Managing Abnormal Liver Tests in Primary Care

Summary guideline August 2015

Main objectives for liver guidance

1. Identify patients at risk of chronic liver disease
2. In people with abnormal LFTs increase testing for treatable liver disease.
3. Identify those with non-alcoholic fatty liver disease (NAFLD), and stratify by level of risk.
4. Improve information on treatable liver disease for clinicians and patients.
5. Audit CCG prevalence of abnormal LFTs and identification of major causes in primary care

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Aim of Guidance

This summary guideline is designed to be used in primary care and outpatient settings to improve the investigation and management of patients with abnormal liver function tests.

The guideline draws on available national and local guidance on managing abnormal Liver Function Tests in primary care, and the identification, risk stratification and management of Non-Alcoholic Fatty Liver Disease (NAFLD).
At present there is insufficient evidence to make definitive evidence based statements in some areas of practice. This guideline aims to provide safe advice for clinicians in areas where clinical uncertainty remains.

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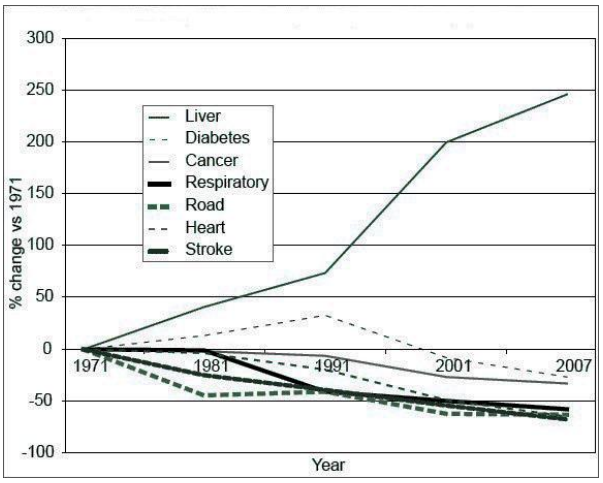
http://fingertips.phe.org.uk/profile/liver-disease

Background

The Chief Medical Officer prioritised liver disease in the 2011 annual public health report. *"Liver disease is the only major cause of mortality and morbidity that is on the increase in England while decreasing among our European neighbours."*
Mortality in England from liver disease rose from 13.9 to 16.6 per 100,000 between 2001 and 2010.
"All the three major causes of liver disease – obesity, undiagnosed infection and, increasingly, harmful drinking – are preventable."

With rising rates of type 2 diabetes and obesity across the UK it is estimated that 20-30% of the adult population will have non-alcoholic fatty liver disease (NAFLD) with approximately 10% of cases having some degree of liver fibrosis and hence at risk of future cirrhosis.



UK 1971-2007, % Increase in mortality from liver disease compared to other conditions. Data from WHO HFA-BD

East London GP recorded prevalence of major liver diseases (adults >18 years).
(*based on GP computer records in March 2015)*

Condition	Number	%	UK Predicted*
Alcoholic Liver Disease	1,407	0.19%	0.3%
Hepatitis B	2,737	0.37%	0.3%
Hepatitis C	2,060	0.28%	0.4%
NAFLD	5,430	0.74%	**17-33%**

**Figures from the Lancet commission and Public Health England*

This suggests under diagnosis and under recording of liver disease in primary care.

Local Audits suggest large numbers of people with abnormal LFTs have insufficient investigation to make a diagnosis.

Among 11,235 adults across inner east London with no recorded liver disease, but two abnormal LFTs in the preceding two years, investigations were as follows:

Two Abnormal LFTs in the past 2 years	11,235 Cases	
Had Audit C	7,010	60.7%
Had Virology	3,228	31.8%
Had Ultrasound	438	3.5%
Had All 3 tests	139	1.1%

Which patients currently get tested for liver disease?

For vague or non specific symptoms full LFTs are frequently ordered by GPs as part of a cluster of investigations.

Choose the ALT (alanine transaminase) **alone** as an initial test ***unless*** there is a suspicion of cholestasis when Bilirubin and ALP are indicated.

The following groups of patients will also benefit from testing:

Look for viral hepatitis in:-
- Those from high risk countries
- At risk sexual contacts
- Intravenous drug users

Look for alcoholic liver disease (ALD) using ALT and GGT in those who drink excess alcohol
(AUDIT C score over 5)

Look for NAFLD using ALT alone in:-
- People with diabetes

Check LFTs in patients on drugs requiring monitoring
- Statins- using ALT alone
- High-risk drugs

Management of abnormal LFTs

(ALT >40) in patients with no liver related symptoms

ALT (alanine transaminase) is the most sensitive marker of liver dysfunction to use in primary care

In this guidance, an ALT over 40 IU is considered abnormal.

Evidence from the Ballets study (see refs) suggests the most cost effective option is to proceed to a full liver screen on finding an abnormal LFT result in a patient with no liver related symptoms.

Evidence shows that abnormal LFTs are persistent, hence a second test in asymptomatic people is usually also abnormal.

Check

Country of birth
Alcohol consumption
Drug and sexual history, (including OTC and recently started prescribed medicines.)
Travel history
Family history of liver disease

Record

AUDIT C /Full AUDIT score and alcohol units/week
BMI

Test

Offer the patient a liver screen. The history will guide you as to the priority of the blood tests. Ensure completion of other tests as prompted by factors in the patient's history e.g Audit C.

A liver screen will include the following blood tests:-

Liver screen

- Full set of LFTs (ALT, AST, ALP, Br, GGT, Total Protein and Albumin)
- Full blood count and platelets
- Ferritin – *may be raised in haemochromatosis*
- HBA1c – *NAFLD very common among people with diabetes*
- Lipid profile – *metabolic syndrome associated with NAFLD*
- Autoimmune screen and immunoglobulins
- Viral hepatitis screen
  Hepatitis B surface antigen
  Hepatitis C antibody
- Clotting screen
- Coeliac screen

If the cause of liver disease remains unclear further specialist tests may be indicated:

- Alpha fetoprotein *raised in hepatocellular carcinoma*
- Caeruloplasmin *low in Wilson's disease*
- Alpha 1 antitrypsin *deficiency of a protease inhibitor that causes both lung and liver disease.*

Which patients need an abdominal ultrasound test?

1. Those with cholestasis or jaundice where intra or extra hepatic obstruction is suspected.
2. Clinical hepatomegaly
3. Where there is a suspicion of cirrhosis.
4. Risk of metastatic or primary liver cancer
5. No features suggestive of ALD or NAFLD

Is a liver ultrasound test needed to make a diagnosis of NAFLD?

The definitive diagnosis of NAFLD requires evidence of excess fat in the liver, which may be seen on USS testing, or by liver biopsy.

However, for those patients who have evidence of the metabolic syndrome (Type 2 diabetes, obesity, CVD, hypertension), and where liver screening is otherwise normal, there is a high probability of NAFLD.

Normal LFTs can be misleading.
Evidence shows that quiescent viral hepatitis and non alcoholic fatty liver disease (NAFLD) can have periods associated with normal ALT and other LFTs.

Chronic Viral Liver Disease

Hepatitis B

Chronic Hepatitis B (HBV) is a highly infectious disease most common in India, the Middle East, South East Asia, China and eastern European countries.
Only 5% of infections become chronic - defined as the presence of Hepatitis B surface antigen for more than six months.
In the UK > 90% of new cases are patients who have arrived from endemic areas where vertical transmission is common.
25-30% of patients will eventually develop cirrhosis.
World wide HBV is the commonest cause of hepatocellular carcinoma.

Within inner east London the GP recorded adult prevalence of HBV is 0.4%

Populations at risk of HBV in the UK include:

- Intravenous drug users current and past
- People from endemic areas, sub-Saharan Africa, the Middle East, China and Vietnam where virtually all transmission is vertical.
- Men who have sex with men
- Prison populations

The Role of Primary Care in Managing Chronic Hepatitis B

1. Screen high risk patients for Hepatitis B
If positive refer to local hepatologist.
2. Offer screening and vaccination to close contacts, including children and carers. Offer post exposure prophylaxis where indicated.
https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book
3. All HbsAg positive patients require regular follow up, (including regular liver USS) to inform decisions on starting active treatment.

What do the tests mean?
Hep B surface antigen HBsAg, a marker of early infection in acute Hepatitis B. It remains positive in chronic Hep B and may only disappear during the recovery phase
Hep B surface antibody antiHBs a marker of past infection or immunisation
HBV DNA or viral load measures replication of the virus (>2000iu/l highly infectious)
AFP, alfa feto-protein, produced by hepatocellular cancers.

NICE advises that patients who are HBsAg positive should be referred to a specialist with an interest in hepatology. http://www.nice.org.uk/guidance/cg165/

Local commissioning schemes may support the follow up of lower risk cases (where HBV DNA <2000iu) in primary care within a shared care arrangement as agreed by CCGs and GPs.

Specialist Treatment of Hepatitis B

Chronic infection with the hepatitis B virus (HBV) follows a fluctuating course .Periods of quiescent disease, when the immune system dominates and suppresses the virus, are interspersed with periods of active disease with high levels of viral replication leading to immunological attack on the infected liver. The changes in disease profile can be rapid. A patient might spend years in a quiescent phase only to develop active disease leading to cirrhosis in less than a year.

Patients with chronic HBV will be observed (usually for a year) when viral load, liver inflammation and extent of liver damage (either by liver biopsy or fibroscan) are assessed. This allows accurate staging of the disease. Patients are then classified as active, fluctuating or inactive. For active disease treatment will be introduced. Those with fluctuating disease will be monitored intensively to identify an optimum moment for intervention. Patients with quiescent disease are monitored on an annual basis.

Intervention may involve either an immune stimulant (interferon) to induce a viral clearing immune response or viral suppression with an oral regime.

New cases of Hepatitis B and C should be notified to the health protection agency (HPA)
North East and North Central London health protection team www.hpa.org.uk
020 3837 7084 out of hours- 020 7191 1860

Hepatitis B and pregnancy
Hepatitis B is part of universal screening in pregnancy. Women with positive results are referred to the liver clinic. Neonates should have a RAPID immunisation schedule with Hep B immunoglobulin (HBIG) given to babies of mothers with high replication (>2000iu/l) HBV. The hospital clinic should provide the first immunisation and HBIG.

Effective immunisation reduces transmission of HBV to babies by 90%.

Practices need to:
Complete the Hep B immunisation schedule and check immunity of immunised babies at 1 year of age.
A fourth booster is given at 1year
A final booster with the pre-school immunisations

Hepatitis C

Hepatitis C (HCV) is transmitted through infected blood products, and in a small percentage by sexual contact. Worldwide up to 3% of the population are infected with HCV. There is currently no vaccine.

Untreated 25% of cases will clear spontaneously, about 5% will go on to develop cirrhosis. A small group of those with cirrhosis progress to hepatocellular carcinoma.
Cure is now possible in over 90% of individuals by elimination of the virus

Chronic infection with all genotypes of HCV results in injury to the liver which over time causes fibrosis, leading to cirrhosis. The time period over which an individual patient will develop cirrhosis varies widely from a few years to decades, and although there are known risk factors such as alcohol consumption, it is not possible to predict the degree of liver injury in an individual patient without specialist testing (by liver biopsy or Fibroscan).
Patients who develop cirrhosis are at increased risk of developing liver failure or liver cancer and this group require regular clinical review and screening for hepatoma.

Within inner east London the GP recorded adult prevalence of HCV is 0.3%

Populations at risk of hepatitis C include

- Intravenous drug users current and past
- People from endemic areas, North Africa, sub-Saharan Africa, Pakistan, Bangladesh, Eastern Europe.
- Those who have had blood transfusions in UK prior to 1991 in particular patients with haemophilia.
- Having medical/dental procedures or tattoos in unsterile circumstances
- Men who have sex with men
- Prison populations

http://www.nice.org.uk/guidance/ph43/

The Role of Primary Care in Managing Hepatitis C

Screen high risk patients for hepatitis C.
If positive refer to local hepatologist for further assessment and treatment if indicated.

Patients who have cleared the virus, or been previously treated, will remain antibody positive. Patients with positive viral load (RNA) are active cases requiring referral.

Offer blood test screening to close contacts.

Specialist Treatments for Hepatitis C

Treatment for HCV currently involves oral anti-viral drugs and interferon – a modulator of the immune response. The large number of side effects associated with interferon (which may be needed for up to 1 year) necessitates careful patient selection, and close monitoring.
New oral anti-viral drugs have recently been approved for use in patients with HCV, which may mean interferon is no longer used. Such drugs as sofosbuvir, simeprevir, daclatasvir, ombitasvir and others promise to transform the management of patients with HCV with cure rates of >90%, treatment durations of a few weeks and minimal side effects.

Acute Viral Hepatitis

Hepatitis A and E present as acute hepatitis cases. Both are enterically transmitted infections spread through faeco-oral route.
Neither virus is likely to cause a prolonged viraemia or chronic liver disease.
Both are important causes of hepatitis in patients who have travelled to high risk countries and have not been vaccinated for Hepatitis A.

Management of such patients should be in consultation with a local hepatologist.
Many can be managed safely at home with regular symptom and blood test monitoring. Other others may need admission to hospital.

Alcohol related Liver Disease

In the UK alcohol is the commonest cause of liver disease. The UK is one of the few European countries where alcohol consumption has risen in the last 50 years.
In east London there is a large population of non-drinkers, but the relatively low rates of hospital admission in comparison with the rest of England is no cause for complacency.

Rates of emergency admissions for alcohol related liver disease *(HSCIC data 2012)*

Tower Hamlets	8.7/100,000
Newham and	6/100,000
City and Hackney	3.4/100,000
ENGLAND	24.7/100,000

The risk of alcohol relates damage increases steadily for women drinking over 35 units per week, and for men over 50 units.

Alcoholic liver disease consists of three stages:

- Fatty liver or steatosis
- Alcoholic hepatitis
- Alcoholic cirrhosis

About 1 in 10 patients who drink heavily will go on to develop cirrhosis. Alcohol related cirrhosis of the liver can occur without preceding clinical episodes of alcoholic hepatitis.

The Role of Primary Care in Managing Alcoholic Liver Disease (ALD)

- Awareness of the physical, psychological and social manifestations of ALD.
- Use the AUDIT C alcohol screening tool at the new patient check and when concerned about alcohol excess.
- Assess and support motivation to change.
- Encourage use of alcohol recovery services.
- Minimise harm for those not ready to change.

Referral to hepatology is indicated for **alcoholic cirrhosis** (often identified on USS). Decompensated liver disease has many complications including: jaundice, oesophageal varices, low platelets, prolonged prothrombin time, low albumin.

AUDIT C alcohol screening tool

Figure 2 AUDIT-C alcohol screening

1. How often did you have a drink containing alcohol in the past year?

Never	(0 points)

If you answered never, score questions 2 and 3 as zero.

Monthly or less	(1 point)
2 to 4 times a month	(2 points)
2 or 3 times per week	(3 points)
4 or more times a week	(4 points)

2. How many drinks did you have on a typical day when you were drinking in the past year?

1 or 2	(0 points)
3 or 4	(1 point)
5 or 6	(2 points)
7 to 9	(3 points)
10 or more	(4 points)

3. How often did you have 6 or more drinks on one occasion in the past year?

Never	(0 points)
Less than monthly	(1 point)
Monthly	(2 points)
Weekly	(3 points)
Daily or almost daily	(4 points)

The AUDIT-C (Alcohol Use Disorders Identification Test–Consumption) is scored on a scale of 0 to 12 (a score of 0 reflects no alcohol use). A score of 3 or more in older adults is considered positive and suggests the need for further evaluation. Generally, the higher the AUDIT-C score, the more likely it is that the patient's drinking is affecting his or her health and safety.[30]

Assess alcohol consumption using Audit C. Also include a record of units/week . A score of 4 and above on Audit C, or more than 6 drinks on any ONE occasion in the last year, should lead to a more detailed enquiry about alcohol consumption.

https://www.nice.org.uk/guidance/cg115

Local Alcohol Services
Local drugs and alcohol recovery teams provide counselling, day programmes or inpatient or home detoxification.

1. Tower Hamlets http://www.rapt.org.uk/content/tower-hamlets-community-alcohol-team-thcat
2. Newham DASL http://www.dasl.org.uk/newham-services.html
3. City and Hackney http://www.eastlondon.nhs.uk/Services/Specialist-Addiction/Specialist-Services/Alcohol-Recovery-Centre-%28ARC%29.aspx Tel: 020 8985 3757

National Alcohol Services
Alcoholics anonymous 08457697555

Non alcoholic fatty liver disease (NAFLD)

NAFLD is an umbrella term for the spectrum of liver damage including fatty liver, non-alcoholic steato-hepatitis and cirrhosis, without alcohol being the causative agent. NAFLD is best considered as the hepatic manifestation of the metabolic syndrome. Obesity and insulin resistance are major risk factors for NAFLD.
A large European study found NAFLD in 94% of obese patients (BMI>30), 67% of overweight patients (BMI>25) and 25% of normal weight patients. Between 40-70% of patients with NAFLD have Type 2 Diabetes.
The combination of increasing diabetes prevalence and increasing obesity in younger populations, particularly among south Asian groups, suggests there will be a large increase in the incidence of NAFLD in east London.

Populations at risk of NAFLD include:

- Those overweight or obese
- Insulin resistance/Type 2 diabetes
- Hypertension
- Hyperlipidaemia
- Ethnicity- Bangladesh

Prevalence and complications of non-alcoholic fatty liver disease (NAFLD)

NAFLD

- Simple steatosis (fatty liver) population prevalence 20-30%, present in up to 70% of people with Type 2 diabetes
- Excess fat builds up in the liver. Asymptomatic, but LFTs may be abnormal.
- REVERSIBLE if the underlying cause (obesity) is tackled.

Over 75% of people with NAFLD have simple steatosis, which is a benign condition, unlikely to progress to fibrosis or cirrhosis.

NASH

- 15% of those with NAFLD have evidence of liver inflammation (non-alcoholic steatohepatitis NASH) and may have fibrosis. LFTs may be abnormal.
- for those who develop NASH 5% will go onto develop hepatocellular carcinoma (HCC)
- Liver damage is REVERSIBLE if the underlying cause (obesity) is tackled .

Cirrhosis

- Cirrhosis
- Occurs in about 10-20% of those with NASH.
  Many will have Type 2 Diabetes.
  Liver function can be preserved by behavioural and lifestyle modification

Liver failure

- Liver failure and hepatocellullar carcinoma.
- Cirrhosis progresses over years, with gradual failure of liver function.

Identification of NAFLD in primary care

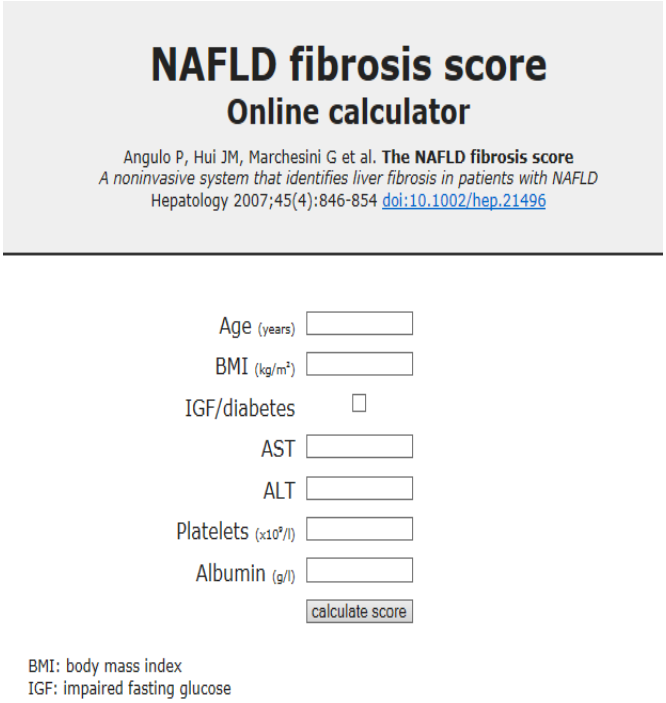
The following features may indicate a diagnosis of NAFLD

- **Negative** alcohol history
- Obesity
- Elements of the metabolic syndrome (Type 2 Diabetes, Hyperlipidaemia, Hypertension)
- AST/ALT ratio ≤ 1
- Negative liver screen (hepatitis B and C, autoimmune screen and immunoglobulins, ferritin)
- Fatty liver on USS

Is a liver ultrasound test needed to make a diagnosis of NAFLD?

The definitive diagnosis of NAFLD requires evidence of excess fat in the liver, which may be seen on USS testing, or by liver biopsy.
However, for those patients who have evidence of the metabolic syndrome (Type 2 diabetes, obesity, CVD, hypertension), and liver screening is otherwise normal, there is a high probability of NAFLD.

The NAFLD Fibrosis score calculator



Risk Stratification of NAFLD

The NAFLD fibrosis score uses routine clinical and laboratory data to estimate the risk of inflammation and fibrosis in patients with NAFLD.
Use of the score can stratify the fibrosis risk, and reduce the number of diagnostic liver biopsies required.

Using the NAFLD fibrosis score in primary care helps to identify which patients can be managed in general practice, and which patients should be referred for specialist investigation and follow up.

An online tool to calculate the NAFLD fibrosis score can be found at www.nafldscore.com

The result should be entered into EMIS Web using the term 'NAFLD fibrosis score'

Using the NAFLD Fibrosis score in practice

Scores < -1.455: predictor of absence of significant fibrosis. *(negative predictive value of 88-93%)*
These patients can be managed in primary care

Scores ≤ -1.455 to ≤ 0.675: indeterminate.

Scores > 0.675 suggest a high risk of fibrosis. *(positive predictive value of 82%-90%)*
Patients should be referred onto secondary care for elastography (fibroscan) or liver biopsy.

Patients with high or indeterminate scores should be referred to secondary care for further assessment. Many will require a liver biopsy or fibroscan to assess the extent of fibrosis.

Management of NAFLD

1. The mainstay of treatment for ***all*** NAFLD patients is advice on lifestyle modification to reduce weight and increase physical activity. This can reverse fatty changes and early liver inflammation (NASH).

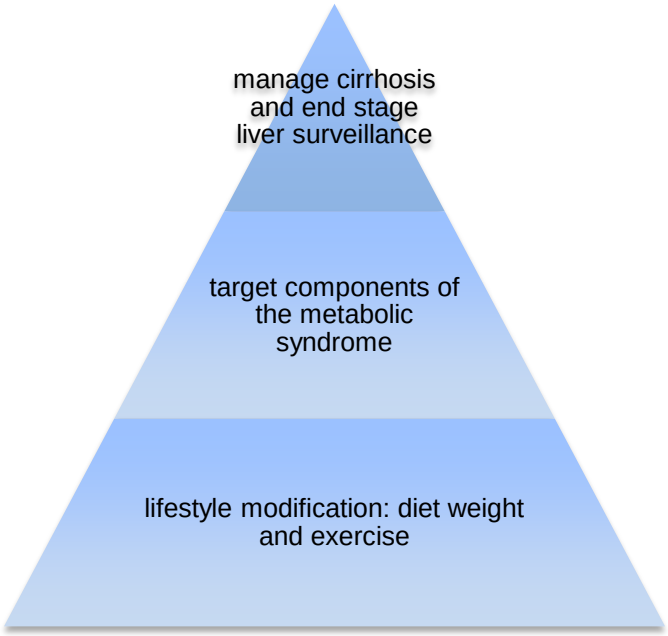
2. Active management of co-existing components of the metabolic syndrome (diabetes, hypertension and dyslipidaemia).

NAFLD patients with simple fatty liver (with a fibrosis Score < -1.455) can be managed in primary care.

NAFLD patients with steato-hepatitis and evidence of fibrosis are at highest risk of progressive liver disease, and will need more aggressive lifestyle modification.

Patients with cirrhosis require specialist surveillance for hepatocellular carcinoma (HCC).

Summary of NAFLD management



Resources for Lifestyle Change

Local resources

- Healthwise- Exercise on prescription. This requires bloods/ BP /pulse and a diagnosis
- Health trainers- In Newham and Tower Hamlets
- Hackney ICARE website http://www.hackneyicare.org.uk/

National resources

- Weight watchers
- Slimming world (small cost to the patient)
- PARKRUN every Saturday morning www.parkrun.org.uk

Information for Patients

Patient information about NALFD is available on NHS choices, patient.co.uk or on EMISWeb systems on entering a diagnosis of NAFLD.
www.patient.co.uk/health/non-alcoholic-fatty-liver-disease

Monitoring LFTs in NAFLD without fibrosis

There is no evidence for benefit of monitoring LFTs in NAFLD where there is simple fatty liver, but no evidence of fibrosis or cirrhosis.

LFTs seem to have little predictive value for severity of liver disease or future mortality risk until late disease when the bilirubin rises or the albumin falls.

Currently there are no effective pharmacological treatments.

Hence, there is little value in monitoring LFTs on a regular basis. Instead focus efforts on lifestyle interventions, and monitoring and treating the individual components of the metabolic syndrome.

Pregnancy related liver disorders:

Cholestasis of pregnancy
(Prevalence - 2% of pregnancies)
Presents with generalised pruritus.
Check LFTs and bile acids. Referral to secondary care is indicated. There will be elevation of alkaline phosphatase and transaminases. Intrahepatic cholestasis can lead to foetal loss due to placental insufficiency.

Acute fatty liver of pregnancy
This rare but serious condition presents with nausea, abdominal pain and hypoglycaemia around 34-36 weeks of pregnancy.
Any woman with these features should be referred immediately to hospital

Less common Liver Disorders include:

Haemochromatosis (bronze diabetes).
(*Prevalence approx.1 in 200 in European populations).*
A genetic disorder resulting in iron overload.
Presents with fatigue, diabetes, hypogonadism, cardiomyopathy, arthralgia, arrhythmias.
Diagnosis by liver biopsy.
Treatment is therapeutic phlebotomy.

Autoimmune hepatitis (AIH)
(Prevalence 10-17 per 100,000 population).
AIH is an immune mediated relapsing liver disease. It is associated with elevated immunoglobulins and transaminases and a positive autoimmune serology.
It is more common in women.

Primary Biliary Cirrhosis
(Prevalence 1 in 4,000, mainly women)
Primary biliary cirrhosis (PBC) is a slowly progressive autoimmune disease of the biliary system causing progressive obstructive jaundice.

Primary Sclerosing Cholangitis
(PSC) is an uncommon condition affecting the bile ducts and liver. Inflammation and scarring of the bile ducts can lead to liver damage and cirrhosis

Wilson's disease
(Prevalence estimated at 1 in 30,000).
A treatable autosomal recessive disorder of hepatic copper deposition. Classically affects the eyes with Kayser Fleischer rings – copper accumulation in the Iris. Hepatic disease includes steatosis and cirrhosis.

Prescribed Drugs and the liver

Statins

Recent guidance from NICE and CEG recommends checking LFTs before starting statins.
Use the ***ALT*** alone.

Statins do not cause liver disease.
They are often associated with mild increases in liver transaminases and rarely > 3 fold rises. These are usually transient.
The benefit of being on a statin usually outweighs the risk of liver damage, particularly in those with NAFLD.

1. Test liver ALT before starting statin therapy to identify pre-existing disease.

2. If the baseline test is normal and there is no previous history of liver disease, no further monitoring of LFTs is required unless clinically indicated.

3. If ALT is raised take a careful history, perform clinical examination and further testing (full liver screen – see P.3)

4. Raised transaminases should not preclude appropriate statin use, though LFTs should be monitored.

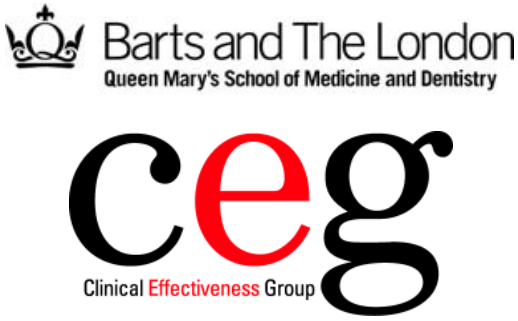
Other Drugs which can affect the liver

Many drugs can potentially damage the liver.
Always consider a drug related cause for abnormalities of liver function, especially following the recent introduction of a new medication.

When prescribing in primary care for a high risk medication *(e.g. methotrexate, azathioprine, mycophenolate*) with a shared care agreement, it is essential for GPs to arrange and record regular monitoring blood tests, with appropriate advice to patients on monitoring intervals and results.

Advice for clinicians

Barts Health NHS Trust http://www.bartshealth.nhs.uk/our-services/ The Royal London Hospital	Hepatology Biochemistry Virology	020 3594 3200 hepatologyservices@bartsandthelondon.nhs.uk 020 3246 1013 020 3246 0364/0331
Barts Health NHS Trust Newham University Hospital	Gastroeterology Virology Biochemistry	020 7363 8084 020 3246 0318 020 7363 8120
Homerton University Hospital NHS foundation trust http://www.homerton.nhs.uk/	Gastroenterology Virology Biochemistry	020 8510 7435 huh-tr.gastro@nhs.net (via BartsHealth) 020 3246 0318 020 8510 7886



Acknowledgements

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