الجامعة السورية الخاصة
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First lecture

- Liver disease
  -Introduction
  -Anatomy &physiology
  -Prevalence of liver disease
  -Jaundice
  -LFTs

2/12

-

LIVE === LIVER

- It was at one time considered the seat of live hence its name ,
- liver the thing we live with

- Ambrose Bierce (1842-1914)

LIVER

- UNIQUE
- >500 vital function
- Holds one pint of blood supply at any given moment(13%)
- organ that can regenerate itself
- 1.2—1.5kg

Functional reserve

- Enormous functional reserve
  Surgical removal of 60% of the liver of a normal person produces minimal and transient hepatic impairment
- Regeneration restores most of the liver mass within 4 to 6 weeks.

Regeneration

- *Regeneration.*
- Cell death or tissue resection (such as in living-donor transplantation) triggers hepatocyte replication, to compensate for the cell or tissue loss.
- ***It is a normal compensatory response to cell death***

It is common

-1/3 OF THE WORLD POPULATION EXPOSED TO VIRAL HEPATITIS B

-The global prevalence of HBV infection in the general population was estimated at 3.5% with about
257 million persons living with chronic HBV infection.
http://www.who.int/wer Position paper WHO2017

More than one million of Syrian population are infected by hepatitis B&C

Winning over ----

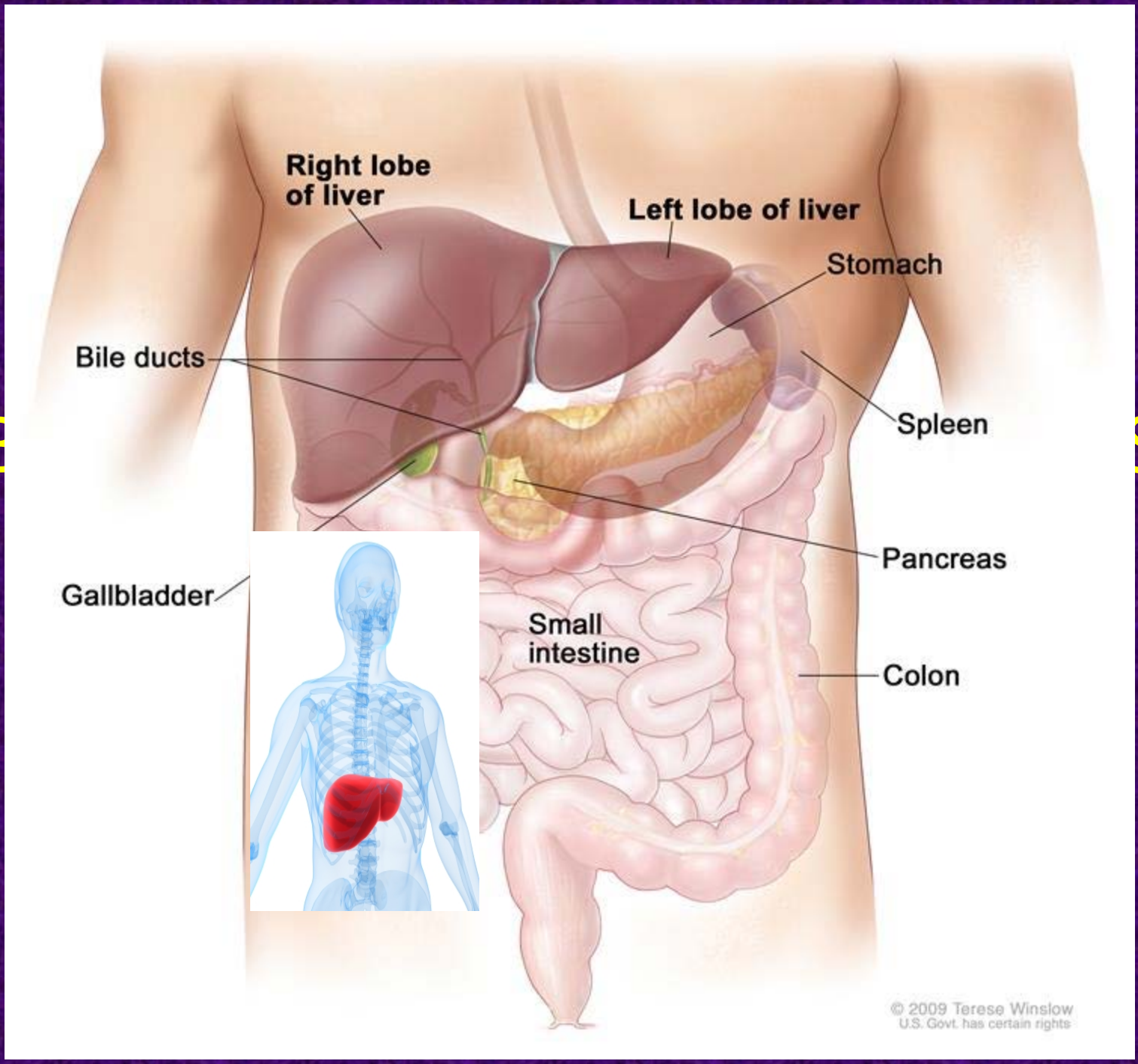
Therapeutic endoscopy

largely replaced surgery for

-Gastrointestinal bleeding

-Tumor palliation

-Biliary diseases.


Right lobe of liver
Left lobe of liver
Stomach
Bile ducts
Spleen
Pancreas
Gallbladder
Small intestine
Colon
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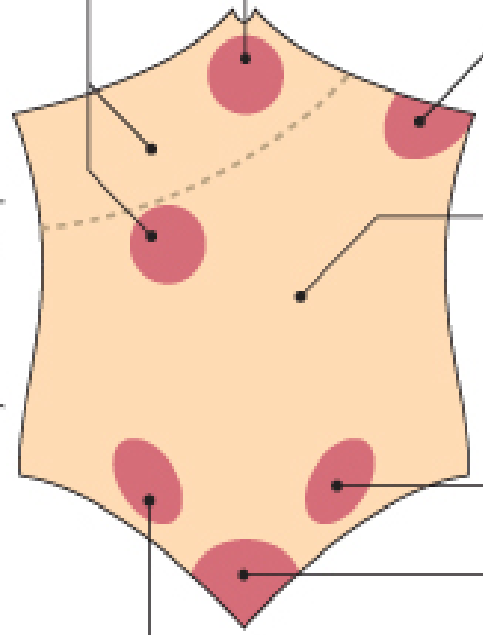
4 ABDOMINAL EXAMINATION: POSSIBLE FINDINGS



Hepatomegaly
Palpable gallbladder

(Ch. 23)

Epigastric mass

Gastric cancer
Pancreatic cancer
Aortic aneurysm

Left upper quadrant mass

?Spleen	*?Kidney*
Edge	Rounded
Can't get above it	Can get above it
Moves towards right iliac fossa	Moves down
Dull percussion note	Resonant to percussion
Notch	Ballotable

Tender to palpation

?Peritonitis	*?Obstruction*
Guarding and rebound	Distended
Absent bowel sounds	Tinkling bowel sounds
Rigidity	Visible peristalsis

Left iliac fossa mass

Sigmoid colon cancer
Constipation
Diverticular mass

Generalised distension

Fat (obesity)
Fluid (ascites)
Flatus (obstruction/ileus)
Faeces (constipation)
Fetus (pregnancy)

Right iliac fossa mass

Caecal carcinoma
Crohn's disease
Appendix abscess

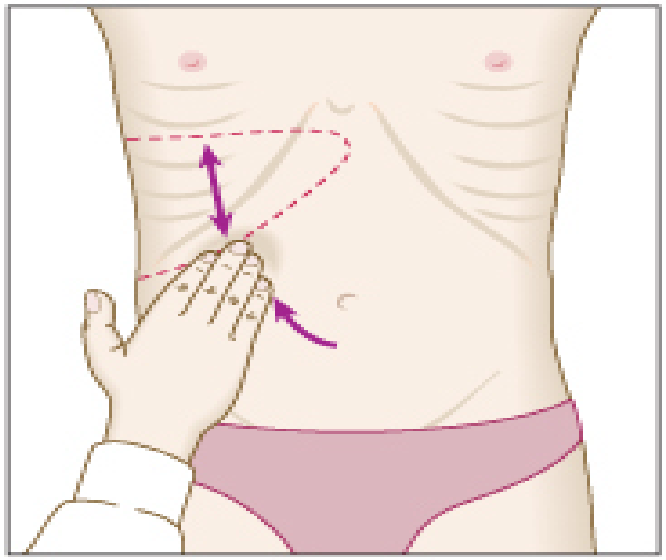
Suprapubic mass

Bladder
Pregnancy
Fibroids/carcinoma

❺ PALPATION OF THE ABDOMEN

Liver

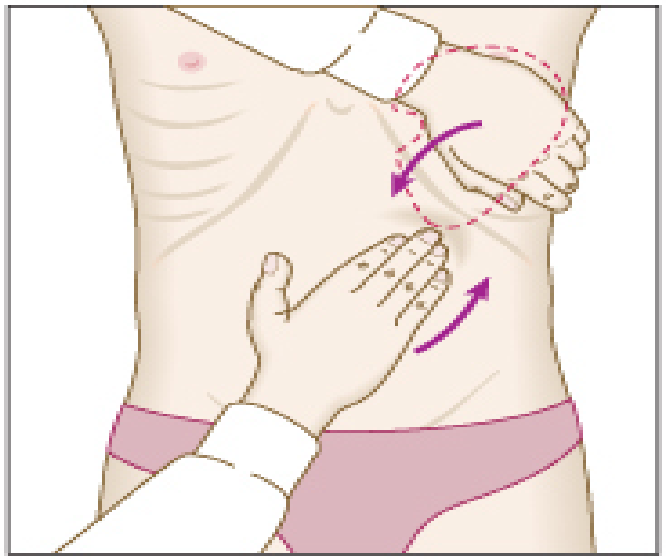
- Start in the right iliac fossa.
- Progress up the abdomen 2 cm with each breath (through open mouth)
- Confirm the lower border of the liver by percussion (see 6).



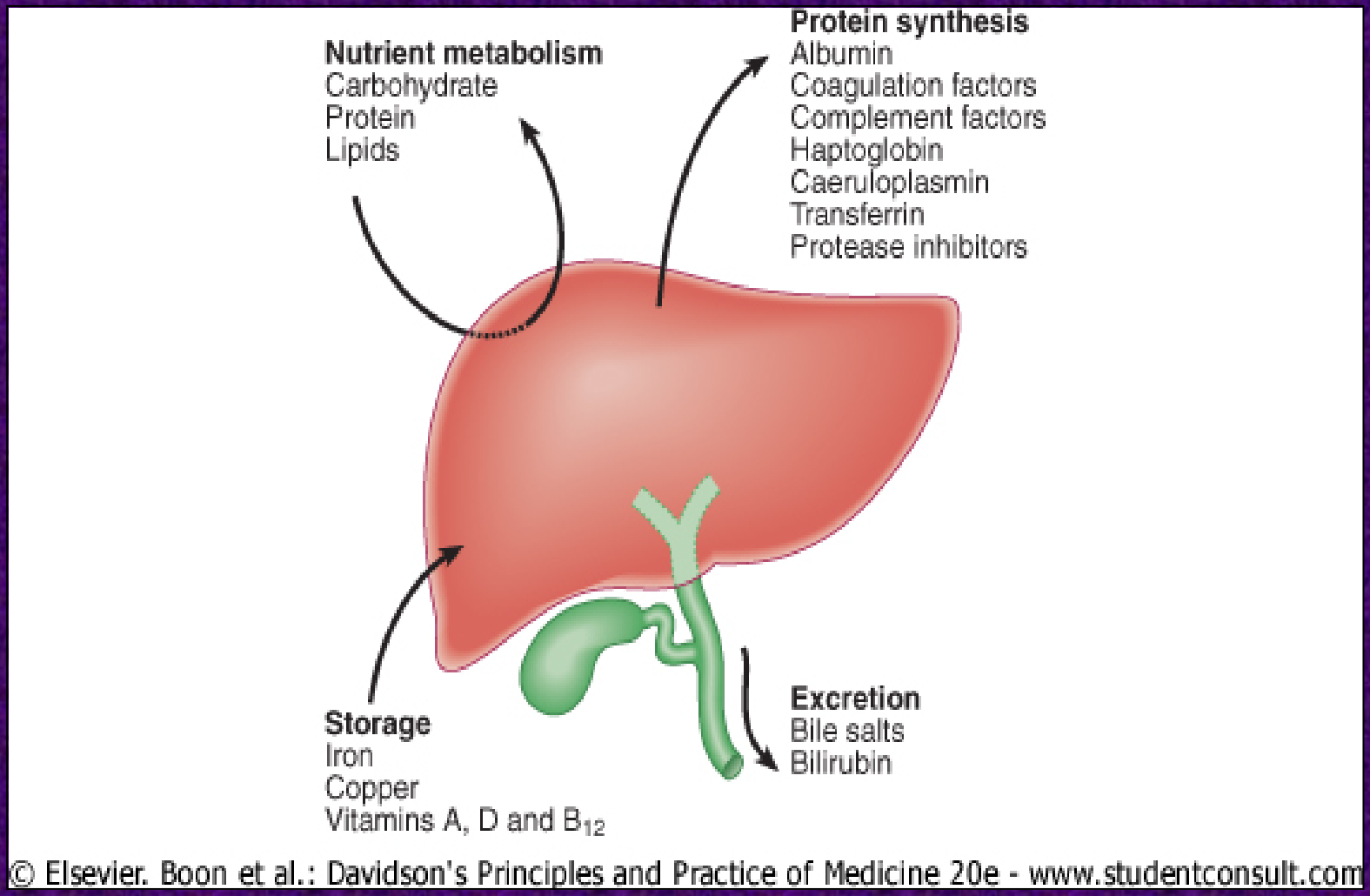
- Detect if smooth or irregular, tender or non-tender; ascertain shape.
- Identify the upper border by percussion (see 6).

Spleen

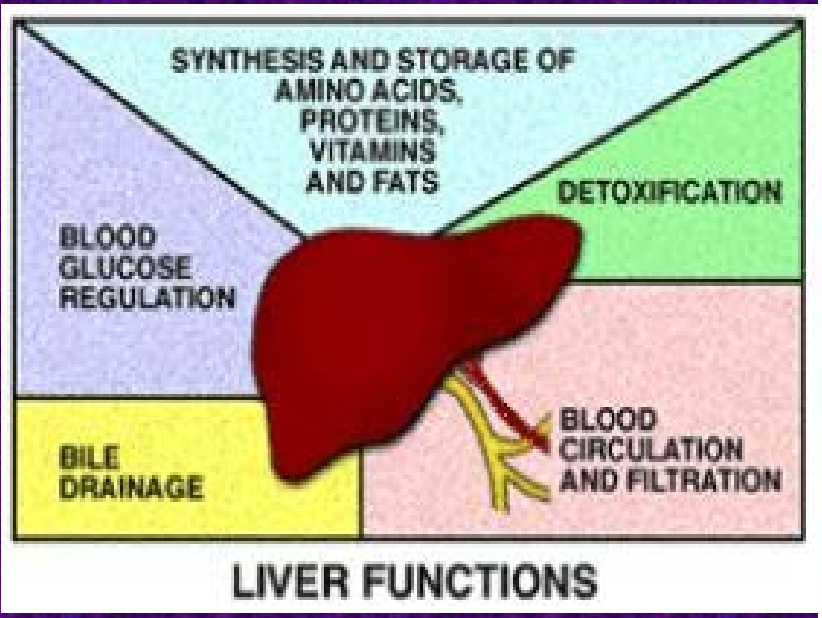
- Start again in the right iliac fossa.
- Progress towards the left upper quadrant at 2 cm intervals.
- Place the left hand around the lower lateral ribs as the costal margin is approached.

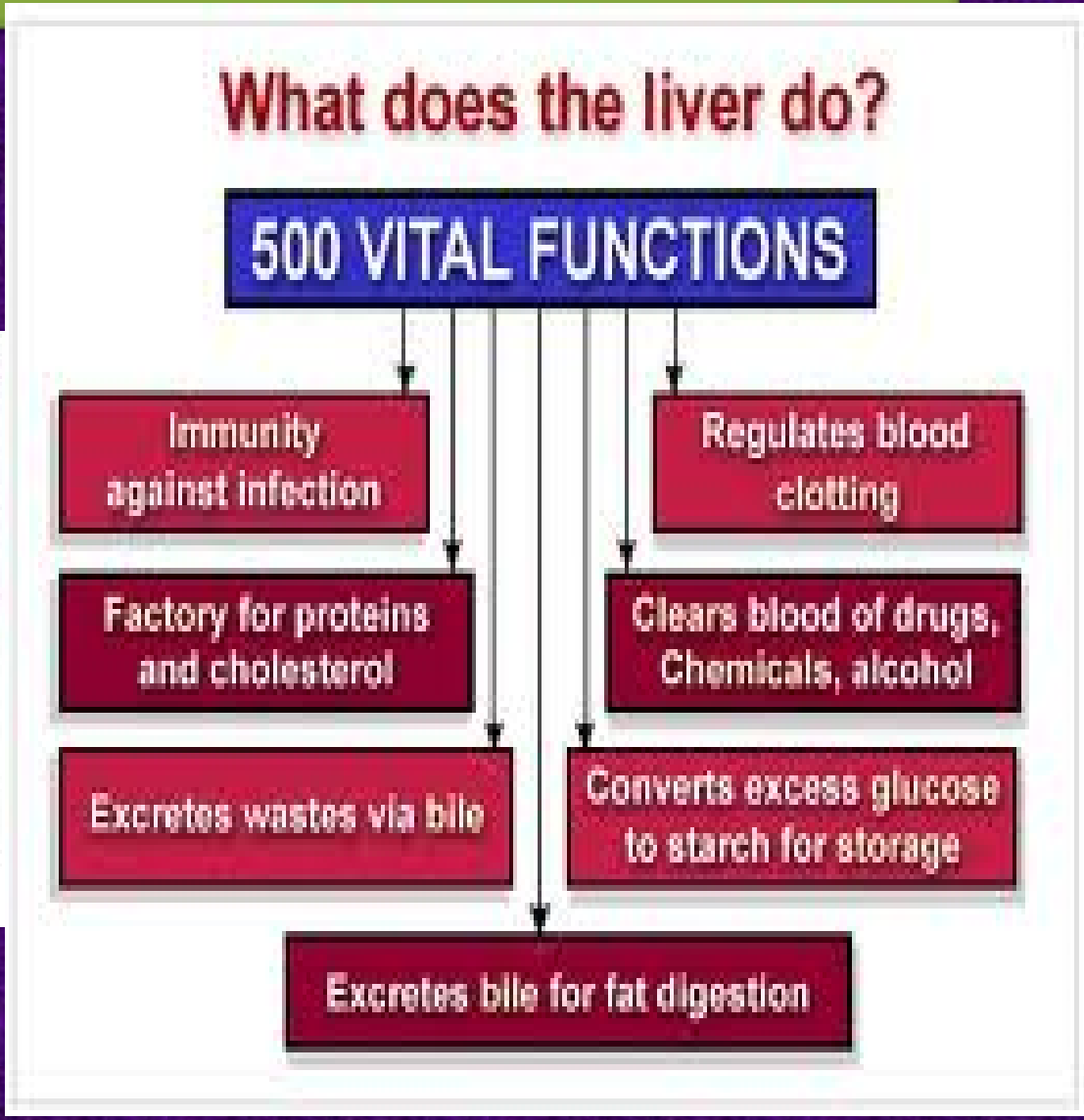


- Note the characteristics of the spleen
  - Notch
  - Superficial
  - Dull to percussion
  - Cannot get between ribs and spleen
  - Moves well with respiration.



Main liver Functions





Metabolism & Production

A. Amino acids

1. Albumin 8-14 mg/day is
2. Clotting factors (II,VII,IX,X) which are in tern modified be vitamin K-dependent enzymes (Vit K is also stored in the liver)
3. Complement factors
4. Haptoglobulin
5. Transferrin
6. Protease inhibitors: eg. alpha1-antitrypsin

Storage

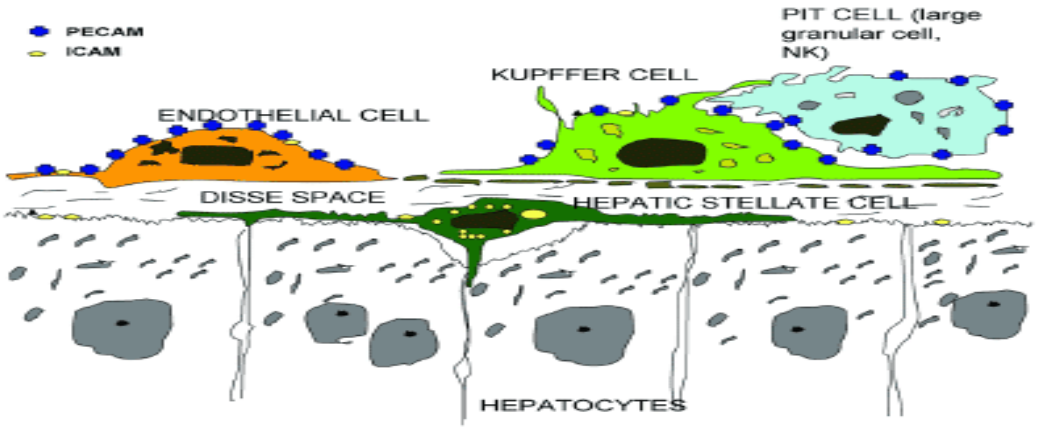
- 1. Vitamin A,D and B12 are stored in large amounts.
- 2. Vitamin K & folate in smaller amounts.
- 3. Iron within 2 compounds (ferritin&hemosiderin)
- 4.copper (also excreted in bile)

Excretion

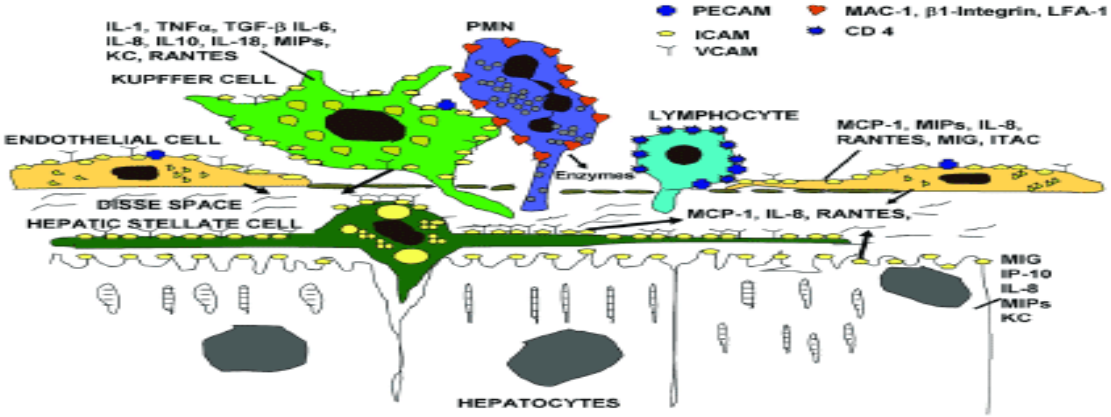
- The main excreted product is the Bile which contains:

1. Bile acids (from cholesterol)
2. Bilirubin (conjugated)
3. phospholipids
4. cholesterol
5. copper
6. Drugs
7. Nutrient metabolism waste products

Immune regulation



A: Sinusoidal structure in normal liver



B: Changes in liver inflammation

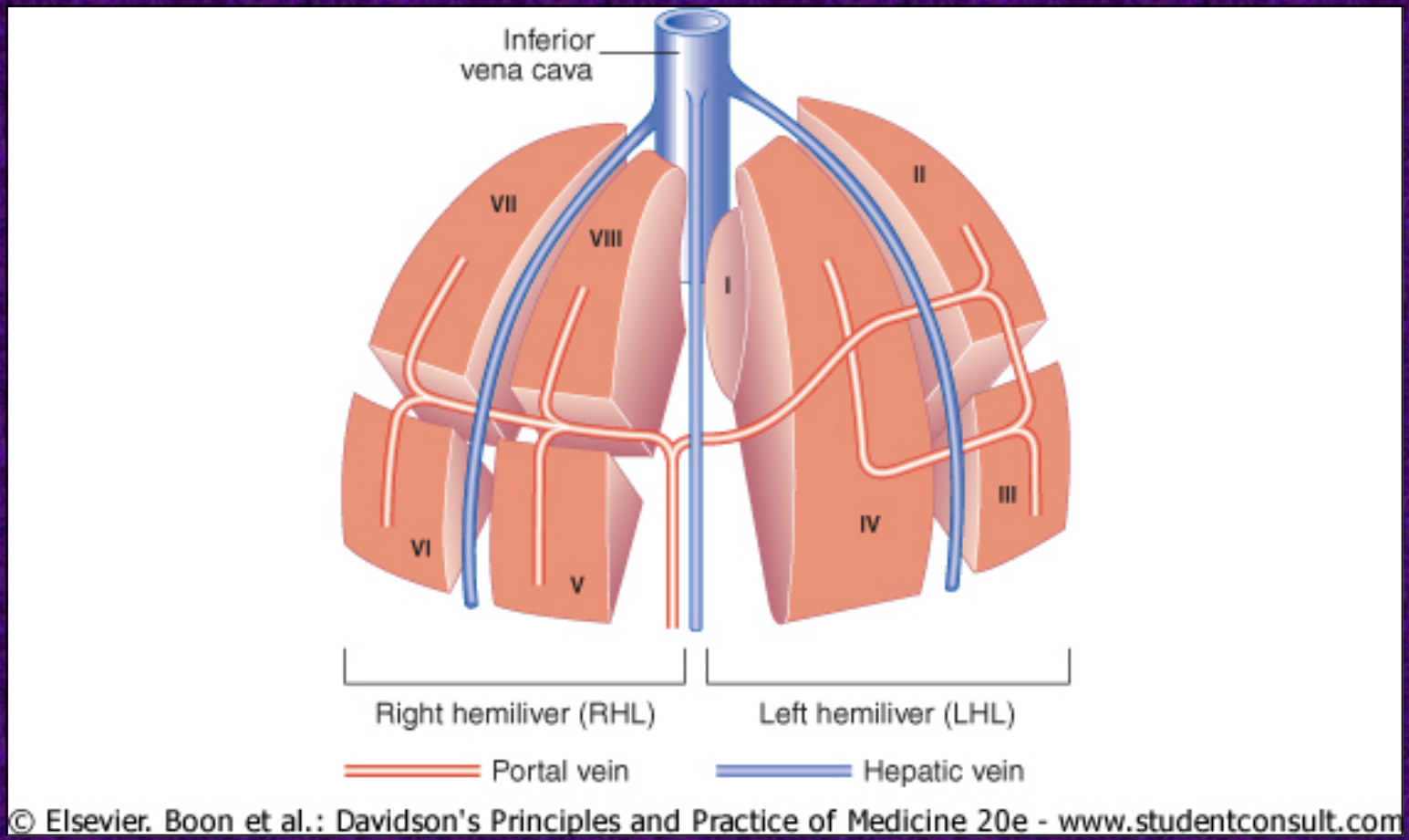
- 9% of normal liver is immune cells.

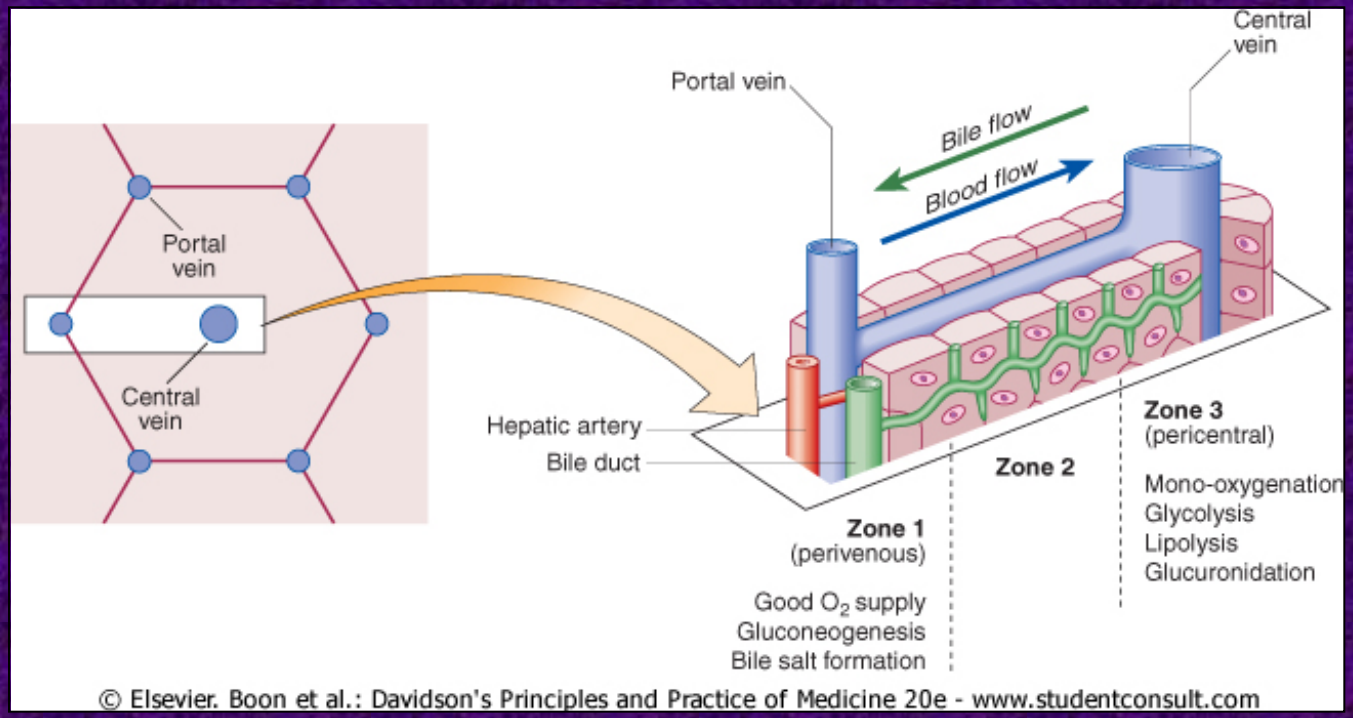
1.Cells for Innate immunity:

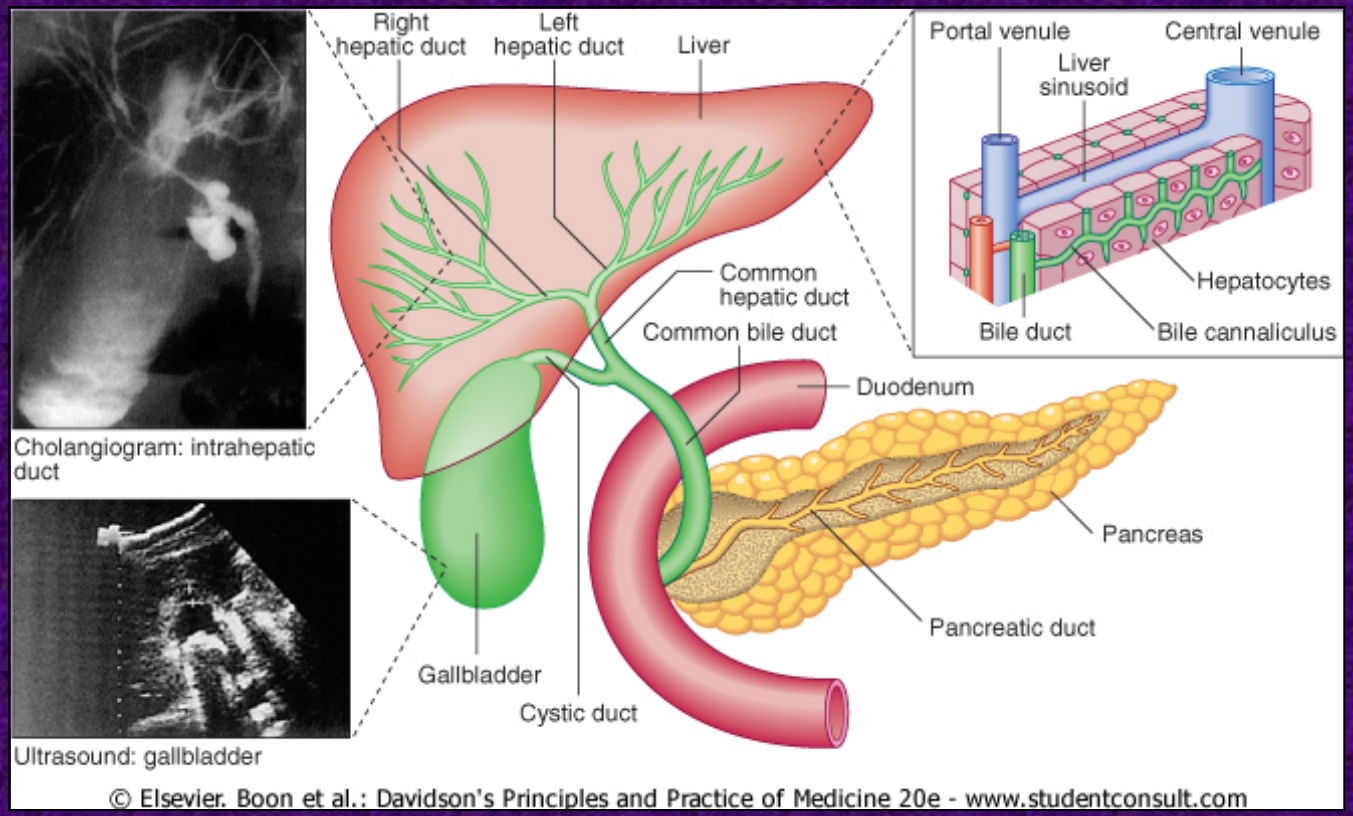
4% Kupffer cells(from blood monocytes)

2.5% Macrophages & Natural killer cells

2. Cells for adaptive immunity: B&T lymphocytes

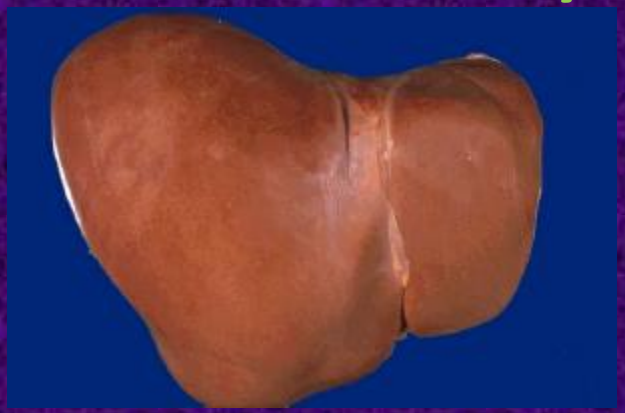




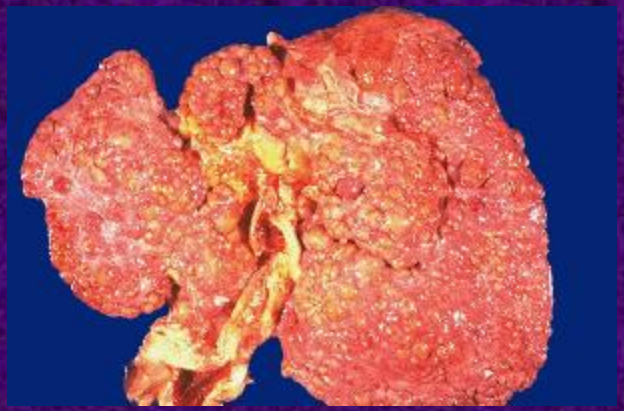


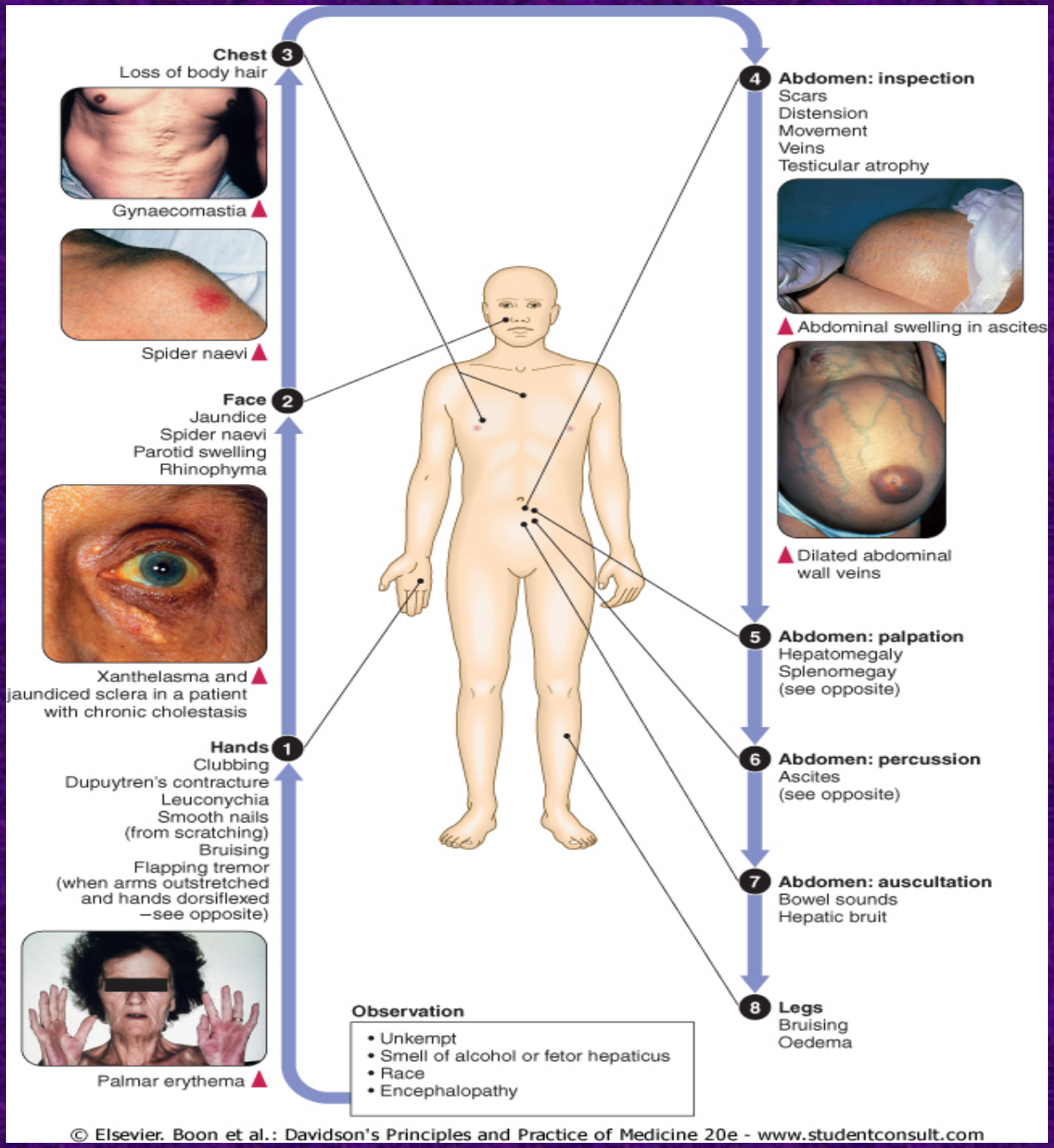
liver from to

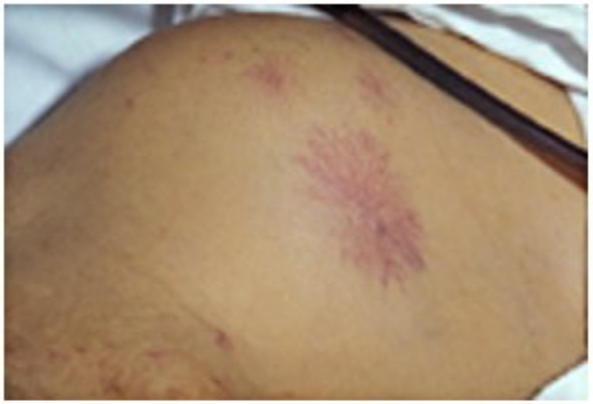
healthy

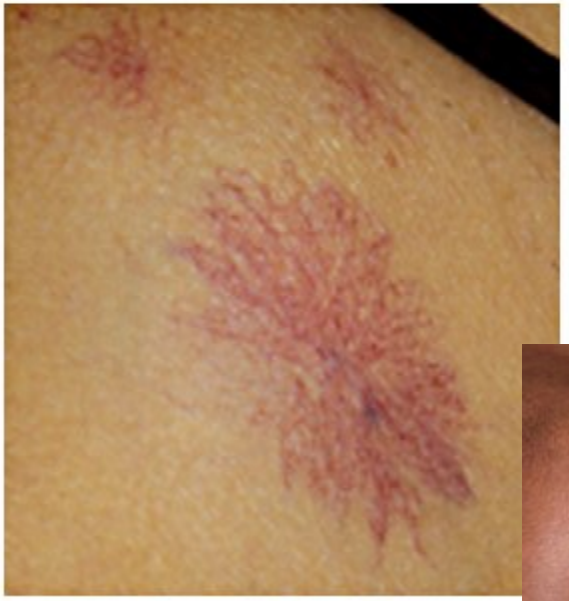


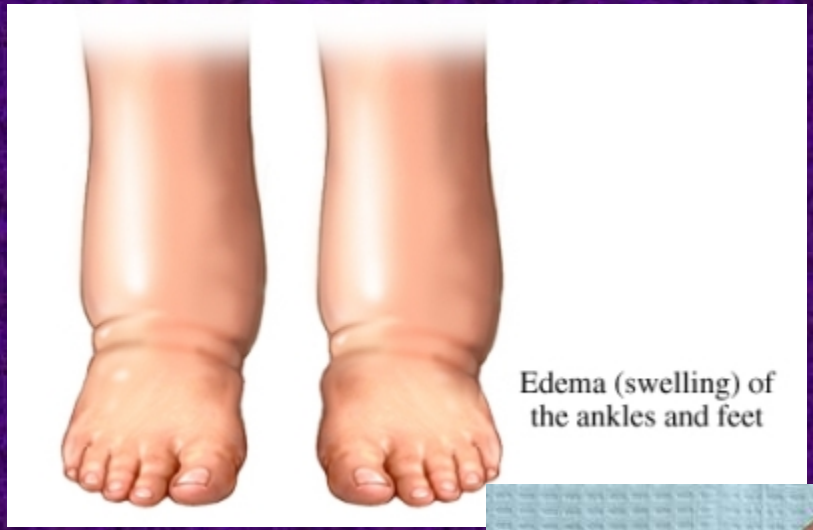
cirrhosis



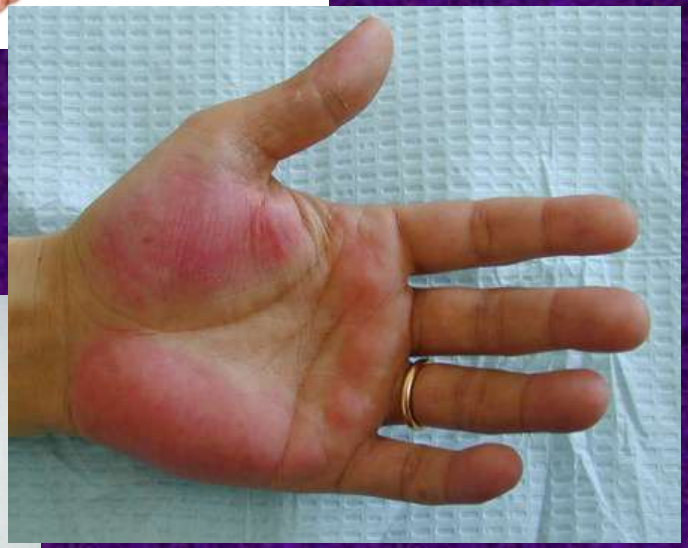








Edema (swelling) of the ankles and feet



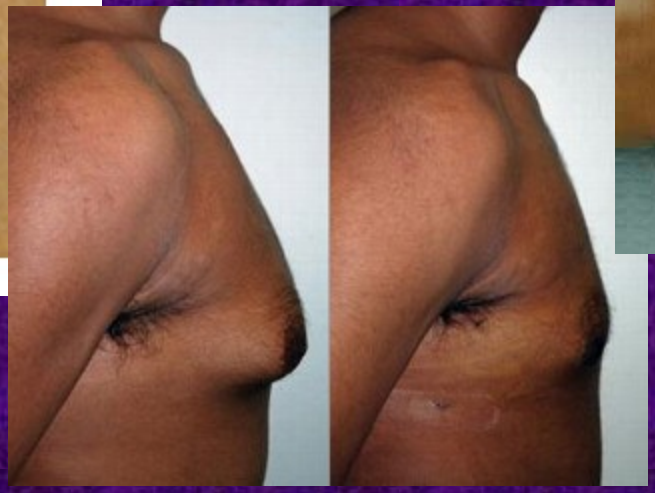
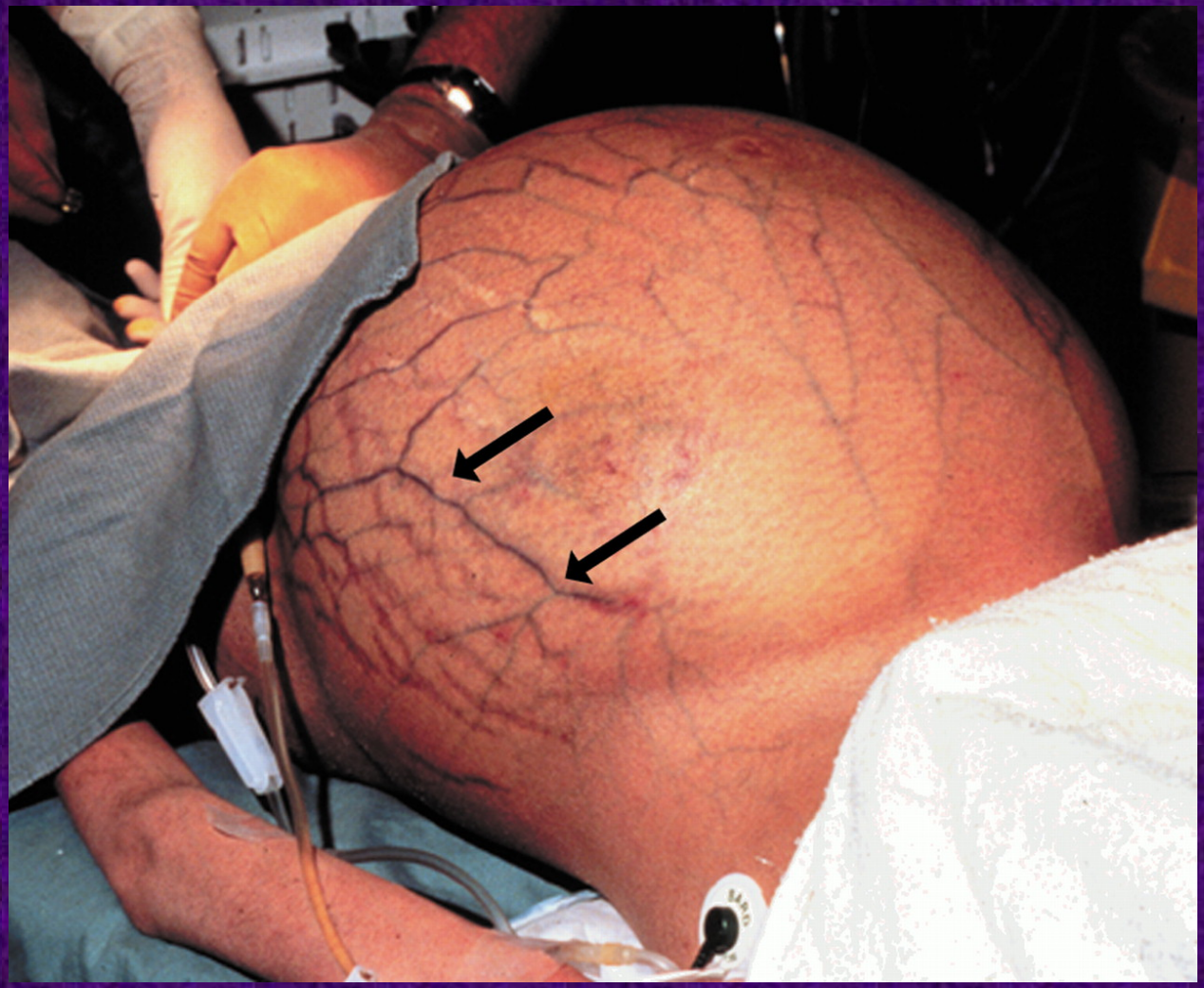
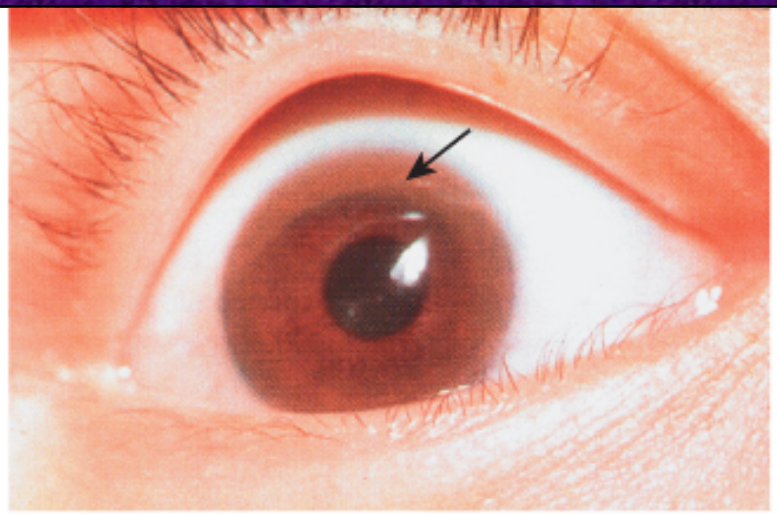


Figure 10. Photograph shows a caput medusae accentuated by a large amount of ascites in a patient being prepared for liver transplantation.

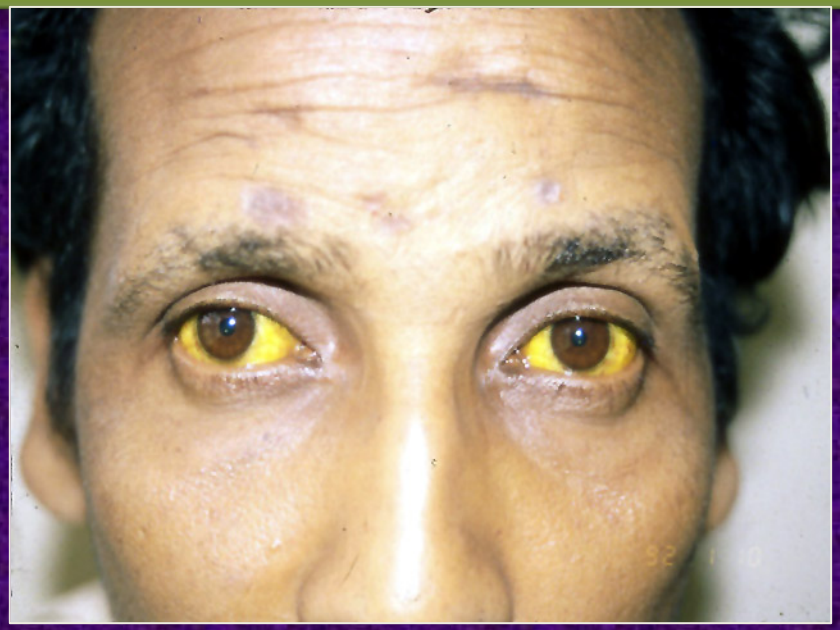


Henseler K P et al. Radiographics 2001;21:691-704

RadioGraphics



Jaundice

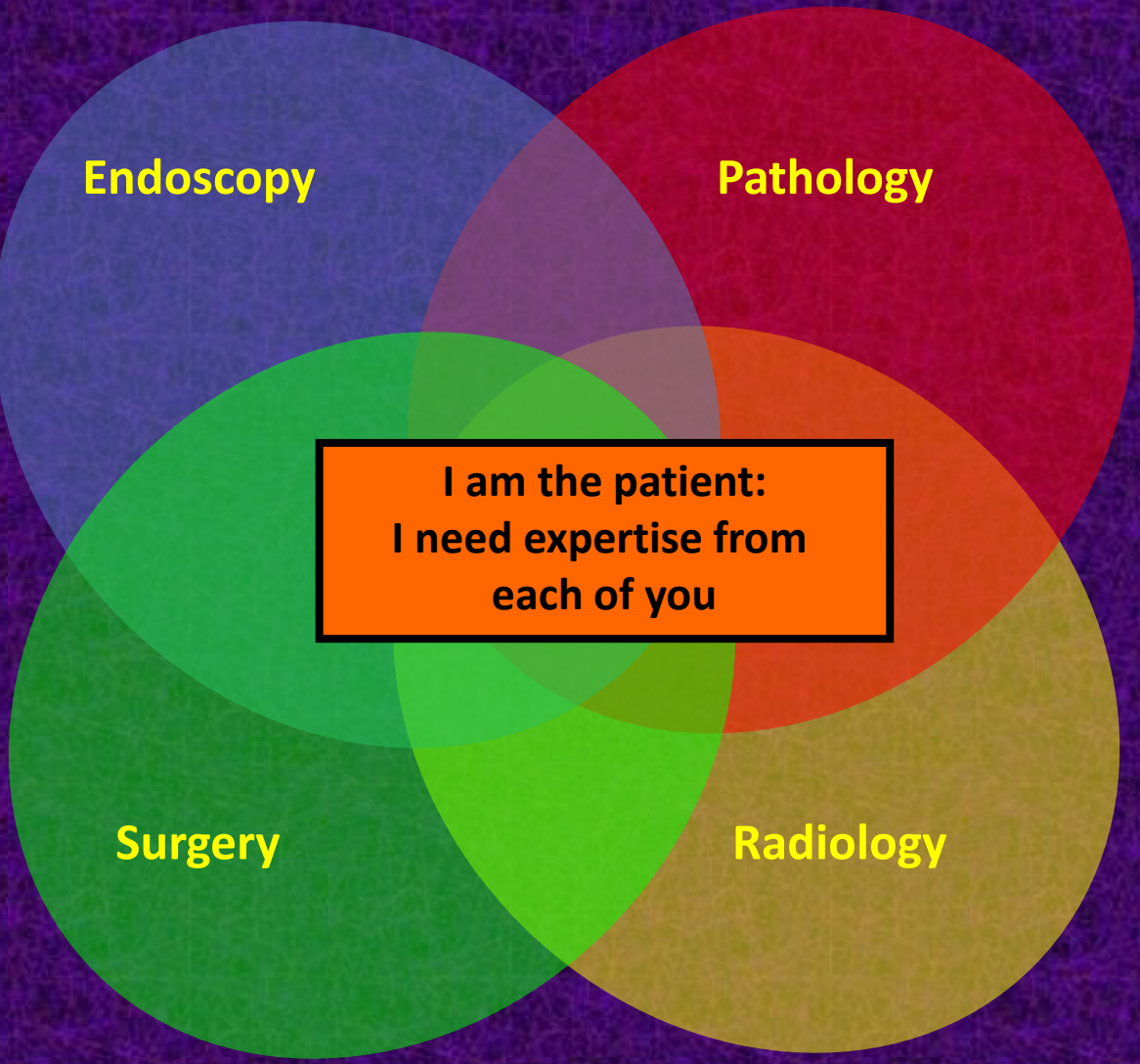


Jaundice is usually detectable clinically when the plasma bilirubin

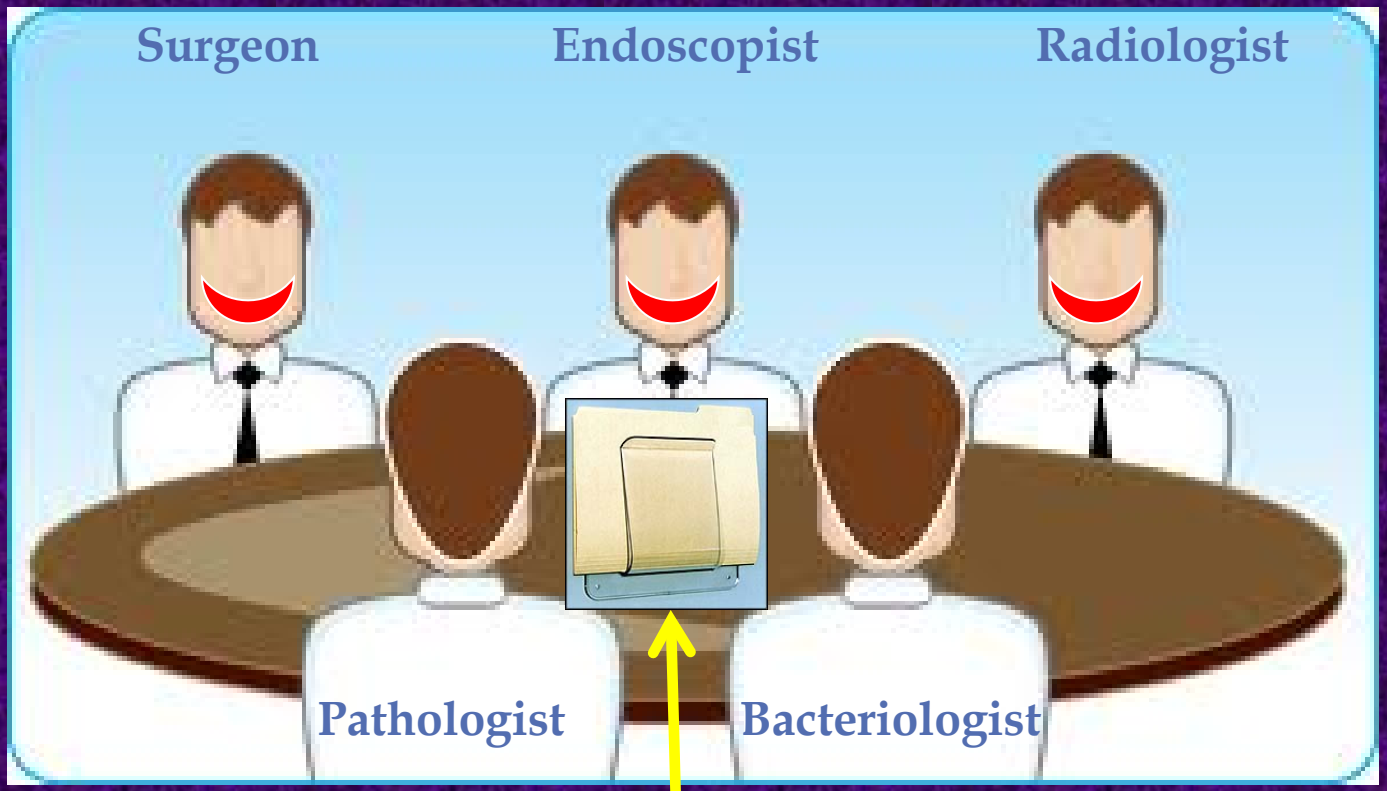
exceeds 40 µmol/L (~2.5 mg/dL). .

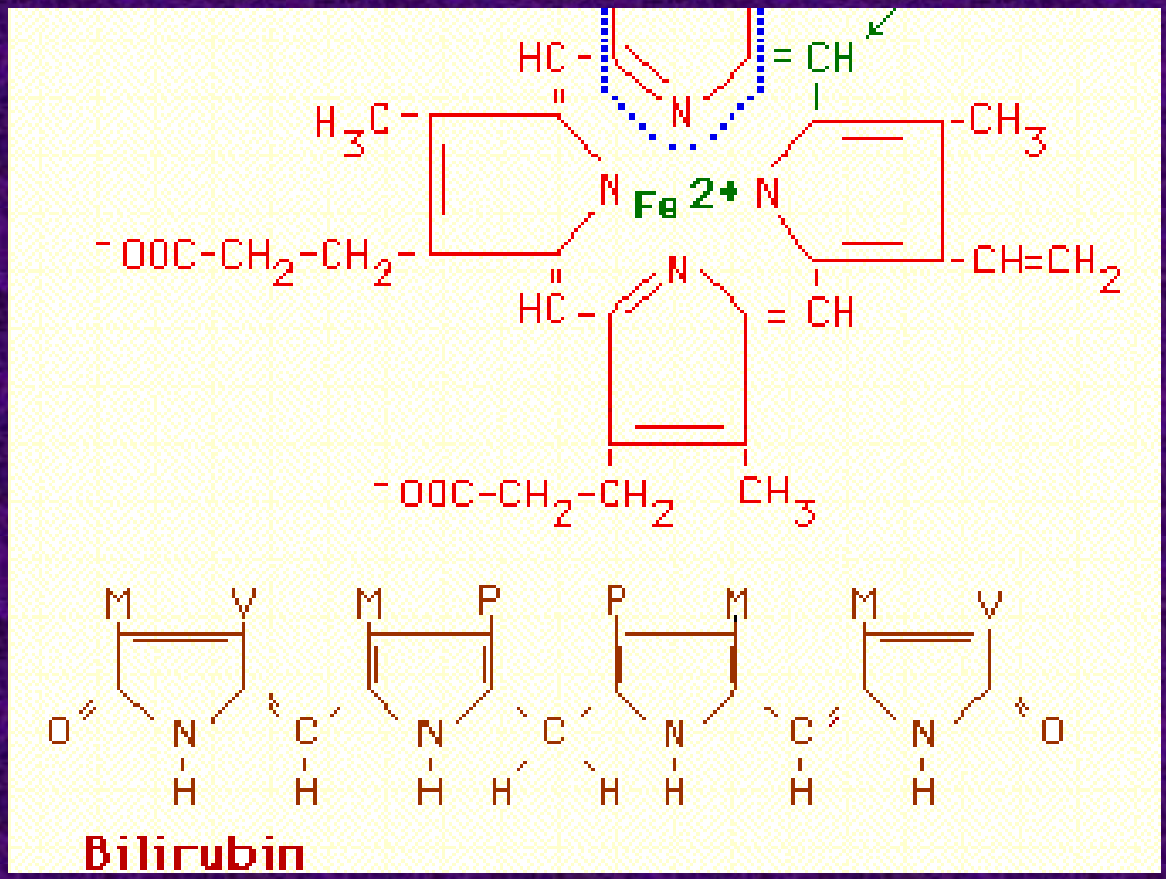
Manifestations

- Liver injury and its manifestations tend to follow characteristic morphologic and clinical patterns, regardless of cause.


Endoscopy
Pathology
I am the patient:
I need expertise from
each of you
Surgery
Radiology

Multidisciplinary approach !



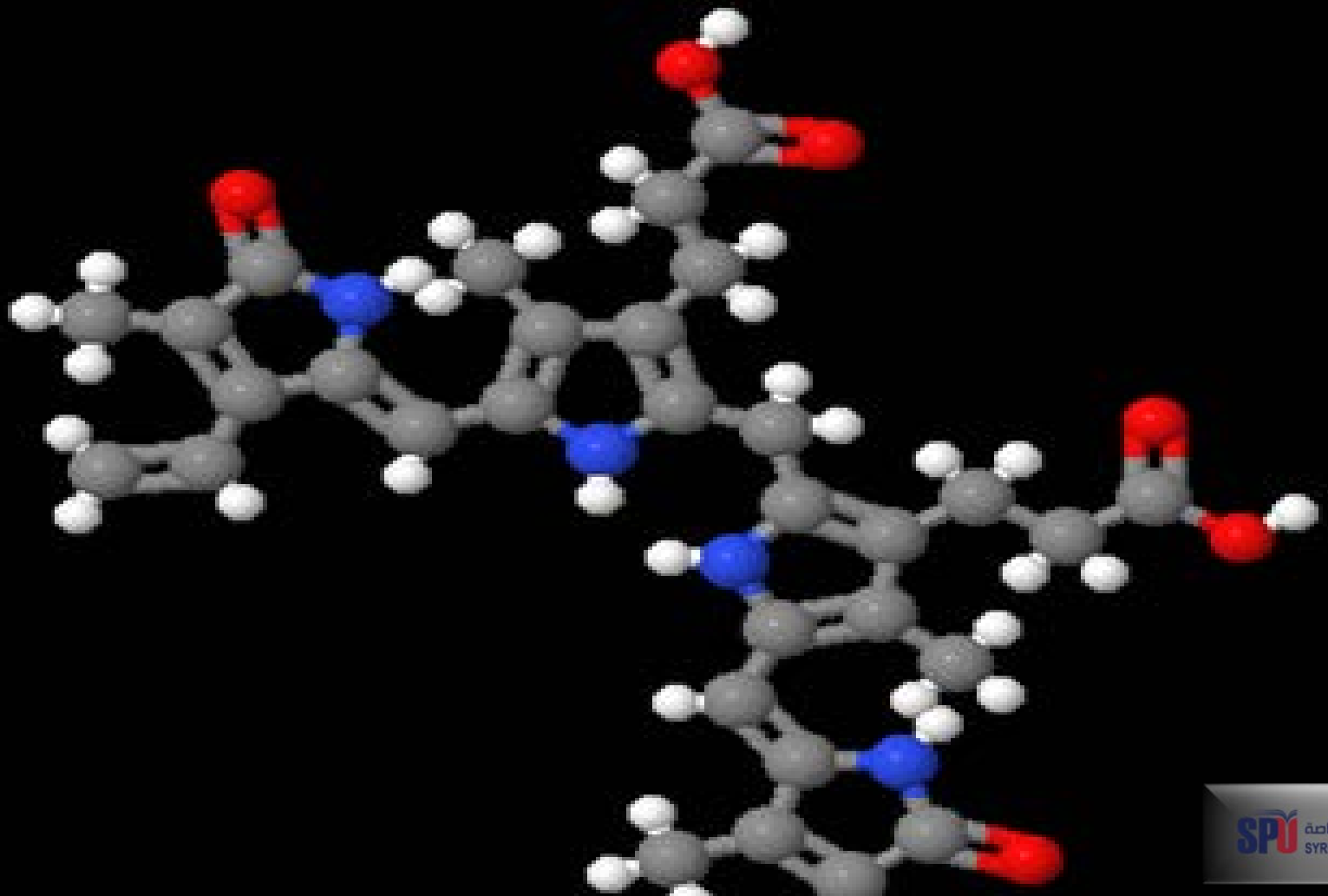


The brake down product of haem

the body usually produces about 300mg of bilirubin

Iron is removed haem molecule and porphyrin ring is opened to form bilirubin

Bilirubin



Bilirubin

Direct: water soluble

Indirect: lipid soluble

Red blood cells

Ineffective erythropoiesis

Other haem protein such as myoglobin and cytochromes

80%

20%

Transport in plasma and hepatic up take

In plasma
((bilirubin bound to albumin))

Not filtered at the glomerulus
unless there is glomerular proteinurea

On reaching the liver the bilirubin is taken into the hepatocyte

unconjugated bilirubin

=

Most of Plasma bilirubin

Conjugation of bilirubin

Endoplasmic reticulum of hepatocyte

Bilirubin + glucuronic acid —(**Bilirubin UDP-glucuronyltransferase**)→ bilirubin glucuronides "conjugated bilirubin" "Water soluble and readily transported into bile"

Bilirubin glucuronides (CONJUGATED BILIRUBIN)
cant be reabsorbed from the gut

degraded by bacterial action mainly in the colon

Urobilinogen
mixture of colorless, water soluble compounds

OXIDISE

UROBILINS AND STERCOBILINS "Brown"

Excreted in faeces

A small percentage of urobilinogen undergoes enterohepatic circulation

Most of it is cleared by the liver

Proportion filtered at the kidney and appears in the urine

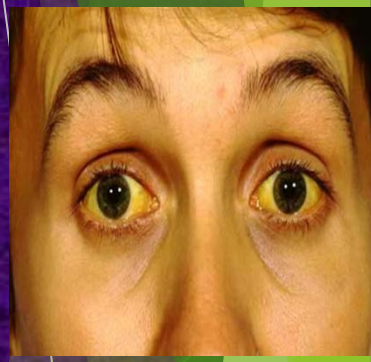
	Urine tests	
Condition	Urobilinogen	bilirubin
Healthy individuals	**Trace**	**Nil**
Gilbert's syndrome	Trace	Nil
Haemolytic disease	Increased	Nil
Hepatitis **•prodormal** **•icteric stage**	**Increased** **Undetectable**	**detectable** **present**
Biliary obstruction	**Undetectable**	**present**

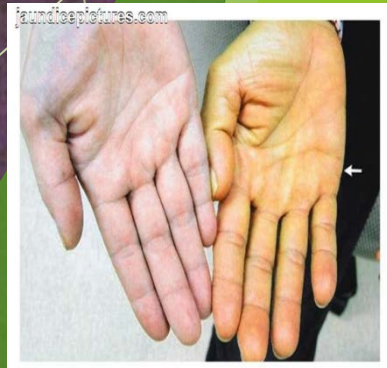
Syndrome	Inheritance	Abnormality	Clinical features/treatment
Unconjugated hyperbilirubinaemia			
Gilbert's	Autosomal dominant	↓ Glucuronyl transferase ↓ Bilirubin uptake	Mild jaundice, especially with fasting No treatment necessary
Crigler–Najjar			
Type I	Autosomal recessive	Absent glucuronyl transferase	Rapid death in neonate (kernicterus)
Type II	Autosomal dominant	↓↓ Glucuronyl transferase	Presents in neonate Phenobarbital, ultraviolet light or liver transplant as treatment
Conjugated hyperbilirubinaemia			
Dubin–Johnson	Autosomal recessive	↓ Canalicular excretion of organic anions, including bilirubin	Mild No treatment necessary
Rotor's	Autosomal recessive	↓ Bilirubin uptake ↓ Intrahepatic binding	Mild No treatment necessary

What is jaundice?

- yellowish pigmentation of the
- skin, the sclera, and other mucous membranes

- Jaundice is usually detectable clinically when the plasma bilirubin exceeds 50 μmol/L





Hepatocellular jaundice

- Both unconjugated and conjugated bilirubin in the blood increase!!!

Hepatocellular jaundice

results from an inability of the liver to transport bilirubin into the bile, as a consequence of parenchymal liver disease.

INABILITY TO SECRETE BILE
CHOLESTASIS

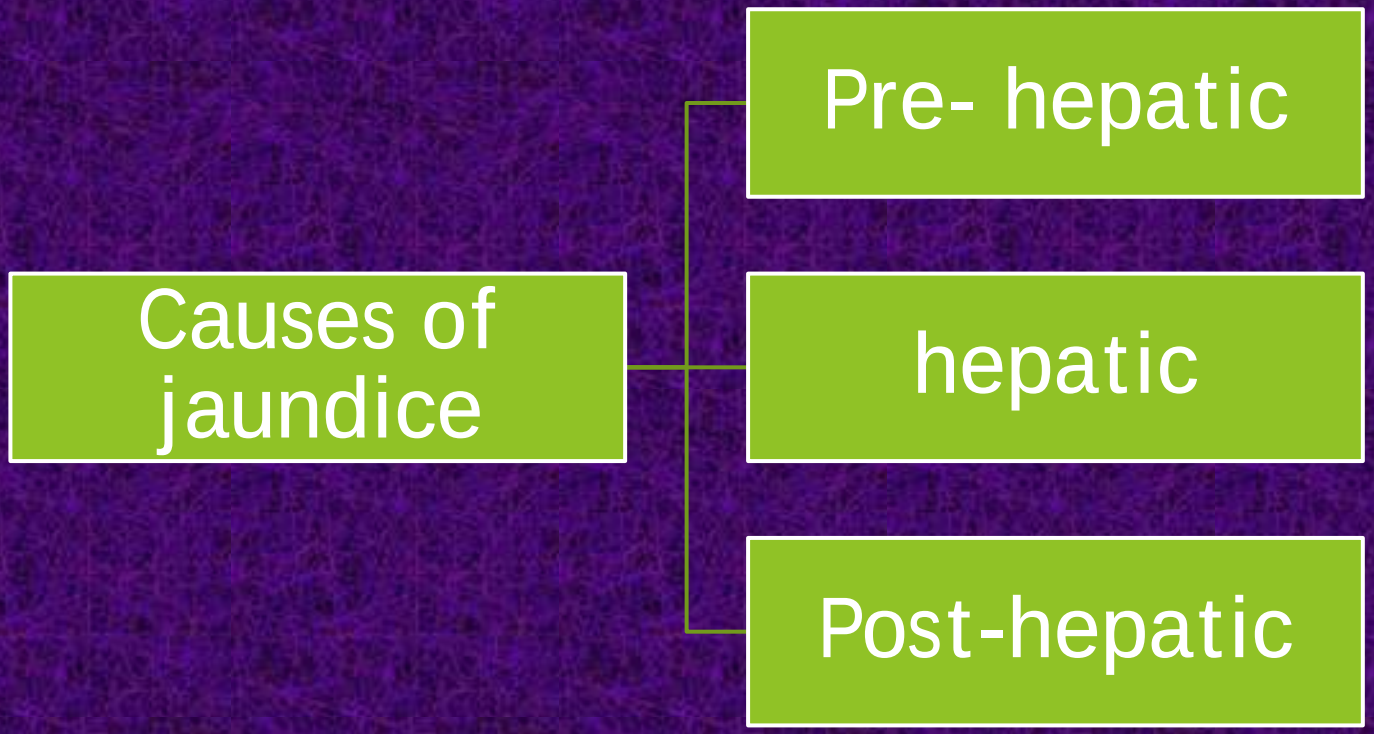
Cholestatic jaundice may be caused by:

- Failure of hepatocytes to initiate bile flow.
- Obstruction of the bile ducts or portal tracts.
- Obstruction of bile flow in the extrahepatic bile ducts.

BILE

The only way in which we can get rid of cholesterol and copper from the body

Enterohepatic circulation 90% of bile is re absorbed


Causes of jaundice
Pre- hepatic
hepatic
Post-hepatic

PRE-HEPATIC JAUNDICE

This is caused either by
1-Haemolysis or
2-congenital hyperbilirubinaemia,
and is characterised by an
isolated raised bilirubin level.

PRE-HEPATIC JAUNDICE

bilirubin load **six times** greater than normal before unconjugated bilirubin accumulates in the plasma.

.

- This does not apply to the newborn, who have a reduced capacity to metabolise bilirubin.

Liver function tests

serum bilirubin

Aminotransferaes ALT/AST

Alkaline phosphatase

Gama-glutamyle transferase GGT

Albumin

Prothrombin time (INR)

HEPATIC SYNTHETIC FUNCTION

PT

Albumin

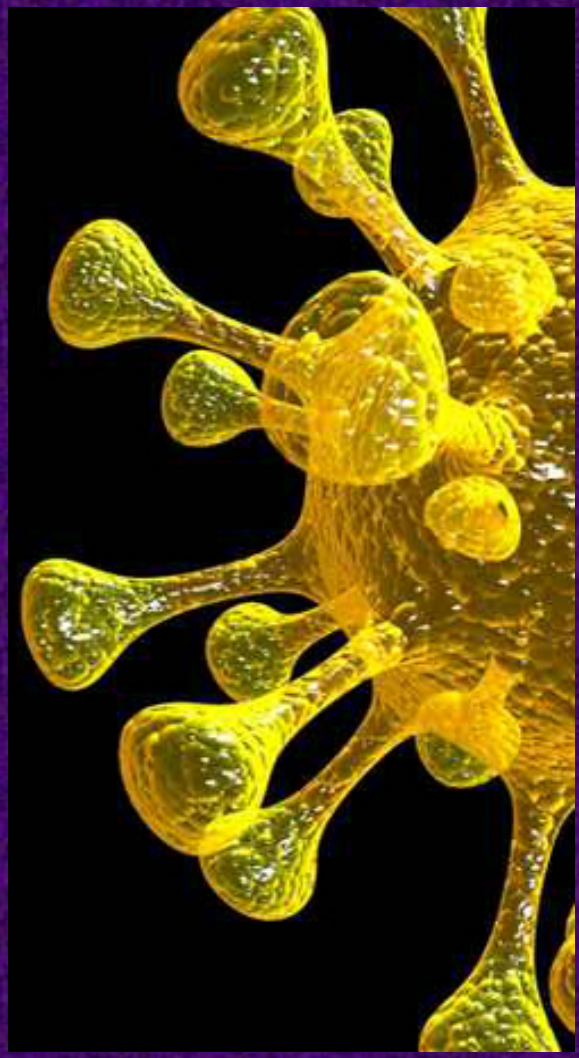
PT

Assess hepatic function

Involves factor II, V, VII, and X, synthesized by the liver

Albumin 8-14g/day

Half-life is 20 days



Aminotransferase

Amino transferase: -ALT

-AST

Both transfer amino group from amino acid to ketoacid producing pyruvate and oxalo-acetate

Tests of hepatic function

Serum albumin
Serum bilirubin
Prothrombin

Tests of hepatocellular injury or cholestasis

Aminotransferase
Alkaline phosphatase
Gama-glutamyl transferase

Common causes of elevated serum transaminases

Minor elevation (< 100 U/L)

- Chronic hepatitis C
- Chronic hepatitis B
- Haemochromatosis
- Fatty liver disease

Moderate elevation (100–300 U/L)

As above plus:

- Alcoholic hepatitis
- Non-alcoholic steatohepatitis
- Autoimmune hepatitis
- Wilson's disease

Major elevation (> 300 U/L)

- Drugs (e.g. paracetamol)
- Acute viral hepatitis
- Autoimmune liver disease
- Ischaemic liver
- Toxins (e.g. *Amanita phalloides* poisoning)
- Flare of chronic hepatitis B

- تكشف اضطرابات الكبد عادة أثناء اجراء فحص دموي روتيني (مثلاً: يظهر ارتفاع بخمائر الكبد لدى 3.5 % من المرضى الذين يتحضرون لعمل جراحي).
  يوجد مرض كبدي ما عند أغلب المرضى الذين لديهم ارتفاع مستمر بهذه القيم

GGT:

Microsomal enzyme
transfer glutamyl groups from gama-glutamyl peptides to other peptides and amino acid

GGT

Alcohol use
BMI

Anticonvulsant
Warfarin
Age gender
Smoking

Alkaline phosphatase

Enzymes Are capable of hydrolysing phosphatesteras at alkaline PH

Bilirubin glucuronides (CONJUGATED BILIRUBIN)
cant be reabsorbed from the gut

degraded by bacterial action mainly in the colon

OXIDISE

STERCOBILINS

Excreted in faeces
"Brown"

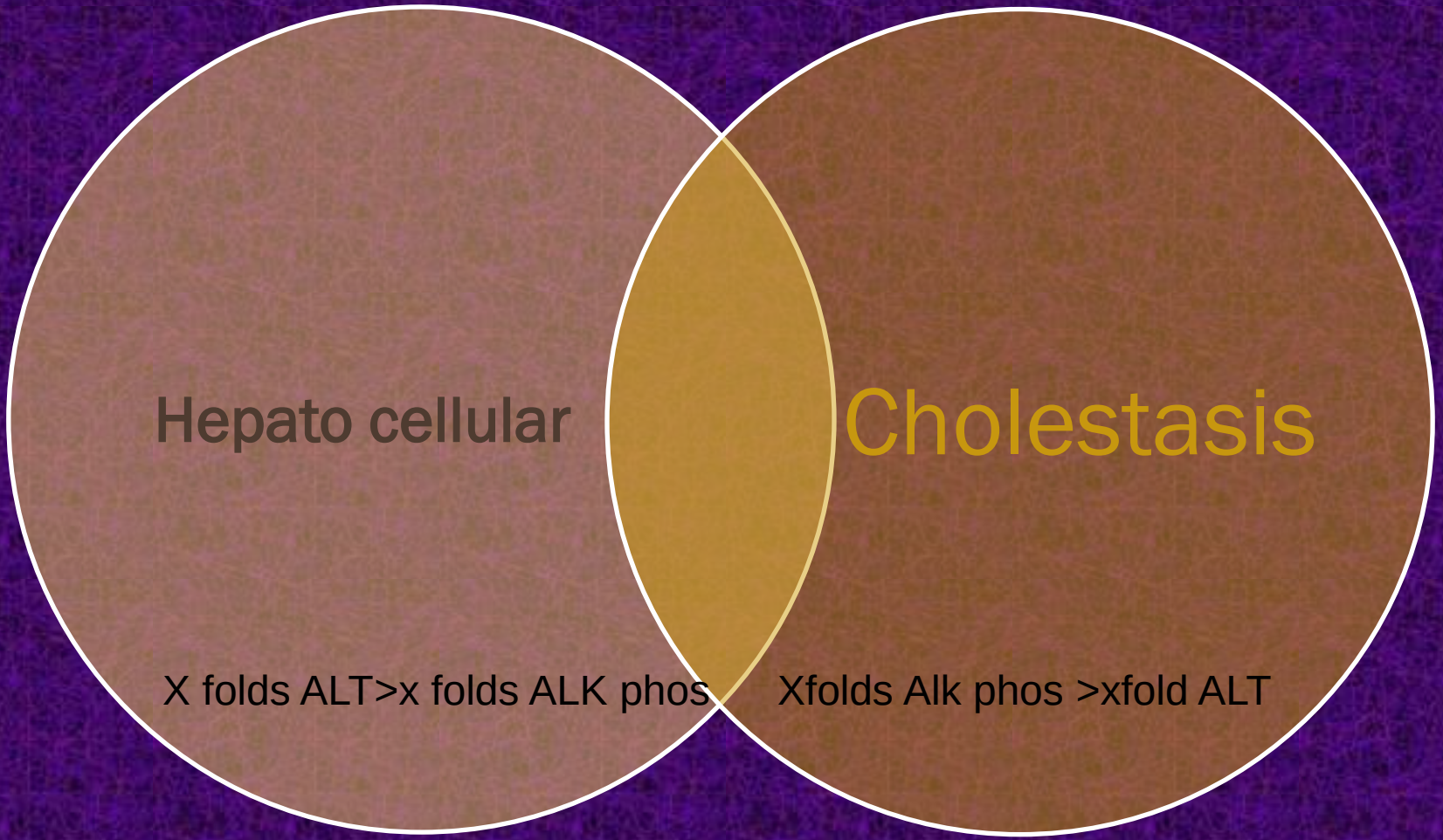
CHOLESTASIS

- Early features
- Jaundice
- Dark urine
- **Pale stool**
- Itching

LATE FEATURES

- Xanthelasma and xanthomas
- Malabsorption
  - Weight loss
  - Steatorrhoea
  - Osteomalacia
  - Bleeding tendency

LIVER DISEASES



	HEPATOCELLUL JARAUNDICE	BILIARY OBSTRUCTION
ALT/AST	> ×6 folds	< ×6folds
Alkaline phosphatase	< ×2.5 folds	>×2.5 folds
Diagnostic likelihood	90%	80%

CAUSES OF CHOLESTATIC JAUNDICE

Primary biliary cirrhosis
Primary sclerosing cholangitis
Benign recurrent intrahepatic cholestasis

Alcohol
Drugs
Viral hepatitis
Autoimmune hepatitis
Cystic fibrosis
Severe bacterial infections
Post-operative
Hodgkin lymphoma
Pregnancy

CHOLESTASIS

- Abdominal pain suggests

1-choledocholithiasis

2-pancreatitis

3-choledochal cyst. Jaundice is progressive in cancer, and fluctuating in sclerosing cholangitis, pancreatitis and stricture. Abdominal examination may reveal irregular hepatomegaly or masses in carcinoma. Faecal occult blood suggests an ampullary tumour

CHOLESTASIS

- . Jaundice is progressive in--- cancer, and fluctuating in

-Sclerosing cholangitis,

-Pancreatitis

3-Stricture. Abdominal examination may reveal irregular hepatomegaly or masses in carcinoma. Faecal occult blood suggests an ampullary tumour

CHOLESTASIS

- . Abdominal examination may reveal irregular hepatomegaly or masses in carcinoma.
- Faecal occult blood suggests an ampullary tumour

LIVER AND COAGULATION

	clotting	Anti-clotting
Vitamin k dependent	II VII IX X	Protein C protein S
independent of Vit K	I V Viii	Antithrombin III

COAGULATION PROTEINS /BALANCING CF

Measurable

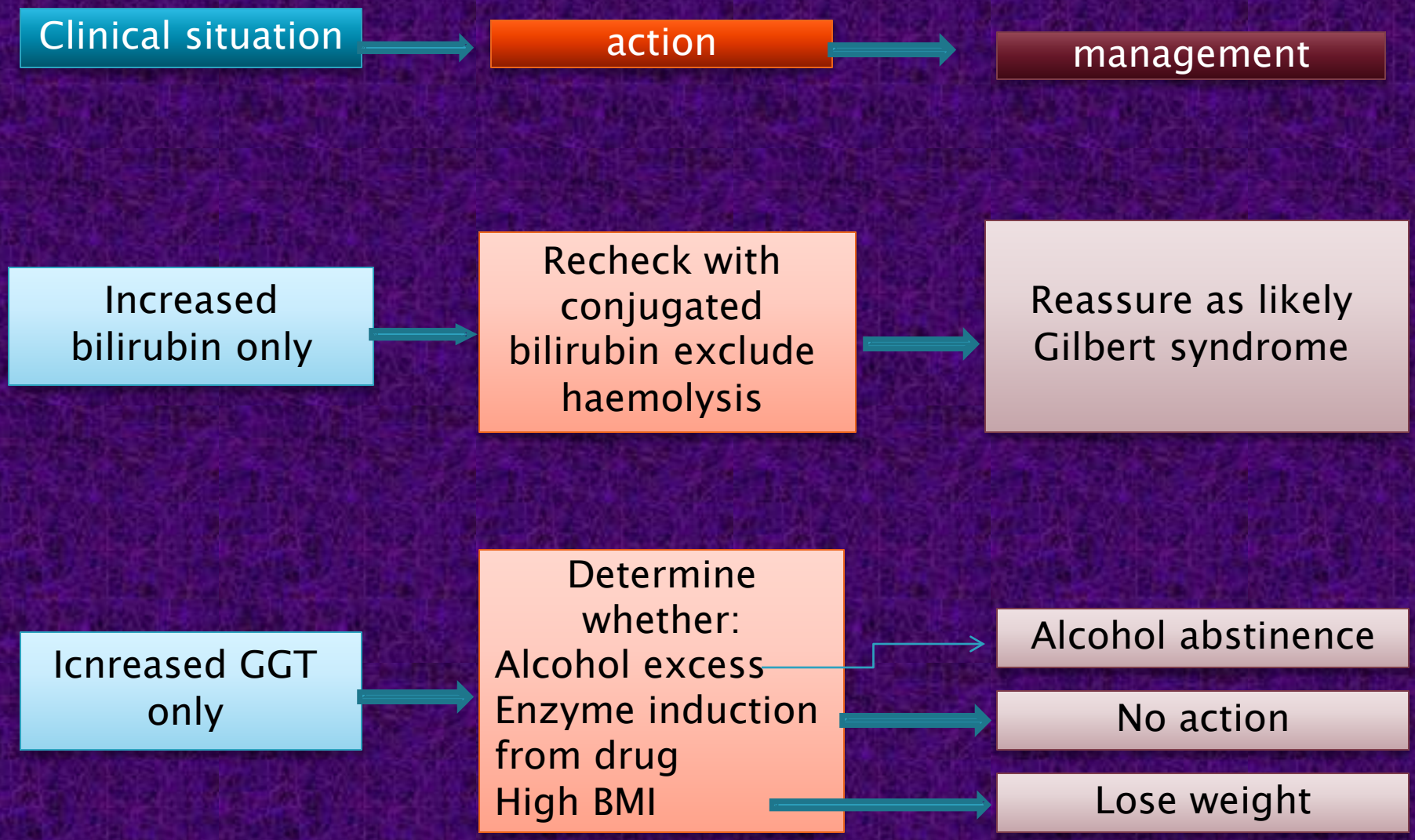
Not Measurable

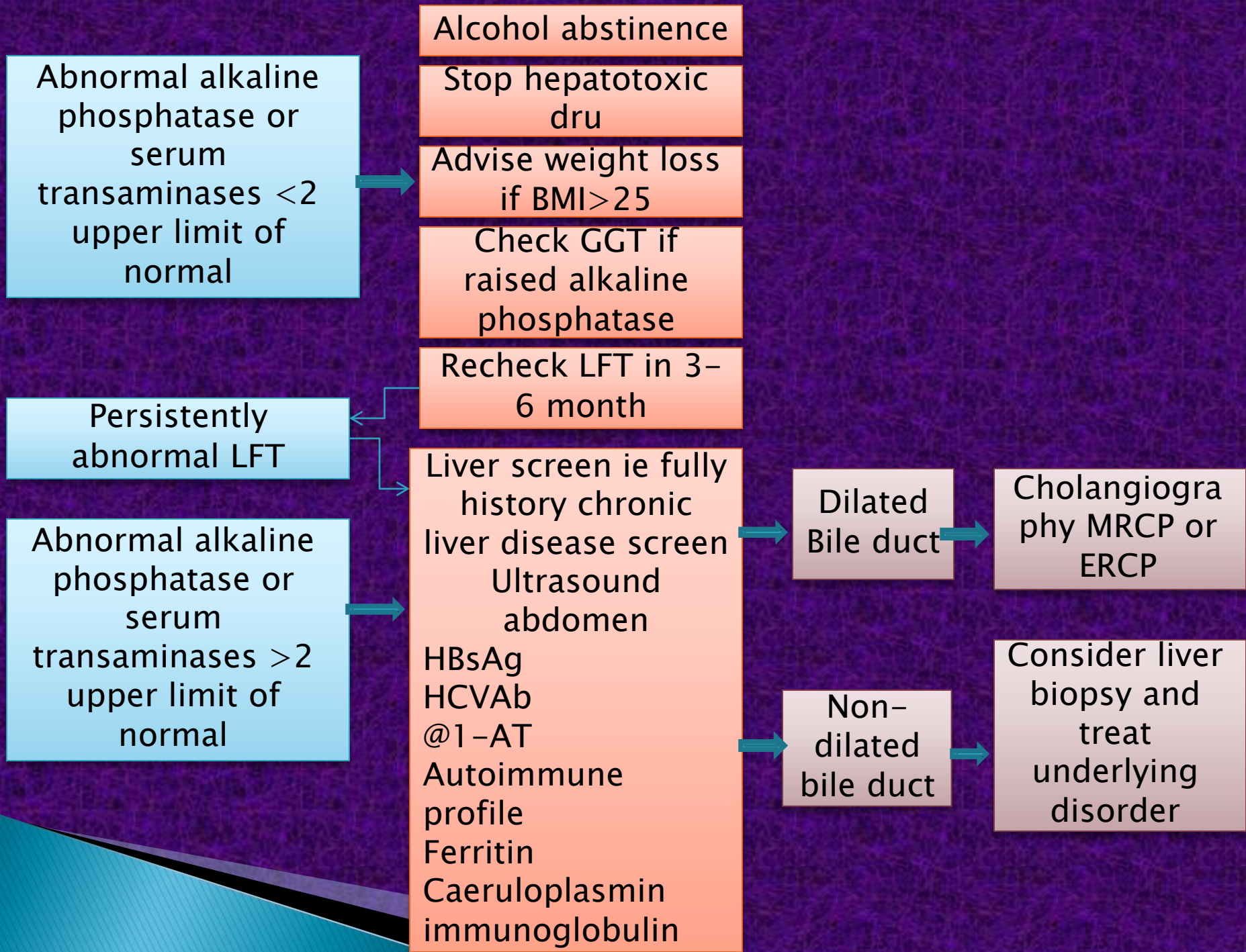
IMPORTANT

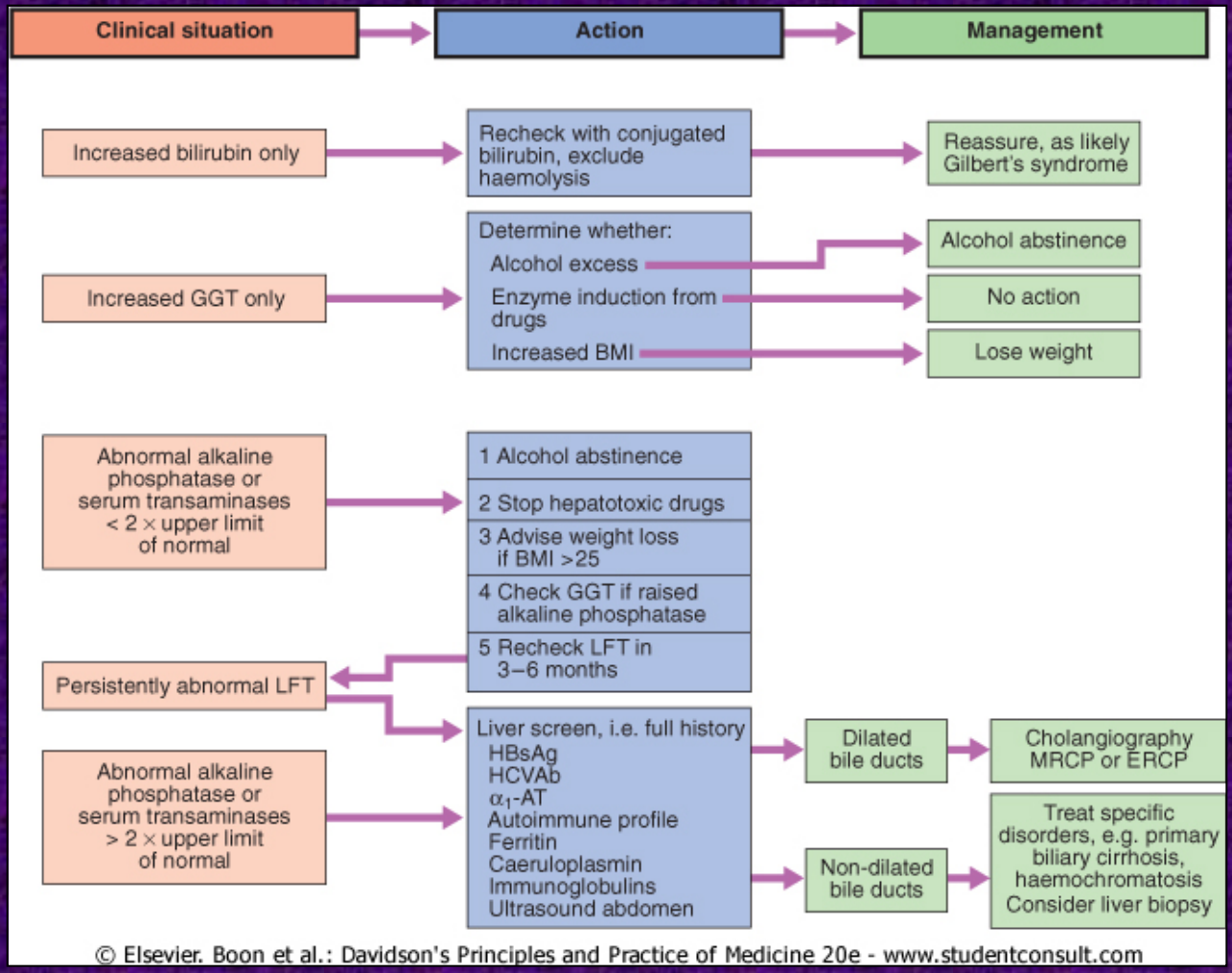
the presence or absence of stigmata of chronic liver disease

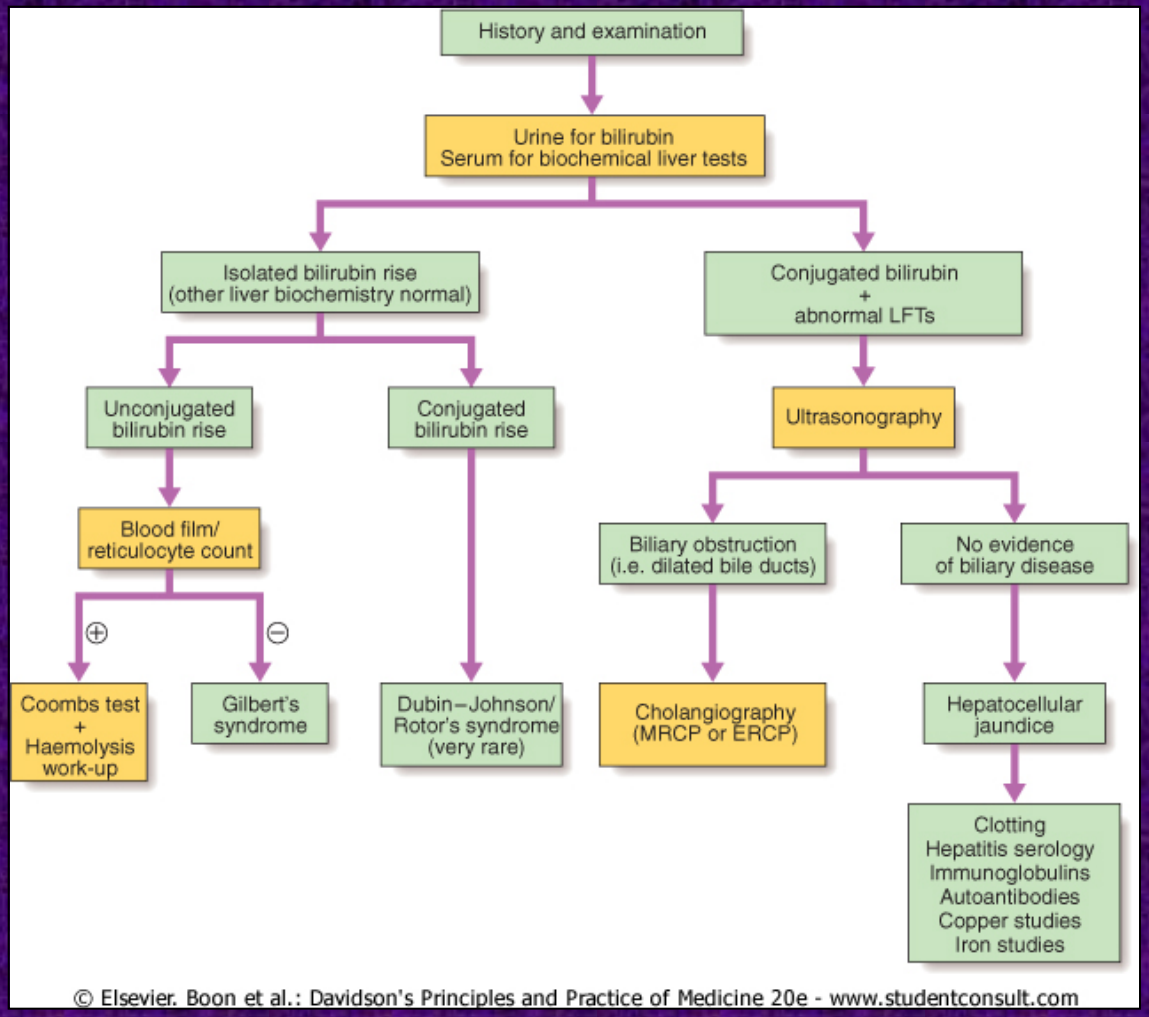
does not reliably identify patients with significant chronic liver disease.

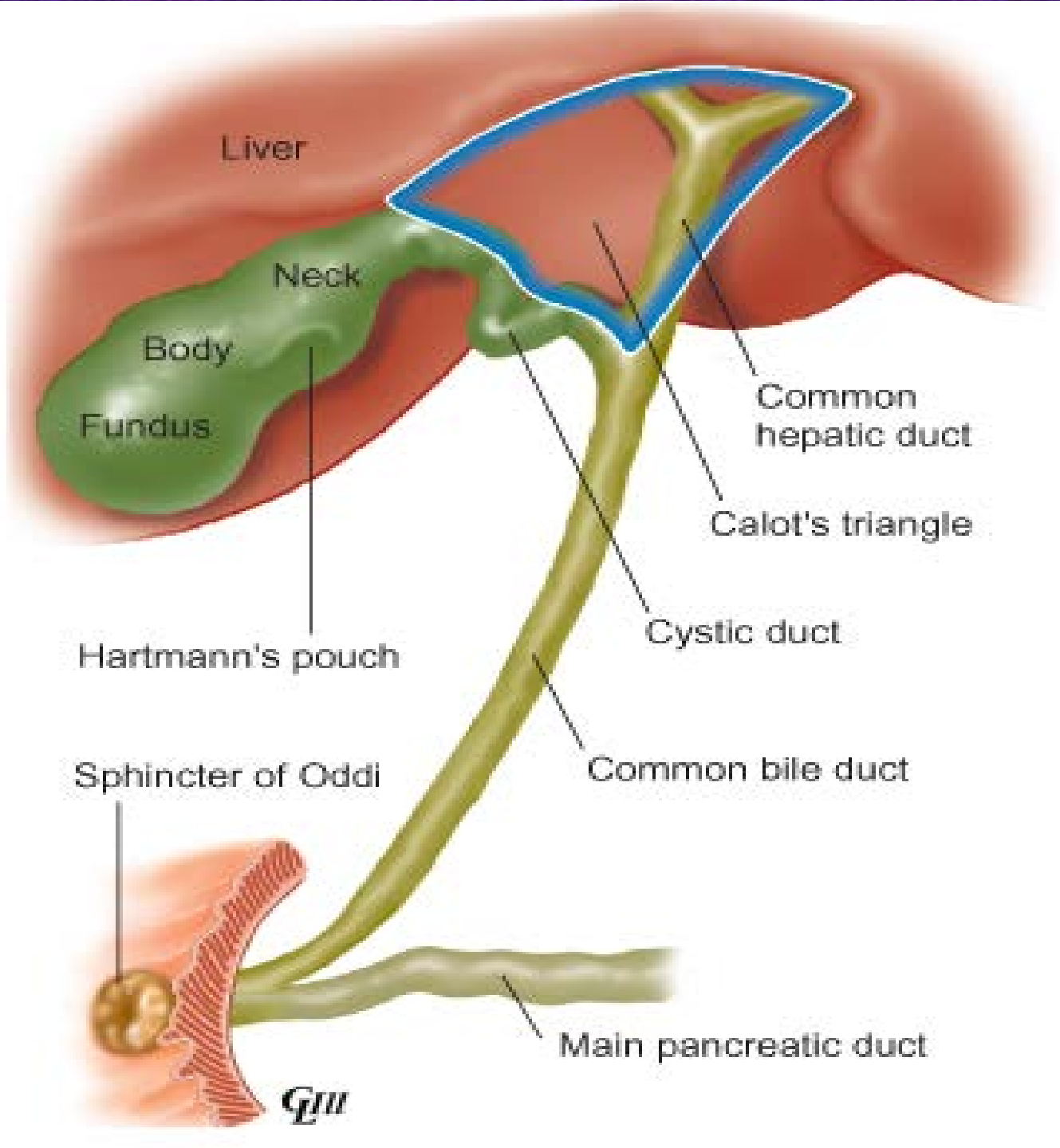
The absence of these stigmata should not therefore preclude further investigation


Clinical situation
action
management
Increased bilirubin only
Recheck with conjugated bilirubin exclude haemolysis
Reassure as likely Gilbert syndrome
Icnreased GGT only
Determine whether:
Alcohol excess
Enzyme induction from drug
High BMI
Alcohol abstinence
No action
Lose weight


Abnormal alkaline phosphatase or serum transaminases <2 upper limit of normal
Alcohol abstinence
Stop hepatotoxic dru
Advise weight loss if BMI>25
Check GGT if raised alkaline phosphatase
Recheck LFT in 3-6 month
Persistently abnormal LFT
Abnormal alkaline phosphatase or serum transaminases >2 upper limit of normal
Liver screen ie fully history chronic liver disease screen
Ultrasound abdomen
HBsAg
HCVAb
@1-AT
Autoimmune profile
Ferritin
Caeruloplasmin
immunoglobulin
Dilated Bile duct
Cholangiography MRCP or ERCP
Non-dilated bile duct
Consider liver biopsy and treat underlying disorder

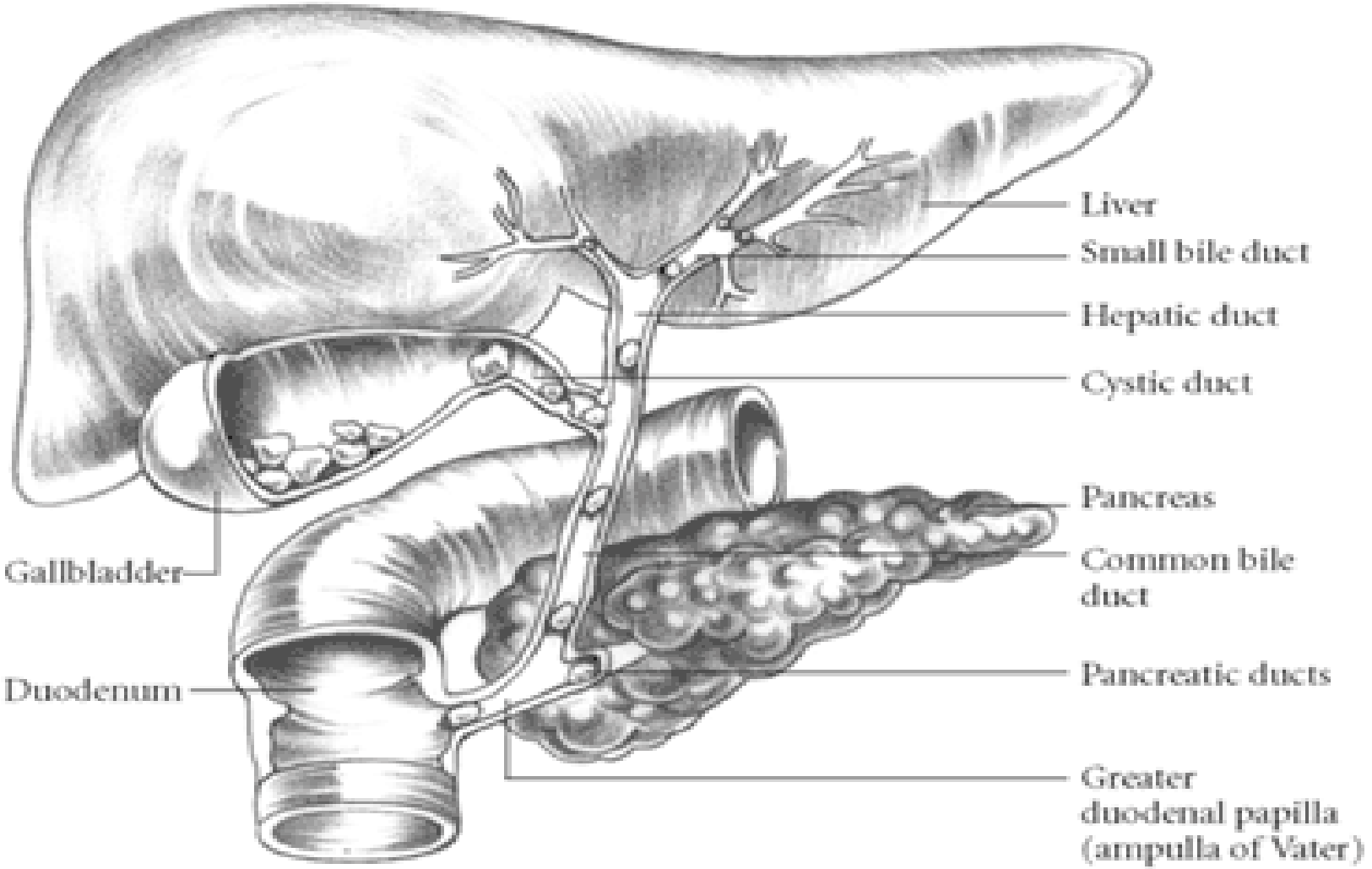


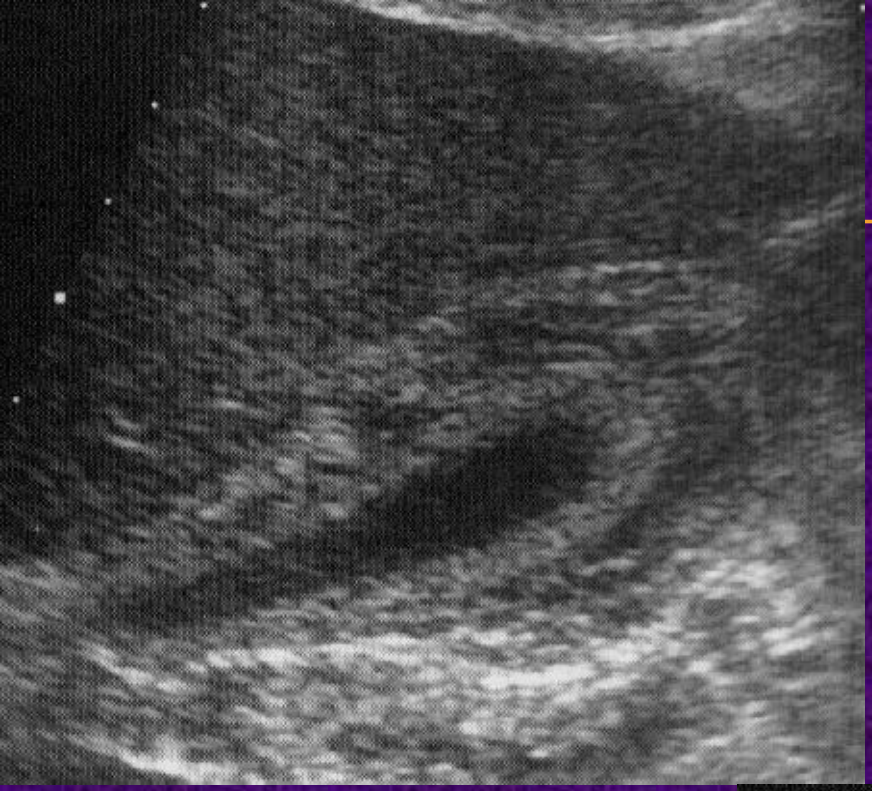


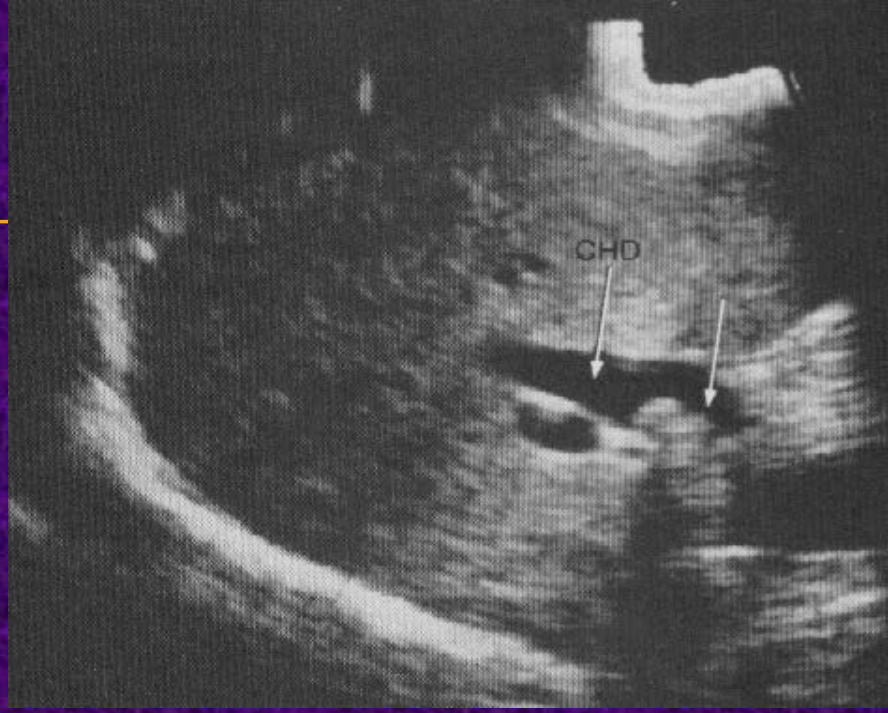

Liver
Neck
Body
Fundus
Common hepatic duct
Calot's triangle
Cystic duct
Hartmann's pouch
Common bile duct
Sphincter of Oddi
Main pancreatic duct

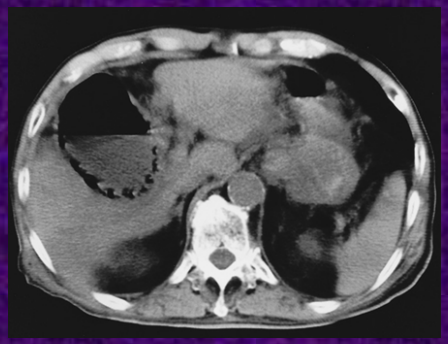
COMMON SITES OF CALCULI FORMATION

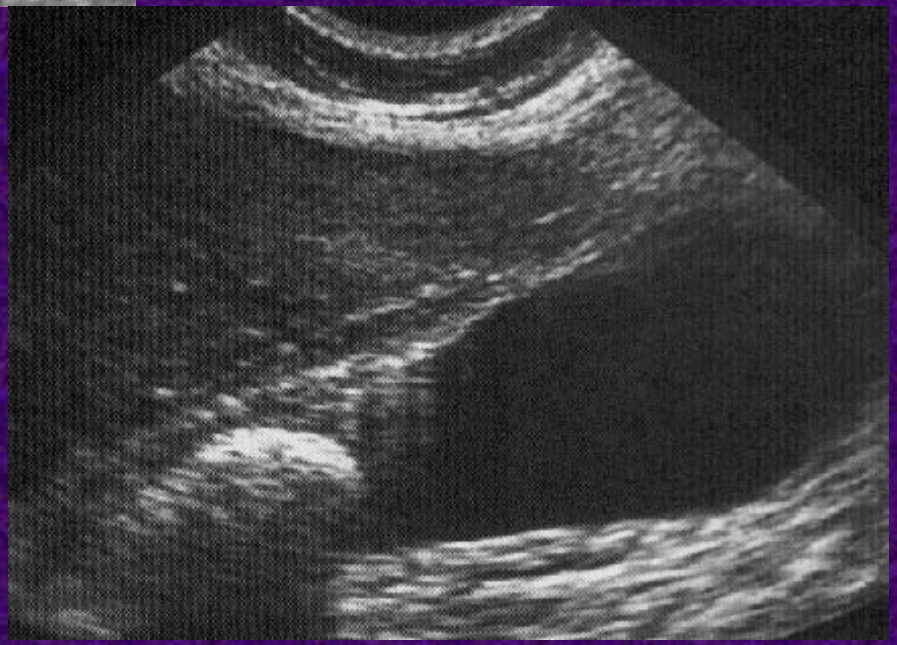
The illustration below shows sites where calculi typically collect. Calculi vary in size; small calculi may travel.



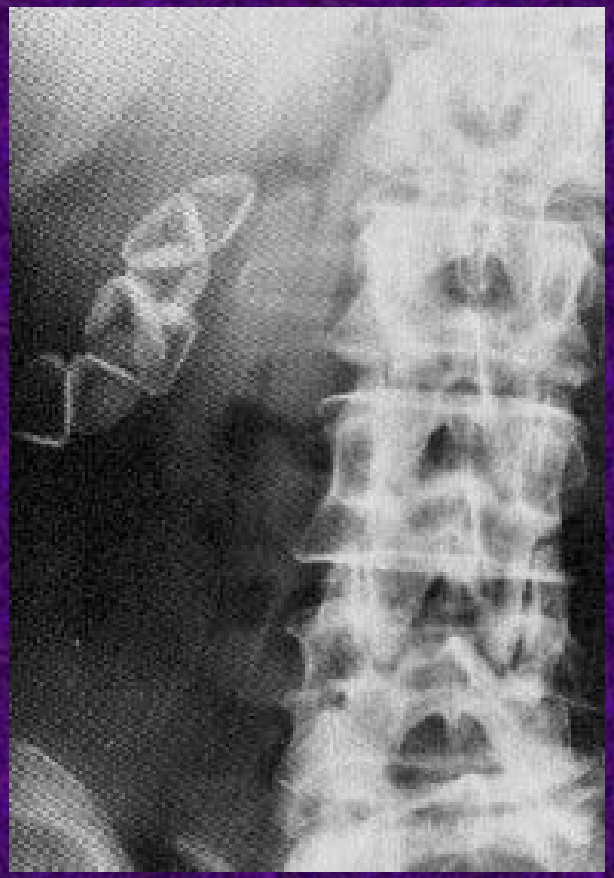



CHD





PLAIN –X-RAY OF ABDOMEN



Calcified gallstones

INCREASED ALP&GGT

ULTRASOUND

Dilated bile duct

- cholangiography
- MRCP or ERCP

IN INCREASED ALP&GGT ULTRASOUND EXAMINATION OF BILIARY TREE MUST BE DONE

Normal bile duct

- Consider liver biopsy
- Treat underlying disorder

IN THE CASE OF INCREASED ALP&GGT ULTRASOUND EXAMINATION OF BILIARY TREE MUST BE DONE

Normal bile duct

- Consider liver biopsy
- Treat underlying disorder

Dilated bile duct

- cholangiography
- MRCP or ERCP

IMAGING

- **Ultrasound**
  - The state of biliary tree(dilated)and gallbladder(stones)
  - Presence of hepatic mass
- **CT/MRCP**
  - MRCP is superior for biliary tree
- Nuclear medicine: DISIDA scan/HIDA scan
  - Limited to patient with bilirubin of 20 mg/dL
  - Sensitive for the presence of acute cholecystitis
  - Presence of bile leak after surgery or ERCP.

CHOLANGIOGRAPHY

MRCP

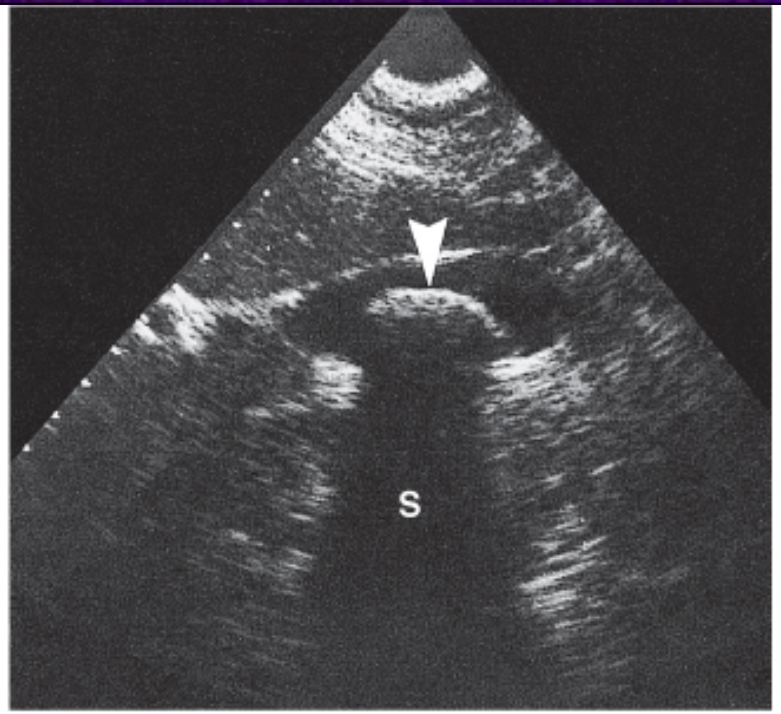
ERCP

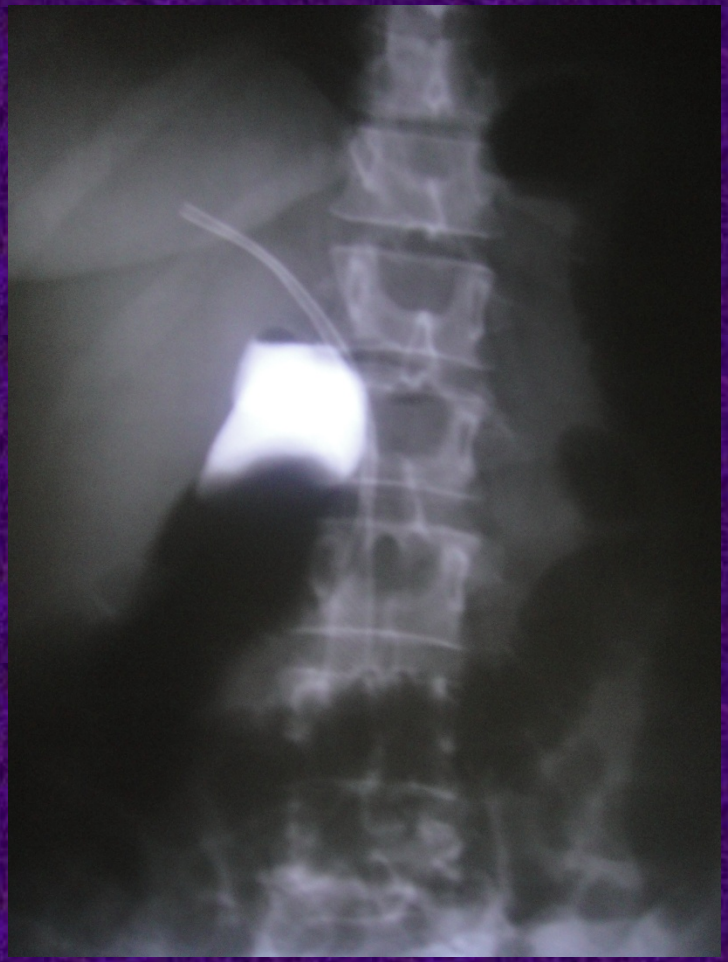
PTC.

- PTC :does not allow the Ampulla of Vater or pancreatic duct to be imaged..

CHOLANGIOGRAPHY

- **MRCP** is as good as ERCP at imaging the biliary tree and does not have the same complications
(pancreatitis in 5% and 1% bleeding if a sphincterotomy is performed);
-
- it is therefore the diagnostic test of choice.

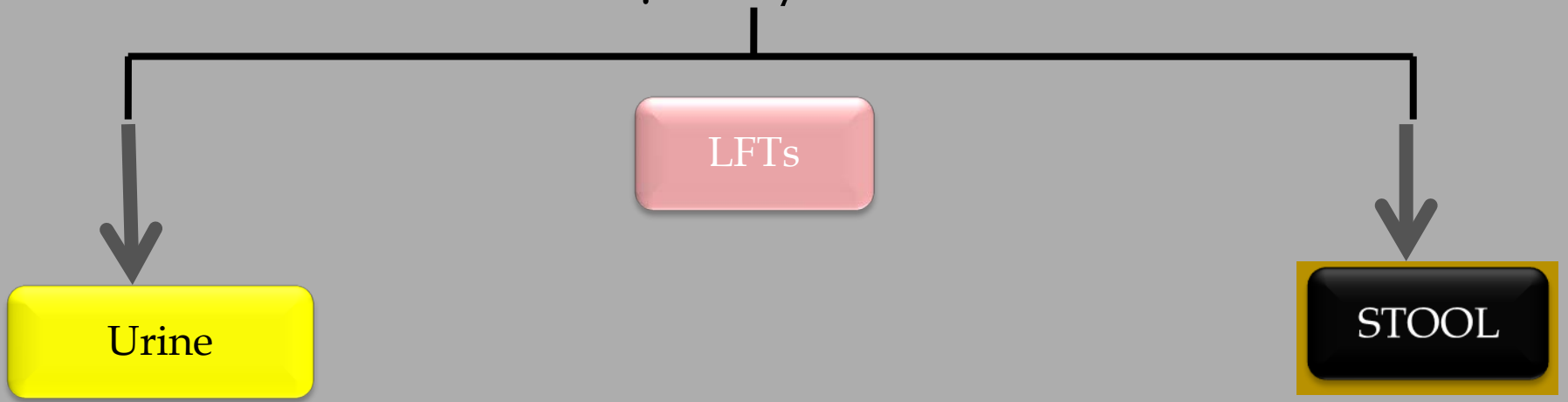




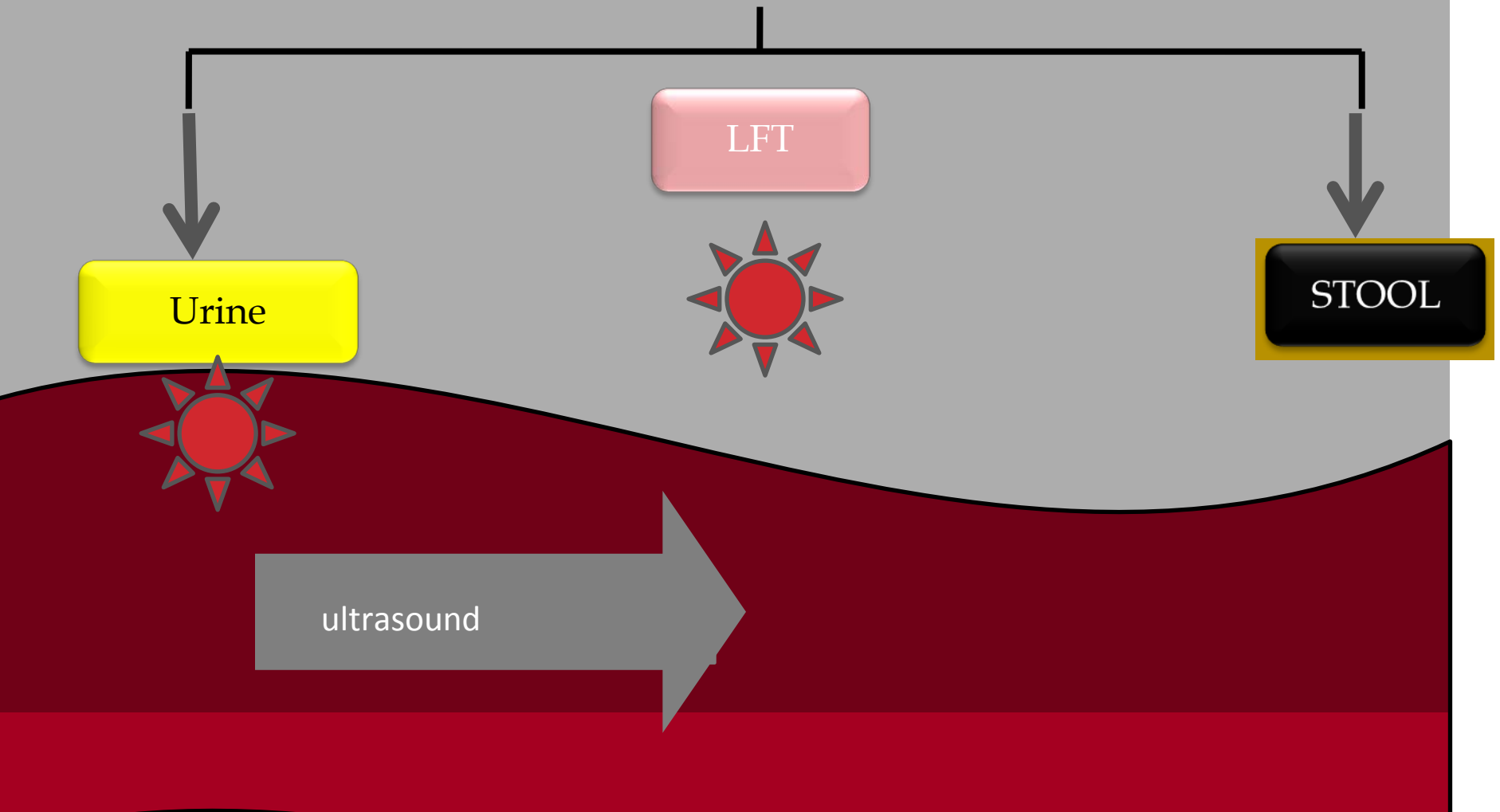
Approach to the Jaundiced Patient

History and examination

Jaundice is usually detectable when the plasma bilirubin exceeds 50 µmol/L

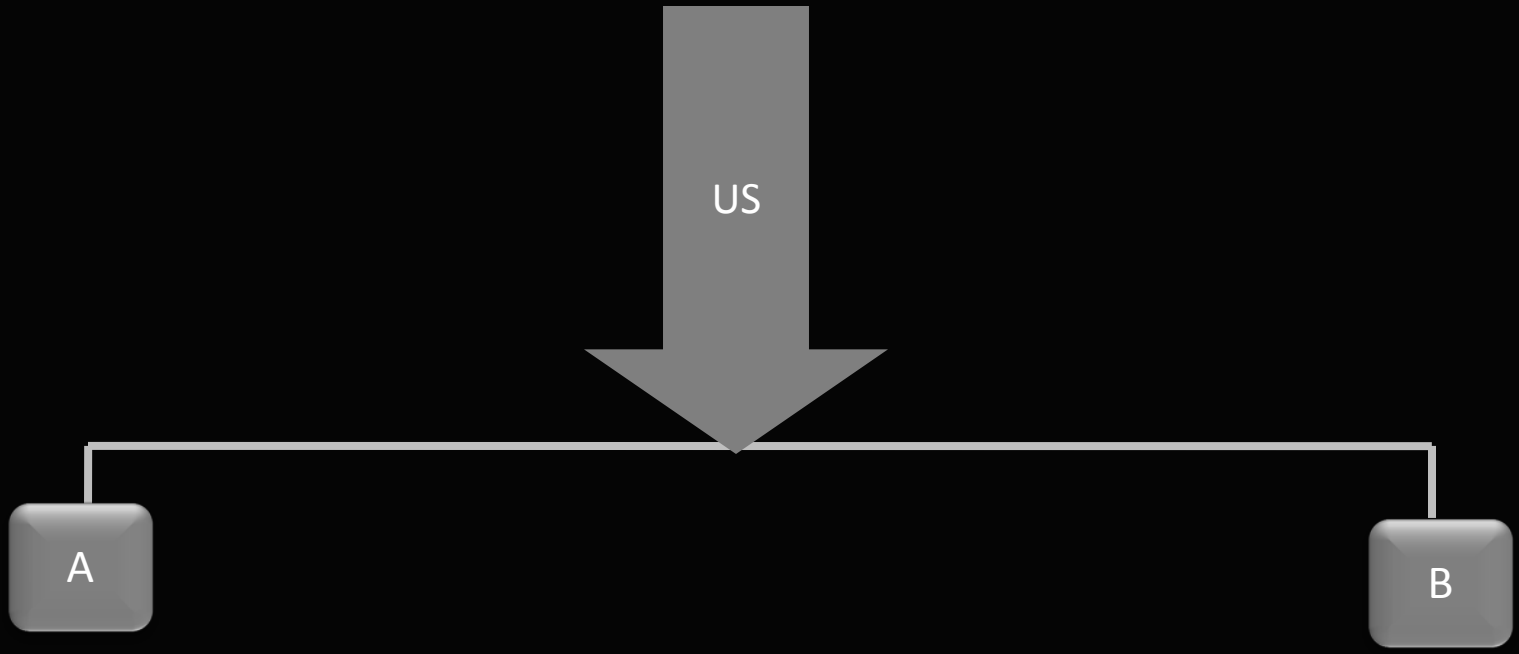


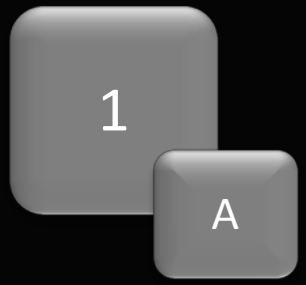
Conjugated bilirubin + abnormal LFTs



1

↑ Conjugated bilirubin + abnormal LFTs



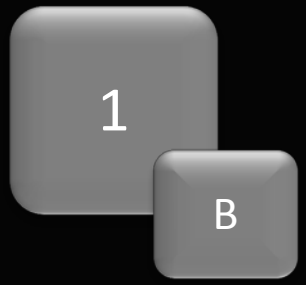


Biliary obstruction (i.e. dilated bile ducts)

Obstructional jaundice
(Greater elevation of ALP and GGT than the aminotransferases)

↓

Cholangiography
(MRCP or ERCP)



No evidence of Biliary disease

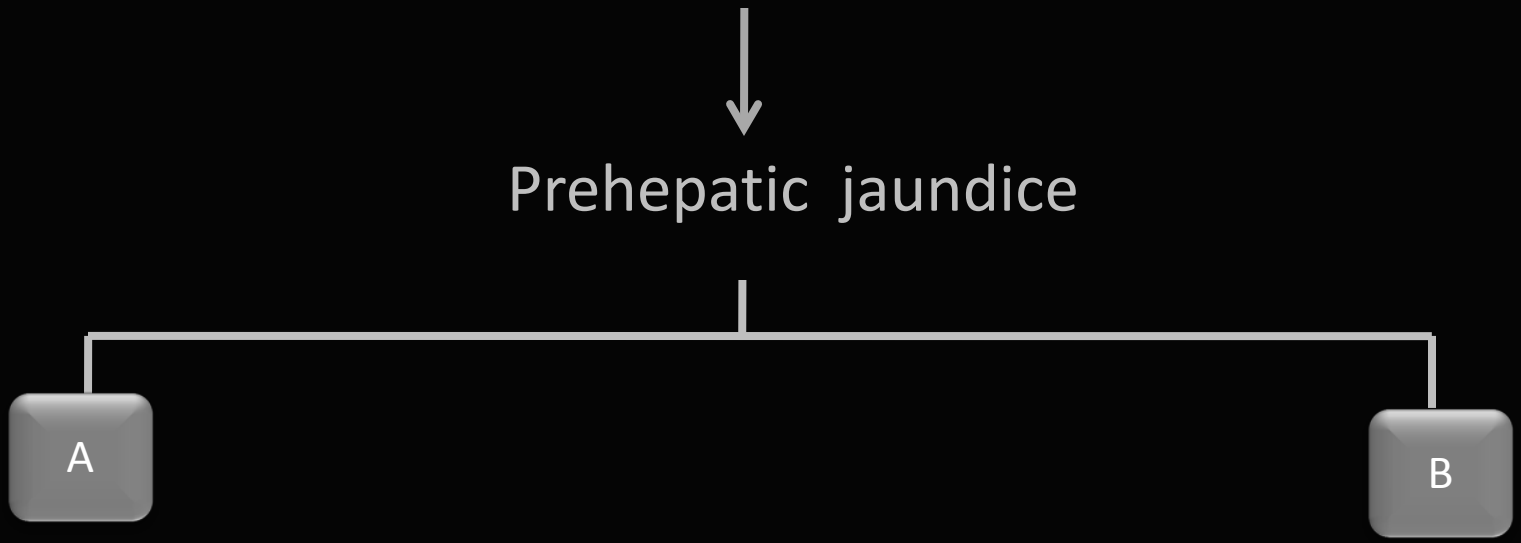
Hepatocellular jaundice

Acute jaundice + AST > 1000 highly suggestive of parenchymal liver disease due to :

- Infection
- Drugs
- ischemia

2

Urobilinogen present , Isolated bilirubin rise , and other liver biochemistry normal



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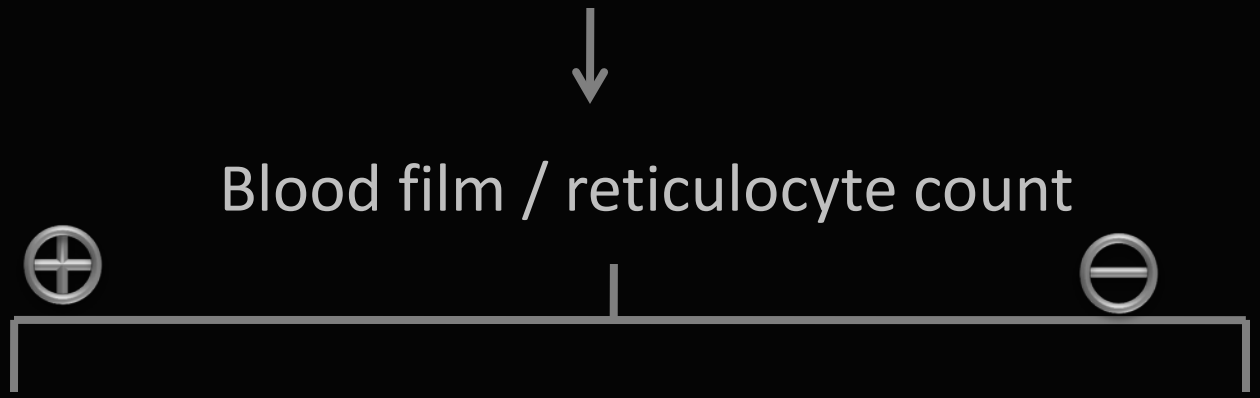
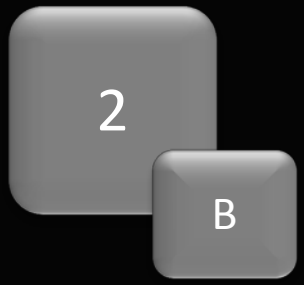
A

Unconjugated bilirubin



Coombs test
+
haemolysis work – up
(Usually mild)

Gilbert's Syndrome
(The most common form of non-heamolytic hyperbilirubinaemia)



conjugated bilirubin

↓

Dubin – Johnson /
Rotor’s syndrome
(very rare)

ETHIOLOGICAL INVESTIGATION