When to consider checking liver blood tests

This pathway is designed to guide primary care clinicians on further investigation and management of patients with abnormal liver function tests. The primary purpose is to identify patients who are at intermediate and high risk of advanced fibrosis with subsequent referral to secondary care.

- Suspected excess alcohol consumption
- Non-specific symptoms inc. fatigue, nausea, anorexia.
- Evidence of chronic liver disease
  - Add clotting with INR if failure suspected
- Conditions associated with high risk of liver disease
  - Includes autoimmune conditions, IBD.
  - Check bloods if symptoms change to suggest development of liver disease.
- Use of hepatotoxic drugs
  - May require monitoring and/or checks before starting.
  - Drugs include:
    - Carbamazepine
    - Methylidopa
    - Minocycline
    - Macrolide antibiotics
    - Nitrofurantoin
    - Statins
      - People with NAFLD who are taking statins should keep taking them. Only consider stopping statins if liver enzyme levels double within 3 months of starting statins, including in people with abnormal baseline liver blood tests (NICE NG49)
    - Sulfonamides
    - Terbinafine
    - Chlorpromazine
    - Methotrexate
- Family history of liver disease
  - E.g. haemochromatosis, Wilson’s disease.
  - In these cases add specific tests for the condition (e.g. ferritin & transferrin saturation, caeruloplasmin etc.)
- Risk factors for viral hepatitis
  - High risk groups such as IVDUs, migrants from high-prevalence areas, prisoners.
  - In these situations, send second line tests (i.e. viral serology) at the same time.
History & Examination

History to include:
- Alcohol history – if suspicious of harmful drinking then complete AUDIT-C questionnaire
- Drug history
- Risk factors for viral hepatitis
- Personal family history
- Comorbidities
- Also measure BMI and check for metabolic syndrome if indicated.

If abnormalities in liver blood tests are found ask about:
- Ethnicity & country of birth
- Travel history
- Further enquiry about specific symptoms
- Occupational exposure
- Tick bites
- Muscle injury
- In children – maternal, neonatal, nutritional and developmental history

Examination to include:
- Body Mass Index
- Abdominal examination looking for hepatosplenomegaly, ascites and other signs of chronic liver disease
1\textsuperscript{st} line investigations to send for potential liver disease

Should include (1\textsuperscript{st} line LFT Investigation):

- Bilirubin
- Albumin
- ALT
- ALP
- GGT
- FBC (if not performed within last year)

If at high risk of viral hepatitis or family history of specific liver disease, also send relevant tests with initial investigations.

The degree of abnormality of liver blood tests is not necessarily a guide to clinical significance – this should be determined by the specific abnormal analyte(s) and the clinical context. Patients with abnormal liver blood tests should be considered for investigation with an aetiology screen irrespective of level and duration of abnormality.

It is not recommended to repeat the same panel of abnormal tests unless there is a high index of clinical suspicion that it is a transient finding. 84% of abnormal liver blood tests remain elevated at 1 year, and 75% at 2 years.
**Isolated Raised Bilirubin**

Most common cause of isolated bilirubinaemia is Gilbert’s syndrome which affects 5-8% of the population. To further investigate a set of fasted blood tests with liver blood tests, full blood count and direct and indirect bilirubin.

- Total bilirubin should rise further with indirect component
- Anaemia should not be present.

Anaemia means that haemolysis must be excluded. In these cases request:
- Reticulocyte count
- Lactate dehydrogenase
- Haptoglobins

Further investigation and referral for haemolysis are outside the scope of this guidance.

If unconjugated bilirubin is more markedly elevated (>40 μmol/L) then consider rarer causes such as Crigler-Najjar syndrome and genetic testing.
URGENT REFERRAL - Urgent USS &/or consider urgent referral or admission

- First presentation of synthetic failure (jaundice, low albumin, prolonged INR) - Discuss with Consultant Hepatologist/Gastroenterologist on-call or acute medics as the patient may require admission.
- If suspecting malignancy (weight loss and marked cholestasis) - urgent 2WW referral.
Standard liver aetiology screen
(for any abnormal results in the initial investigations)

- USS
- Hepatitis B surface antigen
- Hepatitis C antibody (with follow up PCR if positive)
- AMA
- Anti-Sm antibody
- ANA
- Serum immunoglobulins
- Simultaneous serum ferritin and serum transferrin.

*In children ferritin and transferrin may not be indicated but should include anti liver kidney microsomal antibody and coeliac antibodies. Alpha-1 antitrypsin level and ceruloplasmin (age >3) should be included and discussed with metabolic.
Suspected alcohol-related liver disease

- FBC: may reveal macrocytosis
- LFTs:
  - A raised GGT indicates possible alcohol abuse
  - Abnormal ALT reflects hepatocellular damage
  - An AST: ALT ratio that is $>2$ suggests alcoholic damage
- There may be an elevated serum IgA: anti-smooth muscle antibodies may be found

(Source: GP Notebook)
Consider underlying causes including short term viral illness or medication or OTC drugs as causes - consider stopping & repeating LFTS

Use clinical judgement including possibility or short-term viral illness

Medications causing abnormal LFT’s – list not exhaustive

- Amiodarone
- Amoxicillin
- Chlorpromazine
- Ciprofloxacin
- Erythromycin
- Diclofenac
- Fluconazole
- Halothane
- Isoniazid
- Methyldopa
- Oestrogens
- Paracetamol
- Statins
- Rifampin
- Valproic acid
- Herbals
Abbreviations

- ALP - Alkaline Phosphatase
- ALT - alanine aminotransferase
- Anti-Sm - Anti-smooth muscle
- AMA - anti-mitochondrial antibody
- ANA - anti-nuclear antibody
- ARLD - alcohol related liver disease
- BMI - Body mass index
- FBC - full blood count
- FIB-4 - Fibrosis stratification calculator
- GGT - γ-glutamyl transferase
- HIV - human immunodeficiency virus
- LDH - Lactate dehydrogenase
- NAFLD - Non-alcoholic fatty liver disease
- T2DM - Type 2 diabetes mellitus
- USS - Ultrasound scan
Abnormal ultrasound

Fibrosis Risk

AST/ALT ratio <0.8 low risk of fibrosis, >0.8 high risk of fibrosis

FIB4 score:
- ≤ 1.2 Low risk
- > 1.2 Intermediate to High risk
Risk Factors

Management of risk factors and lifestyle advice

Manage risk factors for NAFLD including:
- Hypertension
- High cholesterol
- Diabetes
- Obesity

Lifestyle advice:
- Maintain a healthy weight
- Eat a healthy diet
- Exercise regularly
- Refer to stop smoking services if applicable
- Review alcohol intake