Dr Rachael Harry

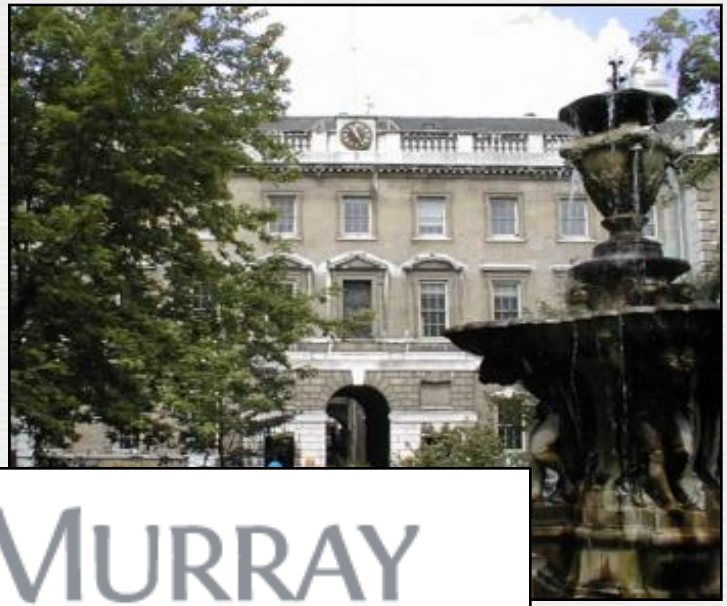
Hepatologist, Auckland

Abnormal Liver Function - Concurrent Workshop Repeated

Saturday, 11 June 2011	Start 2:00pm	Duration: 55mins	Skellerup
	Start 3:05pm	Duration: 55mins	Skellerup

Abnormal LFTs

Dr Rachael Harry
Hepatologist



MACMURRAY
GASTROENTEROLOGY
Phone 09 550 1080 Fax 09 550 1081

Abnormal LFTs

- Introduction
- Cases
  - Who to investigate?
  - How to investigate?
  - When to investigate?
- Guidelines for referral
- What happens next?

THE LIVER FUNCTION TESTS

AST
ALT

ALP
GGT

BILIRUBIN
INR
ALBUMIN

HEPATITIC

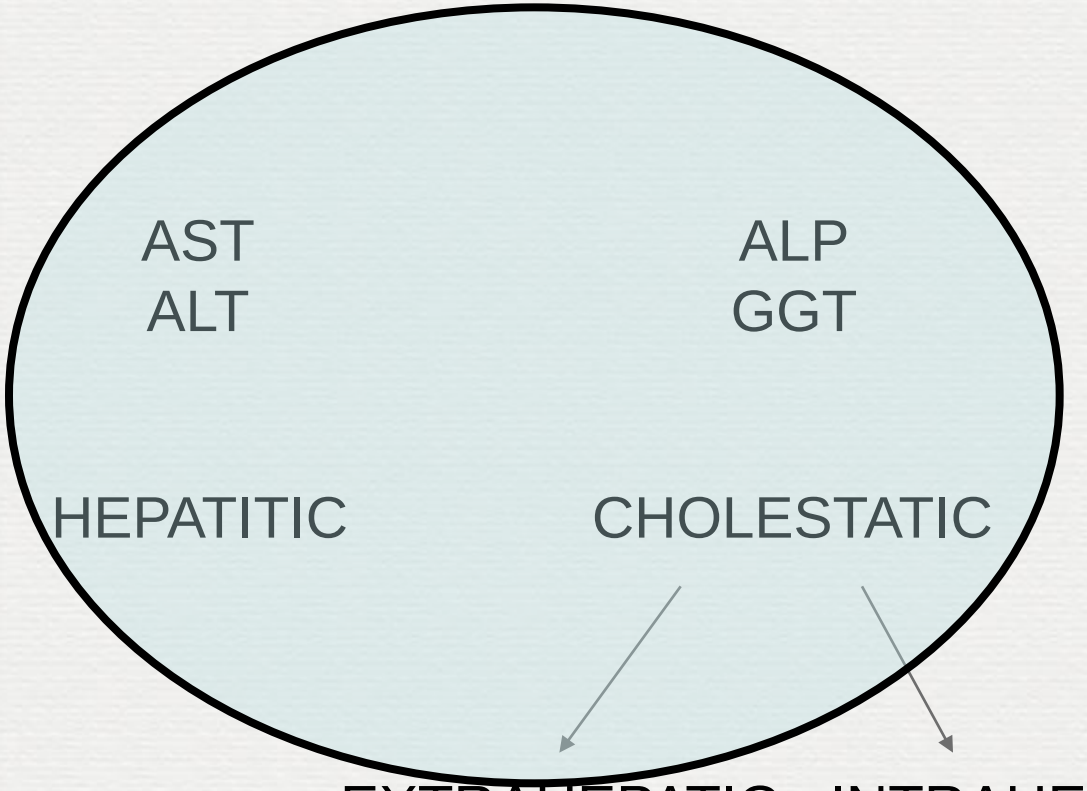
CHOLESTATIC

SYNTHETIC FUNCTION

EXTRAHEPATIC

INTRAHEPATIC

THE LIVER FUNCTION TESTS

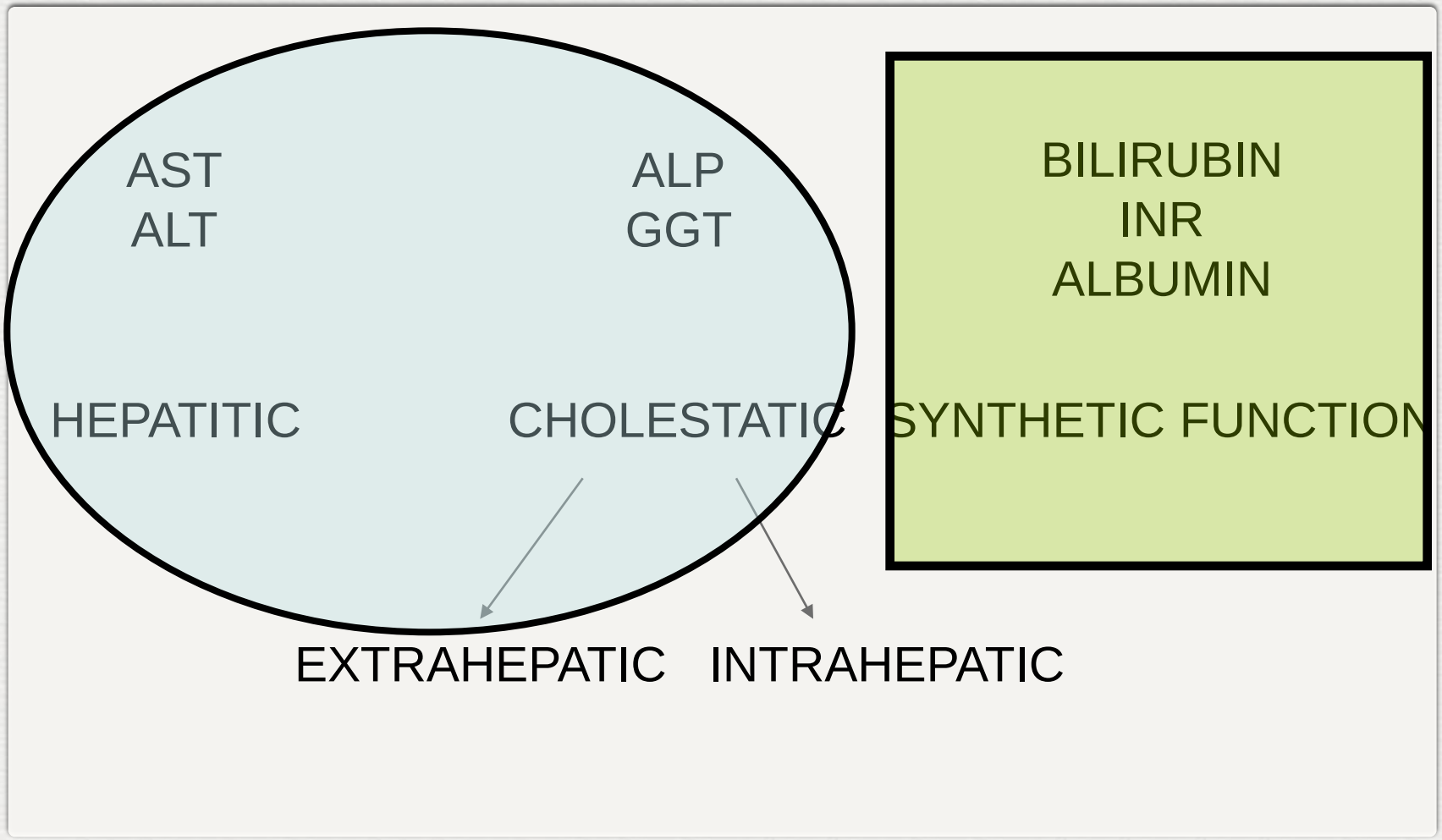


BILIRUBIN
INR
ALBUMIN

Common causes

- Hepatitic - liver parenchymal injury
  - Alcohol/ NAFLD
  - Viral hepatitis
  - Drug induced
- Biliary - intra hepatic bile ducts
  - Primary Sclerosing Cholangitis
  - Primary Biliary Cirrhosis
- Biliary - extra hepatic

THE LIVER FUNCTION TESTS

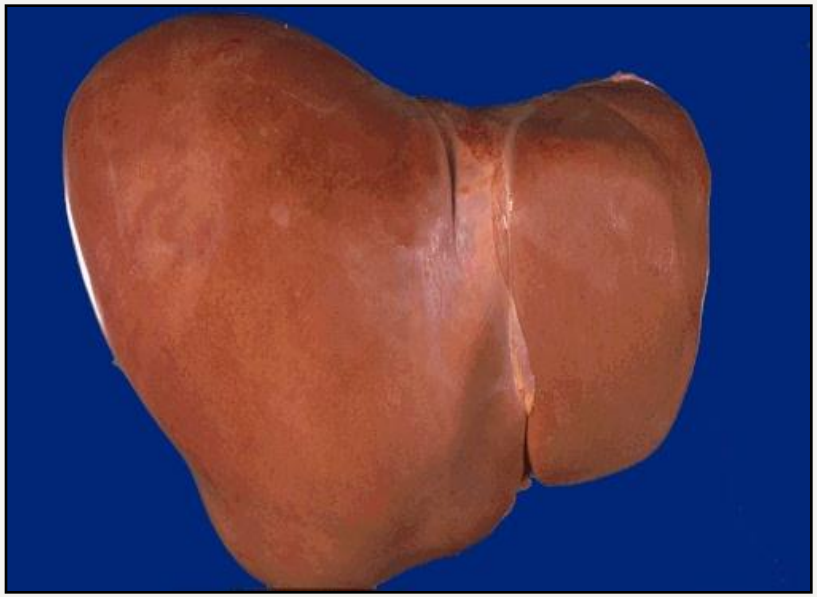


Abnormal Liver function tests

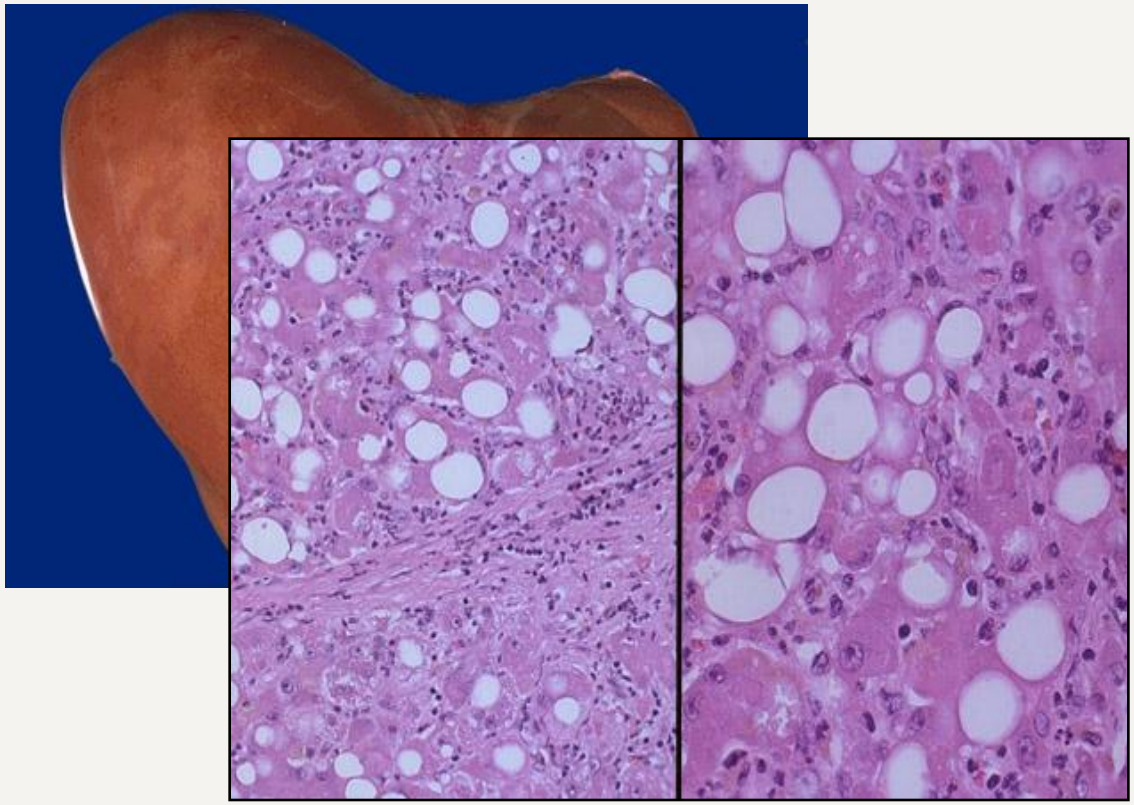
- Indicate liver pathology
- Isolate site of injury
- Function of the liver

- At a given point in time.....

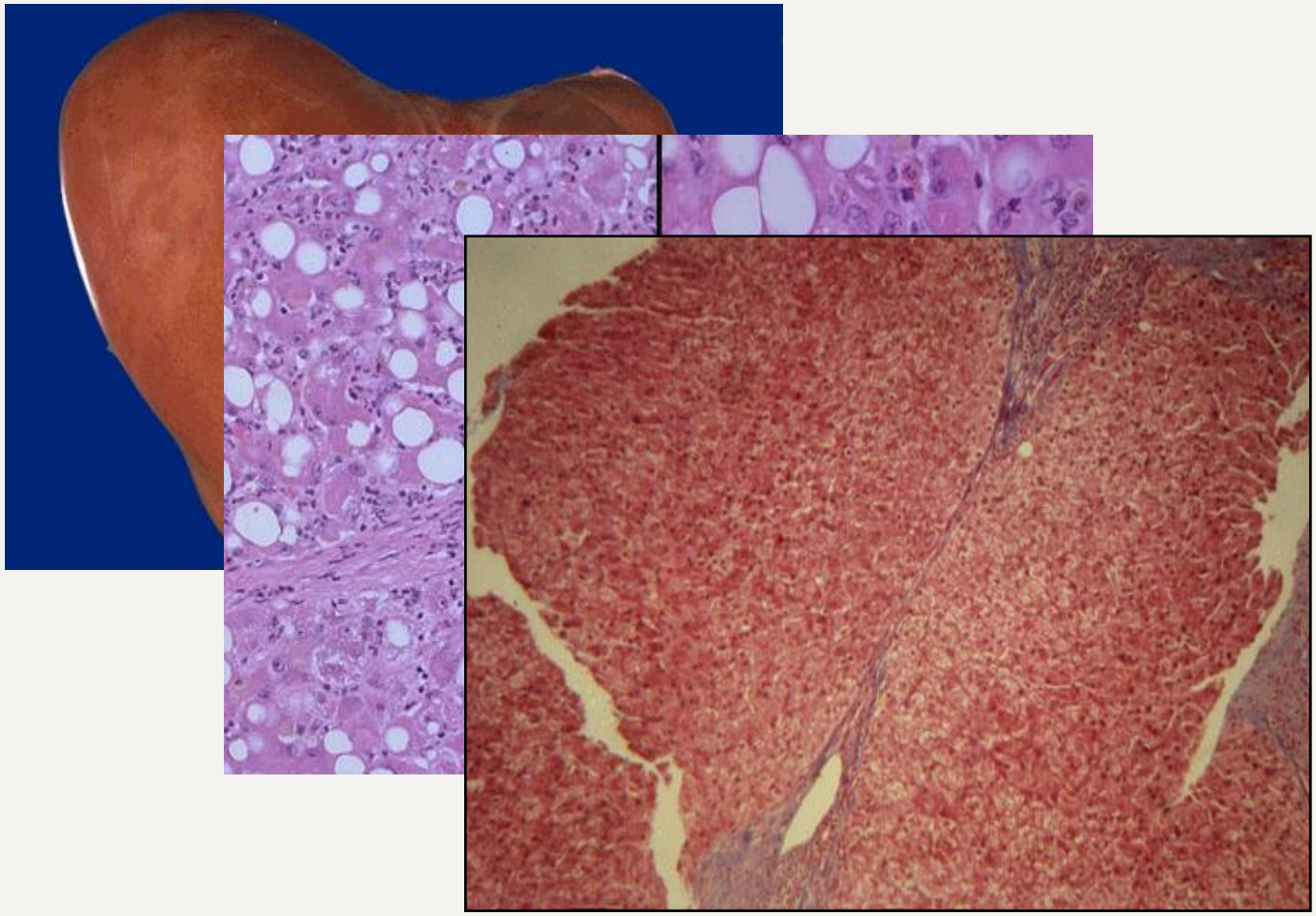
Progression of chronic liver disease



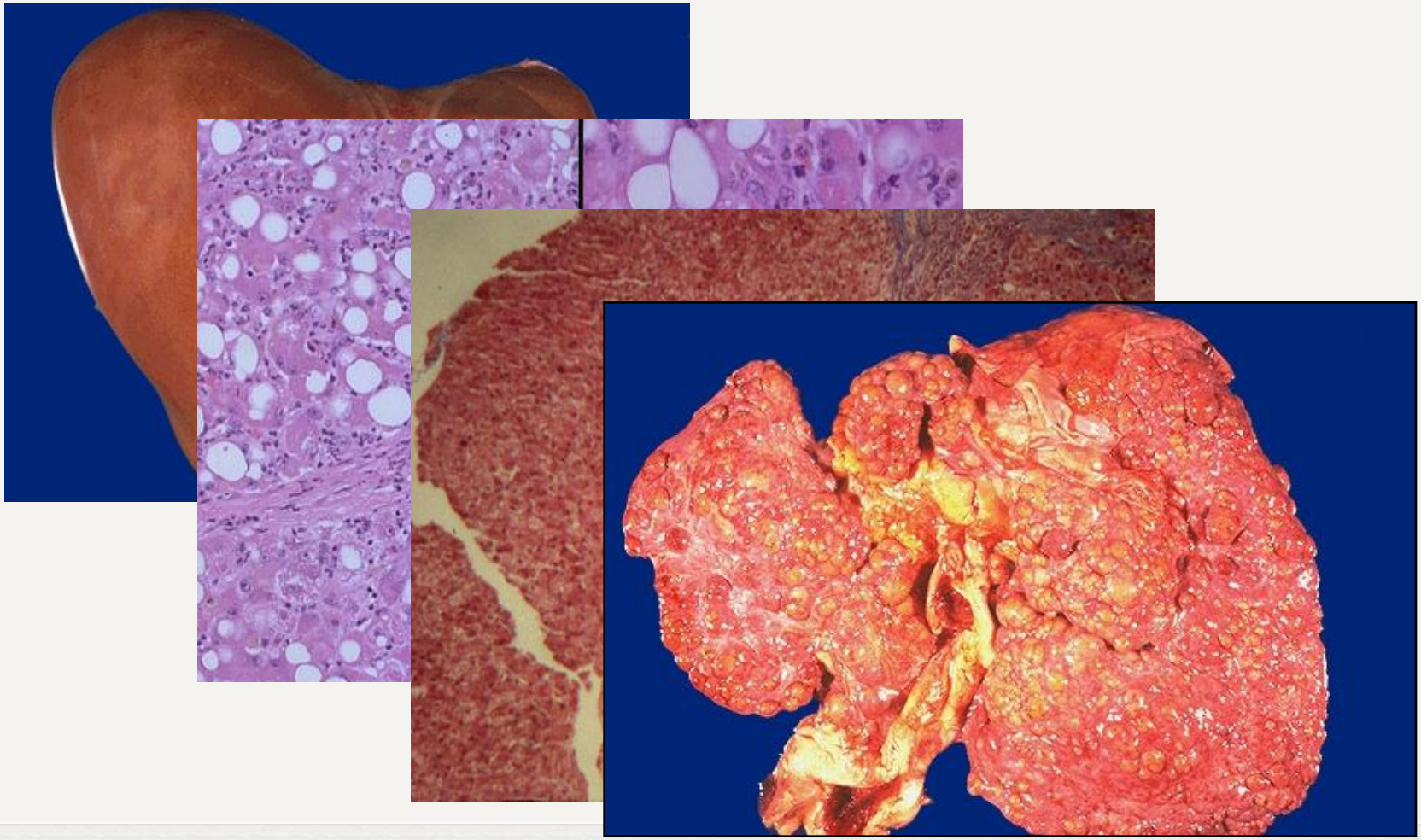
Progression of chronic liver disease



Progression of chronic liver disease



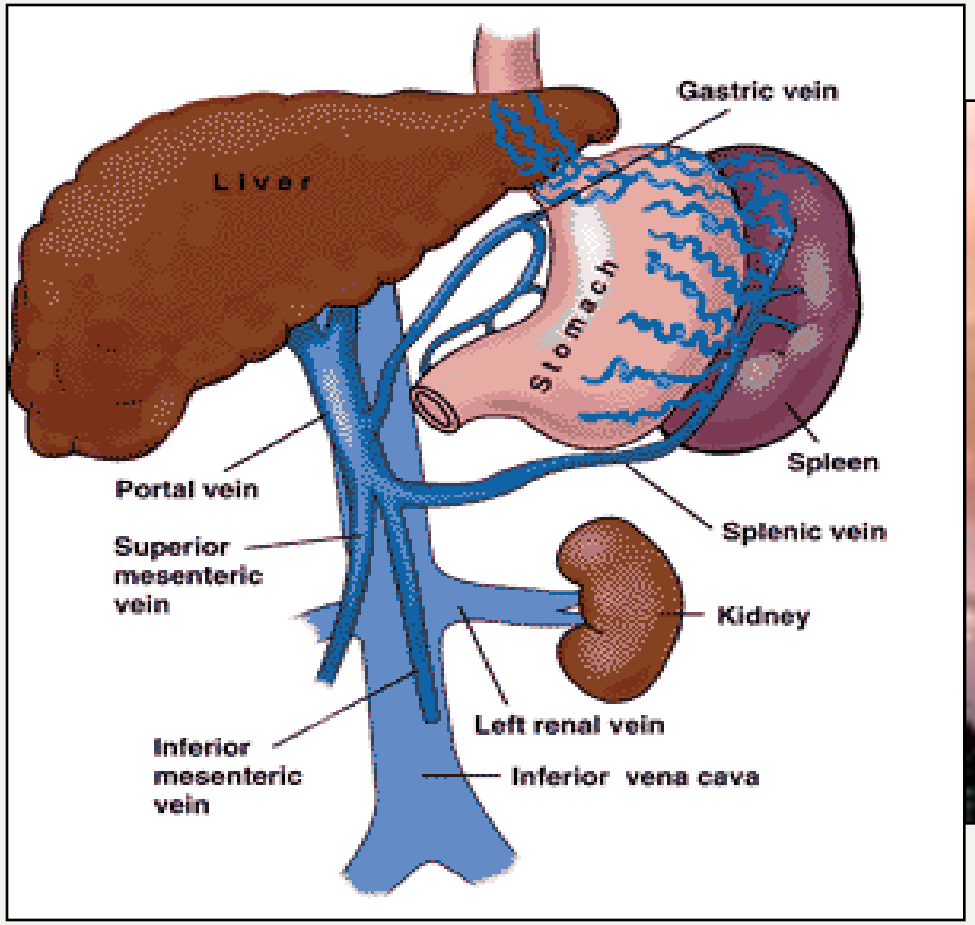
Progression of chronic liver disease

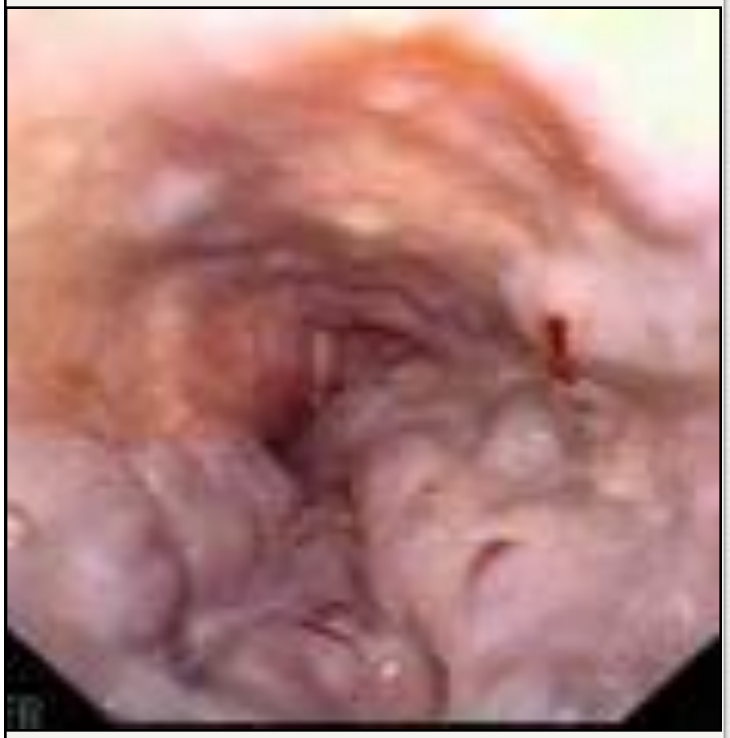


Cirrhosis

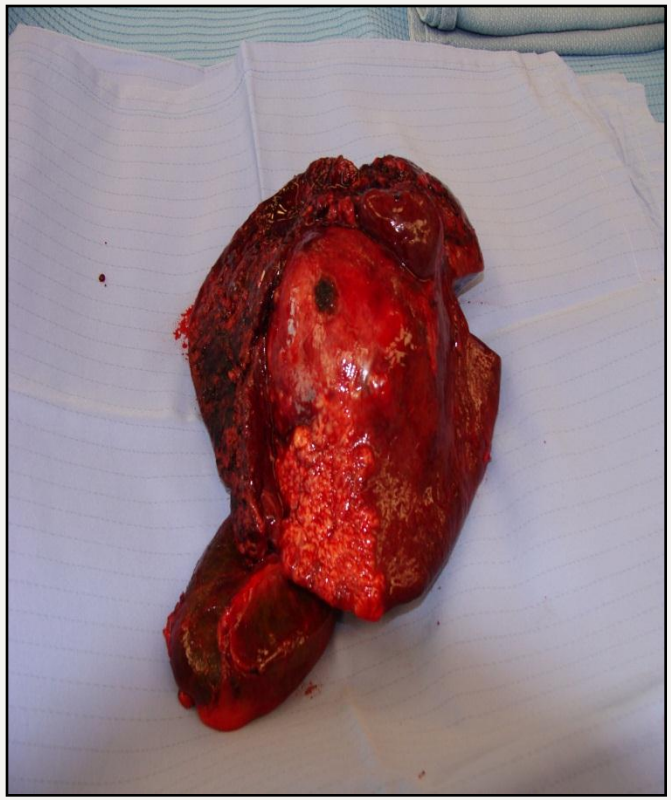
- End stage of any chronic liver disease left untreated
- Responsible for the life threatening complications of most chronic liver disease

Portal hypertension





Hepatocellular carcinoma



- Primary liver tumour
- Common in cirrhosis due to HBV and haemochromatosis
- Treatable if diagnosed early
- Screening USS/ AFP

Liver failure

- The liver fails to meet the demands of the body
- Acute (<12 weeks) or Chronic (cirrhotic)
- Patient presents with evidence of failure of functions of the liver
  - Bilirubin
  - Albumin
  - INR
  - Encephalopathy

Liver function tests

- Indicate liver pathology
- Isolate site of injury

May also:

- Be a screening test for diseases at risk of progression to cirrhosis
- Suggest underlying cirrhosis or complications of cirrhosis

Cases

- Who to investigate?
- When to investigate?
- How to investigate?

A typical patient

- Fit and well
- No FHx, PHx
- No medications
- O/E NAD
- Screening bloods
  - AST 80 ALT 60
  - ALP 120, GGT100

What do we do?

- Ignore it - its only a minor abnormality?
- Repeat it?
- Investigate immediately?

What do we do?

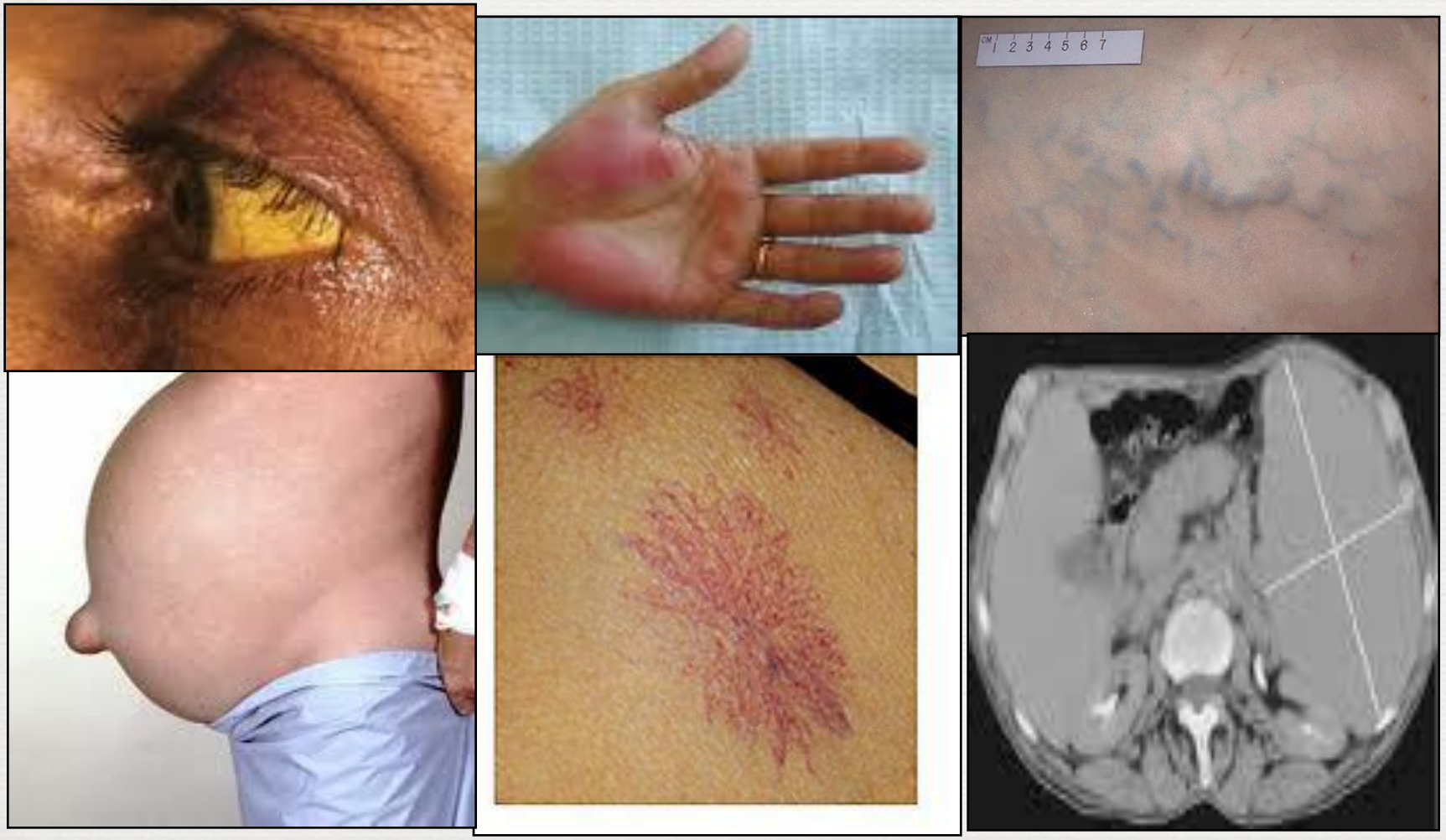
- Ignore it - its only a minor abnormality?
- Repeat it?
  - History, Examination,
  - Exclude cirrhosis or liver failure,
  - Stop drugs/ alcohol
  - Repeat
- Investigate to find cause immediately?

Clues in the history

- HBV: Ethnicity
- HCV: High risk behaviors
- NAFLD: Metabolic syndrome
- Autoimmune hepatitis: woman, other AI conditions
- Primary Biliary Cirrhosis: woman, high cholesterol
- Primary Sclerosing Cholangitis : UC
- Haemochromatosis: Family history
- Alcohol: diary, social consequences, occupation
- Drug: time line of new drugs

How much is too much?

Examination



Clues in tests: AST/ALT

- MINOR (<100 IU/l)
  - Chronic hepatitis C and B
  - Haemochromatosis
  - Fatty liver
- MODERATE (100-300 IU/l)
  - Alcoholic hepatitis
  - NASH
  - Autoimmune liver disease
  - Wilsons
- HIGH (>1000 IU/l)
  - Acute viral hepatitis
  - Autoimmune liver disease
- VERY HIGH (10, 000+)
  - Ischaemic hepatitis
  - paracetamol,

Review in 3/12

- No alcohol
- Stops herbal meds
- Repeat 3/12

- Bili 17, Alb 47, INR 1
- AST 110 ALT 60
- ALP 110, GGT 100

What do we do?

- Ignore it - its only a minor abnormality?
- Repeat it?
- Investigate?

What do we do?

- Ignore it - its only a minor abnormality?
- Repeat it?
- Investigate the underlying cause
  - ?How

What do we want to know?

- Is there a significant liver disease?
- If so, how bad is it?
  - Does she have cirrhosis?
  - Does she have liver failure?
- Might it progress?
- Is it treatable?

‘liver screen’

- Viral hepatitis
- Haemochromatosis
- AIH
- PBC
- Alpha 1 antitrypsin deficiency
- Wilsons
- Sarcoid
- Misc
- Focal lesions/ cirrhosis

‘liver screen’

- Viral hepatitis
- Haemochromatosis
- AIH
- PBC
- Alpha 1 antitrypsin deficiency
- Wilsons
- Sarcoid
- Misc: thyroid, coeliac
- Focal lesions/ cirrhosis

‘liver screen’

- Viral hepatitis
- Haemochromatosis
- AIH
- PBC
- A-1-antitrypsin def
- Wilsons (age)
- Sarcoid
- Misc
- Focal lesions/ cirrhosis

- HBV sAg / HCV ab
- ferritin
- SM Ab, ANA, IgG
- antimitchondrial Ab, IgM
- alpha 1 antitrypsin level
- copper/ caeruloplasmin
- ACE level,
- TFT, coeliac screen
- USS

A typical patient

- HBV/HCV negative
- USS- fatty liver
- Anti SMAB - 1:80
- Other immune markers -ve

- What now?

A typical patient

- Diagnosis NAFLD
  - BP, cholesterol normal
  - No DM
  - Lose weight
- Repeat

A typical patient

- Diagnosis NAFLD
  - BP, cholesterol normal
  - No DM
  - Lose weight
- Repeat

- Repeat bloods 6/12 later
- Bili 17
- AST 70, ALT 60
- ALP115, GGT 120
- What now?

What do we do?

- Ignore it - its only a minor abnormality?
- Repeat it?
- Investigate further?

What now?

- Referred
- Tests repeated!

What now?

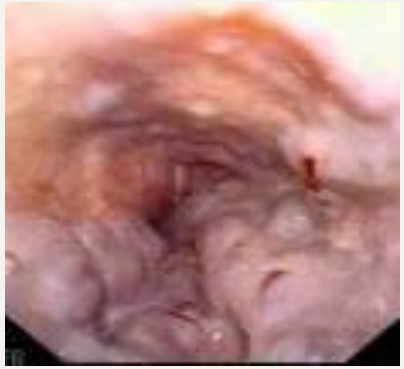
- Referred
- Tests repeated!
- Liver biopsy
  - **established cirrhosis**
  - **consistent with autoimmune hepatitis**

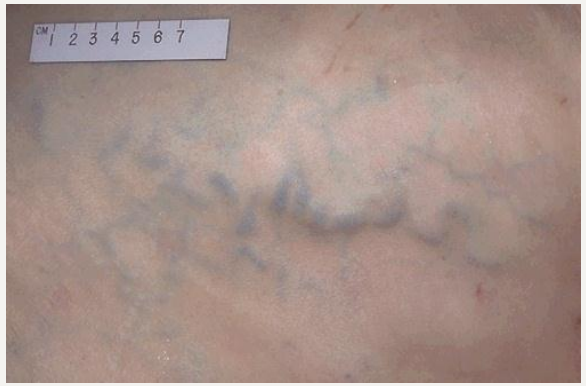
What now?

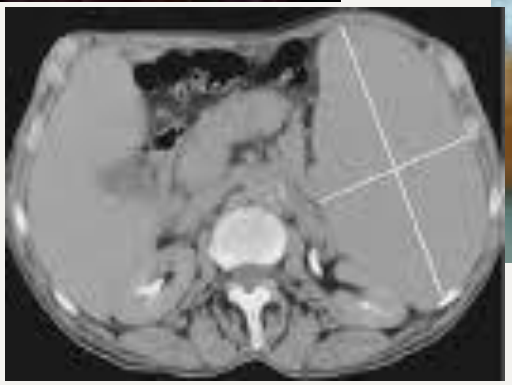
- Referred
- Tests repeated!
- Liver biopsy
  - established cirrhosis
  - consistent with autoimmune hepatitis
- 18/12 after first abnormal LFTs:
- On treatment steroids and azathioprine
- LFTs normal
- USS/AFP 6/12 for HCC screening

Compensated Cirrhosis

- Asymptomatic
- Low platelets, splenomegaly
- Abnormal enzymes but synthetic function normal (Bilirubin, INR, Albumin)







NAFLD

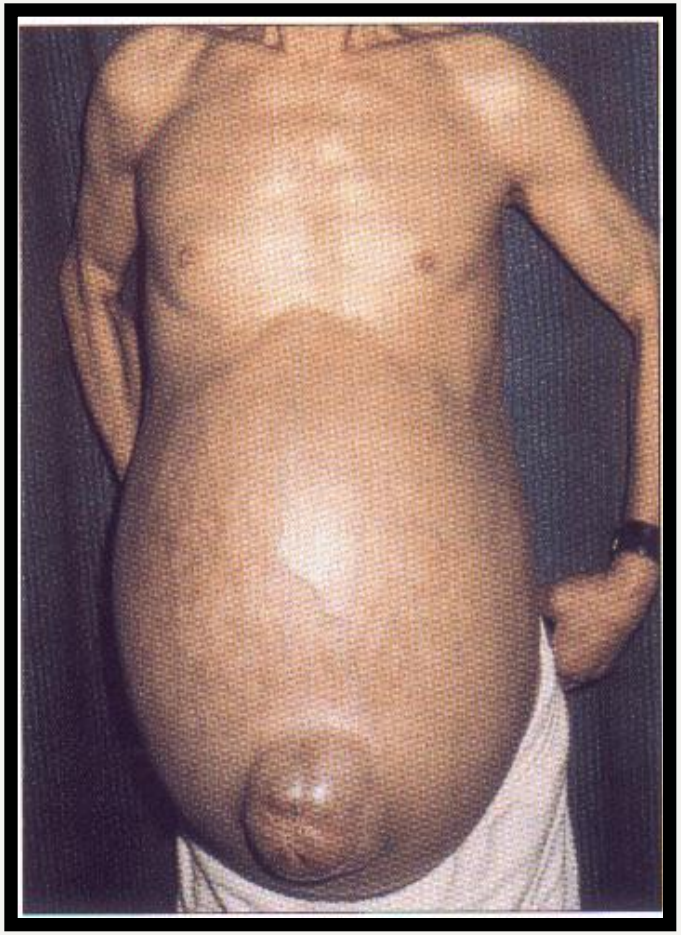
- Is a common cause of low grade LFT abnormalities
- Is associated with obesity, DM, hypercholesterolaemia, hypertension
- Other causes of liver function test abnormalities need to be excluded
- USS finding of echogenic liver does not confimr ath diagnosis
- Treatment is tight control of risk factors
- No specific treatment for NAFLD to reduce progression
- Most patients will die of cardiovascular disease not liver disease

Key points

- **Low grade** abnormality OK to observe before investigation if :
  - No cirrhosis
  - No liver failure
- Beware the diagnosis of NAFLD if
  - no risk factors OR AST/ALT >X2 ULN
- Consider all **reasonable** diagnoses in all patients with **persistent** abnormalities

Another typical patient

- 56 yr old man
- 1/12 Hx abdo swelling
- Bottle whisky/ day
- Nil else on Hx
- O/E



Another typical patient

- Screening bloods
  - bili 17
  - AST 80 ALT 60
  - ALP 120
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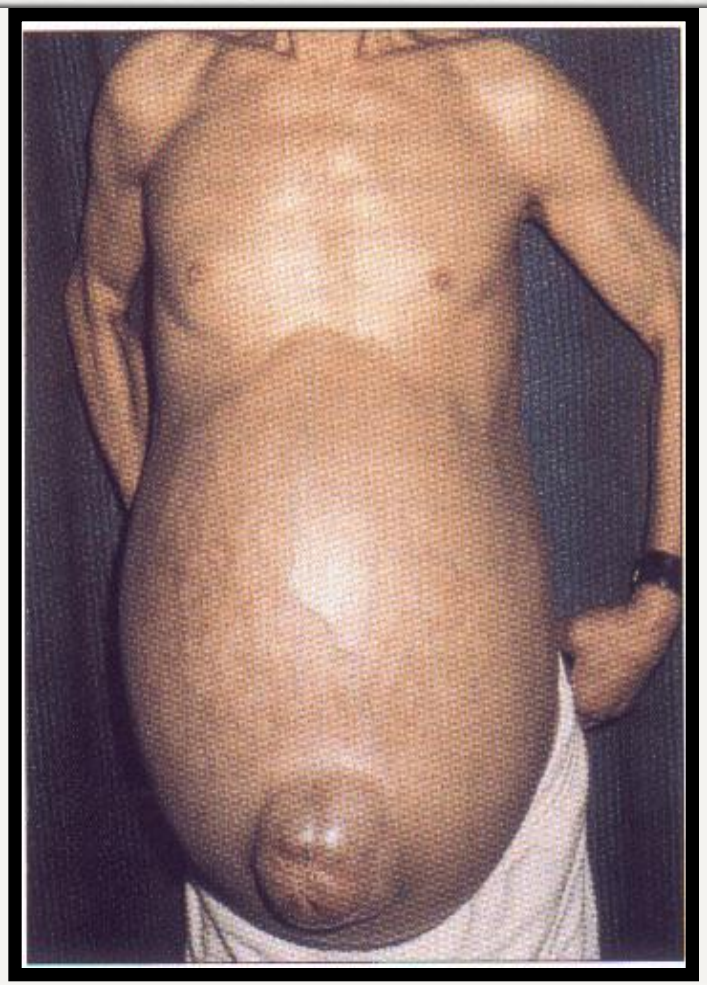
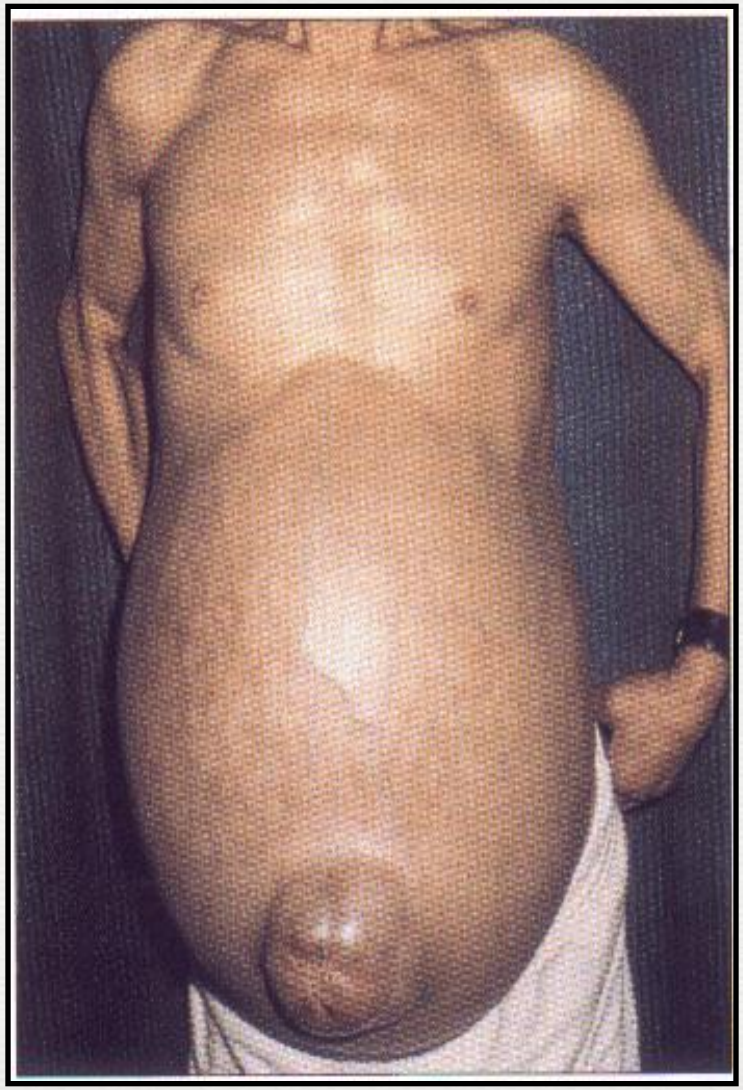
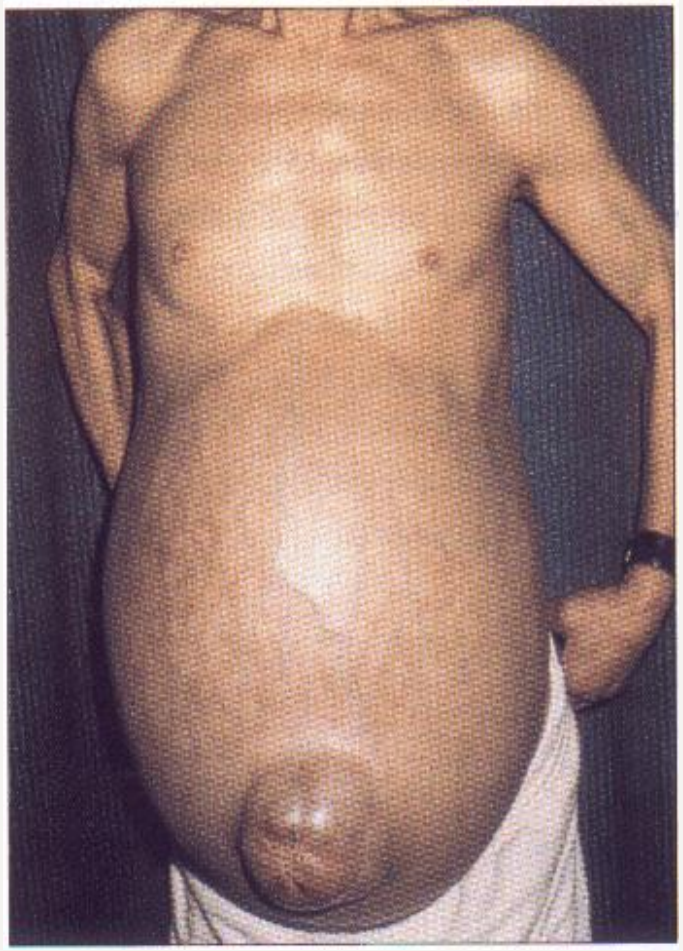


What would you do?

- Tell him to stop drinking and nothing until he does?
- Tell him to stop drinking then investigate?
- Investigate underlying cause immediately?
- Urgent ultrasound?
- Refer?

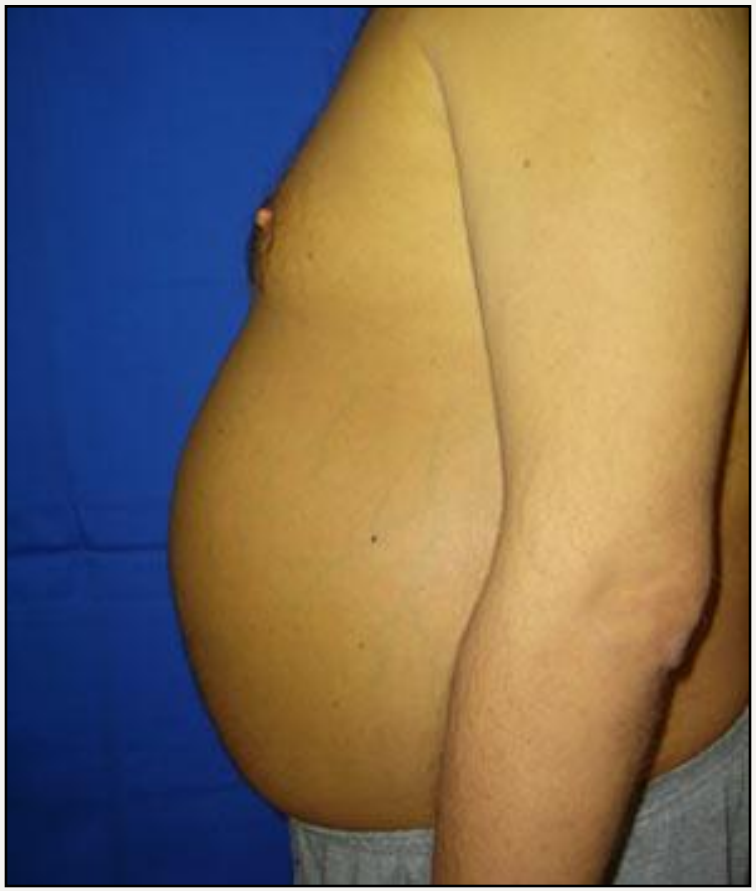


Decompensated cirrhosis



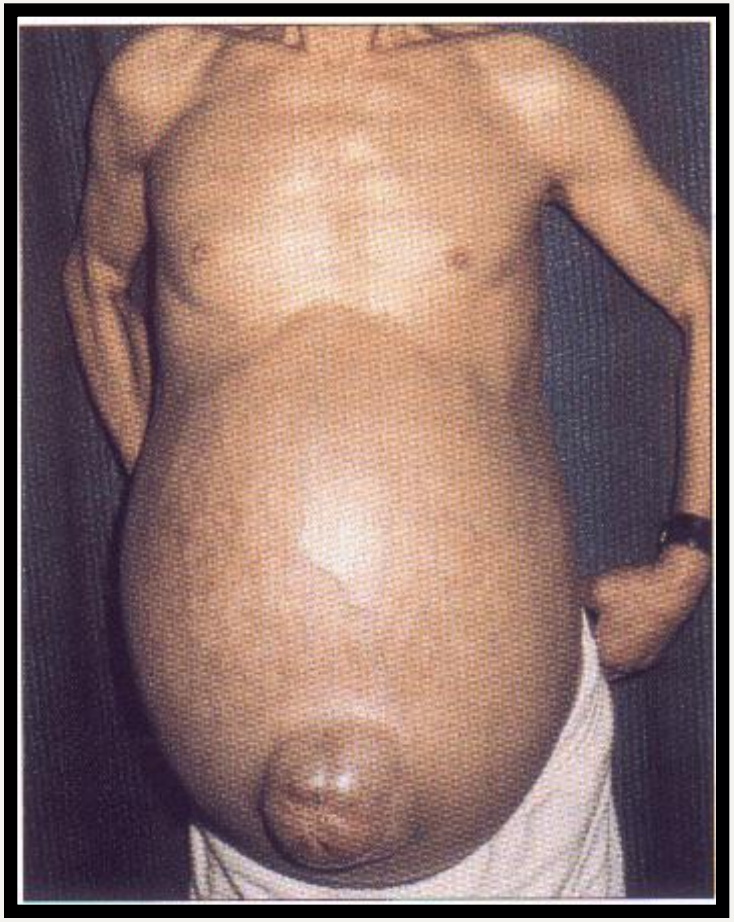
- Increased Bilirubin
- Prolonged INR
- Decreased albumin
- Encephalopathy
- Ascites

Decompensated cirrhosis



- Can be more subtle
- High index of suspicion
- Refer if doubt

Another typical patient

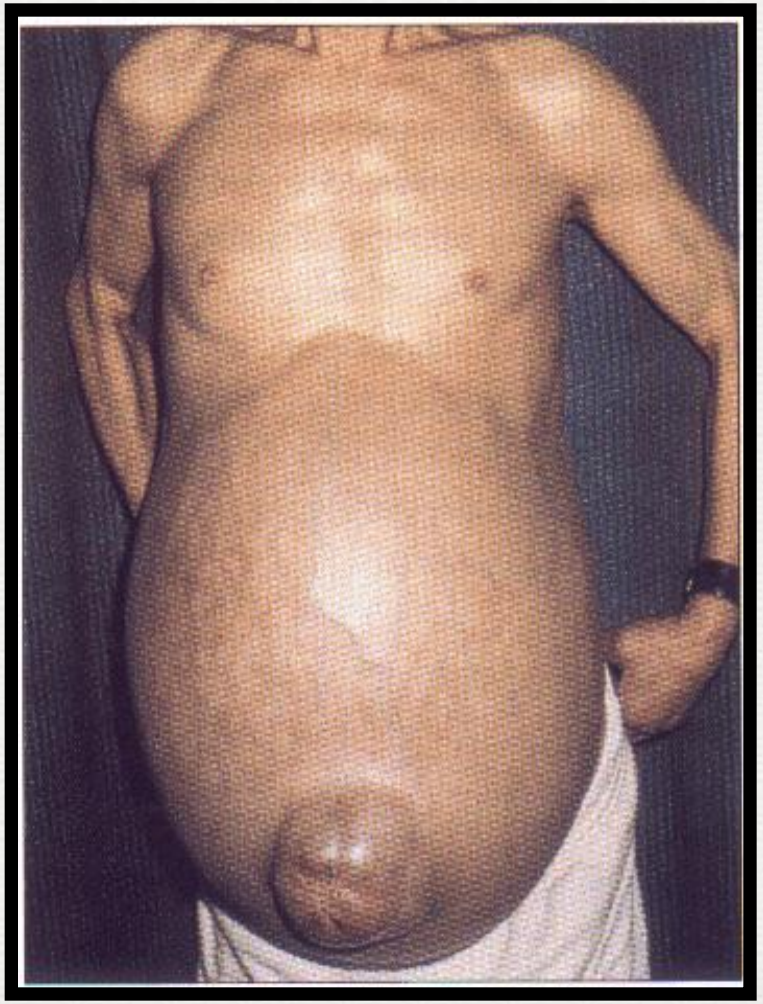


- Liver screen negative
- USS, ascites, small liver
- Almost stops drinking

- What now?

What can you do?????

- Treat ascites ? drain
- Diet
- Abstinence
- ?encephalopathic
- HCC and varices screen
- ?Tx in the future



Importance of cirrhosis

- Prevent it if possible.
- Consider LFTs a screening test
- Treatment may reduce the risk of liver failure or liver cancer even in patients with cirrhosis
- Screening USS/ AFP may detect HCC when treatable
- Is you patient a transplant candidate?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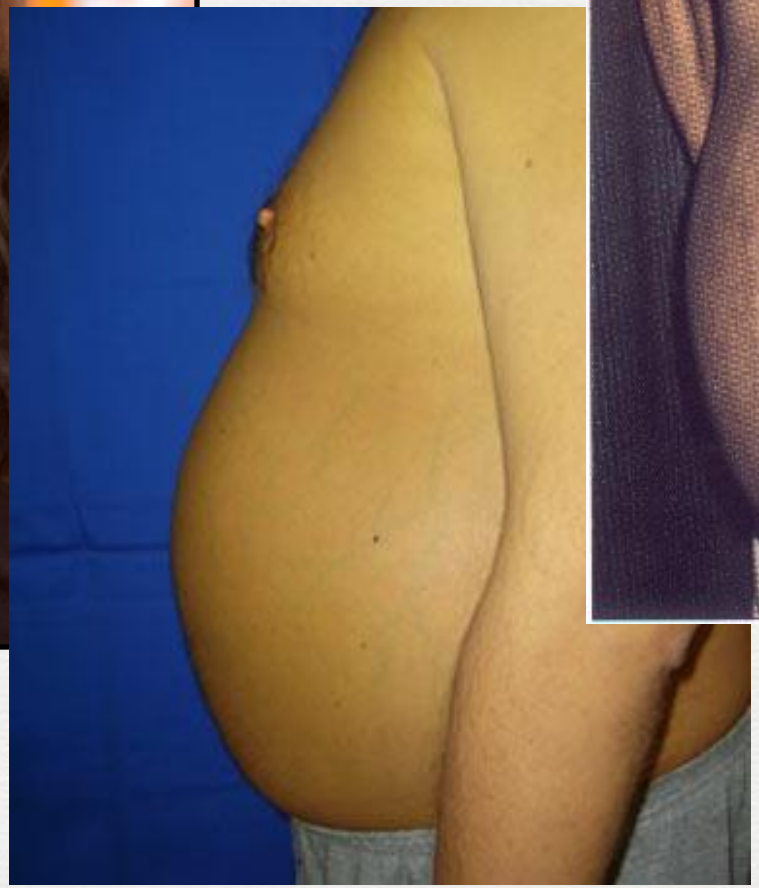

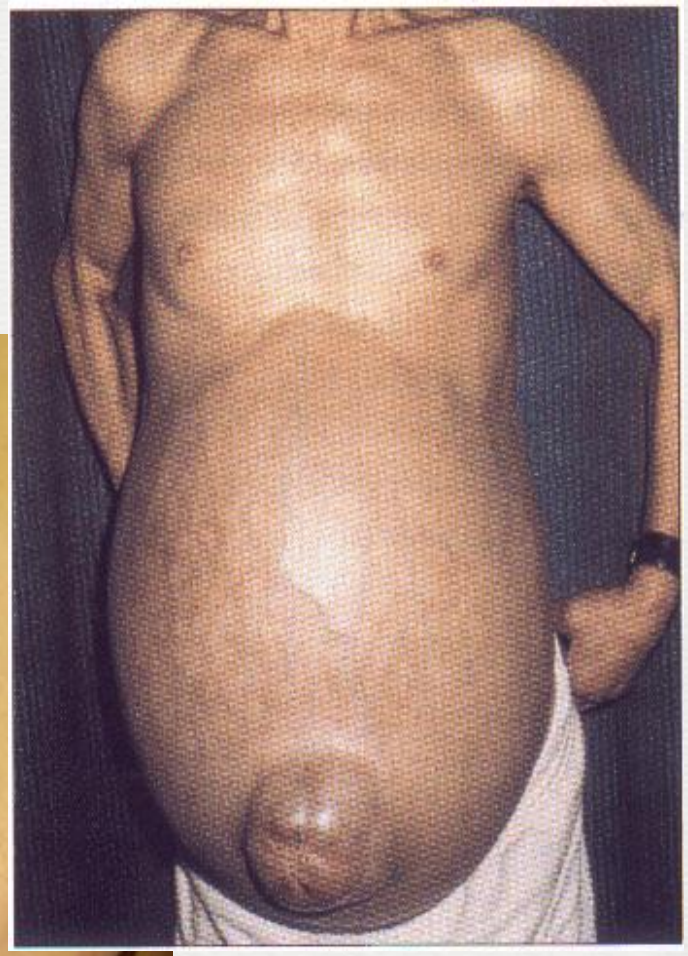

When to refer?

Urgent action required

- Jaundice and evidence of liver failure
  - Immediate discussion and admission
- Jaundice, no liver failure
  - Immediate discussion ?admission
  - Urgent USS, (haemolysis screen)
- Major elevation ALT/ AST (>400)
  - Immediate discussion ?admission
  - Repeat within 24 hours with synthetic function

Less urgent action

- Moderate elevation AST/ALT (>200)
  - INR, Bilirubin, and review early
  - Repeat with 48 hours with liver screen
  - Early referral
- Evidence of cirrhosis, no liver failure
  - Abnormal LFTs, abnormal USS, low platelets
  - Early referral with liver screen

Non urgent action

- Mild Elevation of AST/ALTs(60 - 100)
  - Remove hepatotoxins, Repeat
  - Liver screen in ALL if persistent
  - USS
  - Referral if AST/ ALT > x 2ULN ? liver biopsy
  - Isolated GGT does not require further investigation
  - Fatty liver on USS does not always mean NAFLD

Non urgent action required

- Minor changes (40-60)
  - Remove hepatotoxins, Repeat
  - Liver screen in ALL if persistent
  - USS
- If persists
  - ?risks for NALFD
  - consider referral even if liver screen negative if no risk factors

What do I do? Diagnosis

- Complete liver screen
- Further imaging?
  - Incidental findings or lack of clarity on USS
    - CT, MRI
  - Concern re biliary disease
    - MRCP, ERCP
  - Fibroscan
    - Non invasive, fibrosis only, Good for viral hepatitis

What worries me?

- persistent
- progressive
- variable
- new change
- AST/ ALT>ALP>>GGT
- low platelets or big spleens
- symptoms - itch, nausea, jaundice
- no diagnosis/ never biopsied

To biopsy or not?

- Liver biopsy
  - Concern re diagnosis
    - Possibility of treatable disease
    - Guide treatment decisions
    - Possibility of significant fibrosis
  - Progressive abnormality
  - High grade abnormality
  - Positive screen
  - Diseases with negative liver screen
    - e.g. PBC, atypical AIH, small duct PSC, granulomatous hepatitis, alcohol, NAFLD

And what next?

- Treat the treatable!
- Refer back those at little risk of significant liver disease
  - Persistent abnormality, screen negative, fibroscan / USS normal
    - If abnormality is low grade and non progressive no further diagnostic tests required
      - 3, 6, 12 monthly bloods (LFT, INR, CBC)
      - Attention to risks e.g. alcohol, metabolic syndrome
      - Respond to new complaints e.g. itch
  - If progressive or x 2-3 ULN without explanation
    - re-discuss/ refer ? biopsy

Summary

- **Abnormal liver function tests**
  - Identify liver pathology
  - Point to the underlying cause

- **Identify liver disease in order to**
  - offer patients best possible treatment
  - prevent life threatening consequences of liver disease
  - inform patient choice

Rachael Harry

021 285 1969