Hepatology referral pathways for GPs

1 Scope

For use within hepatology and for referrers to hepatology

Contents

2 Liver blood tests and what they mean

Test	Normal range	What does it mean?	Actions if abnormal
ALT	7-40	Hepatocellular injury if raised May also be muscle-derived	Raised ALT
Bilirubin isolated raised Bilirubin + abnormal LFT	<21	Gilbert's Haemolysis Liver or biliary pathology	Isolated asymptomatic raised bilirubin Refer (routine vs urgent according to values)
Alkaline Phosphatase (ALP)	30-130	Biliary disease (if raised GGT) Bone disease (if normal GGT) Pregnancy (placenta) Acute phase response	Raised ALP and normal ALT
Gamma glutamyl transferase (GGT)	Male 0-73 Female 0-38	Non-specific – can reflect alcohol intake, non-alcoholic fatty liver or biliary disease if associated with raised ALP	Follow pathway relevant to other abnormalities / risks; no referral needed for isolated GGT elevation.
Prothrombin time (PT)		Elevated with impaired synthetic function or biliary obstruction	Refer if suspected liver related
Albumin	35-50	Non-specific, but may represent impaired synthetic function if low	Refer if suspected liver related
Ferritin		Not necessarily iron overload	Raised ferritin
Reduced platelets		Can be a feature of cirrhosis with portal hypertension	Refer if suspected liver related

Chronic liver screen	**Acute liver screen**
U&E, LFT, FBC, PT; FIB-4 if MASLD Hepatitis B & C serology Liver autoantibodies Serum immunoglobulins Ferritin Alpha-1 antitrypsin level Random glucose, HbA1c, lipids Thyroid function Caeruloplasmin (if under 40)	LFT, FBC, PT Hepatitis A, hepatitis B and hepatitis E serology (IgM & IgG), EBV and CMV Liver autoantibodies Serum immunoglobulins Caeruloplasmin (if under 40)

Hepatitis B screen	**Hepatitis C screen**
Chronic liver screen plus: • HBV DNA • Hepatitis A IgG • HIV antibody screen	Chronic liver screen plus: • HCV RNA and genotype • Hepatitis A IgG • HIV antibody screen

3 Hepatology A&G FAQs

RESULT	WHAT IT MEANS
ALP raised with normal GGT	Not likely to relate to liver, more likely bone origin
Low ALT / low ALP	Not concerning in-and-of themselves; often relate to poor nutrition.
Isolated GGT elevation	Most indicative of metabolic risk; only requires referral if another criterion for referral met.
Bilirubin (isolated raised)	Likely Gilbert's if nothing else to suggest liver disease, normal haemoglobin, 'split' bilirubin predominantly unconjugated. NB may have family history
Caeruloplasmin 0.17-0.20	Unlikely to be significant if no other pointers to Wilson's disease
Ferritin raised/normal transferrin saturation	Common in MASLD, Alcohol-related liver disease (ArLD)
FIB-4 <1.3 (<2.0 if over age 65)	Can be requested on T-Quest. Use for MASLD or HCV assessment only. Means low risk of significant fibrosis. Not valid <35 years or >75 years of age.
ELF <9.8	Similar score to FIB-4 but different analytes; indicates low risk of significant fibrosis
FibroScan® <8 kPa	Means low risk of significant fibrosis
Hepatitis C Ab positive	Past exposure – requires HCV RNA (via GP) to assess for active infection
HBcAb +ve & HBsAg -ve	Previous exposure & natural immunity, not chronic infection
IgA raised	Common in MASLD, ArLD – not concerning in itself
SmA/ANA Weak positive	This will always be non-specific, common in MASLD. Not a concern if IgG normal.
Imaging	
Focal lesion on US	If likely benign but report not definitive – repeat at CUH via GP request if done elsewhere otherwise A&G
Gallbladder polyps	Refer to 'HPB surgery' for advice / follow their guidance
Family history	
Of haemochromatosis	Send *HFE* genetics via GP in first degree relatives
Of alpha-1-antitrypsin pathogenic phenotype (not required for MZ)	Send A1AT level via GP in first degree relatives

4 General points

- **For suspected cancer, use the 2WW pathway**
- Parenchymal liver disease does not usually cause pain.
- Pain and deranged liver chemistry most commonly relates to a biliary issue.
- Liver chemistry derangements are common in patients with heart failure and do not require hepatological investigation if likely to relate to overload / back pressure.
- FIB-4, ELF and FibroScan® are tools for assessing risk of fibrosis rather than tools to reach a specific diagnosis.
- FIB-4 is only recommended for use in assessing metabolic-dysfunction associated steatotic liver disease (MASLD) and is not recommended to assess alcohol-related liver disease (ArLD)

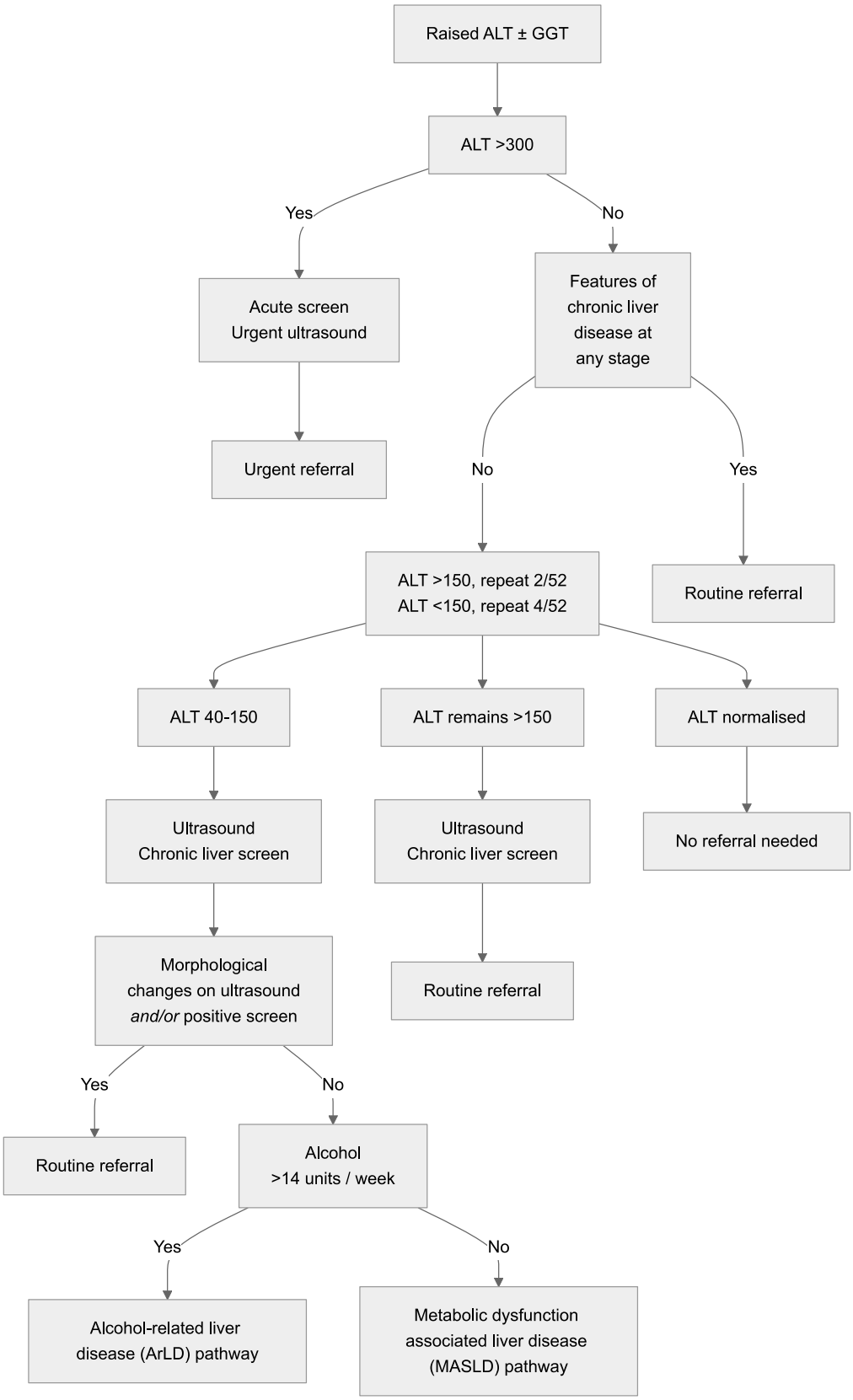
Consider and address risk factors:

- Metabolic syndrome
- Diabetes mellitus
- Alcohol
- Risks for viral hepatitis (ethnicity, drug use)
- Medication
- Vigorous exercise (check CK)

NB Many adults have a combination of central obesity and moderately excessive alcohol consumption. These are synergistic in causing liver damage and this is now called MetALD (metabolic dysfunction and alcohol-related liver disease); follow alcohol-related liver disease pathway if alcohol intake above 14 units / week

5 Isolated raised ALT (+/- GGT)

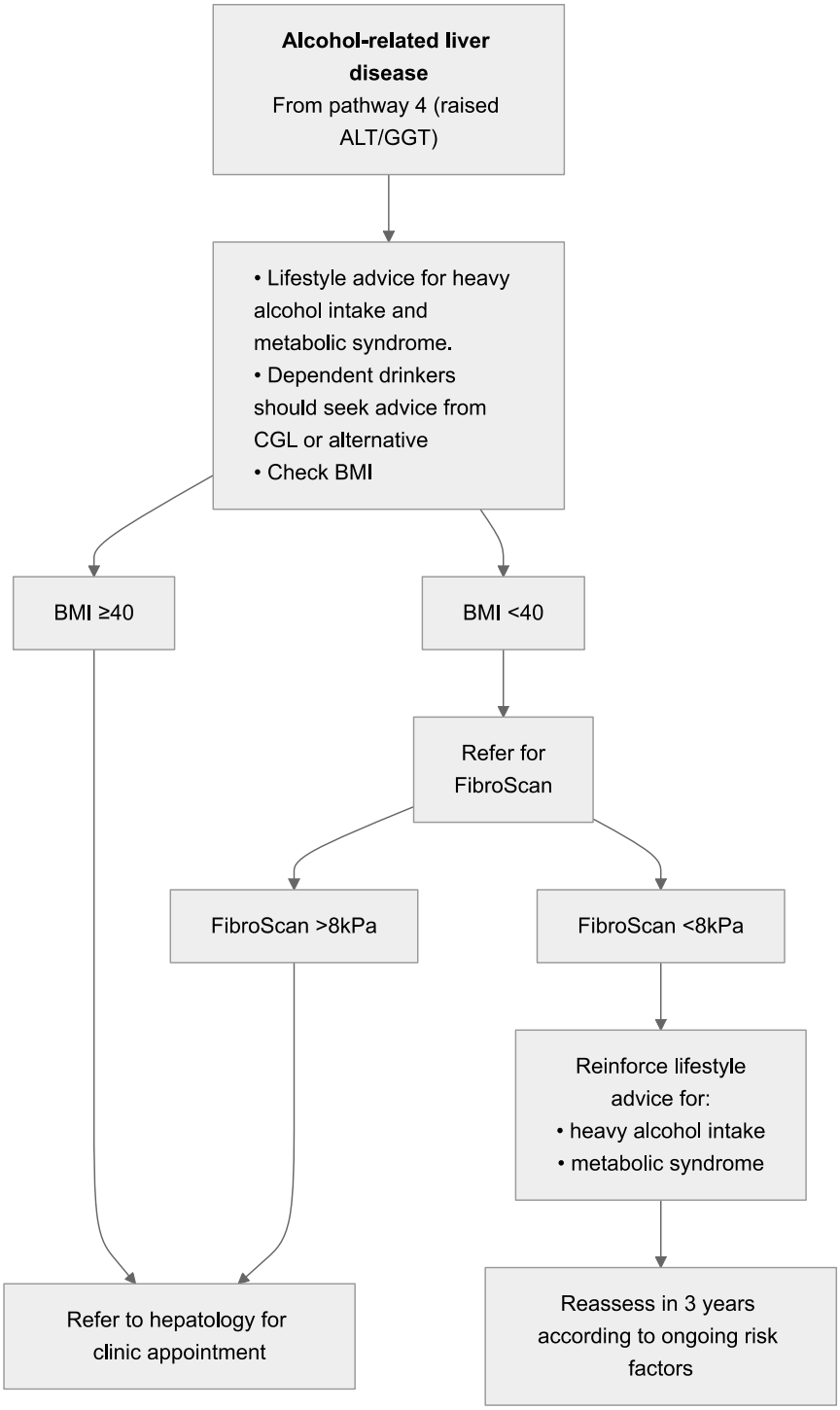
Follow same pathway for isolated elevated aspartate aminotransferase (AST).



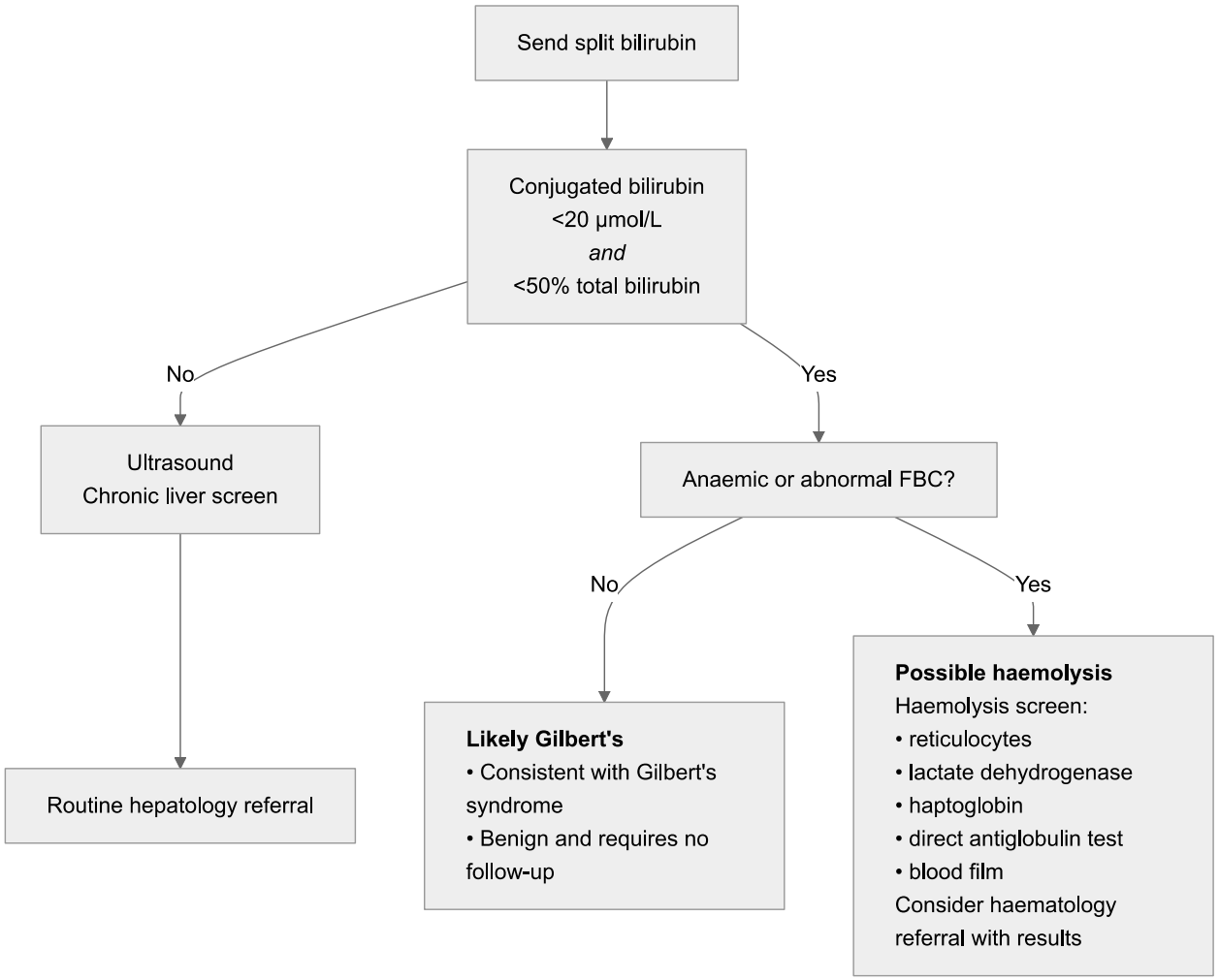
6 Metabolic-dysfunction associated steatotic liver disease (MASLD)

7 Alcohol-related liver disease (ArLD) pathway

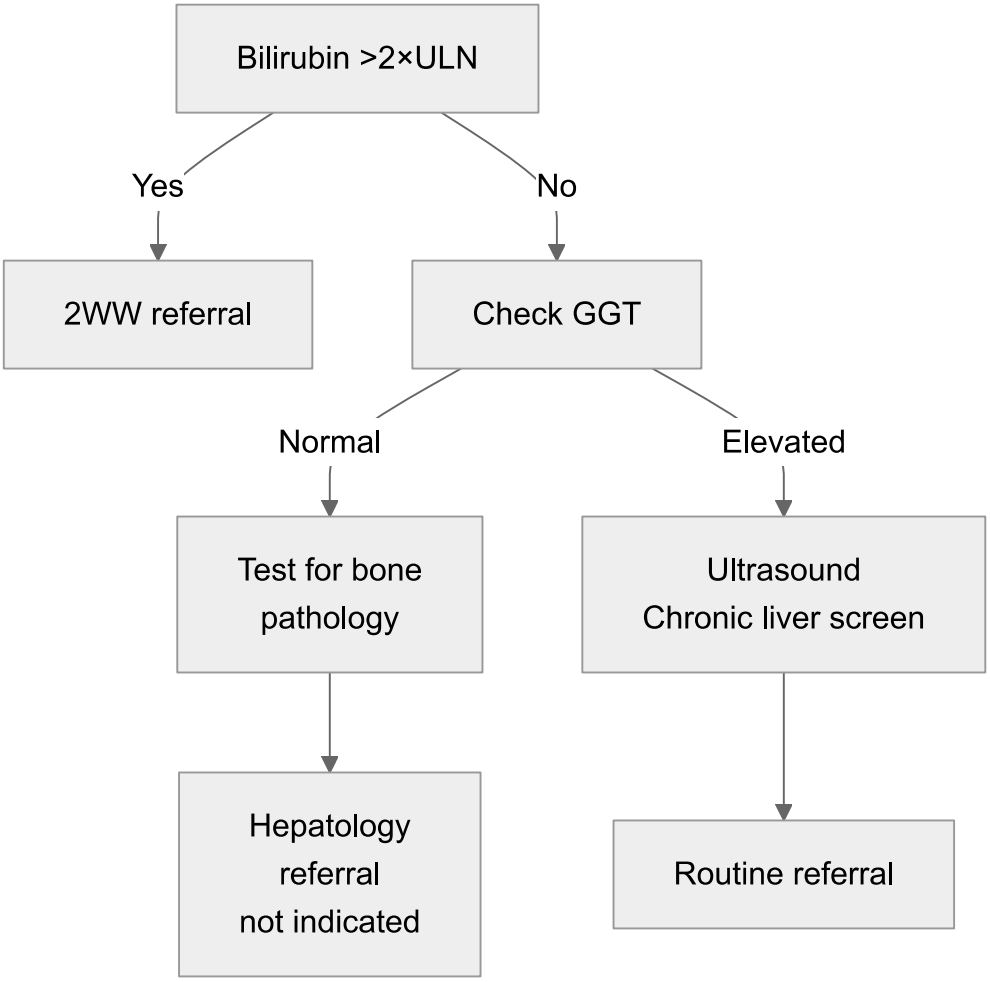
NB Many adults have a combination of central obesity and moderately excessive alcohol consumption. These are synergistic in causing liver damage and this is now called MetALD (metabolic dysfunction- and alcohol-related liver disease); follow alcohol-related liver disease pathway if alcohol intake above 14 units / week. Note that FIB-4 is not recommended for assessment of liver disease in alcohol excess.



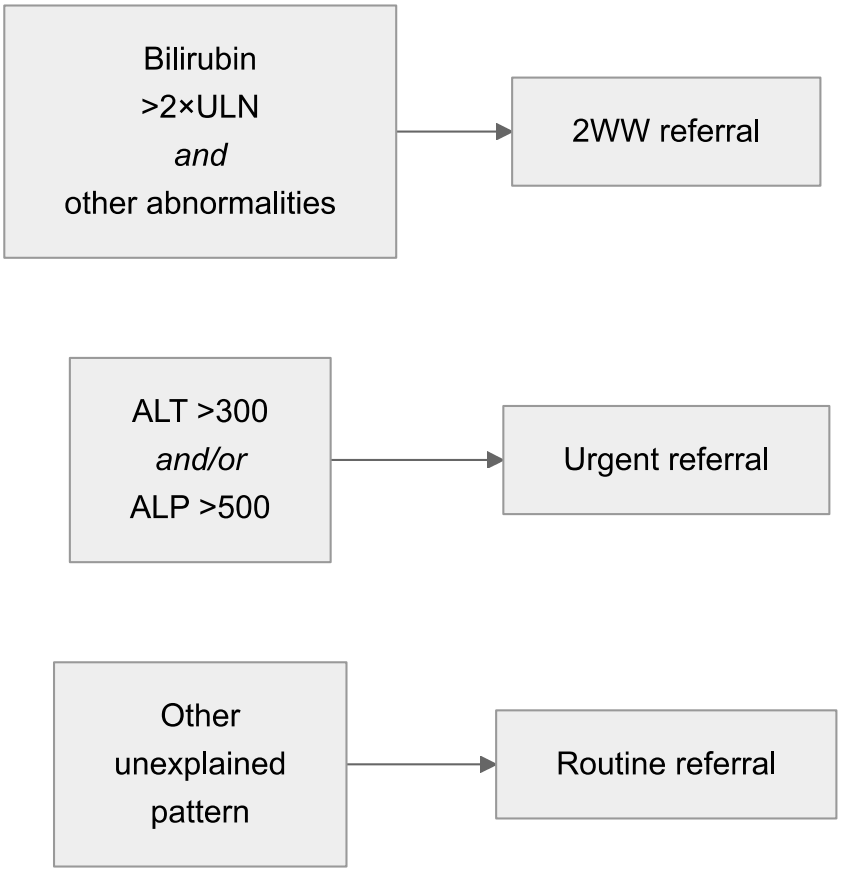
8 Isolated raised bilirubin



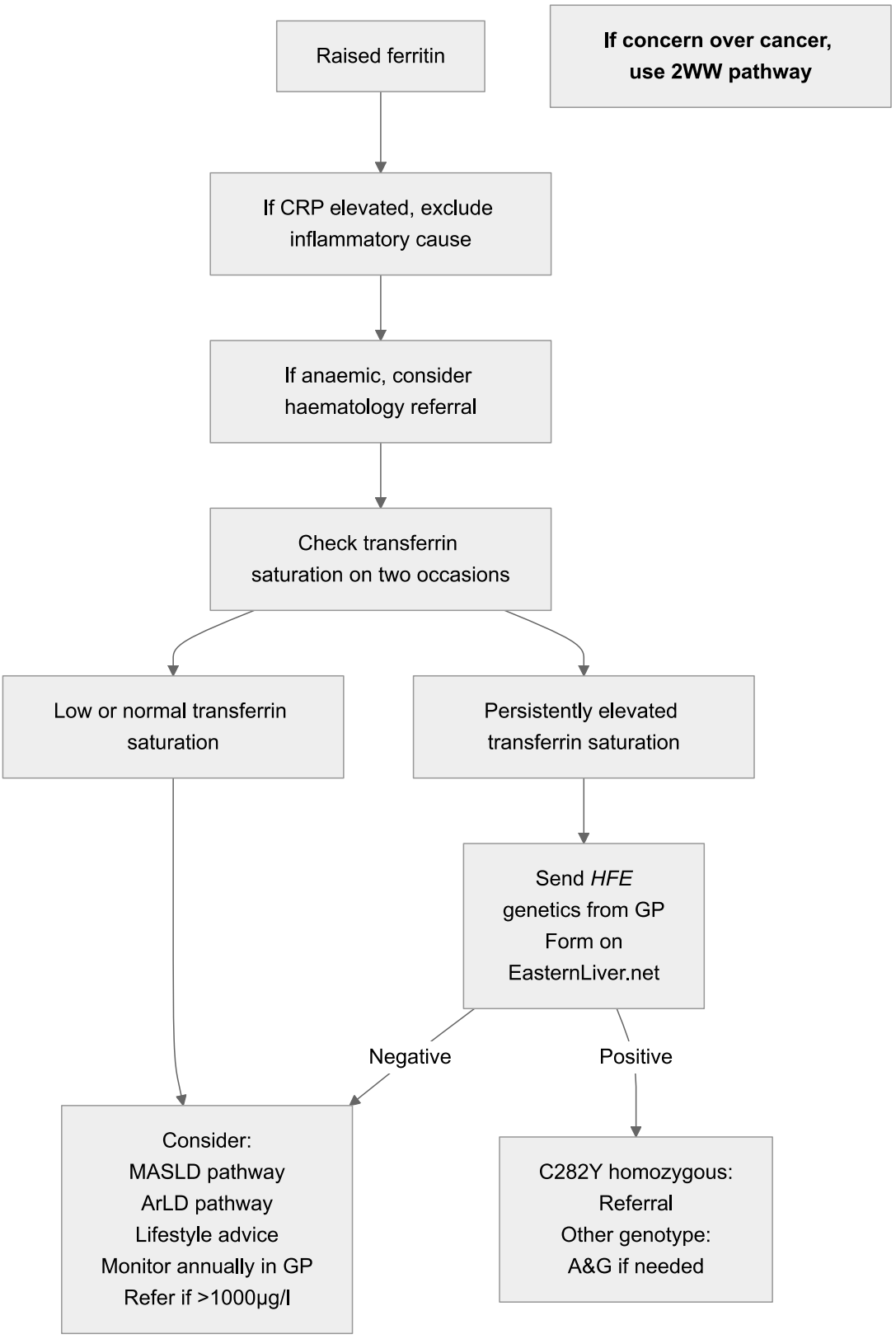
9 Raised ALP and normal ALT



10 Combination of liver chemistry abnormalities

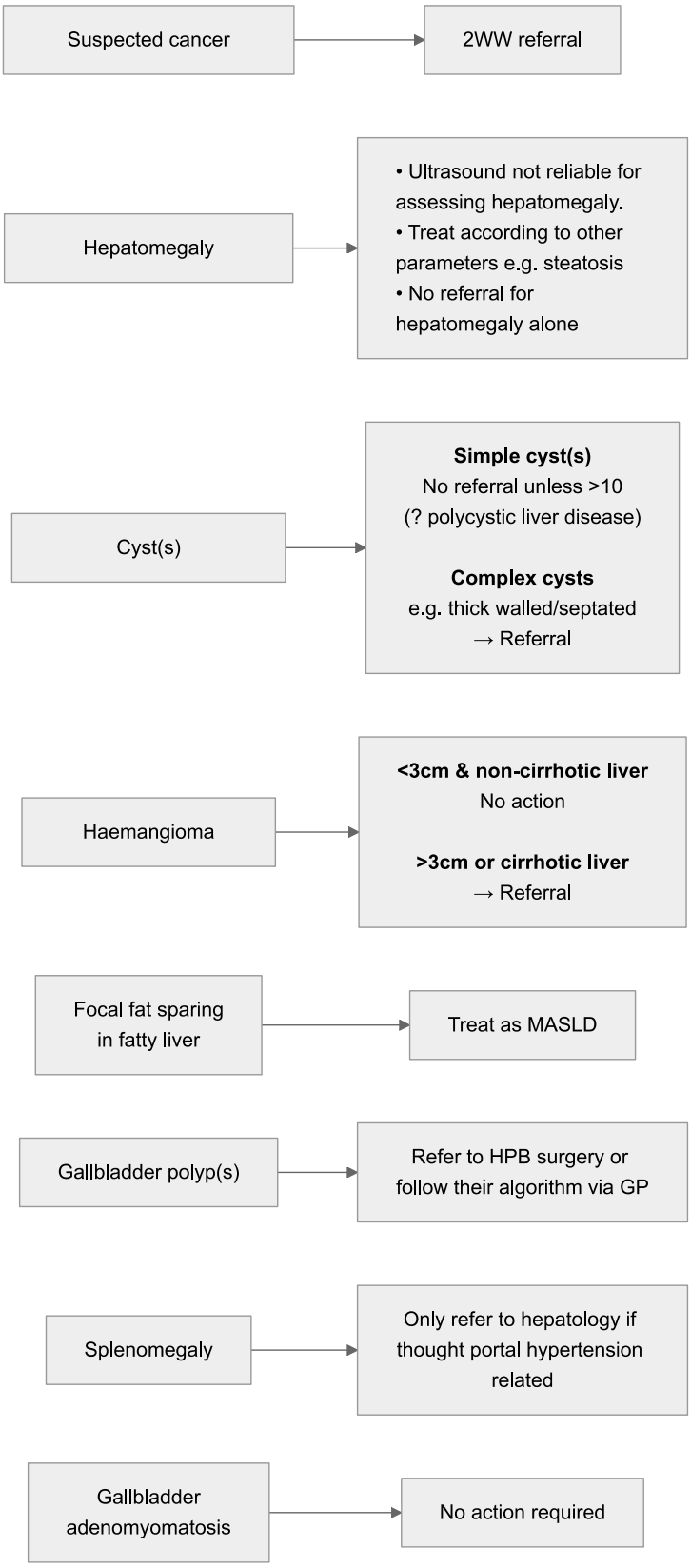


11 Raised ferritin

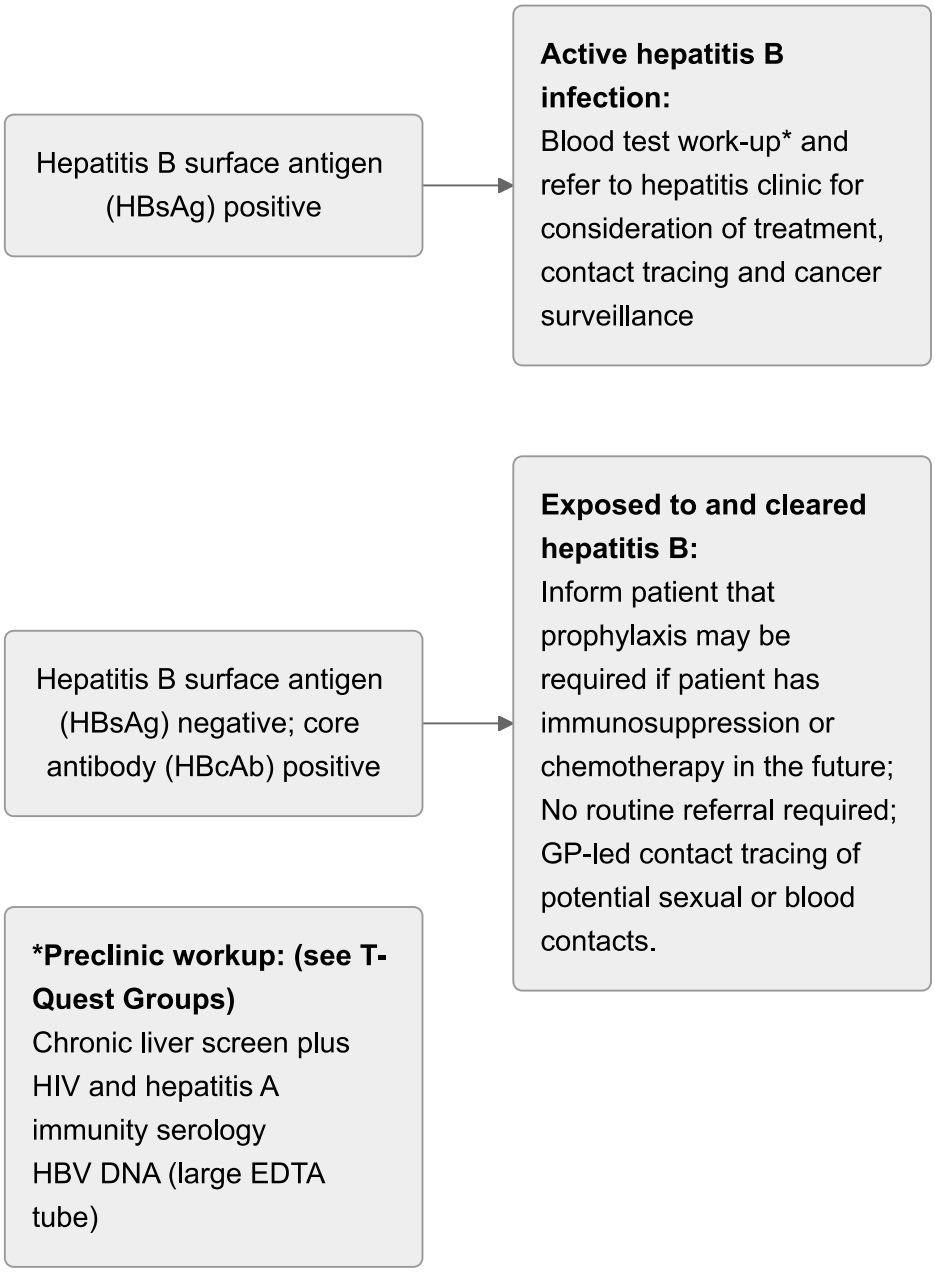


12 Abnormal liver imaging

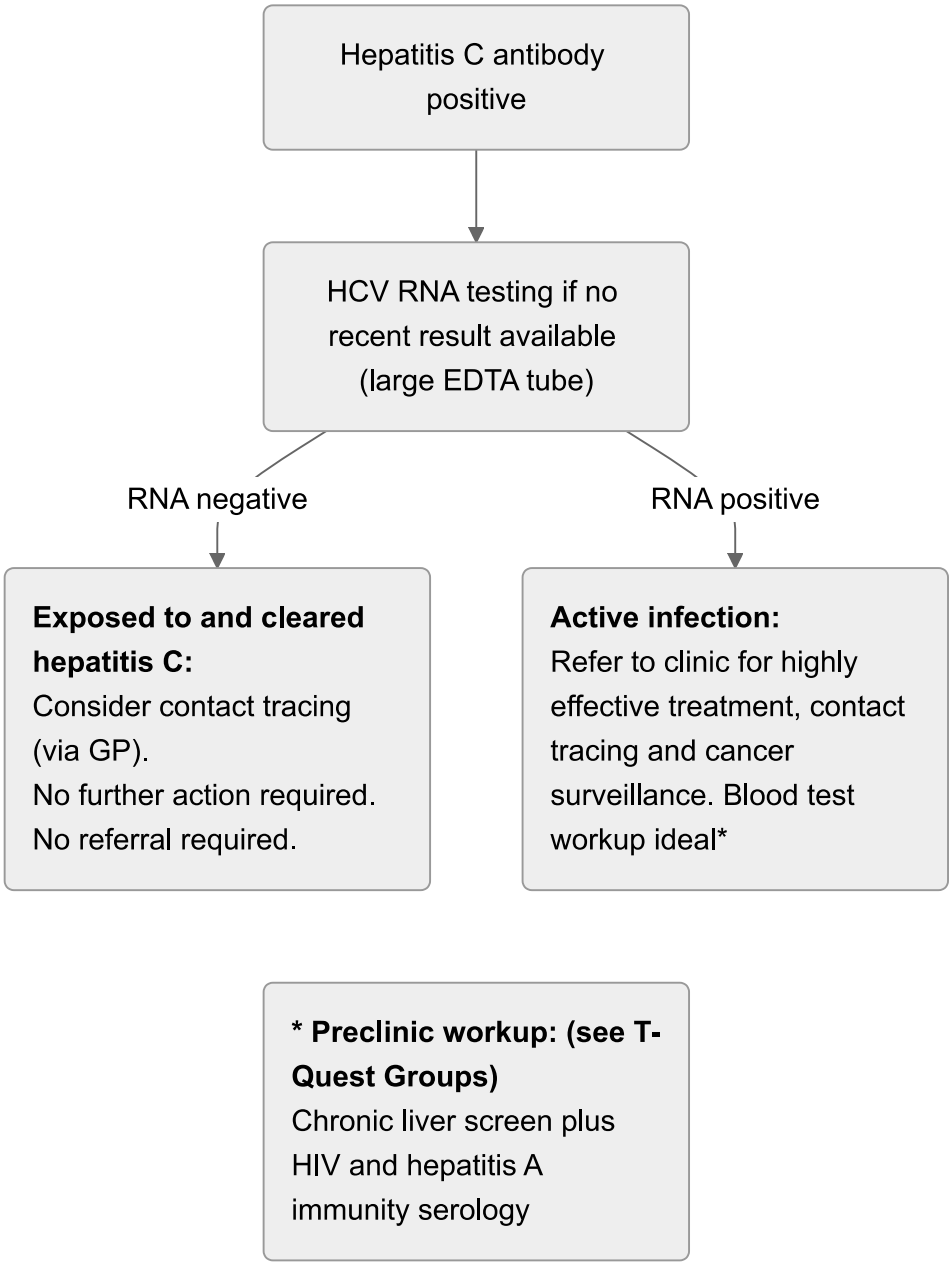
For external ultrasounds, where applicable please raise queries with external provider first.



13 Hepatitis B



14 Hepatitis C



15 Medication issues

15.1 Hormone replacement therapy

Hormone replacement therapy (HRT) appears to be relatively well tolerated in most women with liver disease although on occasion can provoke a worsening in liver enzymes especially in those with a tendency to cholestasis. There is some additional positive in liver disease given the protective effect on bone density. A reasonable approach is to prescribe as normal, to recheck liver chemistry one month after starting, and if there has been no major derangement in liver chemistry to continue standard monitoring appropriate to the patient's liver disease. (O'Donohue & Williams, BJOG 104(1-3) 1997)

Polycystic liver disease: HRT should be avoided in patients with polycystic liver disease because it is associated with the enlargement of hepatic cysts.

Hepatic adenoma: HRT should be avoided in patients with a history of hepatic adenoma.

15.2 Statin therapy

In general, statin therapy can be initiated as standard in patients with liver disease. Monitoring is as standard after introduction with liver and renal chemistry according to NICE guidelines as well as the response to any symptoms that develop.

This includes patients with steatotic liver disease and baseline deranged liver chemistry (although NICE recommend waiting until baseline transaminases are less than 3×ULN).

This includes patients with compensated cirrhosis.

Please discuss considering initiation of statins in patients with decompensated liver disease with hepatology.

For patients with liver transplant patients taking ciclosporin or sirolimus, please consult hepatology prior to prescription; for other transplant patients prescribe as normal.

15.3 Analgesia

In non-cirrhotic liver disease without portal hypertension, prescribe as standard.

In cirrhosis, the avoidance of NSAIDs is recommended.

Pain relief best practice in cirrhotic liver disease with portal hypertension, synthetic dysfunction or decompensation is somewhat undefined.

General principles:

• Paracetamol up to 3g / day.
• Morphine based compounds may be used with caution.
• Major caution with: buprenorphine patches, gabapentin, pregabalin
• Avoid: NSAIDs, tramadol, codeine, oxycodone, amitriptyline

Caution with opioids in relation to accumulation especially with respect to provoking hepatic encephalopathy.

[Ref DOIs: 10.1016/j.jhep.2018.03.024; 10.1002/cld.711; 10.1016/j.amjmed.2023.10.022; PMID: 20000300]

15.4 Direct-acting oral anti-coagulants (DOACs)

May be prescribed as standard in pre-cirrhotic and Child-Pugh class A cirrhosis liver patients.

Please discuss initiation of DOAC in Chid-Pugh class B and C cirrhosis patients with hepatology prior to any prescription.

16 Referral pathways

Urgency	Conditions	Proforma
2WW REFERRAL	Jaundice >40 yrs Suspected liver cancer	2WW proforma
URGENT REFERRAL	Jaundice <40 yrs Tense ascites ALT >300 and/or ALP >500 Suspected cirrhotic decompensation	Urgent CAS referral with hepatology proforma
ROUTINE REFERRAL (please review guidance first)	Abnormal liver chemistry (LFTs) Suspected chronic liver disease Raised ferritin Hepatitis B or C new diagnosis FibroScan® – include ultrasound scan where appropriate	Routine CAS referral with hepatology proforma
	Benign abnormal liver imaging	Referral according to guidance
ADVICE & GUIDANCE		A&G CAS referral with hepatology proforma

- Addenbrooke's Hepatology web page
- Further information: https://easternliver.net

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