Introduction

This chapter will provide a brief overview of the anatomy and physiology of the liver, examining the blood supply, internal structures and the most common hepatic functions. It will provide an overview of the pathophysiology of cirrhosis, subsequent chapters will provide more details on particular problems. This chapter is not an exhaustive guide to liver anatomy and physiology, but it is hoped that the reader will gain an appreciation of how complex and far reaching the liver’s influence over health can be, and how this function is supported by the structure of the liver.

The liver

The liver is the largest solid organ in the body, weighing approximately 1500 g in adults, and comprises of one fiftieth of the total adult body weight. The liver lies in the right upper quadrant of the abdominal cavity covered by Glisson’s capsule, and is therefore protected by the rib cage. The liver has two anatomical lobes (Figure 1.1), with the right being six times larger than the left. The right and left lobes are separated anteriorly by the falciform ligament, and inferiorly by the ligamentum teres. The left lobe also includes the caudate and quadrate lobes. It is
Liver Diseases

separated from these two lobes by the attachment of the ligamentum teres, and
the fissures for the ligamentum teres and the ligamentum venosum (Sherlock
and Dooley, 2002). The hepatic artery, portal vein, afferent and efferent nerve supply
bile ducts and lymphatics enter the liver at a central area known as the hilus. The
liver performs many functions in both health and disease, though only the main
ones will be described in this chapter. Its nerve supply plays a role in many of
these functions (Tiniakos et al., 1996; Sherlock and Dooley, 2002).

The liver has both a venous and arterial blood supply. These provide a total of
around 1350 mL/min of blood – around one quarter of the resting cardiac output.
The portal vein drains the splanchnic circulation and provides 75% of the liver’s
blood supply, the hepatic artery supplies the remaining 25%. The venous outflow
from the liver is through the hepatic vein into the inferior vena cava. The liver
gives very little resistance to the flow of blood from the portal vein, with an average
pressure of 9 mmHg (range 5–10 mmHg). This pressure is sufficient to drive 1 L
of blood through the liver each minute.

Hepatic microstructure

The liver contains hepatocytes, endothelial cells, Kupffer cells, pit cells and hepatic
stellate cells (HSCs). The latter are also called Ito cells, fat-storing cells, perisinu-
soidal cells and lipocytes. Hepatocytes are the liver parenchymal cells and comprise
of approximately 60% of the liver; endothelial cells line the walls of sinusoids (see
below); Kupffer cells are phagocytic cells found on the walls of sinusoids that were
first observed by Karl Wilhelm von Kupffer in 1876 (Haubrich, 2004). Pit cells
are a type of natural killer cell found in the liver, their name comes from their
characteristic cytoplasmic granules resembling the pits in a grape (Wisse et al.,
1976). HSCs are a major regulator of normal liver homeostasis (Li and Friedman,
2001) and are found in the space of Disse (see below).
The portal vein and hepatic artery branch repeatedly until blood from the finest branches of the portal vein and hepatic artery flow into ‘sinusoids’. These are lined with endothelial cells and are similar to capillaries in other tissues. The sinusoids drain into fine central veins which link up with other central veins before draining into the hepatic vein. The arterial and venous supplies are separate until they mix within the sinusoid.

Hepatocytes are arranged in thin layers (hepatic plates) as shown in Figure 1.2, giving a maximum surface area for exchange of substances with the blood. The hepatocytes are separated from the blood by the ‘space of Disse’ and the endothelial cells. The space of Disse contains microvilli projecting from the hepatocytes, HSCs and a low-density extracellular matrix (ECM). HSCs encircle the sinusoid within the space of Disse.

Liver endothelial cells have many holes (fenestrations), not possessed by other endothelial cells, which enable large molecules such as albumin to pass between the blood and the space of Disse. The low-density ECM in the space of Disse


Figure 1.2 The microanatomy of the liver cell plate, showing the relationship of the four non-parenchymal cells to the hepatocytes. Kupffer cells and pit cells lie within the sinusoidal lumen. Endothelial cells separate the sinusoidal lumen from the space of Disse. Stellate cells (lipocytes) lie within the space of Disse. Reproduced from Bacon et al. (2006) with permission from Elsevier.
allows molecules to pass freely but still supports the overall structure, and the hepatocyte microvilli provide a large surface area for passage of substances into and out of the hepatocytes.

Bile canaliculi are minute channels between adjacent hepatocytes that deliver bile into bile ductules in the portal area. The bile is kept apart from the blood and the space of Disse.

Many organs have a ‘functional unit’ that is defined as the smallest section of the organ that can carry out the basic function of that organ. An example is the nephron – the functional unit of the kidney. The functional unit of the liver is not self-apparent, and has been extensively debated. The liver can be imagined as divided into ‘classical’ lobules with a central venule in the middle, and in some of the corners of the polygon (typically drawn as a hexagon) surrounding this is a ‘portal triad’ containing branches of the portal vein and the hepatic artery, and a bile duct.

Rappaport et al. (1954) also defined a functional unit for the liver, the ‘liver acinus’, a volume of liver between a distributory branch of the portal vein and the central vein(s) that it drains into. It is further divided into three zones: zone 1 nearest the liver vascular inflow; zone 3 nearest the central venule where blood leaves the hepatocytes; and zone 2 between them (Figure 1.3). Zone 3 suffers the most from injury whether viral, toxic or anoxic (Sherlock and Dooley, 2002). A slightly different concept was later proposed by Matsumoto and Kawakami (1982). In both concepts the different areas receive different levels of oxygenation and substrates (such as glucose) as blood flows through the liver. They also differ to some extent in the metabolic functions they carry out (Kietzmann and Jungermann, 1997).

Figure 1.3  Hepatic acinus. Reproduced from Bacon et al. (2006) with permission from Elsevier. (HV = hepatic venule; HA = hepatic artery; TPV = portal vein; BD = bile duct).
Carbohydrate metabolism

The liver has a central role in the maintenance of blood glucose levels. It supplies glucose when blood levels are low and takes it up when supply is plentiful.

Glucose is stored within hepatocytes by converting it to glycogen (glycogenesis). Glycogen is a branched polymer, essentially a long string of glucose molecules joined together, with one chain sometimes dividing into two. Storing glucose within the cell as glucose molecules would significantly alter osmotic pressure within the cell leading to problems with intracellular–extracellular fluid balance. Hepatocytes can store up to 5–8% of their weight as glycogen; the adult liver stores on average about 80 g.

Glycogen is readily broken down into glucose (glycogenolysis), so is a good source of energy for sudden, strenuous activity. Glycogenolysis involves enzymes ‘chipping off’ glucose molecules from the glycogen and can be triggered by glucagon (produced in response to a low blood sugar) and adrenaline.

During fasting around 11% of glycogen stores are used each hour. After a few hours the liver increasingly turns to gluconeogenesis to supply glucose. This is the production of new glucose from non-carbohydrates, mainly lactate, amino acids and glycerol (not fatty acids). The supply of glucose shifts between directly supplied dietary glucose, glucose from glycogenesis and glucose from gluconeogenesis over the day (Figure 1.4).

Glucose metabolism is controlled by hormones as described, but there is increasing recognition that it is also controlled by genes cycling in a circadian rhythm (Rudic et al., 2004; Pititsyn et al., 2006). The liver has its own circadian rhythm that is synchronised with the ‘master’ circadian rhythm clock in the suprachiasmatic nucleus in the brain by signals such as glucocorticoid release (Reddy et al., 2007).

Muscle cells can also store glycogen (up to 1–3% of their weight). The much larger total mass of muscle can store more glycogen than liver. However muscle
cells do not possess the enzyme necessary to enable release of glucose from the cell into the blood. A small amount of gluconeogenesis takes place in the kidneys.

Fat metabolism

The liver plays an essential role in the digestion of dietary fats. It produces bile salts which are essential for the emulsification of fats within the gut. Almost all fats in the diet are absorbed from the intestines into the lymphatic system. The fats are broken down into monoglycerides and fatty acids that are absorbed into the intestinal epithelial cells and then enter the lymphatic system as tiny, dispersed particles called chylomicrons.

Functions of the liver in the metabolism of fat can be summarised as:

- Oxidation of fatty acids to supply energy
- Synthesis of cholesterol, phospholipids and lipoproteins
- Synthesis of fats from proteins and carbohydrates

Fatty acids typically contain 16 carbon atoms. To use them for energy the liver splits them into acetyl coA (two carbon atoms long) by beta-oxidation. The acetyl coA can enter the tricarboxylic acid cycle and be used directly as an energy source. Beta-oxidation can take place in all cells in the body, but the liver is particularly efficient at it and can produce more than it needs. The excess acetyl coA is converted into the very soluble acetoacetic acid which can pass easily into other cells where it is converted back into acetyl CoA and used for energy.

Some of the acetoacetic acid is converted into beta-hydroxybutyric acid and very small amounts into acetone. These can also pass easily into other cells around the body where they can be used for energy. Their blood concentrations are normally very low. However in starvation and diabetic ketoacidosis the concentrations of these three substances can rise to many times normal and the presence of acetoacetic acid can be detected in the urine (usually called ketones on the dipstick). This implies that much fat is being metabolised to provide energy.

If an excess of carbohydrates and proteins are presented to the liver they will be converted into fatty acids. Some will be stored in the liver (5% of liver weight is due to fat), the rest will be released into the blood and taken up by adipocytes and stored as fat. Adipocytes can synthesise minute quantities of fat from carbohydrate but the majority takes place in the liver. Fatty acids are continually cycling between the liver and adipose tissue, half the fatty acid in the plasma is replaced every 2–3 minutes.

Protein metabolism

Dietary proteins are digested and broken down into amino acids over several hours. These enter the blood stream and are rapidly absorbed into cells all over the body. Subsequently there is a constant interchange and equilibrium between
plasma amino acids, plasma proteins, amino acids in cells and cellular proteins. Plasma proteins can be rapidly degraded within the reticuloendothelial system. Liver and other cells can rapidly form and degrade proteins. Overall, in health, there is a constant state of equilibrium.

Amino acids can also be used for energy after removing nitrogen, but this leads to the release of the highly toxic substance ammonia (NH₃). The liver removes ammonia from the blood and converts it to urea (and a minor amount into glutamine). The biochemical process for doing this is known as the urea cycle. Some of the chemical steps in the urea cycle are present in other tissues and are important for removal of ammonia from those tissues, but the complete cycle is present only in the liver. Elevated levels of serum ammonia are seen in both acute and chronic liver disease. In acute liver failure this is linked to the impairment in the conversion of ammonia to urea due to hepatic necrosis. In chronic liver disease the rate of urea synthesis is markedly reduced, which is attributed to several factors such as portosystemic shunting and increased intestinal production (Luxon, 2006). Hyperammonaemia has been linked to hepatic encephalopathy and is discussed in depth in Chapter 6.

**Protein synthesis**

The liver can synthesise about 48 g of protein per day. Albumin is the major protein synthesised (approximately 12–15 g) and an important constituent of blood as it is the predominant cause of the oncotic pressure of blood. Albumin also acts as an acid–base buffer and binds drugs and electrolytes in the blood. Its synthesis by the liver is affected by nutritional status, and the blood albumin level is sometimes used as an indicator of nutritional status.

The acute phase response is a non-specific response to tissue injury or infection. This involves a change in the concentration of a number of proteins in the blood known as acute phase reactants. These are defined by having a change in concentration of larger than or equal to 25% by 1 week after the initial injury or infection. Some proteins increase: these positive acute phase reactants are predominantly synthesised by the liver and include alpha-1 antitrypsin, coagulation proteins and C-reactive protein (CRP). Substances whose concentration decreases as part of the acute phase response are known as negative acute phase reactants. These include albumin and transferrin.

CRP is a binding protein (opsonin) that binds to macromolecules released by infective agents or damaged tissue and enhances their phagocytosis. The blood level of CRP is often used as a marker of infection – although it can be raised as part of a general inflammatory response with no infection present.

**Clotting factors**

The liver is the site of synthesis of all clotting factors and their inhibitors (Amitrano et al., 2002). The prothrombin time (PT) is an index of clotting function, which
depends on the production of clotting factors in the liver and can be used as a measure of the liver’s synthetic ability. Liver failure will lead to a prolongation of the PT with the degree of prolongation related to the severity of liver failure. Liver disease can also cause problems with haemostasis in other ways such as causing a drop in platelet numbers and function.

Vitamin K is needed by the liver for the normal production of clotting factors II, VII, IX and X. Vitamin K deficiency will cause a reduction in the levels of these factors (which will be reflected in a prolonged PT). Liver disease does not directly cause a vitamin K deficiency, but vitamin K is a fat-soluble vitamin that needs biliary salts for its absorption. Thus cholestasis can cause reduced absorption of vitamin K.

**Storage of vitamins/iron**

The vitamin stored in greatest quantity in the liver is vitamin A (in hepatic stellate cells), but large quantities of vitamins D and B₁₂ are normally stored as well. Sufficient quantities of vitamin A can be stored to prevent deficiency for as long as 10 months, vitamin D for 3–4 months, and vitamin B₁₂ for over 1 year. The liver is also involved in storage of iron and copper.

**Blood cleansing**

An important non-metabolic function of the liver is the ‘cleansing’ of blood leaving the splanchnic circulation by Kupffer cells. The gut is heavily populated by large numbers of a multiplicity of bacteria and there is a potential for bacteria to be able to leave the gut and enter the vascular system. Any bacteria in the portal vein will pass into the liver and should be phagocytosed by Kupffer cells.

**Processing of drugs and other xenobiotics**

Xenobiotics are substances that are foreign to the body (e.g. drugs). They are potentially toxic and systems have evolved to eliminate them from the body. The most obvious is urinary excretion, though some substances are secreted into bile by the liver (but many are then reabsorbed from the intestine).

Most elimination takes place via the kidneys. These can efficiently eliminate water-soluble xenobiotics but less so lipophilic xenobiotics. The body first metabolises these to less lipophilic substances that can be more easily eliminated by the kidneys. This takes place predominantly in the liver.

Xenobiotic metabolism in the liver involves two kinds of biochemical reaction known as phase I and phase II reactions which often take place sequentially. Phase
I reactions generally involve a family of enzymes known as the hepatic cytochrome P450 system. Phase II reactions involve a chemical reaction in which a large molecule is added to the drug. Again this makes the drug more water soluble and easier to excrete from the body.

Enzymes are often thought of as being specific for a single substrate, but P450 enzymes may metabolise many different drugs. They can be clinically important in a number of ways. When multiple drugs are administered concurrently they can ‘compete’ for metabolism by the same enzyme and inhibit each other’s metabolism. An example is cardiac arrhythmias, or central nervous system (CNS) seizures, caused by an increased theophylline level when it is given with erythromycin. In enzyme induction the normal level of an enzyme is increased and drugs metabolised by that enzyme are metabolised faster than normal. Enzyme induction can be produced by some drugs, foods, alcohol and smoking. The levels of particular P450 enzymes can also be affected by genetics, leading to individual and racial differences in metabolism of drugs.

The portal vein delivers blood from the gut directly to the liver, enterally ingested substances are exposed to the enzymes in the liver before they get to the rest of the body. This is refered to as first-pass metabolism. Some drugs are metabolised so efficiently by the liver that little actually gets through to the rest of the body. The liver also plays a major role in the elimination of hormones and activated clotting factors.

**Exocrine function**

The liver also has an exocrine function. About 500 mL of bile is secreted each day, consisting of water, inorganic electrolytes and organic solutes such as bile salts. Bile salts are the sodium and potassium salts of bile acids and have a detergent-like effect in the gut lumen, emulsifying dietary fat to aid its digestion. Bile secretion is an excretory route for bile pigments, cholesterol, steroids, heavy metals and some drugs. Patients who have jaundice due to intra- or extrahepatic obstruction of the bile duct usually have raised blood levels of cholesterol and alkaline phosphatase. Bile is an alkaline solution containing bicarbonate (secreted by both hepatocytes and biliary duct cells) and aids in the neutralisation of acid chyme entering the duodenum from the stomach.

Two major primary bile acids are synthesised in the liver from cholesterol at the rate of 0.5 g/day (cholic acid and chenodeoxycholic acid). Secondary bile acids are produced within the gut by the action of bacteria on primary bile acids. Cholic acid is converted to deoxycholic acid and chenodeoxycholic acid to lithocholic acid.

Bile is continuously secreted by hepatocytes into biliary canaliculi. Between meals contraction of the sphincter of Oddi causes bile to accumulate in the gall-bladder where the bile salts are concentrated. The most important trigger for relaxation of the sphincter of Oddi and release of bile is return of bile salts to the liver from the splanchnic circulation.
The majority of bile salts (90–95%) are reabsorbed from the small intestine, most from the terminal ileum (meaning that a large proportion remains throughout the small intestine to promote fat absorption). The remaining bile salts enter the colon where more are reabsorbed. Those lost in the stool are replaced by synthesis in the liver. The total pool of bile salts (approx 2.5 g) is recycled up to six to eight times in a day.

Bilirubin

The bile pigments bilirubin and biliverdin are produced from substances containing haem such as haemoglobin. Red blood cells have a life span of around 110 days, with aged red cells being destroyed mainly by the reticuloendothelial cells of spleen, lymph nodes, bone marrow and liver. The haemoglobin is first metabolised by the enzyme heme oxygenase into biliverdin, and then converted to bilirubin. Bilirubin is not soluble in water and in the blood it is transported attached to serum albumin (this is referred to as unconjugated bilirubin).

In the liver the bilirubin has two glucuronate groups attached (conjugated) to it. This conjugated bilirubin is then excreted into the bile canaliculi. Bacteria in the gut convert bilirubin to stercobilinogen, which then forms stercobilin. Most stercobilin is excreted in the faeces and is responsible for the colour of faeces. Some stercobilin is reabsorbed from the gut and can then be re-excreted by either the liver or kidneys.

Liver cirrhosis/fibrosis

Liver capacity for regeneration following a single insult is excellent. A hepactectomy may involve the removal of two thirds of the liver, but the remaining hepatocytes can reproliferate to restore the mass of the organ within days to weeks (Guangsheng and Steer, 2006). However chronic or repetitive injury results in fibrosis, which can develop into cirrhosis (Figure 1.5, Plate 1). Cirrhosis represents the end stage of many different liver disorders, such as alcoholism and chronic hepatitis. Fibrosis and cirrhosis are part of a continuous disease spectrum.

Liver fibrosis is characterised by the production of excess extracellular material in the space of Disse and a loss of fenestrations from the sinusoidal endothelial cells. This is referred to as capillarisation. The microvilli of the hepatocytes disappear and overall there is a reduction in the ability to exchange substances between the blood and hepatocytes.

HSCs are the key cells in fibrosis. Inflammatory cells move into injured areas of liver and these, together with damaged and regenerating hepatocytes, release signalling molecules (cytokines) which ‘activate’ the HSCs. Activated HSCs
proliferate and secrete fibrillar collagens producing an increase in extracellular matrix in the space of Disse. Other changes that take place in HSCs when they become activated are the loss of the retinoid (vitamin A) droplets and the production of smooth muscle actin.

Cirrhosis is characterised by diffuse alteration of the normal liver architecture with nodules of regenerating hepatocytes surrounded by fibrous bands. Blood can be shunted along ‘bypass’ vessels avoiding hepatocytes, and so do not take part in the normal exchange of substances between blood and hepatocyte. There is also interruption of biliary channels which can prevent normal drainage of bile produced by the hepatocytes. Cirrhosis results from necrosis and then nodular regrowth of hepatocytes. It is a diffuse problem, not local to any part of the liver, and the ultimate pattern of damage is much the same regardless of cause. The Child-Pugh score is used to assess the prognosis and appropriate treatment in cirrhosis and is demonstrated in Table 1.1.

Table 1.1 The Child-Pugh score. Adapted from Bacon et al. (2006).

<table>
<thead>
<tr>
<th>Clinical and biochemical assessment criteria</th>
<th>Points scored for increasing abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy (grade)</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>&gt;35</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
</tr>
<tr>
<td>Bilirubin (μmol/L)</td>
<td>&lt;34</td>
</tr>
<tr>
<td>Bilirubin (for primary biliary cirrhosis) (μmol/L)</td>
<td>&lt;69</td>
</tr>
<tr>
<td>Top score</td>
<td>Grade A</td>
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<tr>
<td>Survival in chronic liver disease at 1 year</td>
<td>Grade A</td>
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84%  62%  42%
Table 1.2  Complications associated with liver cirrhosis.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Portal hypertension</strong></td>
</tr>
<tr>
<td>Ascites</td>
</tr>
<tr>
<td>Varices</td>
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<tr>
<td>Oesophagus</td>
</tr>
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<td>Stomach</td>
</tr>
<tr>
<td>Rectum (haemorrhoids)</td>
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<td>Abdominal vein distension (caput medusae)</td>
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<td>Splenomegaly</td>
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<tr>
<td>Anaemia</td>
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<td>Thrombocytopenia</td>
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<tr>
<td>Leucopenia</td>
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<tr>
<td>Portopulmonary shunts</td>
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<tr>
<td>Decreased blood oxygenation</td>
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<tr>
<td><strong>Liver failure</strong></td>
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<tr>
<td>Deranged clotting</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
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<tr>
<td>Elevated bilirubin</td>
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<tr>
<td>Hepatorenal failure</td>
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<tr>
<td>Hepatic encephalopathy</td>
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<td>Immune system dysfunction</td>
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<td>Hypoalbuminaemia</td>
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<td>Oedema</td>
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<tr>
<td>Increased skin pigmentation</td>
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<tr>
<td>Feter hepaticus</td>
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<td>Decreased hormone metabolism</td>
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<tr>
<td>Gynaecomastia</td>
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<td>Testicular atrophy</td>
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<td>Loss of body hair</td>
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<tr>
<td>Spider angiomhas</td>
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<tr>
<td>Palmar erythema</td>
</tr>
<tr>
<td>Menstrual dysfunction</td>
</tr>
<tr>
<td>Increased antidiuretic hormone and aldosterone</td>
</tr>
<tr>
<td><strong>Hepatocellular carcinoma</strong></td>
</tr>
</tbody>
</table>

Cirrhosis can be classified as micronodular or macronodular. In micronodular cirrhosis the regenerating nodules are less than 3 mm in diameter and the fibrous bands separating the nodules are usually thin. In macronodular cirrhosis the nodules are over 3 mm in diameter. There is a tendency for nodules to increase in size over time, and micronodular cirrhosis can become macronodular. Cirrhosis is often classified by its presumed cause, histologically; early stages may show evidence of the cause, but this cannot be determined from the histology later on.

Many health problems are caused by cirrhosis (Table 1.2); some are the result of the development of portal hypertension – an increase in the blood pressure in the portal vein. The cause of this is complex and not completely understood. The disruption of vascular channels caused by alteration of normal liver vascular architecture predisposes to this pressure increase. Additionally, activated HSCs produce smooth muscle actin within the cell and also become sensitive to the powerful vasoconstrictor endothelin. Liver injury also results in a reduction in production
of the vasodilator nitric oxide which would normally oppose the action of the endothelin (Groszmann et al., 2001). This results in the contraction of the HSCs which increase sinusoidal resistance and contribute to the development of portal hypertension.

Portal hypertension leads to further problems. Portosystemic shunts develop as the increased pressure leads to the development of collateral channels between the portal vein and systemic veins. One manifestation of this is varices, thin-walled varicosities that either form in the oesophagus, stomach or rectum. These are prone to rupture which can lead to fatal bleeding (see Chapter 4). Clotting problems caused by deranged liver function can make this complication even more difficult to deal with which is described further in Chapter 4.

Ascites refers to the development of larger than normal quantities of fluid in the peritoneal cavity; patients with severe ascites may have large volumes of fluid with consequent problems such as abdominal discomfort and dyspnoea. The development of ascites is still not completely understood, however Chapter 5 examines the proposed hypothesis. Hepatic encephalopathy is another manifestation of advanced liver disease. Again the pathogenesis is not fully understood, but is thought to be related to the inability of the liver to clear toxic substances from the blood. This is discussed in more depth in Chapter 6.

Fibrosis and cirrhosis can be asymptomatic; the majority of hepatic functional capacity must be lost before hepatic failure ensues. Clinically this is important as many patients do not present until after they have severe structural injury to their liver. Liver fibrosis and cirrhosis have traditionally been viewed as irreversible; however there is evidence now that fibrosis at least is reversible under some conditions (Friedman, 2003). Iredale (2003) looks forward to a future where fibrosis and cirrhosis are treatable.

Chapter summary

This chapter has reviewed the more important aspects of liver anatomy and physiology. It has shown how the normal structure of the liver superbly supports its physiological functions, and how the development of an abnormal structure in cirrhosis is detrimental. An understanding of the functions of the liver will help the health care professional appreciate how liver disease can affect people in so many different ways, and can improve the quality of care given to people with liver disease.

References

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