The aminotransferases are very sensitive indicators of hepatic inflammation and necrosis. Damage to the hepatocyte results in release of the enzymes into the circulation.

Markedly elevated levels (>1,000 U/L) usually indicate viral hepatitis, severe drug or toxic reactions or hepatic ischaemia. However, the level of elevation is not a reliable marker of hepatic dysfunction or damage.

ALT is found primarily in the liver and so is a more specific marker of hepatocellular damage. It is, however, found in other tissues and may be elevated in muscular damage, acute myocardial infarction and renal infarction. Haemolysis is associated with falsely elevated levels.
AST is an enzyme found primarily in the liver, heart, kidney, pancreas and muscles. Elevated levels are seen in cases of hepatocellular damage, acute myocardial infarction (in this case all other liver function tests remain normal), musculoskeletal diseases (e.g. polymyositis, muscular dystrophy, muscle crush injury), intestinal injury, haemolysis, hypothyroidism, pulmonary embolism and necrotic tumours. Vitamin B_6 deficiency and pregnancy are two instances where the enzyme may be decreased.

Bilirubin

Total ..... <20 micromol/L

Direct..... <7 micromol/L

Bilirubin is a breakdown product of haemoglobin that is conjugated and eliminated by the liver. Total bilirubin comprises unconjugated, conjugated and delta bilirubin, whereas direct bilirubin comprises conjugated and delta bilirubin.

Jaundice is usually not detectable until bilirubin is >50 micromol/L. The three main reasons for the elevation of plasma bilirubin are:

- intravascular haemolysis
- failure of conjugation mechanisms within the hepatocytes
- obstruction in the biliary system.

The different causes of jaundice are associated with different patterns of biochemical abnormalities, as shown in Table D.2 below.

Gamma glutamyltransferase (GGT)

Female .....<30 U/L

Male .....<50 U/L

Gamma glutamyltransferase (glutamyltranspeptidase) is a microsomal enzyme believed to be involved in the transport of amino acids and peptides into cells and in glutathione metabolism. It is mainly found in liver cells. Its main clinical applications are as a sensitive indicator of early liver disease or alcoholism. Increased levels occur following microsomal induction, particularly by alcohol, herbal remedies and drugs such as some anticonvulsants.[9]

Metabolic function tests

Ammonium

Adult, plasma ..... <50 micromol/L

Infant.....64–107 micromol/L

Serum ammonia may be elevated in patients with acute or chronic liver disease, resulting in hepatocellular damage. In patients with cirrhosis, portal shunting of blood results in ammonia from the gut bypassing the liver, resulting in hyperammonaemia and hepatic encephalopathy.[11]

Serum ammonia may also be elevated as a result of genetic defects in urea formation. In the most severe

Table D.2 Biochemical abnormalities associated with different types of jaundice

Jaundice type	Causes	Bilirubin	Alkaline phosphatase	AST, ALT
Pre-hepatic	• Haemolysis • Hereditary uptake disorders	↑ (unconjugated)	Normal	Normal
Intra-hepatic damage	• Hepatitis • Drugs	↑ (mostly conjugated)	Normal—↑	↑↑
Intra-hepatic cholestasis	• Viral hepatitis • Biliary cirrhosis • Drugs • Metastases • Cysts	↑ (mostly conjugated)	↑	Normal—↑
Post-hepatic	• Gallstones in common bile duct • Compression of common bile duct	Normal—↑ (conjugated)	↑↑	Normal—↑

Note: AST = aspartate aminotransferase; ALT = alanine aminotransferase.