Barnsley B.E.S.T event
10th December 2014

ABNORMAL LFTS

Abnormal LFT’s

Dr. Kapil Kapur
Dr. Anne Straffen
BDGH

Interactive case 1

- Male 60 yrs, P/C angina, Normal ETT
- BP 147/95, BMI 31, Cholesterol 6.5
- AST 70 (<35), ALT 90 (<35), GGT 120, ALP98, albumin 39, Bili 17 (<25)
- NILS –ve apart from borderline positive ANA, DSDNA-ve
- USS- Bright liver

Interactive case 1

- Likely diagnosis
- Management
- Can he be given a statin?
- Does he need referral to hospital?

LFTs that we assess

- Enzyme tests
  - -AST, ALT, ALP and Gamma-GT
- Tests of synthetic function
  - -Albumin, PT
- Tests of transport capability
  - -Bilirubin

Epidemiology

- Frequently detected due to routine tests
- Range of normal values is defined as those occurring within 2 Standard deviations from the mean
- By definition 5% of healthy individuals will have abnormal LFTs
- 2.5% will have abnormally high results
- Normal LFTs do not exclude liver disease

Epidemiology

- Serious liver disease is uncommon
- Abnormal LFT's in 19 of 20,000 recruits
  - Non invasive screen usually normal
  - Often need a biopsy
  - Steatosis, Steatohepatitis and Alcoholic liver disease the most common causes

Epidemiology

- Likelihood of false positive tests increases as more tests are requested
- e.g. A screening panel of 20 independent tests in a normal individual will yield at least one abnormal test 64% of the time

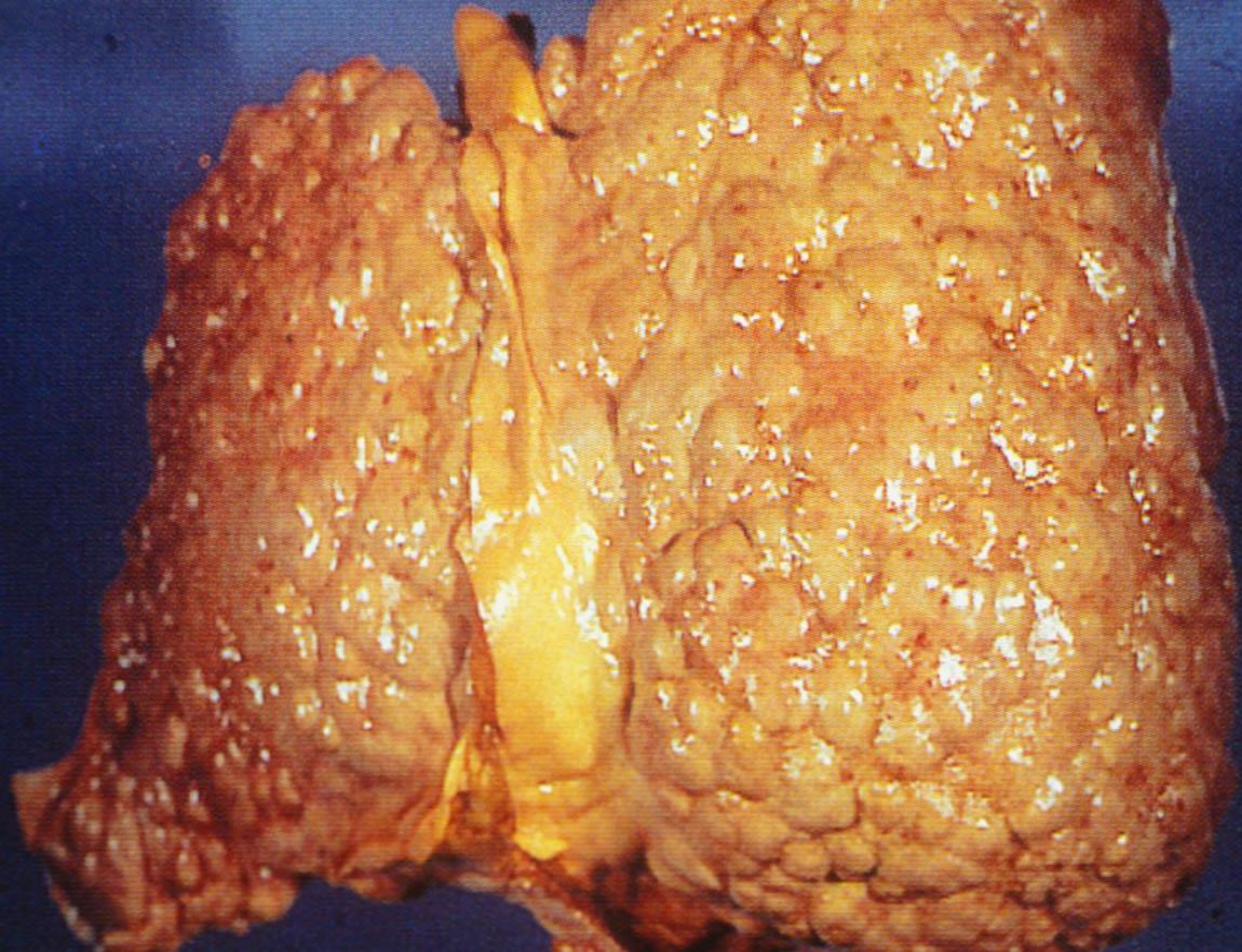
Usual causes of liver disease

- Alcoholic liver disease
- NAFLD
  - Fatty liver, NASH (steatohepatitis)
- Infective hepatitis
  - Hep A, B, C, EBV, CMV, Toxoplasma
- Autoimmune liver disease
- Biliary obstruction
  - Obstructive jaundice---Stones, strictures
  - Intrahepatic cholestasis—PBC, drugs etc

Usual causes of liver disease

- Metabolic liver disease
  - Haemochromatosis, Wilson's disease, Alpha 1 AT deficiency

- Malignancy
  - Secondary
  - Primary



Patterns of abnormal LFT's

- Elevated liver enzymes
  - -AST, ALT, G-GT
- Elevated bilirubin
  - -Isolated or associated
- Cholestatic / obstructive pattern
  - -ALP and G-GT
- Mixed patterns

LFT patterns that indicate aetiology

- Hepatitis like pattern
  - Infections, alcohol, drugs, autoimmune,
- Isolated rise in Bilirubin
  - Gilbert’s, haemolysis
- Cholestatic pattern
  - Intra or extrahepatic obstruction
  - Infiltration
- Mixed
  - Other causes

Making a diagnosis

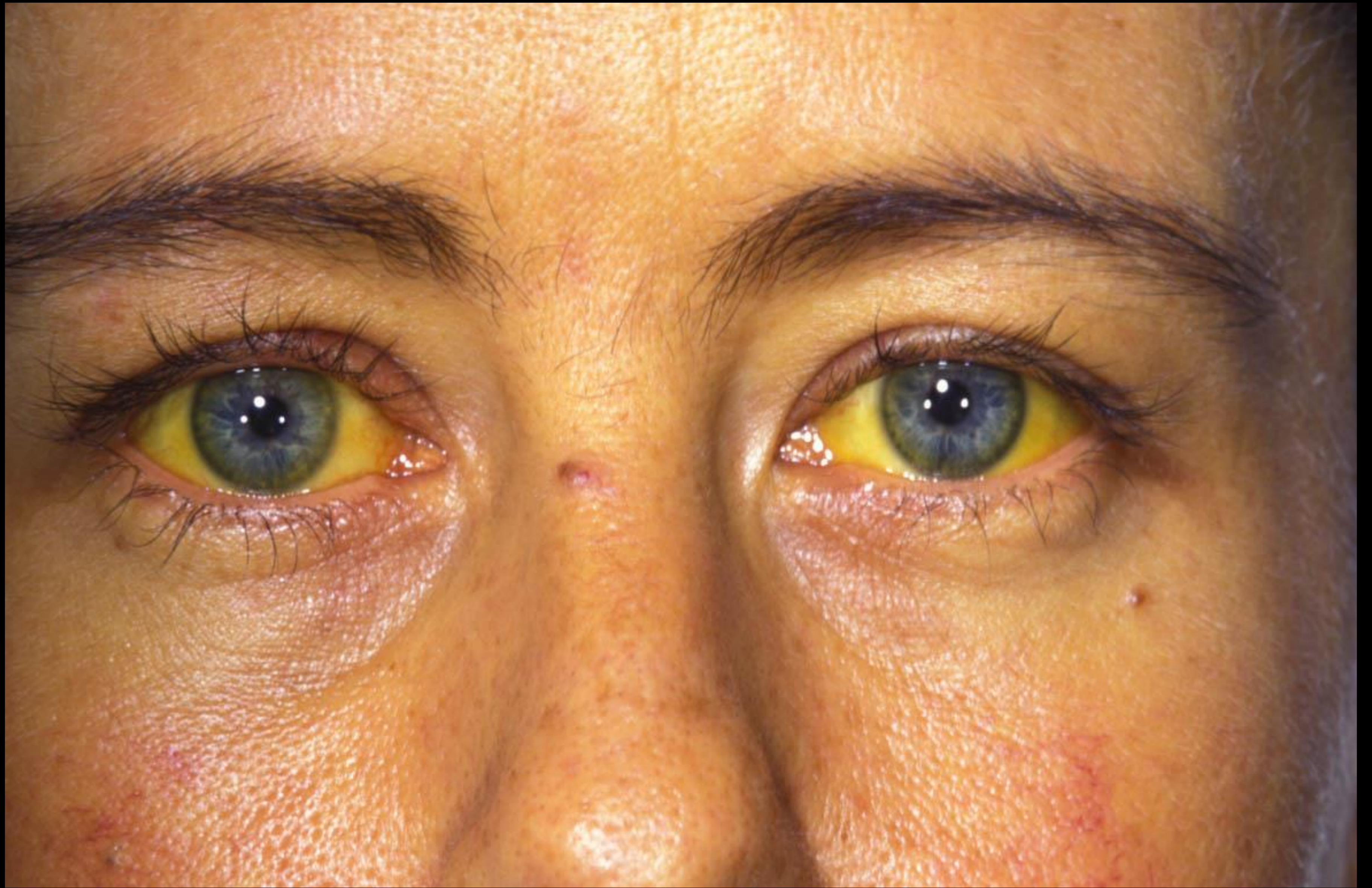
- History
- Clinical examination
- Investigations
  - Primary care
  - Secondary care

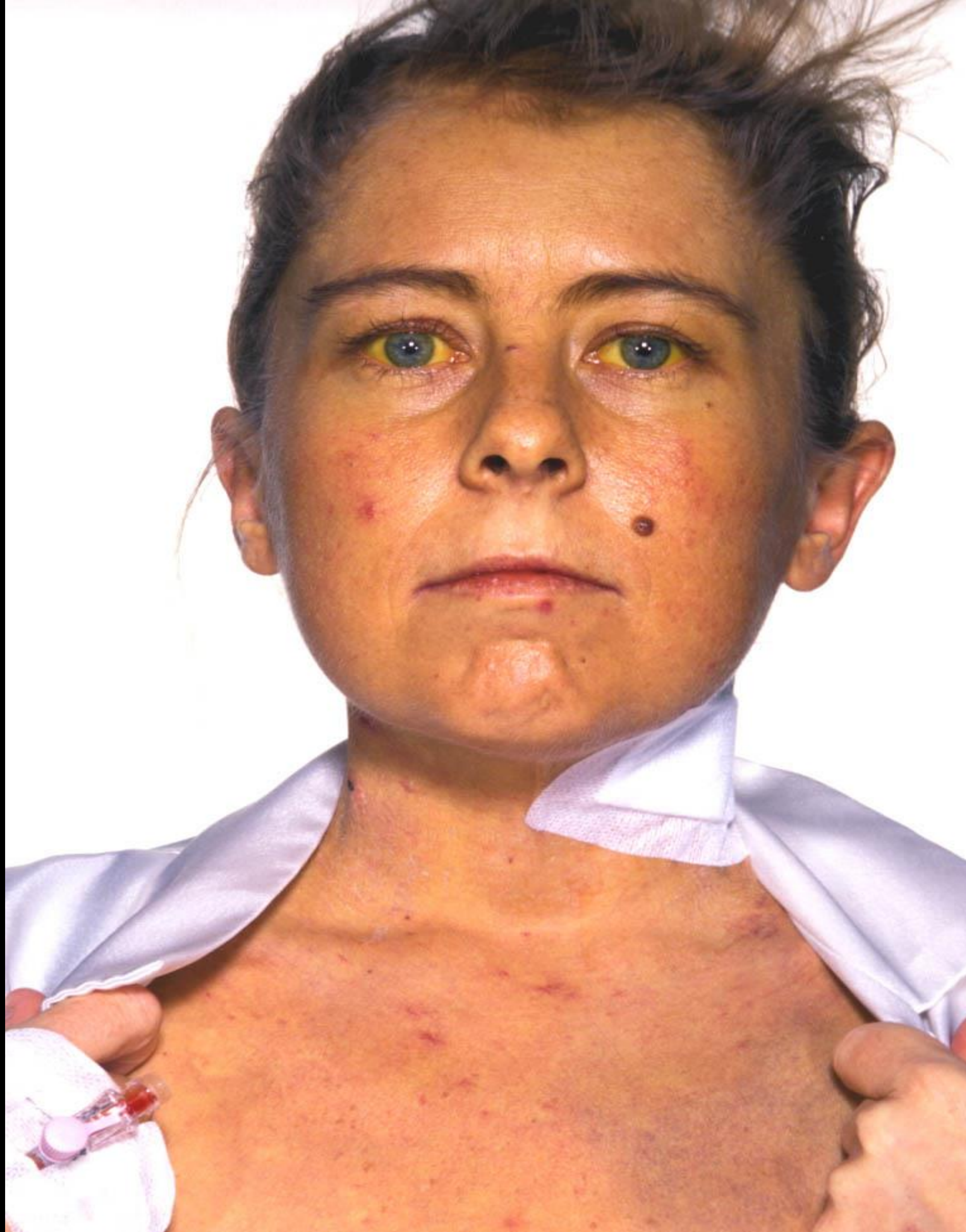
History

- Exposure to drugs and or medication
  - OTC, herbal, NSAIDs, antibiotics, anti-lipid agents
- Occupation
- Ethanol consumption
- Infective contacts
- Preceding symptoms, Weight loss
- History to suggest cholangitis
- Family history

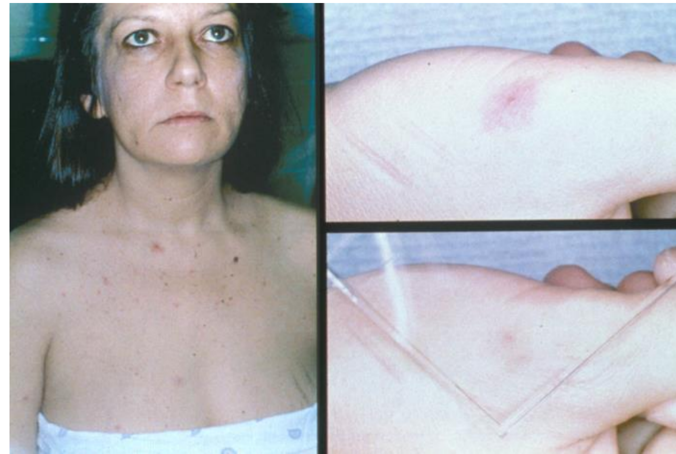
Physical examination

- Jaundice
- Evidence of cholestasis
- Evidence of metabolic syndrome
- Evidence of chronic liver disease
- Evidence of systemic disease

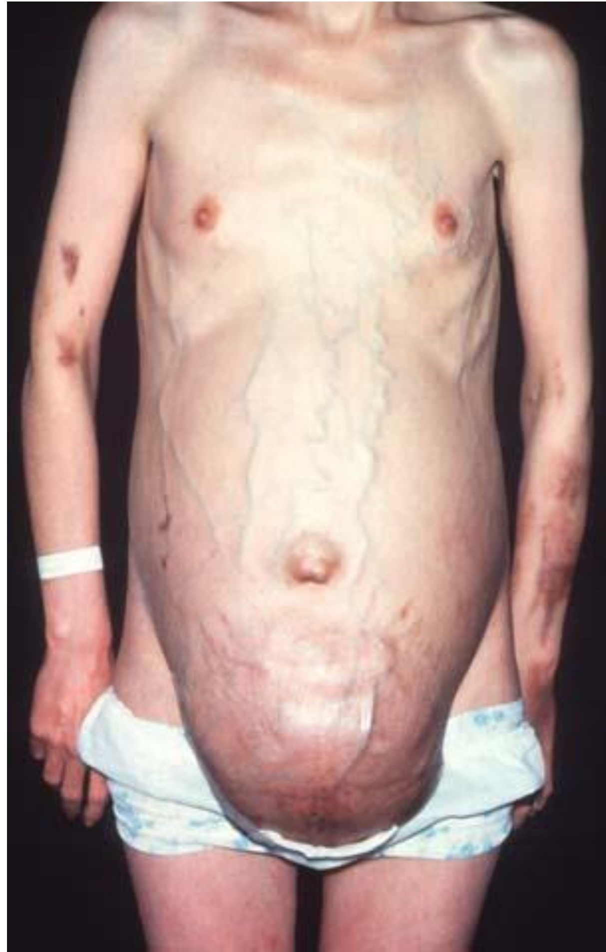




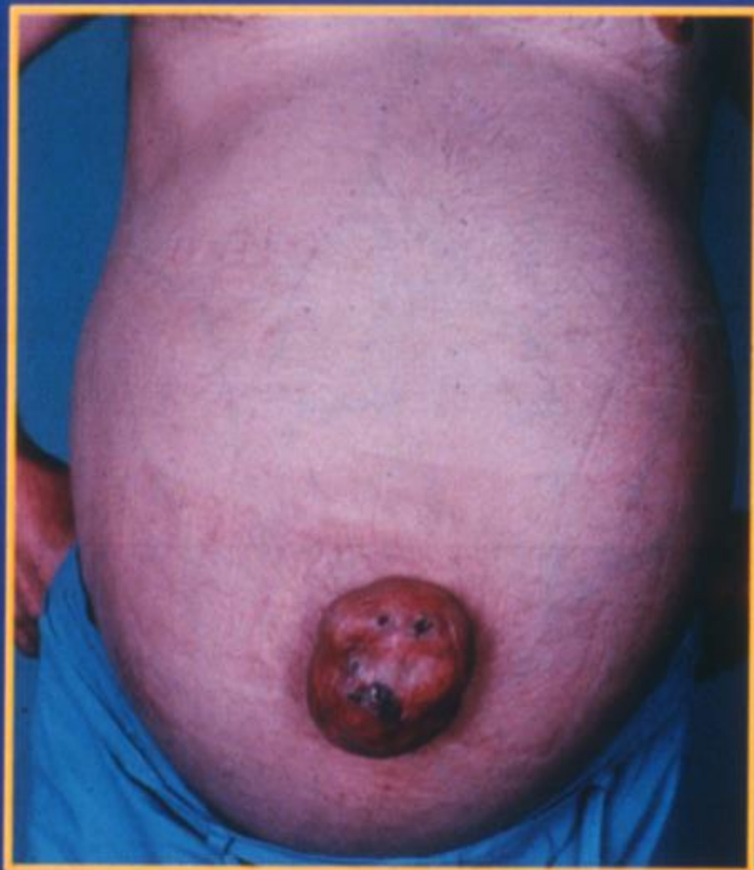
Spider naevi

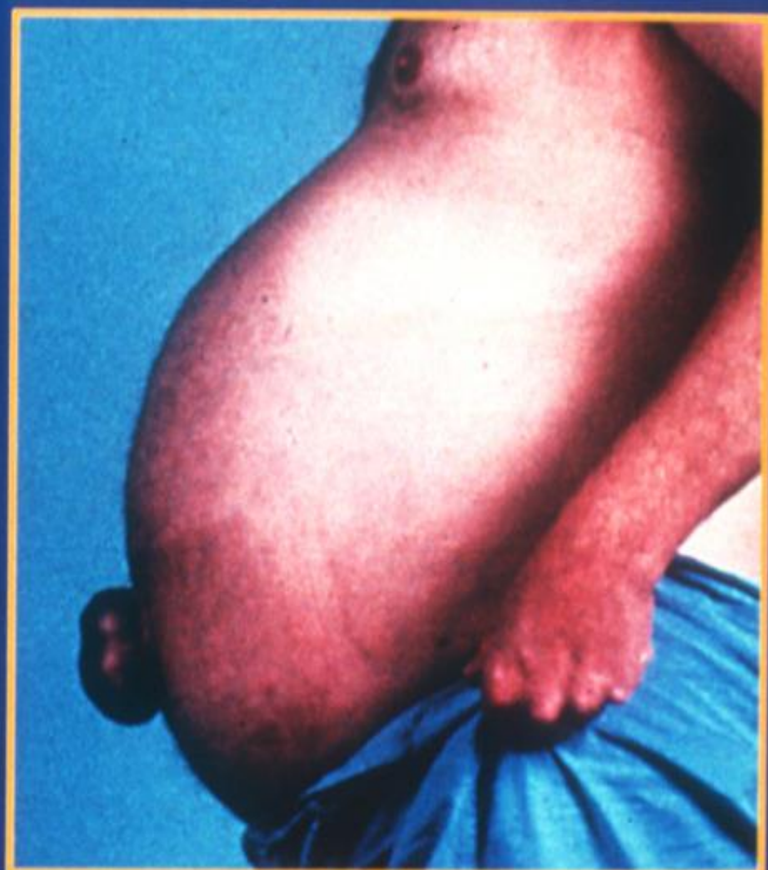


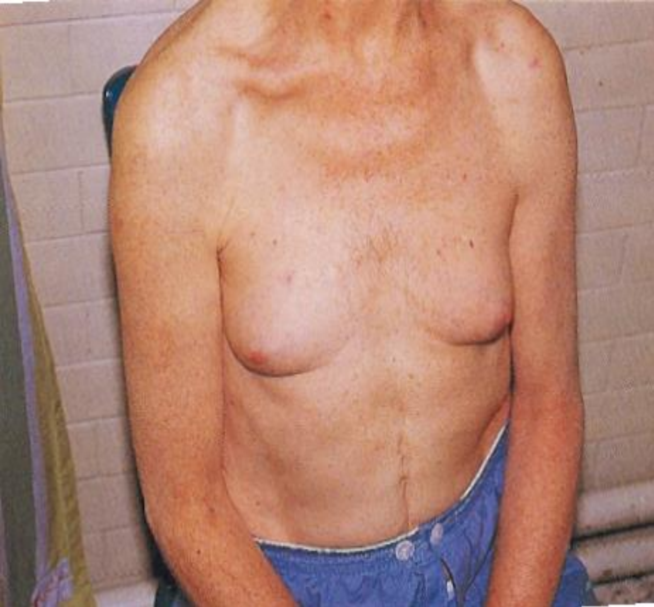
Signs of liver disease

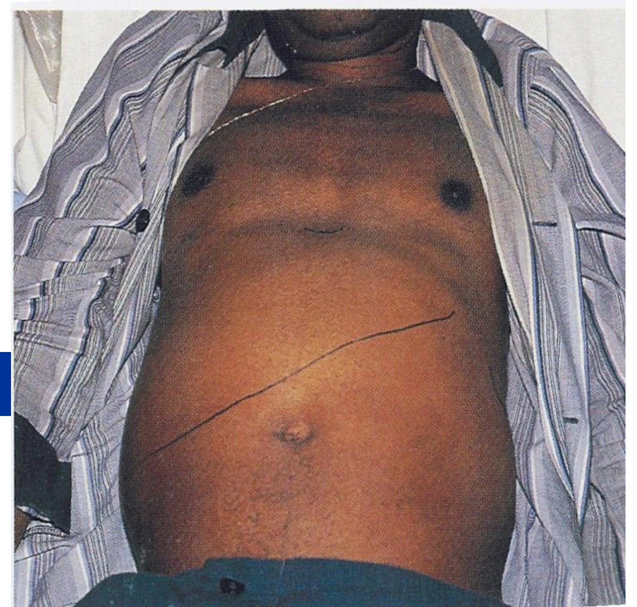


ASCITES

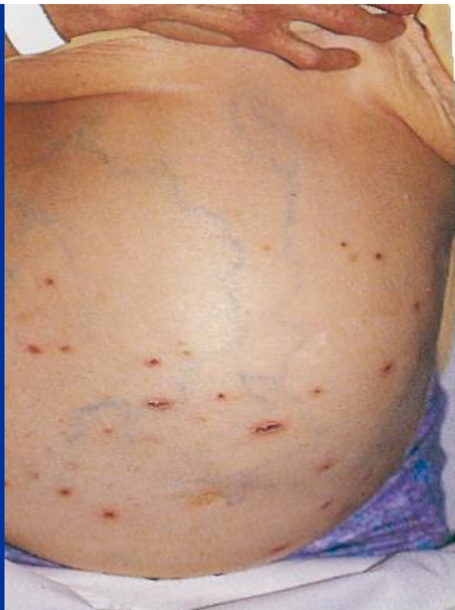


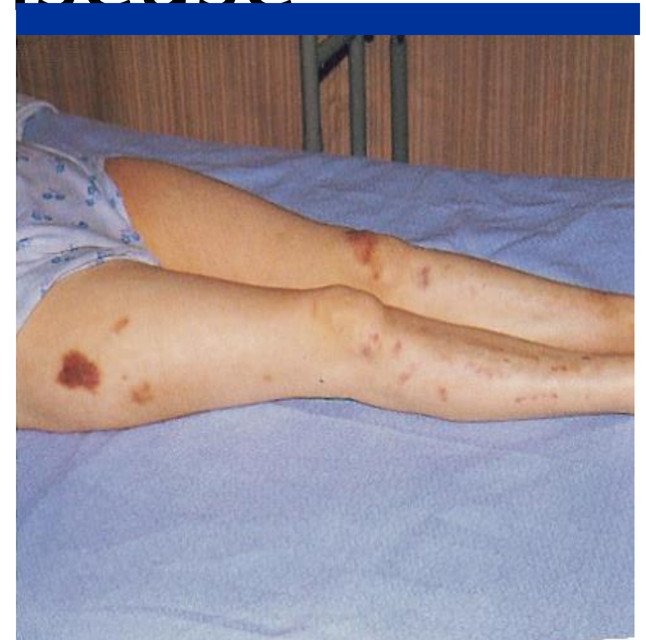






Signs of Liver Disease





Investigations

- Non invasive Liver screen (NILS)

- Imaging
  - -USS
  - -CT abdomen
  - -MRI

- Liver biopsy

Non-invasive liver screen (NILS)

- Hepatitis serology
- Autoimmune profile
- Immunoglobulins
- Ferritin and iron studies
- Caeruloplasmin, Alpha 1 AT levels
- Alpha feto protein

NILS (2)

- Check for diabetes and hyperlipidaemia
  - HbA1c and lipids
- Autoimmune profile
  - Autoimmune hepatitis
    - Antinuclear Ab
    - Anti smooth muscle Ab
    - Anti liver kidney microsomal Ab

NILS (3)

- Primary biliary cirrhosis

  Anti-mitochondrial Ab – raised ALP

- Immunoglobulins

  Often polyclonal

  ↑ IgG – autoimmune hepatitis

  ↑ Ig A – alcoholic LD (↓ coeliac)

  ↑ Ig M – primary biliary cirrhosis

NILS (4)

- Alpha-1-antitrypsin
  - Low (but acute phase protein)
  - Phenotype
  - Many alleles
  - Common deficiency alleles S and Z
  - Family studies

NILS (5)

- Caeruloplasmin

    Wilson's – usually <45 years

    rarely 45 – 50 years

    Age & gender related ref ranges

    Oestrogen dependent – pregnancy, Rx

    Low (but acute phase reactant)

    Serum copper low, urine high

NILS (6)

- TFTs – hyper- and hypothyroidism

  LFTs usually settle once thyroid disorder treated

- tTG – coeliac disease

  LFTs settle on gluten free diet

Role for liver biopsy

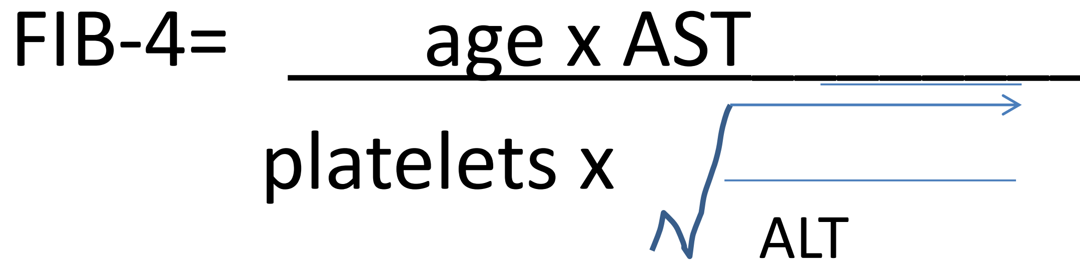
- Persistently abnormal LFTs > 2 fold
- Negative NILS
- No evidence of obstruction on USS
- Influence on the management
  - -Change in management
  - -Influence surveillance for hepatoma
  - -Reassurance to patient and physician

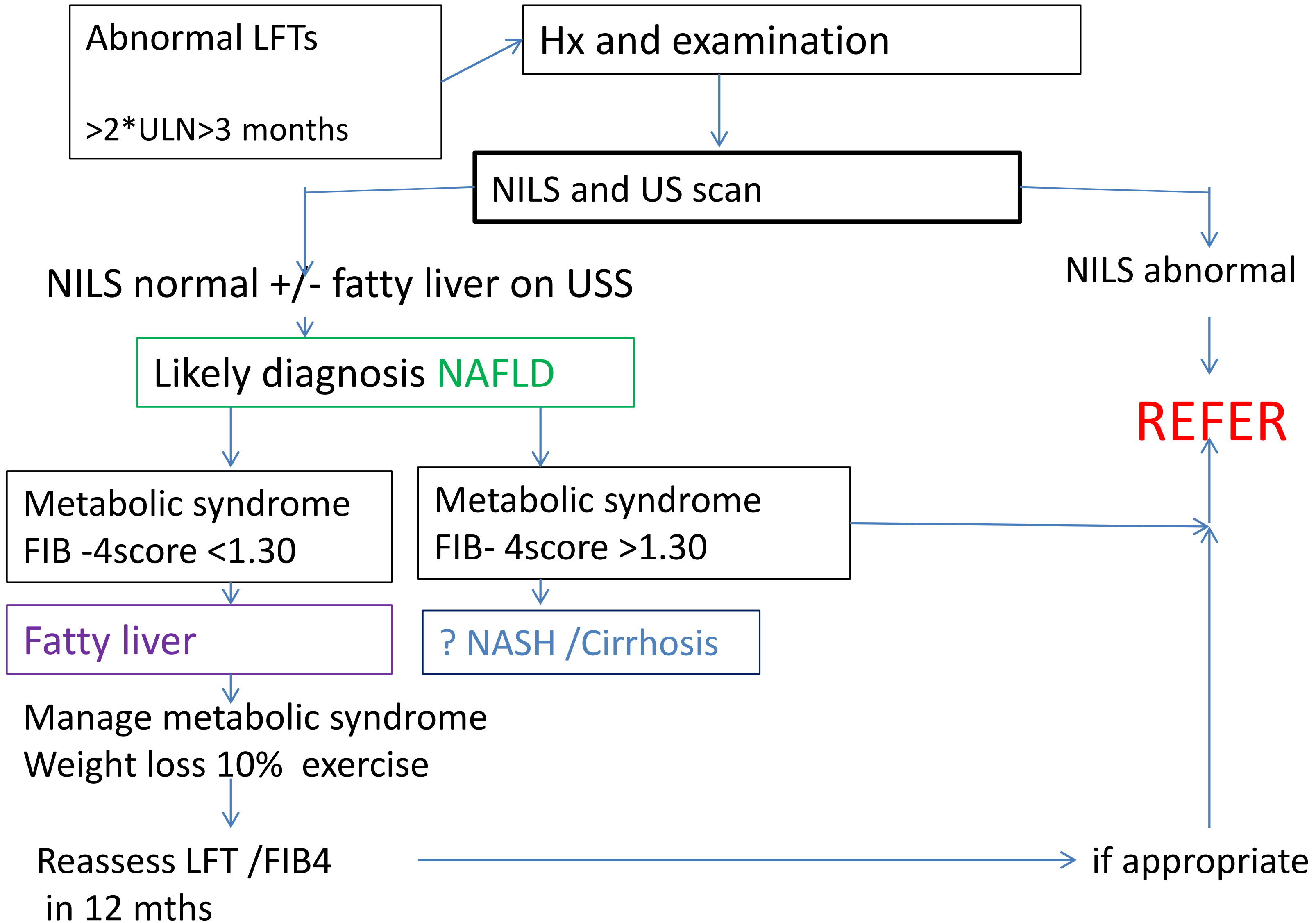
Whom to observe?

- Asymptomatic and well patient
- ALT, AST less than 2 fold elevated
- Normal NILS
- Normal USS

Pathway for abnormal LFTs

Uses FIB -4 Score





ULN- upper limit of normal. NILS (non invasive liver screen). NAFLD – non alcoholic fatty liver disease .
NASH non alcoholic steatohepatitiis

Alcohol

- AST / ALT ratio
  - Typically 2:1 or more (90 %)
  - If 3:1 (96%)
  - Also increased in NASH
- Associated rise in Gamma GT
- Isolated rise in Gamma GT per se is insufficient to make a diagnosis

Isolated hyperbilirubinaemia

- Usually due to Gilbert's syndrome
- Exclude haemolysis
- Investigations
  - Bilirubin fractions – conjugated / unconjugated
  - Haemolytic screen
  - Exclude drugs or medication

Isolated rise in Gamma-GT

- Can be very sensitive but lacks specificity
  - Liver, pancreas, cardiac, renal failure, diabetes, COPD
- Very often medication related
  - Phenytoin, Barbiturates
- May rise in ethanolic liver disease but non specific in isolation
- An isolated rise should not lead to an exhaustive work up

Interactive case 2

- 64 year old male unwell for 4 days
- Ethanol 42 units /wk, Smoker, NIDDM, OA
- Chronic liver disease, firm hepatomegaly, Ascites
- Bili 150, AST 500, ALT 250, GGT 700, ALP 200, Ferritin 1000, AFP 20
- USS-Abnormal coarse echo pattern, Ascites, Splenomegaly

Interactive case 2

- Differential diagnosis
- Complications
- Specific investigations
- Further management

Interactive case 3

- Rotherham GP patient

  54 year old female

  Clinical details: CVD risk

  U&Es

  LFTs

  HbA1c

  Lipids

Interactive case 3

- Bilirubin 39 umol/L
- AST 28 iu/L
- ALT 28 iu/L
- GGT 13 iu/L
- ALP 82 iu/L
- T.Protein 69 g/L
- Albumin 46 g/L

Interactive case 3

- What would you do?
- What advice would you give the patient?

Interactive case 4

- 73 year old male P/C dark urine, itching, wt loss 2 kg, intermittent shivers
- Jaundice, liver edge palpable
- Bili 200, ALP 700, GGT 1000, AST125, ALT 180,
- USS –Dilated CBD, lower end not seen due to gas shadows

Interactive case 4

- Diagnosis
- Possible causes
- Investigations
- Management

Any Questions?