

# Abnormal Liver Function Tests

[Disclaimer](#)

## Contents

Disclaimer.....	1
Red Flags.....	2
<b>Background.....</b>	<b>2</b>
About abnormal liver function tests (LFT's).....	2
<b>Assessment.....</b>	<b>2</b>
 Practice Point - Avoid unnecessary tests.....	2
Risk factors.....	2
Prescribed and over the counter medications.....	3
Complementary and herbal treatments.....	3
Acute hepatitis.....	3
Signs of cirrhosis.....	3
Acute liver failure.....	4
Isolated GGT elevation.....	4
Isolated raised ALP.....	4
Isolated raised bilirubin.....	5
Cholestatic pattern.....	6
Hepatocellular pattern.....	6
Obstetric hepatic conditions.....	7
<b>Management.....</b>	<b>8</b>
Serious hepatic complications.....	8
Confirmed or suspected cause.....	8
Investigations for less common hepatic causes.....	9
<b>Referral.....</b>	<b>9</b>
<b>Information.....</b>	<b>10</b>
For health professionals.....	10
For patients.....	10

## Red Flags

- Increased INR, low platelets, or reduced albumin with abnormal LFTs

## Background

### About abnormal liver function tests (LFTs)

- LFTs include bilirubin, alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), and gamma glutamyl transpeptidase (GGT). In addition, international normalised ratio (INR), prothrombin time (PT), and albumin can be used to assess synthetic liver function.
- The degree of elevation of LFTs does not always correlate with disease severity. Mild increases may be clinically insignificant or cirrhosis may be present with normal LFTs.
- Modest ALT elevations (especially but not exclusively in obese or diabetic patients) may represent non-alcoholic fatty liver disease (NAFLD).
- Recognised patterns of liver dysfunction:
  - Relatively greater increase in ALT and AST compared to ALP and GGT (hepatocellular pattern) – indicates problem with hepatocytes.
  - Relatively greater increase in ALP and GGT compared to ALT and AST (cholestatic pattern) – suggests biliary obstruction.
  - Abnormal synthetic function is suggested by raised bilirubin, elevated INR and PT, and low albumin.
  - Portal hypertension is suggested by low platelet count progressing to pancytopenia in advanced stages.

## Assessment



### Practice Point - Avoid unnecessary tests

Routine monitoring of LFTs in asymptomatic patients is not recommended – request only if signs, symptoms, or risk factors of liver injury or disease.

#### 1. Take a history:

- Consider **risk factors** of liver injury or disease.

#### Risk factors

- Systemic conditions:
  - Infections, e.g. risk factors for viral hepatitis
  - Diabetes, obesity, hyperlipidaemia (fatty liver)
  - Autoimmune disorders
  - Haemochromatosis
  - Coeliac disease
  - Inflammatory bowel disease
  - Cancer
- Pregnancy
- Excess alcohol intake – which also increases toxicity of medications
- Illicit drug use

- Family history of Wilson's disease, haemochromatosis, alpha-1 antitrypsin deficiency, cirrhosis, or liver cancer
- Ask the patient about:
  - **prescribed and over the counter medications.**

### Prescribed and over the counter medications

- Commonly prescribed medications include statins, anticonvulsants and antibiotics, especially flucloxacillin, erythromycin, or amoxicillin + clavulanate.
- Over the counter medications including paracetamol.
- If unsure whether medication is the cause, see the Australian Medicines Handbook, or product information for the drug in your medical prescribing software.

- **complementary and herbal treatments.**

### Complementary and herbal treatments

Examples of complementary and herbal treatments potentially causing hepatotoxicity include:

- Black cohosh
- Chinese herbal medicines
- Germander
- Kava
- Noni juice
- Pennyroyal
- Usnic acid
- Green tea extract
- Weight loss or bodybuilding supplements

2. Assess for clinical features of liver disease:

- **Acute hepatitis**

### Acute hepatitis

- Fever
- Gastrointestinal symptoms – abdominal pain, anorexia, nausea, vomiting
- Icteric features, jaundice, dark urine, pale faeces – may not be present in anicteric hepatitis
- Enlarged tender liver and/or spleen
- Urticaria, and joint pains (particularly in Hepatitis A and B)

- **Cirrhosis**

### Signs of cirrhosis

- Jaundice
- Leukonychia
- Spider naevi
- Palmar erythema
- Gynaecomastia
- Muscle wasting

- *Liver enlargement*
- *Shrunken liver*
- *Hardened liver edge*
- *Ascites*

- **Acute liver failure**

### Acute liver failure

*Defined as a rapid decline in hepatic function characterised by:*

- *jaundice*
- *hepatic encephalopathy*
- *associated with coagulopathy INR > 1.5*

3. Arrange abdominal ultrasound in anyone with significantly abnormal liver enzymes.

4. Further tests:

- Arrange baseline tests for assessment of liver function.
  - FBE – low platelets in portal hypertension, pancytopenia when severe
  - Electrolytes, urea, and creatinine – low albumin indicates impaired synthetic function
  - INR and PT – indicates impaired synthetic function

If increased INR, low platelets, or reduced albumin with abnormal LFTs, consider acute or chronic severe liver disease.

- Arrange further investigations based on pattern of raised LFTs:

- **Isolated raised GGT**

### Isolated GGT elevation

- *Seldom reflects significant liver disease.*
- *Most commonly caused by excess alcohol intake or enzyme induction from medications, e.g. anticonvulsants.*
- *Usually only significant if there are other elevated LFTs.*
- *Can be seen in non-alcoholic fatty liver disease (NAFLD).*

- **Isolated raised ALP**

### Isolated raised ALP

*ALP is derived predominantly from liver and bones – isolated elevation usually suggests bone disorders.*

- *Consider causes of isolated raised ALP:*
  - *Growth in childhood and adolescence, e.g. up to 2 times higher than population average.*
  - *Pregnancy (third trimester) and postpartum.*
  - *Meals – especially fatty meals.*
  - *Older age – mild elevations in the elderly may be normal, but always consider other causes if progressively rising.*
  - *Transient hyperphosphataemia.*
  - **Bone disorders.**

#### **Bone disorders**

- *Paget's disease*

- *Primary or metastatic bone malignancy, e.g. osteosarcoma, multiple myeloma, prostate, breast, or kidney cancers*
    - *Hyperparathyroidism*
    - *Osteomalacia*
  - *If bone disorder suspected, consider requesting:*
    - *calcium, phosphate, vitamin D, parathyroid hormone (PTH).*
    - *bone scan or skeletal survey.*
    - *assessment by the appropriate specialist.*
  - *If suspected liver origin, request isoenzyme analysis:*
    - *Alkaline phosphatase is actually a group of up to 60 different isoenzymes.*
    - *Electrophoresis can be useful to determine the exact isoenzyme elevated and therefore the source.*
- **Isolated raised bilirubin**

### Isolated raised bilirubin

- *Arrange tests for evidence of haemolysis:*
  - *Conjugated:unconjugated bilirubin ratio*
  - *FBE*
  - *Peripheral smear*
  - *Reticulocyte count*
  - *Haptoglobins*
- *Suspect haemolysis if:*
  - *predominant unconjugated bilirubin.*
  - *anaemia with reticulocytosis.*
  - *reduced haptoglobins.*
- *Consider that haemolytic anaemias can be:*
  - *inherited, e.g. spherocytosis, sickle cell anaemia, pyruvate kinase deficiency, glucose-6-phosphate dehydrogenase deficiency.*
  - *acquired, e.g. microangiopathic, immune-mediated, paroxysmal nocturnal haemoglobinuria.*
- *If no evidence of haemolysis, consider **Gilbert's syndrome**.*

#### **Gilbert's syndrome**

- *Common autosomal recessive disorder affecting 3 to 8% of the population.*
- *Fluctuating, moderately elevated levels of unconjugated bilirubin – rarely > 85 micromol/L.*
- *Explain to patient that:*
  - *Gilbert's syndrome has no health implications.*
  - *no special precautions or tests are required.*
  - *they may become jaundiced when unwell from infection or other causes. This does not generally lead to adverse outcomes.*

- **Cholestatic pattern** – indicated by increase in ALP and GGT compared to ALT and AST

## Cholestatic pattern

- Consider **cholestasis causes**.

### Cholestasis causes

- *Space occupying lesion, e.g. abscess, cancer (primary or secondary)*
  - *Biliary dilation:*
    - *Stones in common bile duct*
    - *Benign strictures, e.g. post-operative*
    - *Inflammatory strictures, e.g. chronic pancreatitis, primary sclerosing cholangitis (PSC)*
  - *Hepatic infiltration:*
    - *Malignant infiltrative disorders, e.g. haematologic diseases, metastatic cancer*
    - *Benign infiltrative disorders, e.g. amyloidosis, sarcoidosis*
  - *Intrahepatic cholestasis:*
    - *Drug hepatotoxicity:*
      - *Flucloxacillin and clavulanic acid – common causes even weeks after the medication has finished*
      - *Combined oral contraceptives – may increase ALP or GGT alone*
    - *Familial and congenital causes, e.g. progressive familial intrahepatic cholestasis (PFIC)*
    - *Pregnancy*
    - *Small duct primary sclerosing cholangitis*
    - *Primary biliary cirrhosis (PBC) – a slowly progressive disease that affects middle aged women. If suspected, test for antimitochondrial antibodies (AMA).*
- *Arrange urgent abdominal ultrasound*
- **Hepatocellular pattern** – indicated by increase in ALT and AST (transaminases) compared to ALP and GGT

## Hepatocellular pattern

- Consider **hepatic causes**.

### Hepatic causes

- *Common causes:*
  - *Non-alcoholic fatty liver disease (NAFLD) including non-alcoholic steatohepatitis (NASH)*
  - *Alcohol-related liver disease*
  - *Coeliac disease*
  - *Viral causes: Hepatitis A, B, C, cytomegalovirus, Epstein Barr Virus*
  - *Medications*

- Haemochromatosis
- Rare causes:
  - Wilson's disease
  - Auto-immune chronic hepatitis
  - Alpha-1 antitrypsin deficiency

- Arrange **investigations for liver disorders.**

### **Investigations for liver disorders**

Arrange:

- abdominal ultrasound if not already done.
- hepatitis serology:
  - hepatitis B surface antigen (HBsAg).
  - hepatitis B surface antibody (anti-HBs).
  - hepatitis B core antibody (anti-HBc).
  - hepatitis C virus antibody (anti-HCV).
- iron studies screening for haemochromatosis.
- if personal or strong family history of autoimmune disease, consider early testing for autoimmune causes of hepatitis (check ANA, AMA, anti-SMA, anti-LKM, ANCA, immunoglobulins).
- coeliac serology
- if relevant, testing for other viral causes of self-limiting hepatitis:
  - hepatitis A IgM.
  - cytomegalovirus IgM.
  - Epstein Barr virus IgM.

- 5. If pregnant with abnormal LFTs consider **obstetric hepatic conditions.**

### **Obstetric hepatic conditions**

- Acute viral hepatitis
- Cholelithiasis in pregnancy – symptoms similar to non-pregnant women
- Intrahepatic cholestasis of pregnancy – second half of pregnancy with pruritus of palms and soles of feet and elevated LFTs
- Hyperemesis – in severe cases (hyperemesis gravidarum) will have raised LFTs
- HELLP syndrome (Haemolysis, Elevated LFTs, Low Platelets) – near term and usually with pre-eclampsia
- Acute Fatty Liver of Pregnancy – occurs late in last trimester and is life threatening liver condition

# Management

1. If **serious hepatic complications**, refer to [Emergency Department](#).

## Serious hepatic complications

- [Acute liver failure](#).
  - Aspartate transaminase (AST) > 2,000 U/L.
  - Sepsis in a patient with cirrhosis.
  - Severe hepatic encephalopathy.
  - Severe ascites restricting movement and breathing.
2. Organise [urgent or routine gastroenterology referral](#) if:
    - abnormal liver function tests with:
      - platelet count < 120 x 10<sup>9</sup> per litre.
      - splenomegaly.
      - ascites.
      - hepatic encephalopathy.
      - genetic haemochromatosis (C282Y homozygotes and C282Y/H63D compound heterozygotes only).
    - abnormal liver function test with aspartate transaminase (AST) or alanine aminotransferase (ALT) > 5 times the upper level of the normal range.
    - two abnormal liver function test results performed at least 3 months apart with aspartate transaminase (AST) or alanine aminotransferase (ALT) 2 to 5 times the upper level of the normal range.
  3. If **cholestasis causes**, arrange referral depending on severity and cause:
    - [immediate general surgery referral or admission](#) or [urgent or routine general surgery referral](#)
    - [immediate gastroenterology referral or admission](#) or [urgent or routine gastroenterology referral](#)
    - [immediate oncology referral or admission](#) or [urgent or routine oncology referral](#)
  4. If raised AST and ALT suggesting hepatocellular pattern, manage **confirmed or suspected cause**.

## Confirmed or suspected cause

### **Viral hepatitis**

- If hepatitis A, cytomegalovirus, or Epstein Barr virus:
  - treat symptoms and organise review.
  - re-test LFTs every 6 weeks. If LFTs not improving or deteriorating liver function, arrange [urgent or routine gastroenterology referral](#).
- If hepatitis B or C, follow the [Hepatitis B](#) or [Hepatitis C](#) pathway.

### **Medication-related causes**

- Consider [hepatotoxic drugs](#) and cease likely medication.
- Re-test LFTs every 6 weeks. If not improving, consider other causes.

### **Abnormal iron studies**

- Suspect [haemochromatosis](#) if transferrin saturation > 45%.
- Review serum ferritin. Elevated concentration with normal saturation is often seen with other liver disease e.g., non-alcoholic fatty liver disease (NAFLD), and other inflammatory conditions. May not indicate iron overload.

#### **Alcohol-related liver disease**

- Advise the patient to cease alcohol – see [Alcohol Intervention](#)
- If abstinence achieved and LFTs not normalised in 6 months, consider other causes.
- If patient continues drinking despite appropriate alcohol intervention, request [urgent or routine gastroenterology referral](#).

#### **Non-alcoholic fatty liver disease (NAFLD)**

- Abnormal transaminase levels, or abnormal ultrasound suggestive of hepatic steatosis, and no other identifiable cause of chronic liver disease.
- See [Fatty Liver](#).

5. If cause of abnormal LFTs is still uncertain:

- consider non-hepatic causes. If cause identified, manage underlying disorder and recheck LFTs at 3 to 6 months.
- consider further **investigations for less common hepatic causes**.

#### **Investigations for less common hepatic causes**

- Autoantibodies – ANA, AMA, anti-SMA, anti-LKM, ANCA, immunoglobulins for autoimmune causes.
- Serum alpha-1 anti-trypsin level for alpha-1 anti-trypsin deficiency.
- Serum caeruloplasmin screening for Wilson’s disease. If abnormal result, arrange serum copper and 24-hour urinary copper.

6. If haemolysis suspected arrange [urgent or routine haematology referral](#).

7. In pregnancy, if:

- suspect HELLP syndrome or acute fatty liver of pregnancy, arrange [immediate obstetric referral or admission](#).
- cholelithiasis, arrange [urgent or routine general surgery referral](#).
- acute viral hepatitis, see the [Hepatitis B](#) or [Hepatitis C](#) pathway.
- other obstetric hepatic conditions, arrange [urgent or routine obstetric referral](#).

## Referral

- If [serious hepatic complications](#), refer to [Emergency Department](#).
- Organise [urgent or routine gastroenterology referral](#) if:
  - abnormal liver function tests with:
    - platelet count < 120 x 10<sup>9</sup> per litre.
    - splenomegaly.
    - ascites.

- hepatic encephalopathy.
  - Genetic haemochromatosis (C282Y homozygotes and C282Y/H63D compound heterozygotes only).
- abnormal liver function test with aspartate transaminase (AST) or alanine aminotransferase (ALT) > 5 times the upper level of the normal range.
- two abnormal liver function test results performed at least 3 months apart with aspartate transaminase (AST) or alanine aminotransferase (ALT) 2 to 5 times the upper level of the normal range.
- If ***cholestasis causes***, arrange referral depending on severity and cause:
  - [immediate general surgery referral or admission](#) or [urgent or routine general surgery referral](#)
  - [immediate gastroenterology referral or admission](#) or [urgent or routine gastroenterology referral](#)
  - [immediate oncology referral or admission](#) or [urgent or routine oncology referral](#)
- Do not refer fatty liver with normal liver function tests.
- If haemolysis suspected arrange [urgent or routine haematology referral](#).
- In pregnancy, if:
  - suspect HELLP syndrome or acute fatty liver of pregnancy, arrange [immediate obstetric referral or admission](#).
  - cholelithiasis, arrange [urgent or routine general surgery referral](#).
  - other obstetric hepatic conditions, arrange [urgent or routine obstetric referral](#).

## Information

### For health professionals

#### Further information

- Australian Family Physician – [Liver Function Tests](#)
- Cancer Council Australia:
  - [Optimal Cancer Care Pathway for People with Hepatocellular Carcinoma](#)
  - [Optimal Cancer Care Pathway for People with Hepatocellular Carcinoma: Quick Reference Guide](#)
- Family Practice Notebook – [Hepatotoxic Medication](#)
- RACGP – [Prescribing in Patients with Abnormal Liver Function Tests](#)

### For patients

- Better Health Channel – [Liver Disease](#)
- Gastroenterological Society of Australia – [Health Information Fact Sheets](#)

Last Reviewed: December 2019

[Disclaimer](#)