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Liver Function and Biochemistry

Biochemistry

Functions of the liver, bilirubin metabolism, bile pigments, detoxification, protein synthesis, carbohydrate and lipid metabolism and liver function tests.

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CHAPTER 16

Liver Function and Biochemistry

Metabolic functions, bilirubin, bile pigments, detoxification and liver tests

1. Biochemical functions of the liver

The liver is a major metabolic organ receiving blood from the portal vein and hepatic artery. Hepatocytes process nutrients, synthesize proteins, produce bile, metabolize drugs and help maintain blood glucose and lipid homeostasis.

Function	Biochemical role
Carbohydrate metabolism	Glycogenesis, glycogenolysis and gluconeogenesis
Protein metabolism	Albumin and most clotting factor synthesis, transamination and urea cycle
Lipid metabolism	Fatty acid oxidation and synthesis, ketogenesis, cholesterol and lipoprotein synthesis
Bile production	Bile salts facilitate digestion and absorption of fats
Storage	Glycogen, iron, vitamin A and vitamin B12, among other nutrients
Detoxification	Biotransformation and excretion of endogenous and foreign compounds

2. Bilirubin and bile pigment metabolism

1. 1. Macrophages degrade haem from ageing red cells; haem oxygenase forms biliverdin, iron and carbon monoxide.
2. 2. Biliverdin reductase forms unconjugated bilirubin, which is poorly water-soluble and transported bound to albumin.
3. 3. Hepatocytes take up bilirubin; UGT1A1 conjugates it with glucuronic acid to increase water solubility.
4. 4. Conjugated bilirubin is secreted into bile and enters the intestine.
5. 5. Gut bacteria form urobilinogen. Most is converted to stool pigments such as stercobilin; some is reabsorbed and a small amount excreted in urine as urobilin.

3. Types of jaundice

Pattern	Main mechanism	Typical findings
Prehepatic (haemolytic)	Excess bilirubin production	Predominantly unconjugated bilirubin; urine bilirubin usually absent
Hepatocellular	Impaired uptake, conjugation or secretion	Mixed bilirubin elevation possible; ALT/AST often elevated
Cholestatic / obstructive	Reduced bile flow	Conjugated bilirubin and ALP/GGT often elevated; dark urine, pale stools possible

Jaundice is a sign, not a diagnosis. Neonatal jaundice has age-specific assessment and treatment thresholds. Unconjugated bilirubin can be neurotoxic in newborns at sufficiently high concentrations.

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4. Detoxification and drug metabolism

Phase I reactions include oxidation, reduction and hydrolysis; cytochrome P450 enzymes are important. Phase II conjugation reactions include glucuronidation, sulfation and glutathione conjugation. Transporters help excrete metabolites into bile or blood. Biotransformation may also activate prodrugs or generate toxic metabolites. Glutathione helps detoxify reactive compounds; paracetamol overdose may overwhelm protective pathways and requires urgent treatment.

5. Liver function tests (LFTs)

Test	Illustrative adult range	Interpretation
ALT	~7-56 U/L	Hepatocellular injury; relatively liver-enriched
AST	~10-40 U/L	Liver or muscle injury
ALP	~40-130 U/L	Cholestasis or increased bone activity
GGT	Lab/sex-specific	Supports hepatobiliary origin of raised ALP
Total bilirubin	0.2-1.2 mg/dL	Production, conjugation or excretion abnormality
Albumin	3.5-5.0 g/dL	Synthetic function and other systemic factors
PT / INR	INR ~0.8-1.2 off anticoagulants	Clotting factor synthesis, vitamin K status and anticoagulant effects

ALT and AST primarily reflect injury rather than liver function. Albumin and PT/INR can help assess synthesis but are affected by other factors. A normal enzyme level does not exclude chronic liver disease. Interpret patterns and trends using local laboratory ranges.

6. Liver enzyme patterns and synthetic function

Pattern	Typical findings
Hepatocellular injury	ALT and AST rise disproportionately to ALP
Cholestatic injury	ALP rises disproportionately; GGT can support hepatic origin
Impaired synthetic function	Prolonged PT/INR and/or reduced albumin, with other causes considered
Altered bilirubin handling	Raised total bilirubin; direct and indirect fractions aid assessment

The magnitude of a transaminase elevation does not necessarily measure remaining liver functional capacity. INR may also be influenced by anticoagulants and vitamin K deficiency.

7. Nursing applications

Assess jaundice, pruritus, abdominal symptoms, bleeding, nutrition and mental status. Record medication and alcohol history respectfully; observe for confusion or reduced consciousness. Obtain specimens correctly, report critical results and support prescribed care. Suspected acute liver failure with encephalopathy or coagulopathy requires urgent escalation.

8. Important Examination Questions

Long Answer Questions

1. 1. Discuss liver biochemical functions, bilirubin metabolism and LFTs.
2. 2. Explain bilirubin metabolism and the biochemical basis of jaundice.
3. 3. Describe liver function tests and distinguish hepatocellular and cholestatic injury.

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Short Answer Questions

1. 1. Write a short note on Types of jaundice.
2. 2. Write a short note on phase I/II reactions.
3. 3. Write a short note on ALT versus ALP.

Very Short Answer Questions

1. 1. Which enzyme conjugates bilirubin? - UGT1A1.
2. 2. Which bile pigment is formed first from haem breakdown? - Biliverdin.
3. 3. Which liver protein supports plasma oncotic pressure? - Albumin.
4. 4. Which test reflects coagulation factor function and can indicate impaired hepatic synthesis? - PT/INR, interpreted in context.

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Additional objective question

Which enzyme conjugates bilirubin? - UGT1A1.

9. Quick Revision

- The liver synthesizes most plasma proteins and urea.
- Unconjugated bilirubin travels bound to albumin; conjugated bilirubin is water soluble.
- ALT and AST mark injury rather than directly measuring synthetic function.
- ALP and GGT help identify cholestatic patterns.

Conclusion

Liver biochemistry explains nutrient metabolism, detoxification, bilirubin excretion and laboratory patterns of hepatic injury and dysfunction.

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Practice questions

Choose one best answer. The answer key and explanations follow the questions.

1. Which enzyme conjugates bilirubin with glucuronic acid in hepatocytes?

A. Haem oxygenase
B. Biliverdin reductase
C. Amylase
D. UGT1A1

2. Which liver-test pattern is typically cholestatic?

A. ALT rises disproportionately to ALP
B. ALP rises disproportionately, with GGT supporting hepatic origin
C. Isolated reduction in albumin with normal enzymes
D. Isolated unconjugated bilirubin elevation

3. How is unconjugated bilirubin transported in blood?

A. Bound to albumin
B. Bound to haemoglobin within platelets
C. Freely dissolved without a carrier
D. Stored inside chylomicrons

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Answer key and explanations

1. D - UGT1A1

UGT1A1 conjugation increases bilirubin water solubility.

2. B - ALP rises disproportionately, with GGT supporting hepatic origin

Disproportionate ALP elevation is a cholestatic pattern; GGT helps support hepatic origin.

3. A - Bound to albumin

Poorly water-soluble unconjugated bilirubin travels bound to albumin.

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