Hepatology referral pathways for GP

1 Scope

For use within hepatology

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# 2 Liver blood tests and what they mean

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal range</th>
<th>What does it mean?</th>
<th>Actions if raised</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>7-40</td>
<td>Hepatocellular injury</td>
<td>Raised ALT</td>
</tr>
<tr>
<td>Bilirubin isolated raised</td>
<td>&lt;21</td>
<td>Gilberts Haemolysis</td>
<td>Isolated asymptomatic raised bilirubin</td>
</tr>
<tr>
<td>Bilirubin with abnormal LFT</td>
<td></td>
<td>Liver or biliary pathology</td>
<td>&gt;42 urgent referral</td>
</tr>
<tr>
<td>Alkaline Phosphatase (ALP)</td>
<td>30-130</td>
<td>Biliary disease (if raised GGT)</td>
<td></td>
</tr>
<tr>
<td>Gamma glutamyl transferase (GGT)</td>
<td>Male 0-73, Female 0-38</td>
<td>Non-specific – can reflect alcohol intake, non-alcoholic fatty liver or biliary disease if associated with raised ALP</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (PT)</td>
<td></td>
<td>Elevated with reduced synthetic capacity or biliary obstruction</td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>35-50</td>
<td>Non-specific, but may represent reduced synthetic capacity</td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td></td>
<td></td>
<td>Raised ferritin</td>
</tr>
<tr>
<td>Reduced platelets</td>
<td></td>
<td>Can be a feature of cirrhosis with portal hypertension</td>
<td></td>
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</table>

**Chronic liver screen**
- LFT, FBC, PT, APTT, INR
- Hepatitis B & C serology
- Liver autoantibodies
- Serum immunoglobulins
- Ferritin
- Alpha-1 antitrypsin
- Random glucose, HBA1c
- If under 50 caeruloplasmin

**Acute liver screen**
- LFT, FBC, PT, APTT, INR
- Hepatitis A, Hepatitis B and Hepatitis E serology (IgM & IgG)
- Liver autoantibodies
- Serum immunoglobulins
- If under 50 caeruloplasmin

**Hepatitis B screen**
- Chronic liver screen plus:
  - HBV DNA
  - Hepatitis A Immunity
  - HIV screen

**Hepatitis C screen**
- Chronic liver screen plus:
  - HCV RNA and genotype
  - Hepatitis A Immunity
  - HIV screen
3 Raised ALT

THINK about and address Risk Factors
- Metabolic syndrome
- Diabetes
- Alcohol
- Risks for viral hepatitis (ethnicity, IV drug use)
- Medication

**ALT > 300**
- Urgent USS, Acute Liver Screen

Raised ALT + abnormal billirubin or ALP or albumin or prothrombin time or platelets
- See pathway

**Isolated raised ALT < 300**
- USS Chronic liver screen

150 - 300
- USS Chronic liver screen

50 - 150
- Repeat ALT 6/52

< 50
- Reinforce lifestyle advice

**Do all features below apply?**
- >35 years
- Echo-bright liver
- NO signs cirrhosis or portal hypertension
- Clinical features of metabolic syndrome
- Normal chronic liver screen
- Alcohol intake < 10 units per week

**Likely NAFLD**
If > 75 yrs old, reasonable to reinforce lifestyle advice only

If < 75 yrs old, risk stratification with FIB-4 to assess risk of NASH (non-alcoholic steatosis)
Higher risk if metabolic syndrome or type 2 diabetes. Advanced fibrosis is usually asymptomatic.

FIB4 request via T-Quest or calculate at from age, AST, ALT, platelets:
http://gihep.com/calculators/hepatology/fibrosis-4-score/

Low Risk
- 1.3 (age 35-64)
- 2.0 (age ≥65)

- Lifestyle advice
- Reassess FIB-4 annually and if > 1.3

Intermediate Risk
- 1.30 to 2.67

- Routine referral for further stratification with Fibroscan and to consider long term follow up

High Risk
- > 2.67

- Routine referral
4 Isolated asymptomatic raised bilirubin

Split bilirubin, FBC and prothrombin time

Unconjugated hyperbilirubinemia
NO clinical stigmata of cirrhosis, normal albumin, prothrombin time and platelets

YES

Anaemia?

YES

Haemolysis screen
reticulocytes
lactate dehydrogenase (LDH)
haptoglobin
Direct Antiglobulin Test (DAT)
Blood film

+/- refer haematology

NO

Unconjugated hyperbilirubinemia

NO

Ultrasound, 
Chronic liver screen

ROUTINE REFERRAL

NO

Likely Gilbert’s syndrome
(inherited defect in ability to conjugate bilirubin that is benign and requires reassurance and no follow up)

5 Raised ALP and normal ALT

Bilirubin > 2x upper limit normal

YES

URGENT REFERRAL

NO

Check GGT
Is it raised?

YES

Ultrasound, 
Chronic liver screen

ROUTINE REFERRAL

NO

Tests for bone pathologies

Consider bone profile, vitamin D, ESR/CRP, PSA
6 Raised ALT +/- Raised ALP +/- raised bilirubin (combination of abnormalities)

- Bilirubin > 2x upper limit normal: **URGENT REFERRAL**
- ALT >300: Urgent USS Acute Liver screen: **URGENT REFERRAL**
- ALP or ALT >100-300: USS Acute Liver Screen Chronic Liver screen: **ROUTINE REFERRAL**

7 Raised ferritin

- If CRP elevated – exclude inflammatory cause / repeat after interval. Exclude anaemia (haem ref)
- Check fasting transferrin saturation (tf sat) and LFTs / family history
- Low tf sat
- Borderline/raised tf sat or family history
- Normal ALT: Lifestyle advice (moderate alcohol consumption and metabolic RFs) and monitor ferritin with referral if no response to these measures
- Elevated ALT: **Raised ALT pathway**
- HFE genotyping (EDTA to Molecular Genetics for simple HFE1 genotype – see form at end of document)
- C282Y homozygous, C282Y/H63D or clinical concern
- Refer to Bill Griffiths, Consultant Hepatologist (further guidance [here](#))
8 Abnormal liver imaging

**Hepatomegaly**

- Chronic liver screen
- Refer to hepatology

**Cyst/s**

- Simple cyst/s
  - No referral required
- Complicated cysts
  - thick-walled /septated /multiple
  - Repeat US at CUH if non-CUH scan
  - Refer A&G if CUH scan

**Haemangioma**

- Small (< 2cm) incidental haemangioma
  - No referral required
- Large (> 2 cm)/complex
  - Repeat US at CUH if non-CUH scan
  - Refer A&G if CUH scan

**Focal fat sparing on background of “fatty liver”**

- NAFLD pathway

**Suspected primary liver CA**

- Urgent referral

**Ultrasound scan shows gall bladder polyp**

- > 1 cm
  - Referral to **HPB surgery** for cholecystectomy
- < 1 cm
  - Adverse features:
    - Biliary pain
    - Background Primary Sclerosing Cholangitis
  - Yes
    - Yes
    - Cholesterol polyp
      - Yes
      - No follow up
      - No
      - USS surveillance at 6 months then annually
    - No
    - Polyp growth
  - No
9 Hepatitis B

Hepatitis B surface antigen (HBsAg) positive

Refer to hepatitis clinic for assessment of the need for treatment, contact tracing and cancer surveillance *

Exposed to and cleared hepatitis B.
Contact tracing with GP.
Referral only required if patient takes immunosuppression or chemotherapy (or does so in the future)

Hepatitis B core antibody (anti-HBcAb) positive
Hepatitis B surface antigen (HBsAg) negative

10 Hepatitis C

Hepatitis C antibody positive

Perform HCV RNA test (large EDTA)

+ve

Refer to hepatitis clinic for assessment of the need for treatment, contact tracing and cancer surveillance *

-ve

Exposure and clearance
Contact tracing
Confirm with repeat HCV RNA and if negative no further action required.

* Pre-clinic workup: (see T-Quest Groups)
For HBV and HCV: Chronic liver screen plus HIV and hepatitis A immunity serology
For HCV: HCV RNA and genotype (large EDTA tube)
For HBV: HBV DNA (large EDTA tube)
11 Referral pathways

URGENT REFERRAL

<table>
<thead>
<tr>
<th>Jaundice</th>
<th>Letter or referral proforma to:</th>
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<tr>
<td>Acute hepatitis (ALT &gt; 300)</td>
<td><a href="mailto:add-tr.NHSOutpatientreferrals@nhs.net">add-tr.NHSOutpatientreferrals@nhs.net</a></td>
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<tr>
<td>Suspected cirrhotic decompensation</td>
<td></td>
</tr>
<tr>
<td>Tense ascites</td>
<td></td>
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<tr>
<td>Suspected liver cancer</td>
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ROUTINE REFERRAL – please review guidance

<table>
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<th>Re-referral of patient lost to follow up</th>
<th>Letter or referral proforma to:</th>
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<tr>
<th>Abnormal LFTs</th>
<th>E-referral to general hepatology clinic (non-viral)</th>
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<td>Suspected chronic liver disease</td>
<td></td>
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<tr>
<td>Raised ferritin</td>
<td></td>
</tr>
<tr>
<td>Hep B or C new diagnosis</td>
<td>E-referral to hepatitis clinic</td>
</tr>
<tr>
<td>Benign abnormal liver imaging (if pathway suggests referral)</td>
<td>Advice and guidance referral for MDT review</td>
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- Further information: [https://easternliver.net](https://easternliver.net)

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Document management

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<tr>
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<td>Dr Will Gelson</td>
</tr>
<tr>
<td>Pharmacist:</td>
<td>n/a</td>
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REGIONAL GENETICS LABORATORIES TEST REQUEST

All tests requested will be reviewed against departmental criteria. If testing is not arranged, the samples will be stored and the referring clinicians informed. After testing, samples may be used anonymously for the development of new tests and for quality monitoring.

Venous blood samples: Adult: 5ml; Children: 1-5ml
☐ DNA test: EDTA tube
☐ Chromosomes: Lithium Heparin tube
☐ Microarray: Lithium Heparin and EDTA tubes

Other samples:
☐ Cord/Placenta/insertion site/skin
☐ Products of Conception (whole specimen in sterile pot)
☐ Amniotic Fluid
☐ CVS
☐ Other (please contact the laboratory)

Sample obtained by (Signature)……………………………
Printed Name ……………………………………………..
Date………………………………………………………….

Clinical Synopsis Please provide clinical synopsis and pedigree with relevant family history to help the team generate a laboratory report

Tests Required:
HFE1 p.(Cys282Tyr) and p.(His63Asp) genotypes.
Please send EDTA tube to Regional Genetics Laboratory (See address overleaf).

Storage Only (no testing at this time): ☐

Gestation in weeks (If pregnant):

Partners Name and DOB:

Index Case (if not this patient):

The Laboratory does NOT report results via the telephone
All samples MUST be labelled with FULL name, date of birth and NHS number
Processing of samples will be delayed if information is incomplete

Send samples at room temperature by 1st class post or courier to:
East Anglian Medical Genetics Service, Genetics Laboratories, Box 143
ATC Level 6, Addenbrooke’s Hospital, Hills Road, Cambridge, CB2 0QQ

Laboratory opening hours: 8.30am - 5.30pm Monday to Friday
Telephone: 01223 348866 Fax: 01223 348712
E-mail: geneticslaboratories@nhs.net

For further information about sample requirements and tests available see: www.cuh.org.uk/genetics-labs

Indication for Genetic Testing:

1. To establish a diagnosis  ☐
2. Guide clinical management  ☐
3. Information regarding prognosis/recurrence risk  ☐
4. Predictive testing  ☐
5. PGD/Prenatal diagnosis  ☐

Has the test been discussed at a clinical meeting?  ☐
If so, please provide information on clinical meeting
(i.e.: Neurology meeting, cancer meeting)

Is the test urgent?  ☐
(i.e. pregnant or will alter management)

Please confirm that your department will fund the test*  ☐

Has the test been approved by patient’s consultant  ☐

* Please see UKGTN website (http://ukgtn.nhs.uk/) for approximate cost or contact the duty scientist (tel: 01223 348866)