas is both an exocrine and endocrine gland.

**The exocrine pancreas**

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

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

**The endocrine pancreas**

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

![Figure 1 The pancreas in relation to the duodenum and biliary tract.](image)

**Liver**

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

**Organ associated with the liver**

Superiorly and anteriorly: diaphragm and anterior abdominal wall

Inferiorly: stomach, bile ducts, duodenum
Posteriorly oesophagus, inferior vena cava, aorta, gall bladder, lower ribs and diaphragm.

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

**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 branches from the abdominal aorta. Nerve fibres, sympathetic and parasympathetic, enter here. The right and left hepatic ducts leave, carrying bile from the liver to the gall bladder. Lymph vessels leave the liver, draining lymph to abdominal and thoracic nodes.

**Structure**

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

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

Fat metabolism
Stored fat can be converted to a form in which it can be used by the tissues to provide energy.

Protein metabolism
Deamination of amino acids: This process:

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

Synthesis of plasma proteins: These are formed from amino acids and include albumins, globulins and blood clotting factors.
Breakdown of erythrocytes and defence against microbes:
This is carried out by phagocytic hepatic macrophages (Kupffer cells) in the sinusoids although breakdown of red blood cells also takes place in the spleen and bone marrow.

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

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

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

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

Storage: Stored substances include:
- glycogen
- fat-soluble vitamins: A, D, E, K
- iron, copper
- some water-soluble vitamins, e.g. vitamin B12.

Composition of bile
Between 500 and 1000 mL of bile is secreted by the liver daily. Bile consists of:
- water
- mineral salts
- mucus
- bile pigments, mainly bilirubin
- bile salts
- cholesterol.

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

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

**Excretion of bilirubin:** Bilirubin is one of the products of haemolysis of erythrocytes by hepatic macrophages (Kupffer cells) in the liver and by other macrophages in the spleen and bone marrow. Bilirubin is insoluble in water and is carried in the blood bound to the plasma protein albumin. In hepatocytes it is conjugated (combined) with glucuronic acid and becomes water-soluble enough to be excreted in bile. Microbes in the large intestine convert bilirubin into stercobilin, which is excreted in the faeces. Stercobilin colours and deodorises the faeces. A small amount is reabsorbed and excreted in urine as urobilinogen.

**Gall bladder**

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

**Structure**

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

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

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

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

**Functions of the gall bladder**

- 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.

**Digestion and absorption of nutrients**

<table>
<thead>
<tr>
<th>Mouth</th>
<th>Stomach</th>
<th>Digestion</th>
<th>Absorption</th>
<th>Large intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>Salivary amylase: digests starches to disaccharides</td>
<td>Hydrochloric acid: denatures and stops action of salivary amylase</td>
<td>Pancreatic amylase: digests starches to disaccharides; Sucrase, maltase, lactase (in enterocytes): disaccharides to monosaccharides (mainly glucose)</td>
<td>Into blood capillaries of villi</td>
</tr>
<tr>
<td>Proteins</td>
<td>Hydrochloric acid: pepsinogen to pepsin; Pepsin: proteins to polypeptides</td>
<td>Enterokinase (in enterocytes): chymotrypsinogen and trypsinogen (from pancreas); to chymotrypsin and trypsin; Chymotrypsin and trypsin; polypeptides to di- and tripeptides; Peptidases (in enterocytes): di- and tripeptides to amino acids</td>
<td>Into blood capillaries of villi</td>
<td>–</td>
</tr>
<tr>
<td>Fats</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Into the lacteals of the villi</td>
</tr>
<tr>
<td>Water</td>
<td>–</td>
<td>Small amount absorbed here</td>
<td>Most absorbed here</td>
<td>Remainder absorbed here</td>
</tr>
<tr>
<td>Vitamins</td>
<td>–</td>
<td>Intrinsic factor secreted for vitamin $B_{12}$ absorption</td>
<td>Water-soluble vitamins absorbed into capillaries; fat-soluble ones into lacteals of villi</td>
<td>Bacteria synthesise vitamin $K$ in colon; absorbed here</td>
</tr>
</tbody>
</table>

**Metabolism**

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

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

Two types of process are involved:

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

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

**Metabolic pathways**

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

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

**Disorders of GIT**

**Thrush (oral candidiasis)**

This acute fungal infection is caused by the yeast Candida albicans, which occurs when the commensal microbe grows in white patches on the tongue and oral mucosa. In adults it causes opportunistic infection mainly in debilitated people and in those whose immunity is lowered by, e.g., steroids, antibiotics or cytotoxic drugs. In children it occurs most commonly in bottle-fed babies. Chronic thrush may develop, affecting the roof of the mouth in people who wear dentures.

**Gingivitis**

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

**Squamous cell carcinoma**

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

**Mumps**

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

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

**Gastro-oesophageal reflux disease (GORD)**

This condition, the commonest cause of indigestion (or ‘heartburn’), is caused by persistent regurgitation of acidic gastric juice into the oesophagus, causing irritation, inflammation and painful ulceration. Haemorrhage occurs when blood vessels are eroded. Persistent reflux leads to chronic inflammation and if damage is extensive, secondary healing with fibrosis occurs. Shrinkage of mature fibrous tissue may cause stricture of the oesophagus.

This condition sometimes gives rise to Barrett’s oesophagus (see below). Reflux of gastric contents is associated with:

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

**Achalasia**

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

**Peptic ulcer disease**

Ulceration involves the full thickness of the gastrointestinal mucosa and penetrates the muscle layer. It is caused by disruption of the normal balance between the corrosive effect of gastric juice and the protective effect of mucus on the gastric epithelial cells. It may be viewed as an extension of the gastric erosions found in acute gastritis. The most common sites for ulcers are the stomach and the first few centimetres of the duodenum.

The underlying causes are not known but there is a strong association with H. pylori infection. It is believed that H. pylori, some drugs, e.g. non-steroidal anti-inflammatory drugs (NSAIDs),
and smoking may impair the gastric mucosal defences in some people. However, H. Pylori is present in many people who show no signs of peptic ulcer disease. If gastric mucosal protection is impaired, the epithelium can be exposed to gastric acid causing the initial cell damage that leads to ulceration. The main protective mechanisms are: a good blood supply, adequate mucus secretion and efficient epithelial cell replacement.

**Gastritis**

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

**Acute gastritis**

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

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

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

**Chronic gastritis**

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

**Cholera**

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

**Dysentery**

**Bacillary dysentery**: This infection of the large intestine is caused by bacteria of the Shigella group. The severity of the condition depends on the organisms involved. Shigella dysenteriae causes the most severe type of infection and it occurs mainly in developing countries. Children and older debilitated adults are particularly susceptible. The only host is humans and the organisms are spread by faecal contamination of food, drink, hands and fomites. The intestinal mucosa becomes inflamed, ulcerated and oedematous with excess mucus secretion. In severe infections, the acute diarrhoea, that contains blood and excessive mucus, causes dehydration, electrolyte imbalance and anaemia. When healing occurs the mucous membrane is fully restored.

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

**Inflammatory bowel disease (IBD)**

This term includes Crohn’s disease and ulcerative colitis. Their aetiology is unknown but is thought to involve environmental and immune factors in genetically susceptible individuals. Both conditions typically have a pattern of relapse and remission.

**Crohn’s disease**

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

Complications include:

- secondary infections, occurring when inflamed areas ulcerate
- fibrous adhesions and subsequent intestinal obstruction caused by the healing process
- fistulae between intestinal lesions and adjacent structures, e.g. loops of bowel, surface of the skin

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➢ perianal fistulae, fissures and skin tags
➢ 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. From there it may spread proximally to involve a variable proportion of the colon and, sometimes, the entire colon. The main symptom is bloody diarrhoea. There are periods of remission lasting weeks, months or years. Individuals may develop other systemic problems affecting, for example, the joints (ankylosing spondylitis), skin and liver. In long-standing cases, cancer sometimes develops.

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

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

Outcomes include:
➢ spontaneous reduction, i.e. the loop of bowel slips back to its correct place when the intra-abdominal pressure returns to normal
➢ manual reduction, i.e. by applying gentle pressure over the abdominal swelling
➢ strangulation, when reduction is not possible and the venous drainage from the herniated loop of bowel is impaired, causing congestion, ischaemia and gangrene.

In addition there is intestinal obstruction.

**Hepatitis A**
Previously known as ‘infectious hepatitis’, this type often occurs as epidemics in all parts of the world. It affects mainly children, causing a mild illness although it is often asymptomatic.

Infection is spread by the faecal–oral route, e.g. via contaminated hands, food, water and fomites. Viruses are excreted in the faeces for 7–14 days before clinical symptoms appear and for about 7 days after. Symptoms may include general malaise followed by a period of jaundice that is accompanied by passing of dark urine and pale faeces.

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Antibodies develop and confer lifelong immunity after recovery. Subclinical disease may occur but not carriers.

**Hepatitis B**

Previously known as ‘serum hepatitis’, infection occurs at any age, but mostly in adults. The incubation period is from 50 to 180 days. The virus enters the blood and is spread by contaminated blood and blood products.

People at greatest risk of infection are those who come in contact with blood and blood products in the course of their work, e.g. health-care workers. The virus is also spread by body fluids, i.e. saliva, semen, vaginal secretions, and from mother to fetus (vertical transmission).

Others at risk include intravenous drug users and men who have sex with men. Antibodies are formed and immunity persists after recovery. Infection usually leads to severe illness lasting from 2 to 6 weeks, often followed by a protracted convalescence. Carriers may, or may not, have had clinical disease. Hepatitis B virus may cause massive liver necrosis and death. In less severe cases recovery may be complete. In others chronic hepatitis (see opposite) may develop; live viruses continue to circulate in the blood and other body fluids. The condition also predisposes to cirrhosis and liver cancer.

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

**Hepatitis C**

This virus is spread by blood and blood products, which accounts for the infection of many people with haemophilia. The infection is very frequently asymptomatic although a carrier state occurs. Infection is usually diagnosed later in life when cirrhosis or chronic liver failure becomes evident.

**Cirrhosis of the liver**

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

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

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

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

**Jaundice**

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

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

Metabolic pathways
Anabolism and catabolism usually involve a series of chemical reactions, known as metabolic pathways. These consist of ‘small steps’ that permit controlled efficient and gradual transfer of energy from ATP rather than large intracellular ‘explosions’. Metabolic pathways are switched on and off by hormones, providing control of metabolism and meeting individual requirements. Both catabolic and anabolic processes occur continually in all cells. Very active tissues, such as muscle or liver, need a large energy supply to support their requirements.

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

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

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

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

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

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

Basal Metabolic Rate (BMR)
The metabolic rate is the rate at which energy is released from the fuel molecules inside cells. As most of the processes involved require oxygen and produce carbon dioxide as waste, the metabolic rate can be estimated by measuring oxygen uptake or carbon dioxide excretion.
The basal metabolic rate (BMR) is the rate of metabolism when the individual is at rest in a warm environment and is in the postabsorptive state, i.e. has not had a meal for at least 12 hours. In this state the release of energy is sufficient to meet only the essential needs of vital organs, such as the heart, lungs, nervous system and kidneys. The postabsorptive state is important because the intake of food, especially protein, increases metabolic rate.

**Basal metabolic rate (BMR)** is the rate of energy expenditure per unit time by endothermic animals at rest. It is reported in energy units per unit time ranging from watt (joule/second) to ml O₂/min or joule per hour per kg body mass J/(h·kg). Proper measurement requires a strict set of criteria be met. These criteria include being in a physically and psychologically undisturbed state, in a thermally neutral environment, while in the post-absorptive state (i.e., not actively digesting food).

Metabolism comprises the processes that the body needs to function. Basal metabolic rate is the amount of energy per unit of time that a person needs to keep the body functioning at rest. Some of those processes are breathing, blood circulation, controlling body temperature, cell growth, brain and nerve function, and contraction of muscles. Basal metabolic rate (BMR) affects the rate that a person burns calories and ultimately whether that individual maintains, gains, or loses weight. The basal metabolic rate accounts for about 60 to 75% of the daily calorie expenditure by individuals.

**Central metabolic pathways**

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

The preferred fuel molecule is glucose, but alternatives should glucose be unavailable include amino acids, fatty acids, glycerol and occasionally nucleic acids. Each of these may enter the central energy-producing pathways and be converted to energy, carbon dioxide and water. There are three central metabolic pathways:
• glycolysis
• the citric acid (Krebs) cycle
• oxidative phosphorylation.

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

**Carbohydrate and energy release**

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

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

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

**Oxidation of glucose**

**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.

**Protein metabolism**

Dietary protein consists of a number of amino acids. About 20 amino acids have been named and nine of these are described as essential because they cannot be synthesized in the body. The others are non-essential amino acids because they can be synthesised by many tissues. The enzymes involved in this process are called transaminases.

Digestion breaks down dietary protein into its constituent amino acids in preparation for absorption into the blood capillaries of the villi in the small intestine. Amino acids are transported in the portal circulation to the liver and then into the general circulation, thus making

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them available to all body cells and tissues. Different cells choose from those available the particular amino acids required for building or repairing their specific type of tissue and for synthesising their secretions, e.g. antibodies, enzymes or hormones. Amino acids not required for building and repairing body tissues cannot be stored and are broken down in the liver.

**Amino acids and energy release**

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

**Fat metabolism**

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

**Fatty acids and energy release**

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

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

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

**Glycerol and energy release**

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.

*Summary of the fates of the three main energy sources in the central metabolic pathways.*
Creatine Phosphate (CP)

Phosphocreatine, also known as creatine phosphate (CP) or PCr, is a phosphorylated creatine molecule that serves as a rapidly mobilizable reserve of high-energy phosphates in skeletal muscle, myocard, and the brain to recycle adenosine triphosphate, the energy currency of the cell.

In the kidneys, the enzyme AGAT catalyzes the conversion of two amino acids — arginine and glycine — into guanidinoacetate (also called glycocyamine or GAA), which is then transported in the blood to the liver. A methyl group is added to GAA from the amino acid methionine by the enzyme GAMT, forming non-phosphorylated creatine. This is then released into the blood by the liver where it travels mainly to the muscle cells (95% of the body's creatine is in muscles), and to a lesser extent the brain, heart, and pancreas. Once inside the cells it is transformed into phosphocreatine by the enzyme complex creatine kinase, which makes it able to donate its phosphate group to convert adenosine diphosphate (ADP) into adenosine triphosphate (ATP). This process is an important component of all vertebrates' bioenergetic systems. For instance, while the human body only produces 250g of ATP daily, it recycles its entire body weight in ATP each day through creatine phosphate.

Creatine phosphate can be broken down into creatinine, which is then excreted in the urine. A 70-kg man contains around 120g of creatine, with 40% being the unphosphorylated form and 60% as creatine phosphate. Of that amount, 1–2% is broken down and excreted each day as creatinine.

Function

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