Liver Function Tests And Interpretation

The liver performs different kinds of biochemical, synthetic and excretory functions, so no single biochemical test can detect the global functions of the liver.

LFTs comprise a panel of blood tests used to assess various aspects of liver function, including hepatocellular integrity, biliary excretion, and synthetic capacity. Due to the liver's multifunctional role, no single test can comprehensively evaluate its function.

I. Clinical Significance of Liver Function Tests

Uses

- **Screening:** Non-invasive, sensitive tests for detecting liver dysfunction.
- **Pattern Recognition:** Helps differentiate hepatocellular, cholestatic, or infiltrative liver diseases.
- **Disease Monitoring:** Assesses disease severity and progression in conditions such as:
    - Primary biliary cholangitis (PBC)
    - Autoimmune hepatitis
- **Therapy Monitoring:** Evaluates response to treatment and guides management.

Limitations

- **Sensitivity:** LFTs may remain normal in early or mild liver diseases.
- **Specificity:** Most LFTs are not disease-specific.
- **Extrahepatic Influences:** Elevations may occur due to non-hepatic conditions (e.g., hemolysis, muscle injury).
- **Serum Bile Acids:** More liver-specific, yet less commonly used in routine panels.

II. Classification of Liver Function Tests

A. Tests of Excretion and Detoxification

1. **Serum Bilirubin (Total, Direct, Indirect)**
2. **Urine Bilirubin**
3. **Urine Urobilinogen**

B. Tests of Hepatocellular Injury

1. **Aminotransferases (AST, ALT)**
2. **Other Cytosolic Enzymes** (e.g., LDH, SDH)

C. Tests of Synthetic Function

1. **Serum Albumin**

2. **Prothrombin Time (INR)**

D. Tests of Cholestasis

1. **Alkaline Phosphatase (ALP)**
2. **Gamma-Glutamyl Transferase (GGT)**

III. Detailed Review of Key Liver Tests

A. Bilirubin Metabolism

Bilirubin is a breakdown product of hemoglobin. The Van den Bergh reaction distinguishes:

- **Direct (Conjugated) Bilirubin** : Water-soluble; excreted in bile.
- **Indirect (Unconjugated) Bilirubin** : Albumin-bound; not excreted in urine.

Type	Normal Range	Clinical Significance
Total Bilirubin	0.2–1.2 mg/dL (2–20 µmol/L)	General liver health
Direct Bilirubin	<0.3 mg/dL (5.1 µmol/L)	Conjugation & biliary obstruction
Indirect Bilirubin	Calculated (Total – Direct)	Hemolysis, Gilbert's Syndrome

Prognostic Value:

- Deep jaundice in acute liver failure correlates with higher mortality.
- Decreased by agents like salicylates, sulfonamides, and free fatty acids.

B. Urine Bilirubin

- Only conjugated bilirubin appears in urine (due to renal filtration).
- Indicates hepatobiliary disease.
- May be detected even with normal serum bilirubin.

C. Urobilinogen in Urine

- Formed in the intestine; reabsorbed and excreted in urine.
- **Elevated in:** Hemolysis, early hepatitis, alcoholic liver disease.
- **Decreased in:** Cholestasis or obstructive jaundice.

Detection: Ehrlich’s aldehyde reaction (purple color).

D. Aminotransferases (AST, ALT)

Enzyme	Tissue Source	Localization	Clinical Use
ALT	Liver-specific	Cytosol	More liver-specific
AST	Liver, heart, muscle, brain	Cytosol & mitochondria	Also elevated in extrahepatic diseases

Elevation Patterns:

- **Severe (>20x normal; >1000 U/L)** : Acute viral hepatitis, toxins, ischemia.
- **Moderate (3–20x)** : Chronic hepatitis, autoimmune liver disease, alcoholic hepatitis.
- **Mild (1–3x)** : NASH, cirrhosis, fatty liver, myositis, strenuous exercise.

AST/ALT Ratio

- **>2:** Alcoholic liver disease (due to pyridoxine deficiency reducing ALT synthesis).
- **<1:** Viral hepatitis, NASH.
- **>1:** Suggests progression to cirrhosis in chronic liver disease.

Special Notes:

- AST elevations may reflect mitochondrial injury.
- Low aminotransferase levels: Seen in long-term dialysis, uremia.

E. Alkaline Phosphatase (ALP)

- **Found in:** Liver (bile canaliculi), bone, placenta, intestine.
- **Elevation in:** Cholestasis, bone disease, pregnancy, infiltrative liver diseases (e.g., granulomas, metastases).
- **Normal Variability:** Elevated during growth spurts (children/adolescents), increases with age.

Preanalytical Considerations:

- Use unhemolyzed serum.
- Avoid citrate/EDTA; they chelate zinc and inhibit ALP activity.

Summary Table: Diagnostic Use of Liver Function Tests

Parameter	Primary Role	Elevated In	Decreased In
ALT	Hepatocellular injury	Hepatitis, NASH	ESRD, pyridoxine deficiency
AST	Mitochondrial damage	Alcoholic hepatitis	Uremia
ALP	Cholestasis marker	Biliary obstruction, bone disease	—
Bilirubin	Excretory function	Hemolysis, obstruction	Drugs, binding changes
Albumin	Synthetic function	—	Cirrhosis, malnutrition
PT/INR	Coagulation synthesis	Liver failure	—