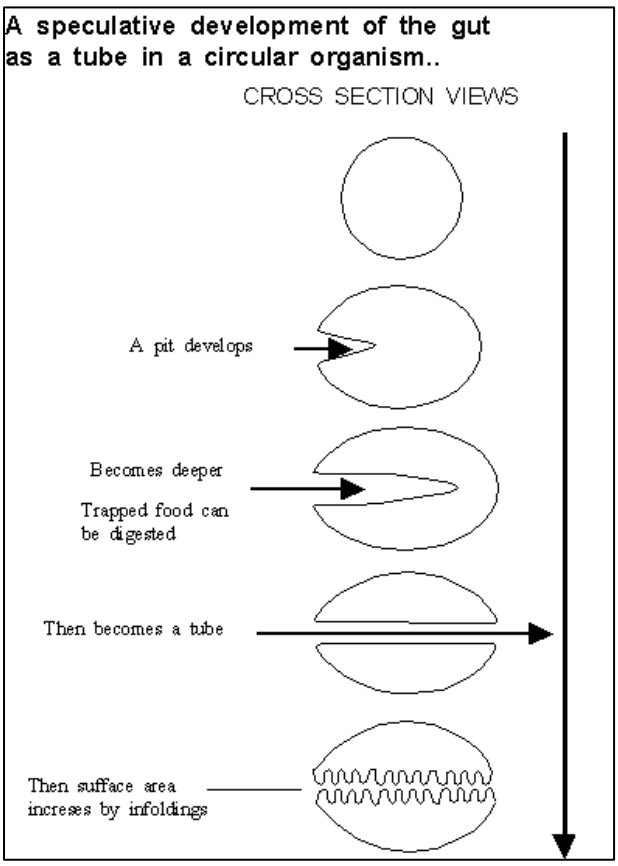
A TRIP DOWN THE GUT WITH A FEW DIVERSIONS

We need food for energy, growth, tissue repair, maintenance of body temperature and maintenance of body functions. Humans eat almost anything and thus we are at the top of a multitude of food chains. Our food comprises carbohydrates, proteins, fats, minerals, vitamins, and water, all of which are ultimately derived from absorption by the gut.

- The gut is in simple terms a tube running from mouth to anus which:
- Takes in food and water
- Stores food and water
- Acts on food by physically using teeth, and by the churning of food by stomach and intestines
- Acts on food chemically utilising oral, stomach, liver, pancreatic and gut secretions
- Absorbs water and the products of digestion from the greatly (up to 600-fold) increased gut area associated with villi and microvilli
- Stores waste products and then excretes them

FORMATION OF THE GUT AND ITS DERIVATIVES

Unicellular organisms rely upon diffusion to obtain nutrients and excrete waste products. Initially this would also suffice for small multicellular organisms. To enhance absorption pits would have developed to allow nutrients to be trapped and processed. Obviously the deeper the pit the better. A deep pit that passed through the organism would allow food to be processed more effectively.

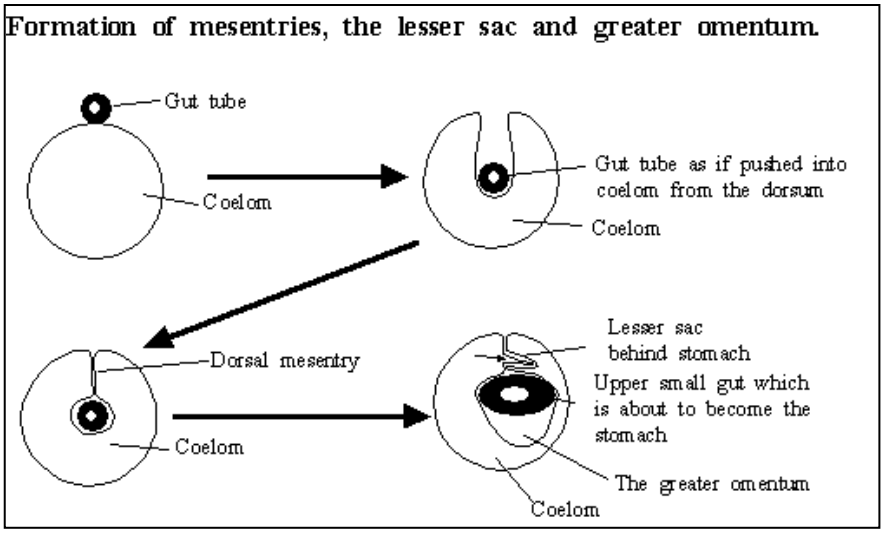


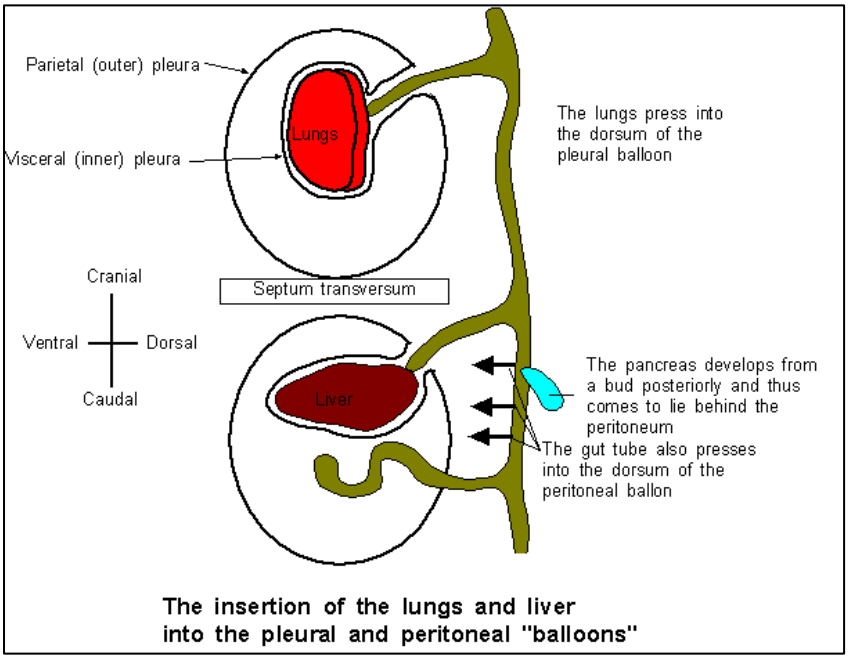
Various organs, including the pancreas and liver can be considered as outgrowths from the gut. The coelom (= hollow cavity) is formed by a split in the embryonic mesenchyme. This allows the gut a degree of movement. The coelomic lining is a membrane made of flat cells that secrete fluid to assist lubrication to allow movement of some internal organs. Mesenteries are thickened sheets continuous with coelomic membranes.

Although more complex in reality, it is almost as if the straight gut tube had been pushed separately into the back of the "coelomic balloon" the wall of which is the peritoneum (+ outside of the cavity) with the gut being suspended by the infolded two balloon surfaces (the mesentery),

with the gut later becoming elongated.

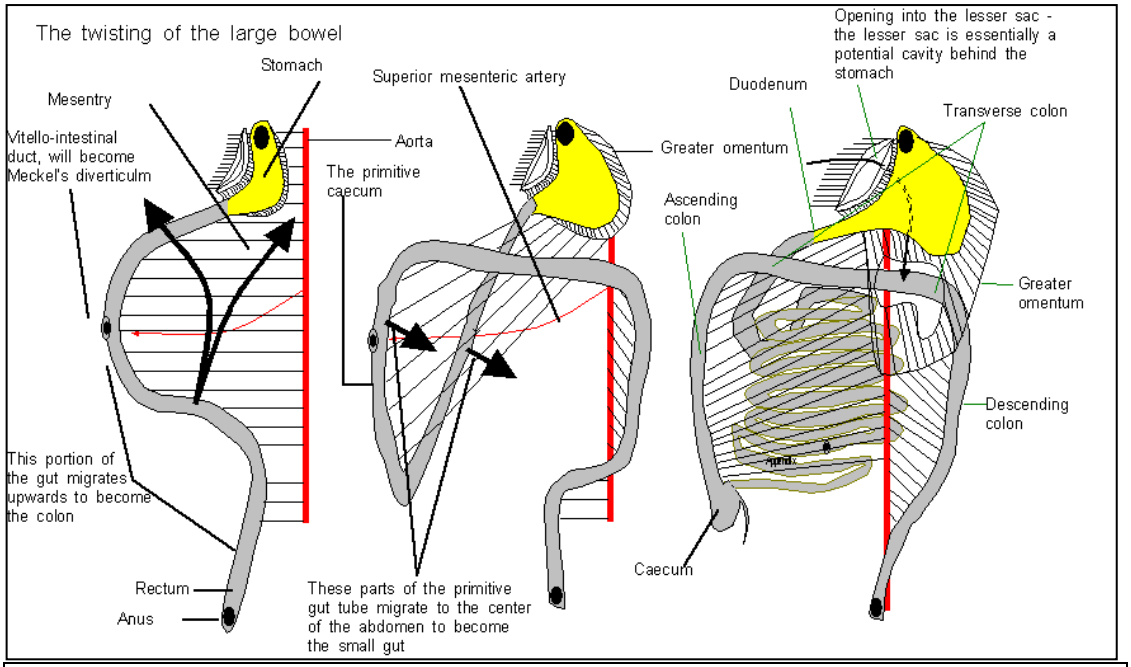
This mythical original coelomic balloon is divided by the transverse septum (which later forms part of the diaphragm through which the gut and blood vessels have to pass) into chest (pleuropericardial) and abdominal (peritoneal) balloons.

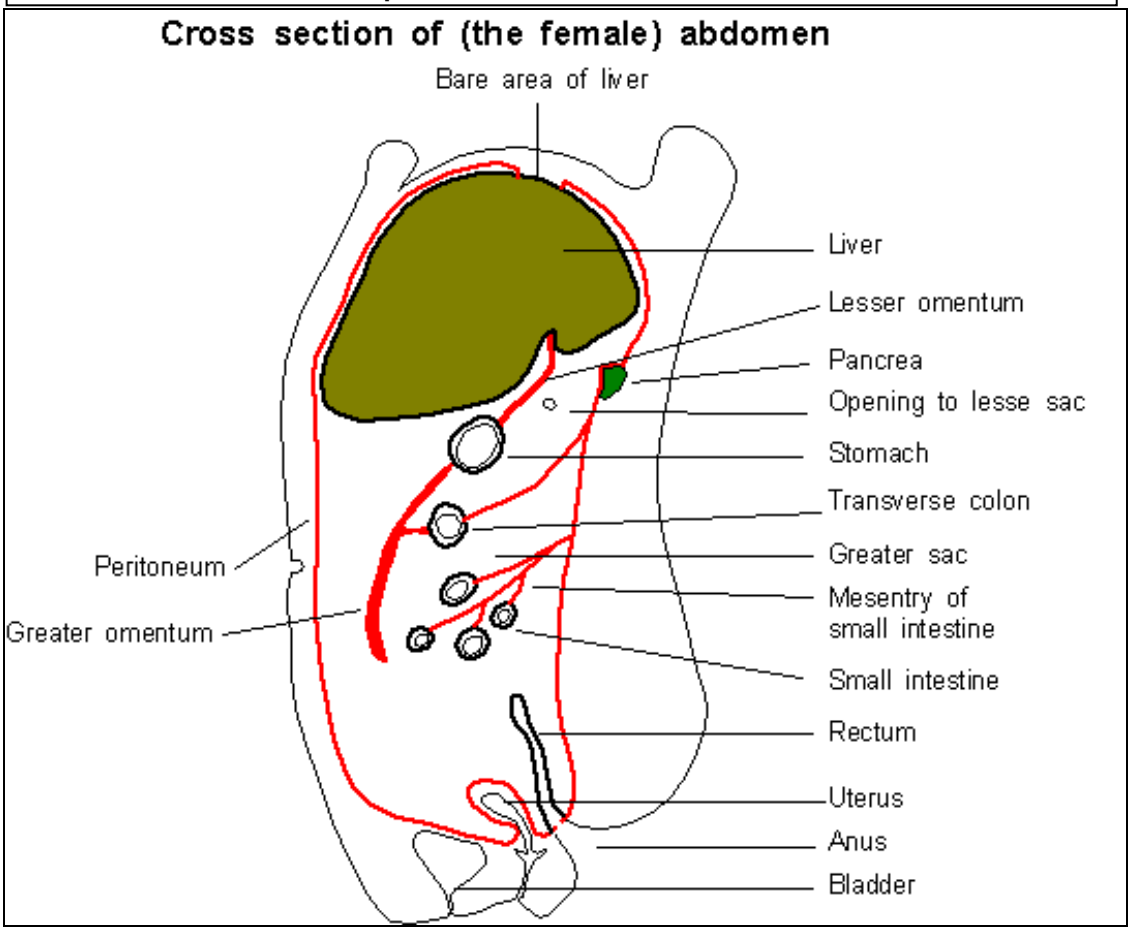




The diaphragm is derived from tissue that was initially more cranial in situation, thus explaining its innervation from the cervical spinal cord (C3,4,5).

The cranial portion of the gut tube that will eventually become the stomach rotates and enlarges to the left, giving rise to the lesser and greater curvatures and a sheet of mesentery (= mesenchyme of the gut = connective tissue), the greater omentum which hangs off the greater curvature (like a chef's apron) over most of the upper abdominal contents. A small sac (the lesser sac) develops as if pushed from right to left behind the stomach.





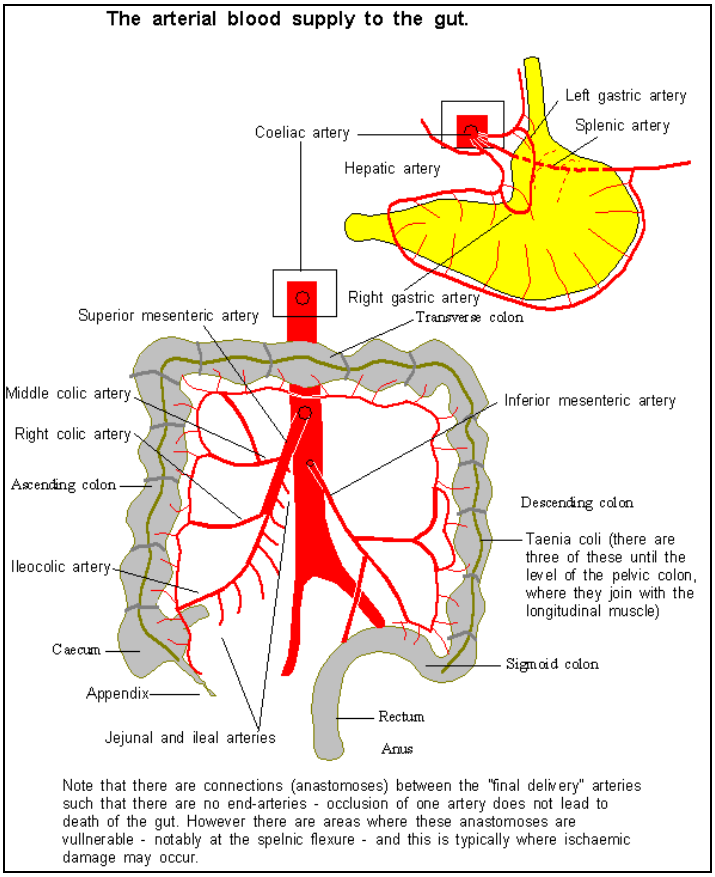
The liver grows as though it was pushed caudally and ventrally into the top of the peritoneal balloon. The lesser omentum is the membrane that lies dorsal to the stalk of the liver bud as it pushes away from the gut tube.

The pancreatic buds grow posteriorly and thus come to lie behind the peritoneum. The gut then twists so that the shorter and wider large gut acts as a picture frame for

the longer thinner small gut. The top of this frame is “slotted in” dorsal to the stomach.
Meckel's diverticulum is a small pouch about two feet from the junction of the small and large gut and is all that remains of the yolk sac.

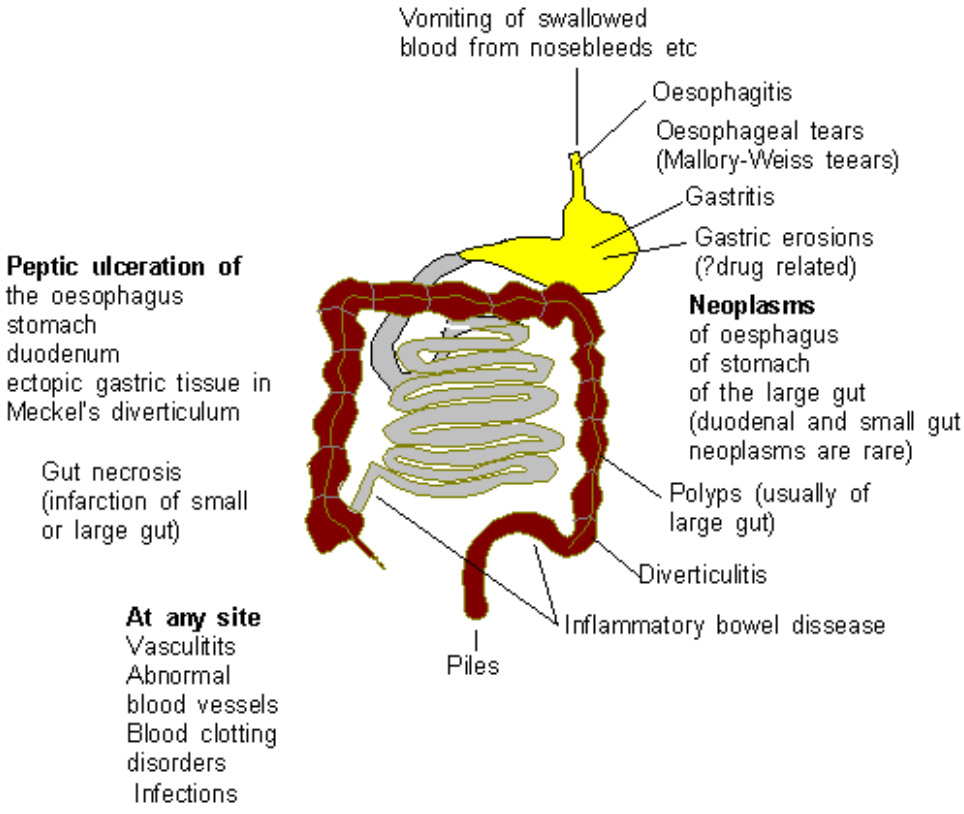
The secretion of digestive fluids and enzymes is evoked by the presence of food in the gastrointestinal tract using nerve, hormone, and mechanical stimuli. Secretions of the gut are initiated by the X (Vagus) nerve, by hormones or hormone-like substances produced by the gut or other tissues. Sympathetic and parasympathetic nerves modify the intrinsic contractility of the gut.

THE BLOOD SUPPLY TO THE GUT.



Bleeding into the upper gastrointestinal tract usually presents as vomiting of blood (haematemesis) or passage of black tarry loose stools (melaena) of a distinctive smell caused by partially digested blood which rushes through the gut.

Possible sites of gastrointestinal bleeding



Vomiting of blood (haematemesis) usually results from bleeding proximal to the ileum.

Passage of black tarry stools (melaena) usually results from blood that has been partially digested (and thus exposed to small gut enzymes) and this usually implies a source higher than the small gut.

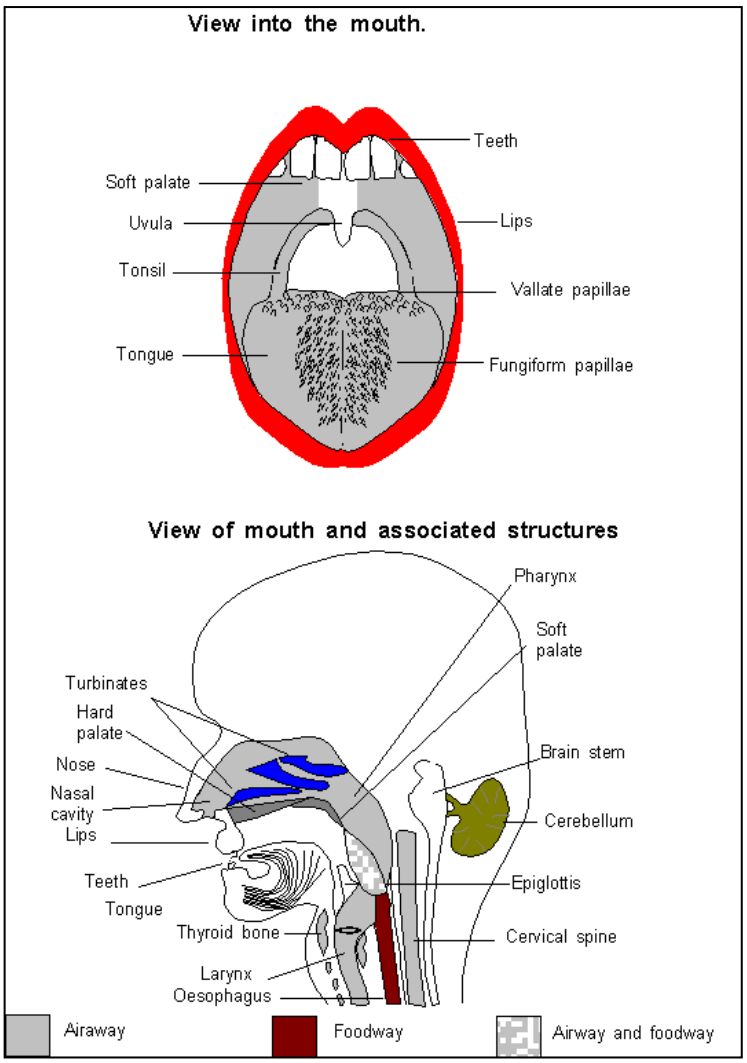
Bright red blood passed from the rectum suggests a source low down in the large gut (occasionally intestinal hurry can cause a brisk upper gastrointestinal haemorrhage to present with dark red blood).

Blood which splashes from the anus is from a source close to the anus, often from piles.

Blood mixed in with the stool often comes from the colon above the rectum.

Mouth and oesophagus

Food is chewed in the mouth and mixed with saliva, made into swallowing units - boluses - and propelled onwards into the pharynx. Most of the pharynx is comprised of striated muscle which merges with the smooth muscle of the oesophagus. The first third of the oesophagus is striated muscle, the middle third a transition zone, and the last third is smooth muscle.

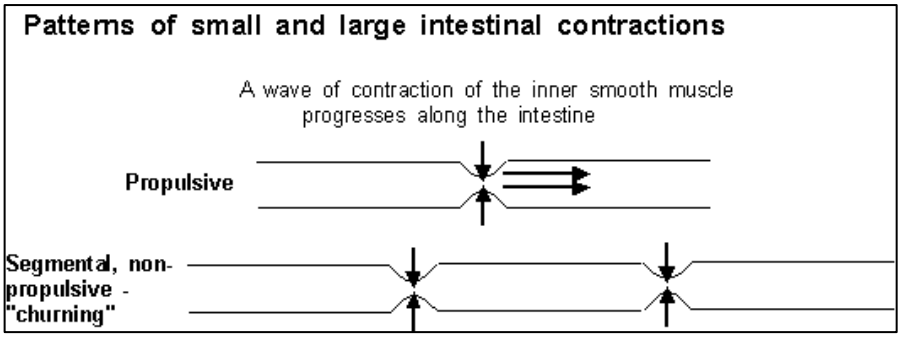


Swallowing is voluntarily initiated but thereafter becomes a brainstem reflex:

- the mouth is closed
- the bolus of food is delivered to the back of the mouth
- the soft palate rises to close off the nasopharynx
- respiration is temporarily inhibited
- the larynx rises
- the entrance to the larynx is closed off by the sphincter-like muscle which surround it
- the food bolus passes over or around the epiglottis which is situated, cowl-like, over the laryngeal orifice (however the epiglottis can be absent without significant effect on swallowing)
- the oesophageal muscle and surrounding muscles relax to allow the bolus to pass

Thereafter the progression of food along the gut is almost exclusively automatic until defaecation.

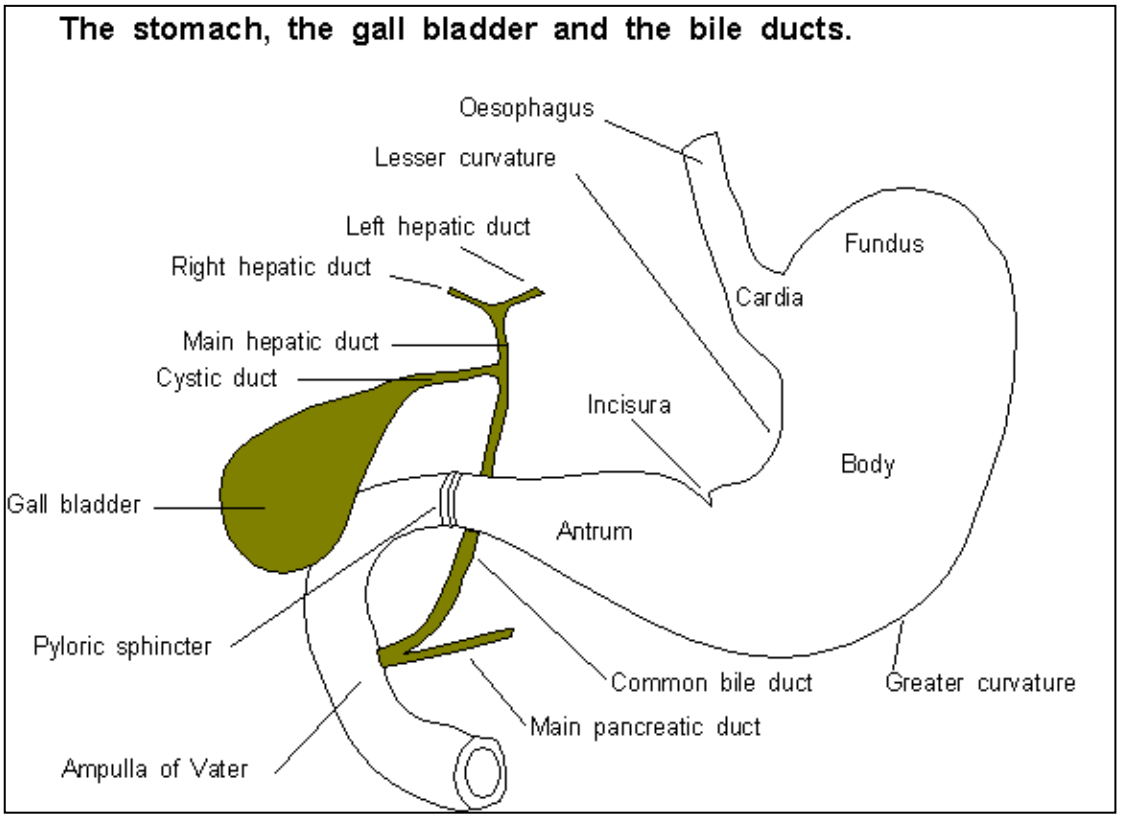
The gut tube is smooth muscle which contract in (peristaltic) waves to propel food onwards.



Heartburn is caused by reflux of acid, bile, food, or fluid from the stomach into the oesophagus. It is usually caused by loss of tone in the lower oesophageal sphincter, either alone or associated with conditions (such as obesity or pregnancy) in which there is raised intra-abdominal pressure.

The stomach

The stomach has three areas, the fundus, body and antrum. In the stomach food is exposed to gastric juice which contains hydrochloric acid and digestive enzymes. The parietal cells of fundus and body produce hydrochloric acid and the antrum produces gastrin, a hormone that causes gastric acid secretion in response to gastric distention, dietary protein or vagus nerve action.



Absorption by the stomach is in practical terms limited to fluids. The stomach has four main functions:

- Secretion of hydrochloric acid which breaks down pepsinogen into the enzyme pepsin. Hydrochloric acid also reduces the number, or kills, most bacteria ingested in food
- Secretion of enzymes including pepsin. Pepsin breaks down protein into polypeptides
- A reservoir which also churns food
- A producer of intrinsic factor. Dietary vitamin B12 is bound to intrinsic factor. The complex is absorbed in the terminal ileum (and thus may be reduced in patients with terminal ileal diseases such as Crohn's disease). Haematological aspects are covered under haematology

Within a few hours all food has left the stomach via the pyloric sphincter (pyloric = gatekeeper) into the duodenum where it meets pancreatic juices and biliary secretions arriving from the common bile duct via the ampulla of Vater.

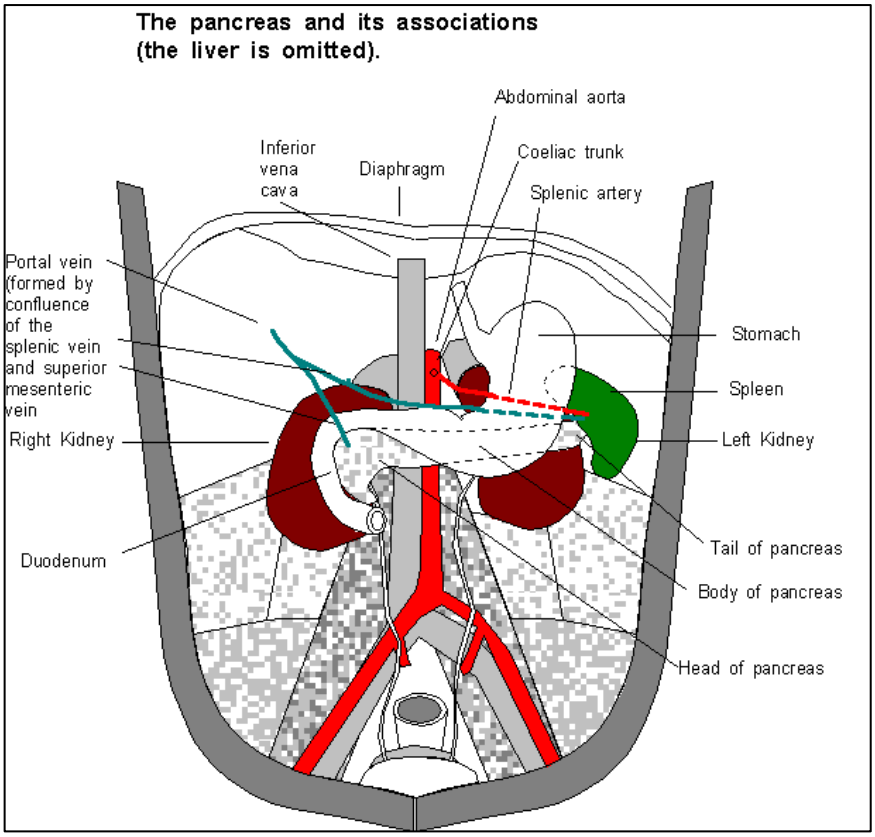
Peptic ulcers may occur in the oesophagus, stomach, duodenum, Meckel's diverticulm or in post-operative stomachs) Associations of chronic peptic ulcers include:

- *Helicobacter pylori* infection of the gastric antrum (90 percent of duodenal ulcers)
- Smoking
- Hyperacidity
- Ingestion of drugs which damage the stomach mucosa including non-steroidal anti-inflammatory agents, corticosteroids or aspirin
- Stress (only proven for the stress of head injury or burns)

In the duodenum food is acted upon by the bile and pancreatic secretions. The pancreatic duct and the bile duct usually join just before draining into the duodenum via the ampulla of Vater. The presence of food in the duodenum evokes the secretion of secretin (a hormone which causes secretion of bicarbonate by the pancreas).

The pancreas

The pancreas secretes enzymes including *trypsinogen* which is broken down to *trypsin* (which breaks down proteins to polypeptides), *amylase*, *maltase* and *lipase*. Bicarbonate is also secreted so that the contents of the small gut are approximately neutral.



Cholecystokinin, produced by the duodenum in association with the parasympathetic nervous system, evokes secretion of (exocrine) pancreatic enzymes *trypsin* and *chymotrypsin* which break down proteins, *lipase* which breaks down fats, and *amylase* which breaks down starch.

The exocrine pancreas also produces maltase, which breaks down maltose to two molecules of glucose, and bicarbonate. The alpha cells of the (endocrine) pancreas produce glucagon, which maintains the serum glucose, whereas the beta cells secrete insulin, which decreases the serum glucose. Somatostatin is secreted by the pancreas and gut and reduces gut secretions.

Acute inflammation of the pancreas causes amylase to leak out into the bloodstream. Chronic pancreatic inflammation eventually causes deficiencies of the exocrine and endocrine functions.

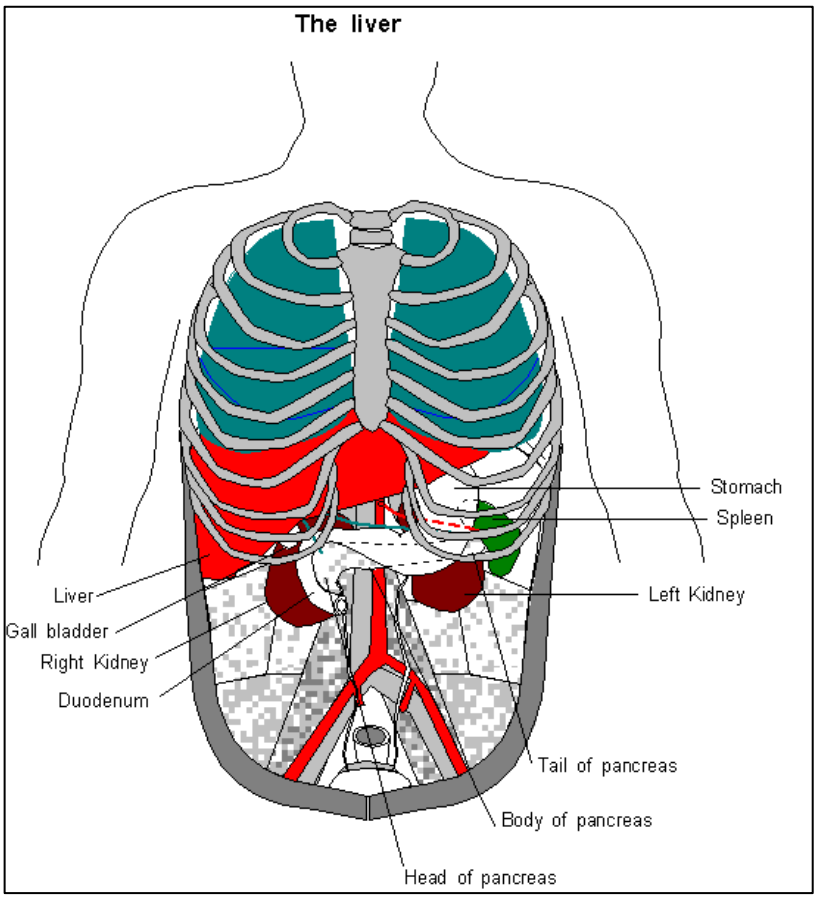
If the pancreas fails then there may be:

- Protein malabsorption
- Fat malabsorption
- Weight loss
- Diabetes mellitus. Pain and bile duct obstruction may also occur, depending on the cause of pancreatic failure.

Cystic fibrosis is a multisystem disease in which there are hyperviscous secretions with plugging of various tubular systems (including that of the pancreas) with

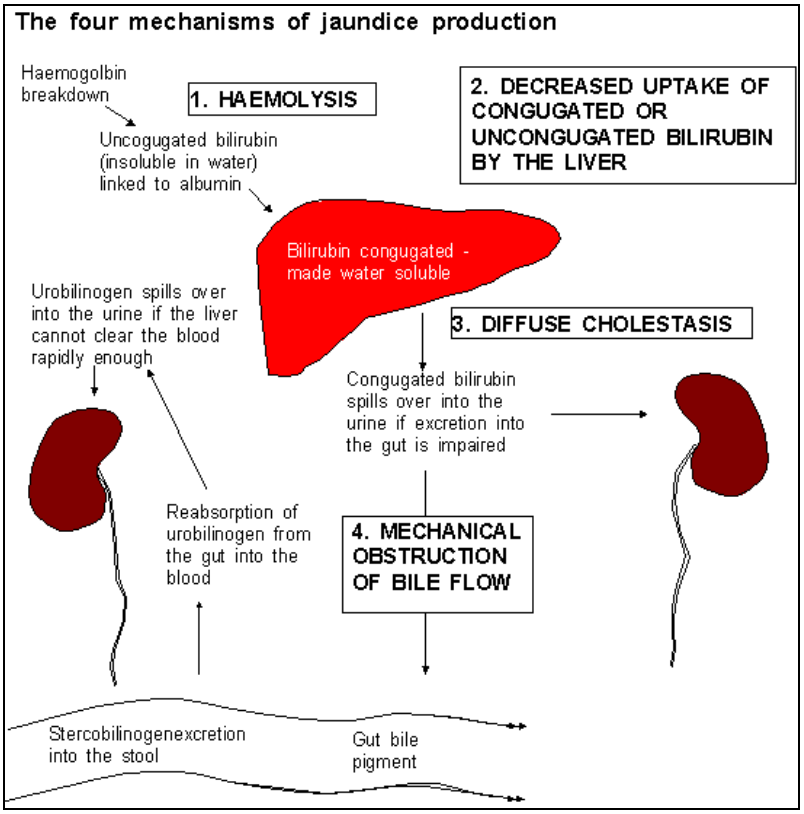
destruction of pancreatic glandular tissue predominantly causing pancreatic exocrine deficiency. The neonatal gut may be clogged up with hyperviscous meconium (the initial contents of the neonatal gut) leading to obstruction, volvulus, perforation, or intussusception.

The liver

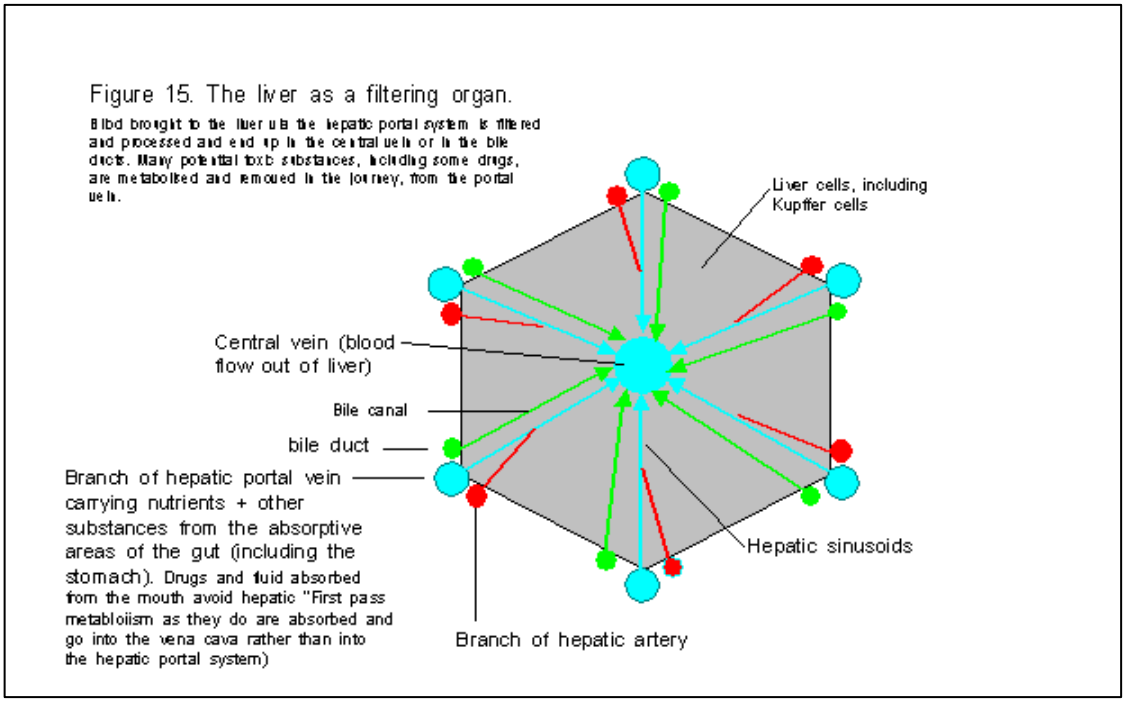


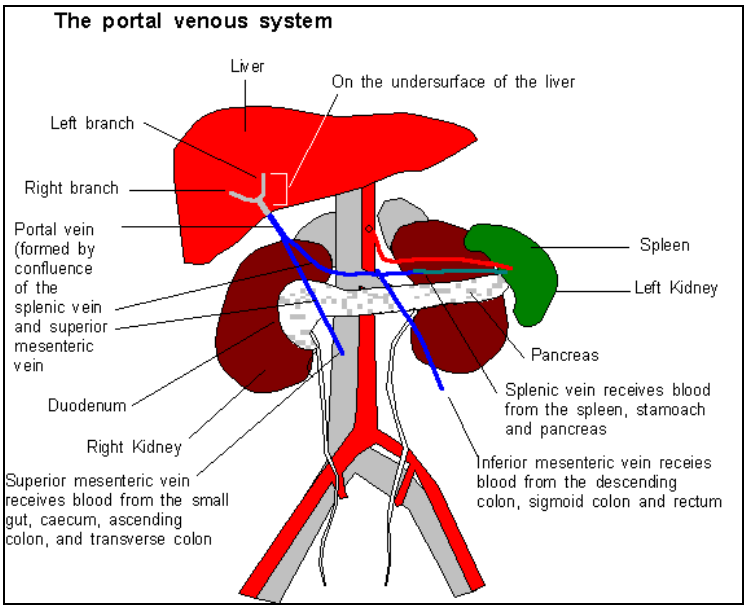
The liver has five main functions:

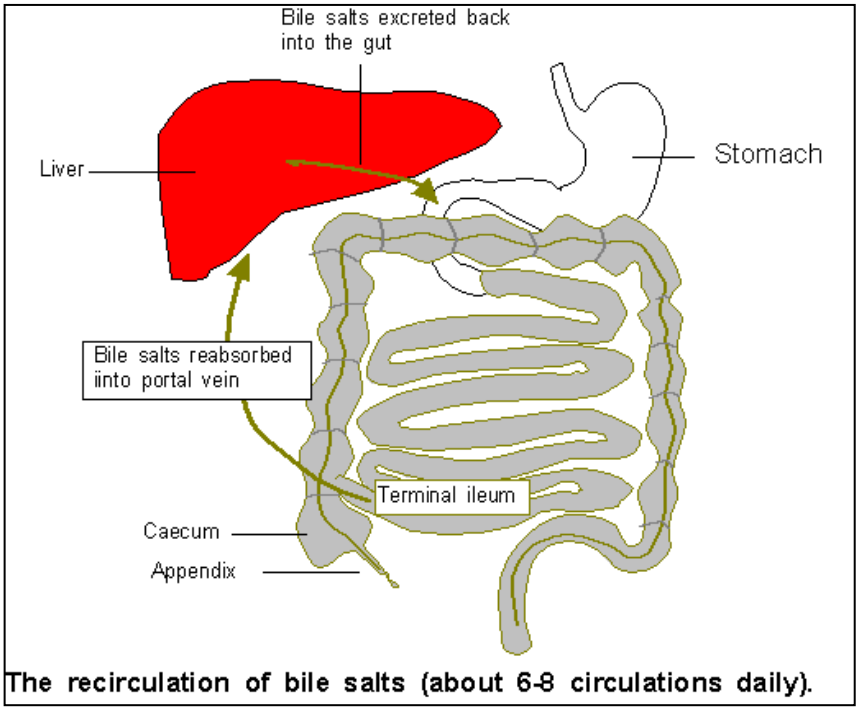
- Dealing with food absorbed by the gut
- Dealing with "benign" metabolic products
- Removal of unconjugated (insoluble) bilirubin resulting from haemoglobin breakdown and converting it to conjugated (soluble) bilirubin which can then be excreted into the gut. If either form of bilirubin is present in excess then jaundice results
- Dealing with potentially toxic metabolic products
- Dealing with drugs and some other ingested compounds



The liver is a filtering organ with blood in the sinusoids (= hollow spaces) exposed to the hepatic cells (the hepatocytes) and phagocytic cells. Both sinusoids and canaliculi have microvilli to increase the available surface area for secretion and/or excretion. Canaliculi collect and drain bile. Bile mostly serves to assist in the digestion of fats. Bile is stored in the gallbladder and its ejection into the duodenum is enhanced by cholecystokinin, a hormone which is released when food, particularly fatty food, enters the duodenum.







About 80 percent of blood arriving at the liver arrives via the portal vein.

The other 20 percent arrives via the hepatic artery. Blood from the intra-abdominal part of the gut (but excluding the anus), spleen, pancreas, gallbladder and its ducts drains into the liver via the portal vein and, after passing through the hepatic filtering system, enters the hepatic veins and then drains into the inferior vena cava. If there is an impaired portal blood flow through the liver then the pressure in the portal vein rises and portal blood has to find other ways of returning to the systemic veins. Consequently veins distend at communicating sites between portal and systemic venous systems.

These sites are:

- at the lower end of the oesophagus to produce oesophageal varices (= tortuous dilated veins). Oesophageal varices are relatively unsupported and, being easily traumatized, may bleed torrentially
- the rectum
- the abdominal wall - blood wells up in the umbilical area and travels outwards (cranially to the superior vena cava system, caudally towards the inferior vena cava system).

In the liver carbohydrate is stored as glycogen which can be broken down to maintain the serum glucose level (glycogenolysis). If starvation is severe fats are converted to ketone bodies in the liver which can be metabolised to produce energy. Glucose can also be made from protein in the liver (gluconeogenesis). In severe liver failure the blood glucose may be pathologically low (hypoglycaemia).

Lipids (cholesterol and its esters, phospholipids, and triglycerides) are carried in the blood as lipoproteins which are produced by the liver and to a lesser extent by the gut. Triglycerides are transported from gut to the liver as chylomicrons (=small globules). In liver disease the serum cholesterol rises, probably because of a combination of a failure of cholesterol excretion and an excessive production of cholesterol by the failing liver.

Cholestasis (=bile stillness) can be caused by mechanical obstruction to the common bile duct or by defective excretion of bile salts into bile canaliculi. In the liver cholesterol becomes part of cholic and chenodeoxycholic acid which then combine with taurine or glycine to form the bile salts. Bile salts assist in the digestion of fats by aggregating and surrounding them to form structures known as micelles. Some bile is stored in the gall bladder, where it may precipitate to form gallstones if the bile becomes oversaturated with lipids. These bile salts pass into the liver canaliculi into the duodenum and passes down to the terminal ileum where they are mostly (95 percent) reabsorbed and returned to the liver - the enterohepatic circulation.

Failure to reabsorb bile salts in the lower small gut (as may occur in Crohn's disease) leads to irritation of the large gut which causes diarrhoea.

The liver synthesizes most of the plasma proteins including albumin which maintains the osmotic pressure of the blood, and several blood clotting factors including fibrinogen, and prothrombin (made from Vitamin K) Breakdown of proteins into amino acids can occur in many tissues but amino acids can only be broken down to urea in the liver. Thus a low urea is a feature of fulminant liver failure.

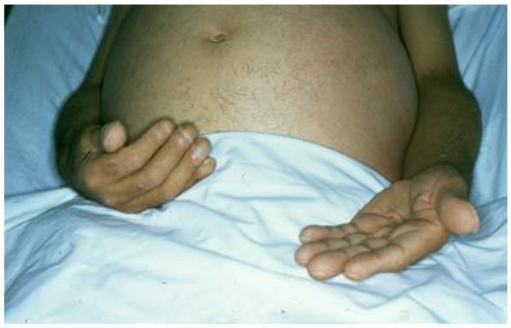
The liver can break down some potentially harmful proteins and some potentially harmful substances, including some drugs. In contrast some drugs are metabolized to their active forms in the liver - the liver usually deactivates drugs which are fat soluble or of high molecular weight.

The "standard" tests of liver function as measured in the blood are:

- *Bilirubin* which is increased in haemolysis, hepatitis, or mechanical obstruction of the bile flow (Fig 14) and a few other rare disorders of bilirubin metabolism
- *Alanine aminotransferase* which is released by inflamed liver cells. The aspartate transminase level also rises but this is less liver-specific because cardiac or skeletal muscle damage can cause rises.
- *Alkaline phosphatase* is released by irritated (usually meaning mechanically obstructed) biliary tract epithelium, even if the obstruction is not severe enough to cause jaundice (an elevated alkaline phosphatase is also found in some bone diseases and in pregnancy)
- *Albumin* as a measure of hepatic synthesis capability. As the half life of albumin is three weeks a low level implies chronic liver disease (malnutrition or malabsorption can also reduce serum albumin)
- *Prothrombin time* is an important measure of hepatic synthetic capability
- *Glucose* (often forgotten as a liver function test) is a measure of glycogen reserves in the liver

In liver failure there may be:
- Jaundice
- Confusion
- Fluid retention
- Bleeding
- An impaired conscious level leading to coma
- Abnormal movements
- A low blood glucose
- A low blood urea (because of failure of hepatic synthesis)

Ascites is an accumulation of fluid within the peritoneal cavity.



Ascites, when caused by liver disease, usually results from a combination of:
- obstructed portal venous return
- hypoalbuminaemia
- the kidney responsing to the resulting low osmotic pressure, with increases in renin and aldosterone leading to sodium and water retention
- failure of the liver to detoxify fluid retaining hormones

Cirrhosis is a disorganization of lobular architecture with regeneration nodules and fibrosis. In general, small nodules (micronodular cirrhosis) tend to occur when there is continuing liver cell damage such as caused by chronic alcoholism whereas large nodules (macronodular cirrhosis) occurs when there is low grade inflammation and necrosis.

Hepatic encephalopathy, diffuse dysfunction of brain tissue caused by liver dysfunction, usually only occurs if there is a substantial reduction in liver cell mass with diversion of (and thus failure of the liver to detoxify) portal blood into the general circulation which then poisons the brain.

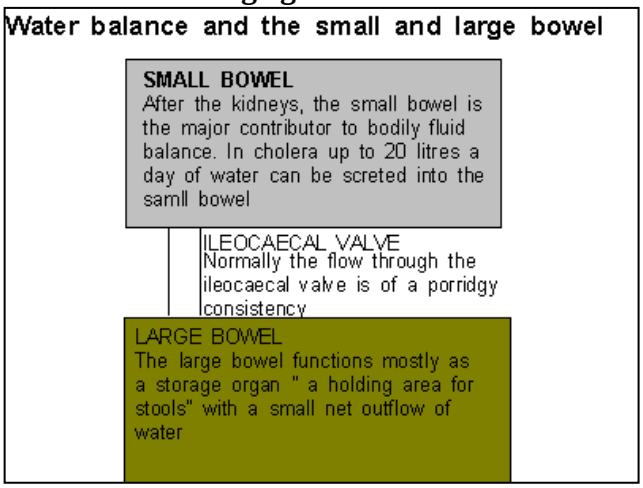
The spleen

Functions of the spleen include:

- Breakdown and removal of effete blood cells (red blood corpuscles, white cells and platelets)
- Formation of red and white blood cells in adults, but usually only when the bone marrow has failed
- Removal of certain abnormal structures in the blood (e.g. malarial parasites)

The splenic artery branches soon after entry into the spleen, and blood flows through the splenic pulp where it is filtered and effete blood cells are removed. The venous blood then flows to the liver in the portal vein which is formed by the confluence of the superior mesenteric and splenic vein. If the portal venous pressure is high then the spleen becomes congested and may become anatomically enlarged and overactive to produce hypersplenism in which the counts of red blood corpuscles, white cells and platelets may all be reduced.

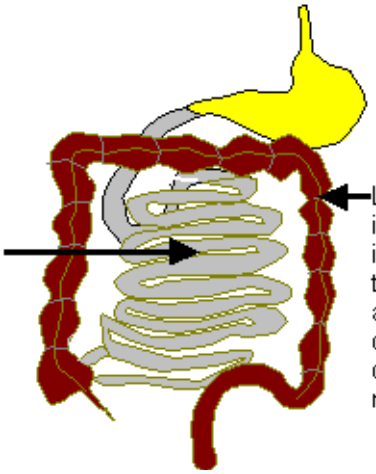
The small and large guts



Small bowel diarrhoea differs from large bowel diarrhoea in several respects.

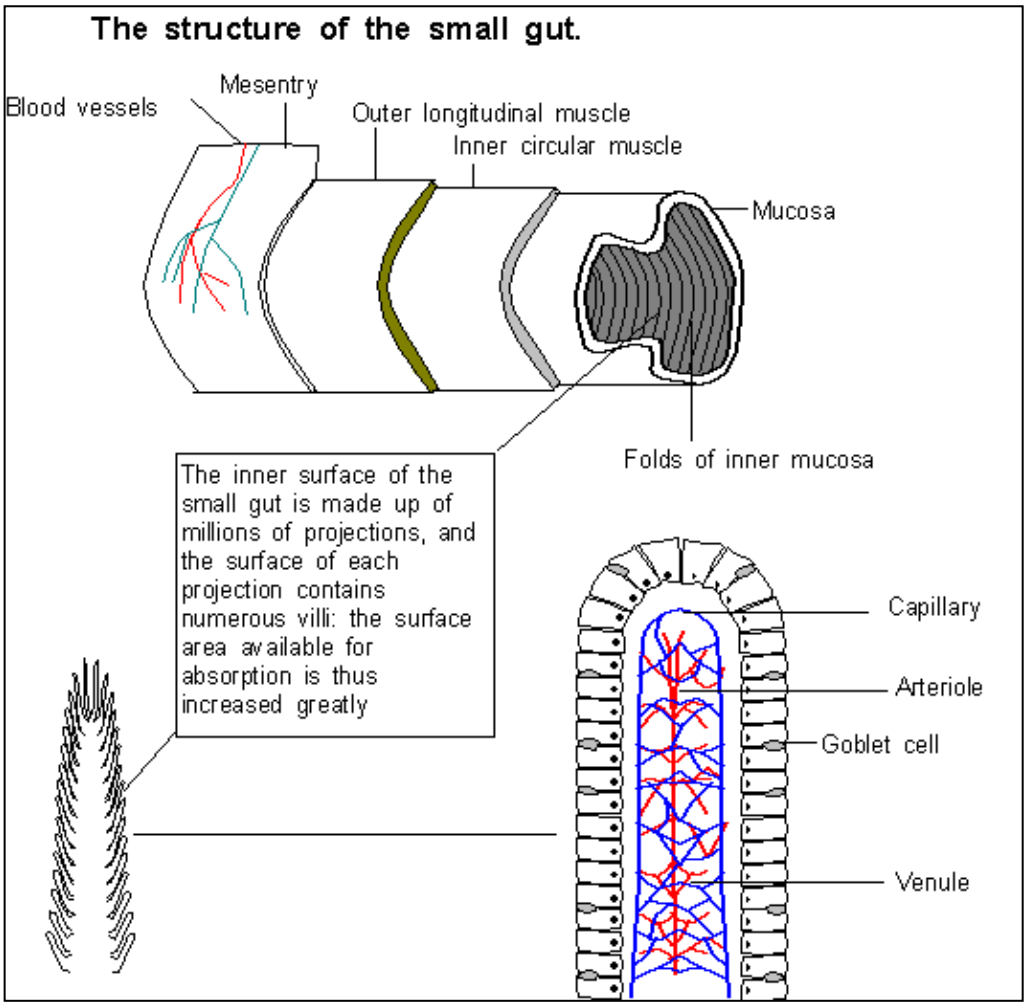
Small and large bowel diarrhoea

SMALL BOWEL DIARRHOEA is either malabsorptive in type or watery, reflecting the main functions of the small gut (absorption and fluid balance). Usually the large gut can continue its reservoir function and thus larger amounts of diarrhoea result than with large gut problems



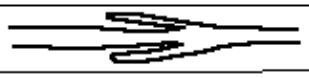
LARGE BOWEL DIARRHOEA is usually caused by inflammatory conditions in which the large gut cannot function as a reservoir. There is passage of small amounts of porridgy diarrhoea, possibly with blood, mucus, or pus

Both the small and large gut tubes have an outer longitudinal and an inner circular layer of smooth muscle with a nerve plexus situated between the two.



There are a surprising number of disease processes that can occur to a tube.

Possible problems with the gastrointestinal tube

Problem	Nature of problem	Examples	Possible results include
Narrowing	Anatomical — Benign	Pyloric stenosis	Vomiting
	Anatomical — Malignant	Cancer	Death
	Spasm	Achalasia	Obstruction
Haemorrhage	Blood loss from vascular compartment	Bleeding duodenal ulcer	Shock
Failure of peristalsis	Failure of propulsion of gut contents	Paralytic ileus	Distension
Failure to absorb	Metabolic defects, lack of digestive secretion, previous resection	Coeliac disease	Malnutrition
Strangulated	Gut blood supply cut off	Incarcerated hernia	Necrosis
Obstructed	Complete failure of onward food movement	Malignant stricture	Vomiting, distension
Herniation	Loop of gut or portion of gut wall extruded through a small aperture	Inguinal hernia	Obstruction and/or ischaemia and/or tissue death
Ischaemia	Blood supply inadequate for normal function	Partial strangulation	Ishcaemic pain
Tissue death (necrosis, infarction)	Tissue death	Total strangulation	Infection Death
Perforation	Leakage of gut contents into peritoneal cavity	Perforated ulcer	Peritonitis, Death
Irritability	Spasm	Irritable bowel syndrome	Colic
Overloaded	Too much to move	Constipation	Pain
Infected	Irriating microorganisms and/or toxins	Salmonella food poisoning	Vomiting, diarrhoea
Twisted (volvulus)	Anatomical blockage plus damage to blood supply	Large bowel volvulus	Pain perforation
Polyp formation	Possible blood loss, malignant potential, or twisting		Anaemia pain
Outpouching - diverticulae	Bacterial colonisation — Small gut	----------	Malabsorption
	Bacterial colonisation — Large gut	----------	Diverticulitis
Idiopathic inflammation		Ulcerative colitis, Crohn's disease	Diarrhoea
Intussusception			
Ulceration		Peptic ulcer	Pain, haemorrhage
Reflux		Hiatus hernia	

The small gut

The small gut is concerned with fluid balance, enzyme secretion, digestion, and absorption of food.

The small gut has propulsive peristaltic waves but there are also non-propulsive contractions of two types (segmental and linear) which serve to mix the food. The X nerve (vagal) and sacral parasympathetic outflow increases gut tone and peristalsis whilst the sympathetic outflow reduces muscle tone and peristalsis.

The mucous membrane of the small gut has about 5 million projections (villi) which increase the surface area available for absorption.

Each villus contains an artery and a vein. Columnar cells covering the villi are known as enterocytes and each enterocyte has about 1,000 microvilli. The human ileum thus has a fine velvet appearance. There is a fast turnover of villus cells which is maximum in the ileum (5-7 days).

The small gut absorbs carbohydrates as monosaccharides glucose, fructose or galactose.

At a maximum (with cholera) the small gut can secrete up to 20 litres of fluid a day into its lumen, but even with this secretion rate the small gut continues to absorb fluids.

Small gut enzymes, along with pancreatic enzymes, digest larger molecules of carbohydrate, protein and fats, but not cellulose (which has to be processed for us by herbivores that have the necessary enzymes). Water, salts, most vitamins and glucose are absorbed unchanged but vitamin B_{12} requires to be complexed with gastric intrinsic factor before it can be absorbed.

The small gut delivers a porridgy paste containing about 1,000 mls of water each day via the ileo-caecal valve into the large gut. Absorption of foodstuffs is almost total (95 percent of fat and 90 percent of protein).

Small gut diarrhoea (see Figure 19) is either malabsorptive in type with greasy stools (caused by fat malabsorption) or watery (after the kidney the small gut is the second most important fluid regulating tissue of the body). Fat malabsorption occurs in most diffuse disorders of the small gut. Many small gut pathologies tend to spare the large gut which can thus continue its function as a reservoir. With small gut diarrhoea large amounts of diarrhoea are passed often because the large gut still functions as a reservoir. There is usually no blood, mucus or pus.

Appendicitis is inflammation in the blind-ended tube that is the appendix.

The large gut

The large gut functions mostly as a reservoir but absorbs some water. There is no significant enzyme secretion.

Faeces contain undigested or indigestible food residues, desquamated gut lining cells and bacteria. Defaecation normally requires integration of both voluntary and

involuntary nervous systems. The internal sphincter is autonomic (involuntary) and the external sphincter is voluntary.

Large gut diarrhoea is usually caused by pathogens or pathologies that invade and irritate the gut wall which then cannot function as a reservoir. Large gut diarrhoea is thus frequent passage of small amounts often of "porridgy" stool, possibly with blood, mucous or pus.

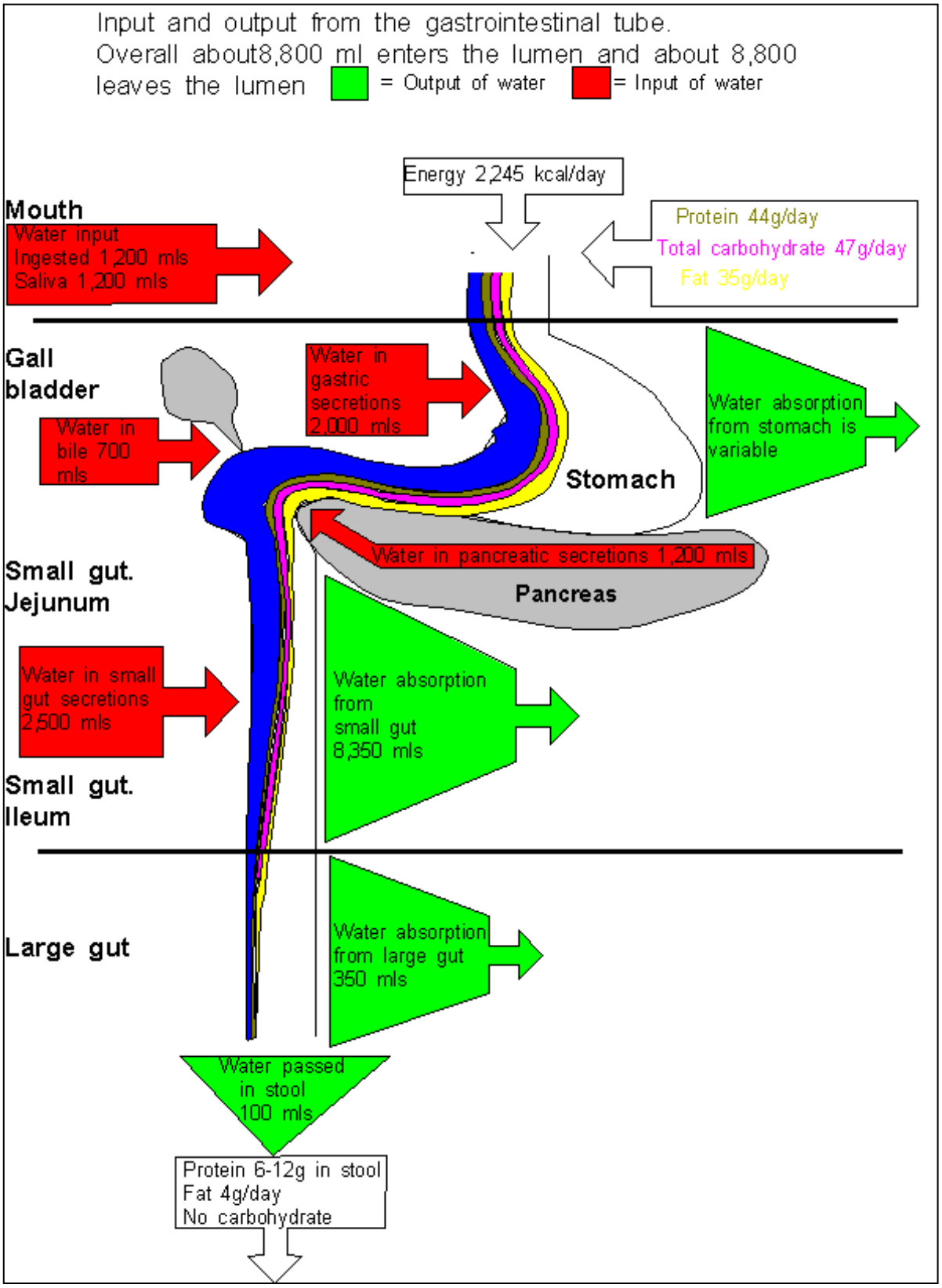
Most people pass stools once or twice a day. The range of normality is between three times daily to three times weekly. *Changes* in bowel frequency may be important even if within the "normal" range. Constipation may occur:

- In old age when gut muscle tone is reduced
- If there is dehydration
- If there is obstruction, twisting, of failure of blood supply to the gut
- If there is anorectal pain
- If there is neurological impairment (e.g. diabetic or other autonomic neuropathy)
- If there is endocrinological abnormality (e.g. hypothyroidism or a high plasma calcium)
- As a drug effect (e.g. anticholinergics, aluminium based antacids, opiates)
- In those on low residue diets

Diarrhoea (more frequent passage of unusually loose stools) may be caused by:

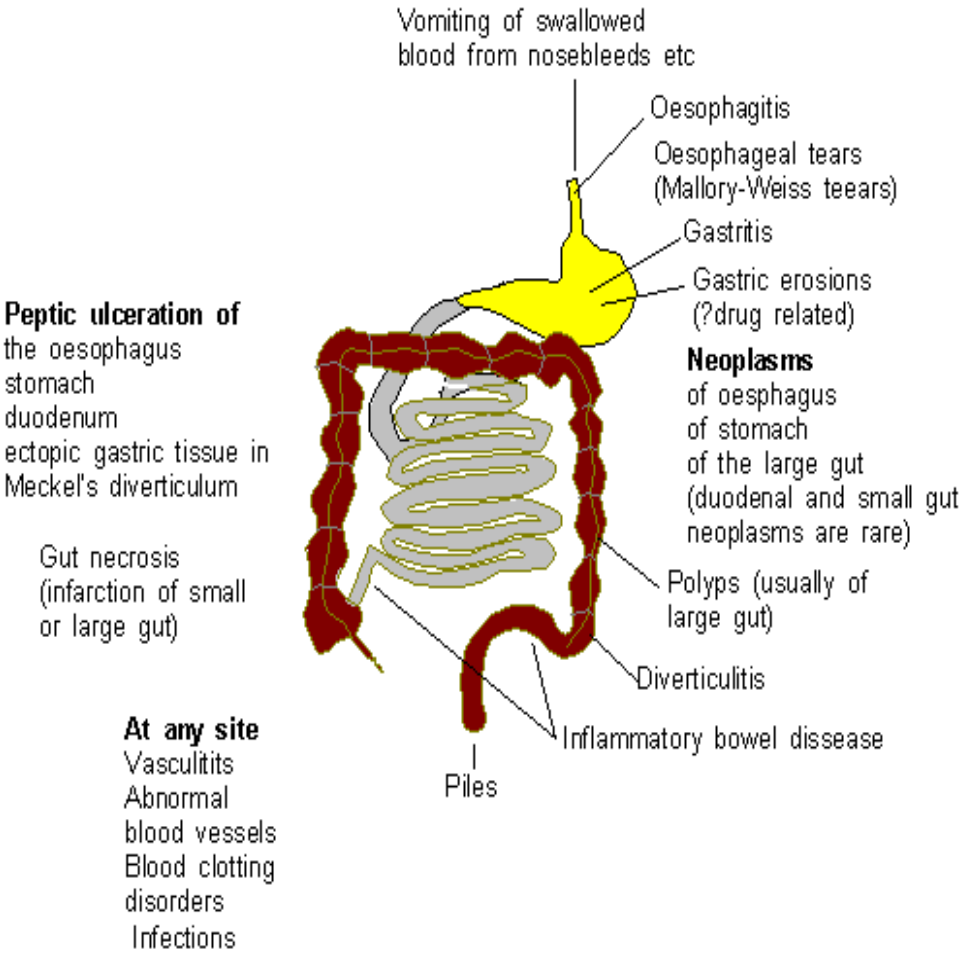
- Excessive secretion of water into the gut (usually in the small gut)
- Excessive retention of water in the gut (osmotic purgatives)
- Malabsorption of osmotically active foods, which draw excessive fluid into the gut.
- Metabolic deficits. For example lactase deficiency causes accumulation of lactose (the carbohydrate in milk in the gut)
- Failure of absorption of fats (steatorrhoea)
- Short gut syndromes (after surgery)
- Failure of reabsorption of bile acids
- Hypersensitivity of the gut. For example to the gliadin fraction of wheat in coeliac disease
- Irritation of the gut (by infections and other processes)
- Small gut ischaemia
- Gut wall inflammation
- Small gut tumours (rare)
- Irritable bowel syndrome "spastic colon" with hyperactivity and/or lowering of the gut pain threshold.
- Drugs (including iron and alcohol)

Inflammation in *ulcerative colitis* is, in contrast to that in Crohn's disease, limited to the inner mucosa and only affects the rectum and large gut.



Gastrointestinal bleeding can occur from many sites.

Possible sites of gastrointestinal bleeding



Vomiting of blood (haematemesis) usually results from bleeding proximal to the ileum.

Passage of black tarry stools (melaena) usually results from blood that has been partially digested (and thus exposed to small gut enzymes) and this usually implies a source higher than the small gut.

Bright red blood passed from the rectum suggests a source low down in the large gut (occasionally intestinal hurry can cause a brisk upper gastrointestinal haemorrhage to present with dark red blood).

Blood which splashes from the anus is from a source close to the anus, often from piles.

Blood mixed in with the stool often comes from the colon above the rectum.

A JOURNEY DOWN THE GUT TUBE

The average person eats about 35-70g fat, about 45g of protein and about 150g of carbohydrate. The progression of food along the gut is almost exclusively under autonomic control until defaecation, a journey of about 4.5 metres.

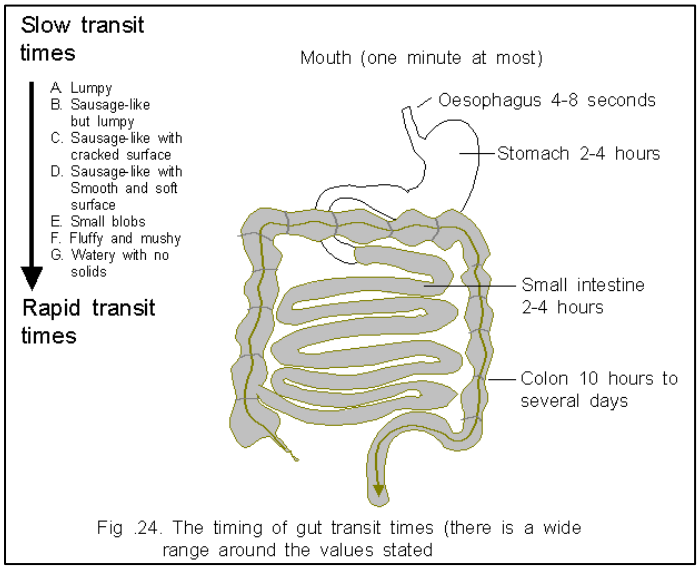


Fig .24. The timing of gut transit times (there is a wide range around the values stated

Although individual variation is wide, barium taken by mouth reaches the ileo-caecal valve in about 4 hours, the hepatic flexure of the large gut within 6 hours, the splenic flexure by 9 hours, the pelvic large gut by 12 hours. Three-quarters of the barium is expelled within 72 hours.