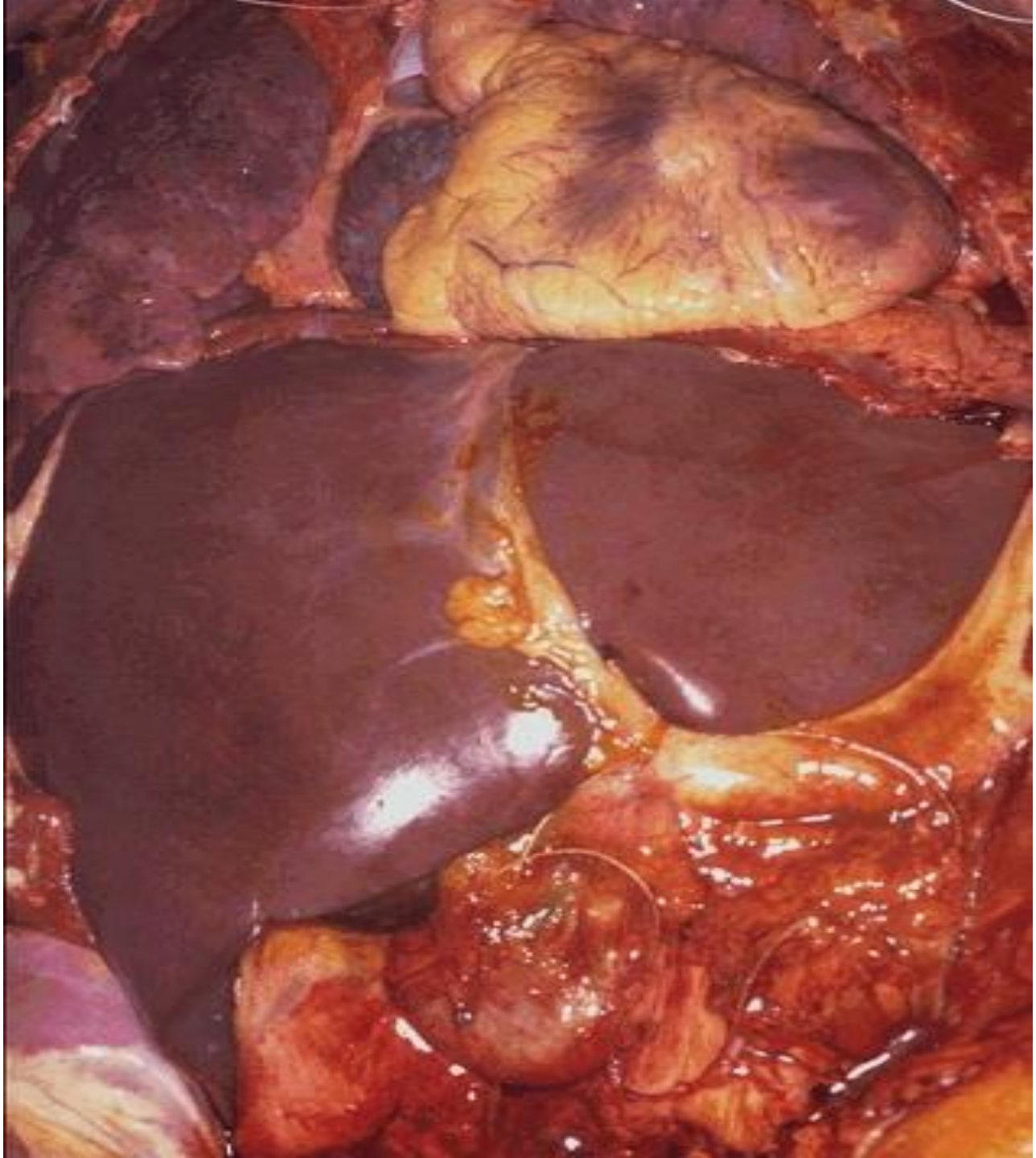
Symptoms and Diagnosis in LIVER and BILIARY TRACT DISEASE

Koray Topgül, MD, Prof



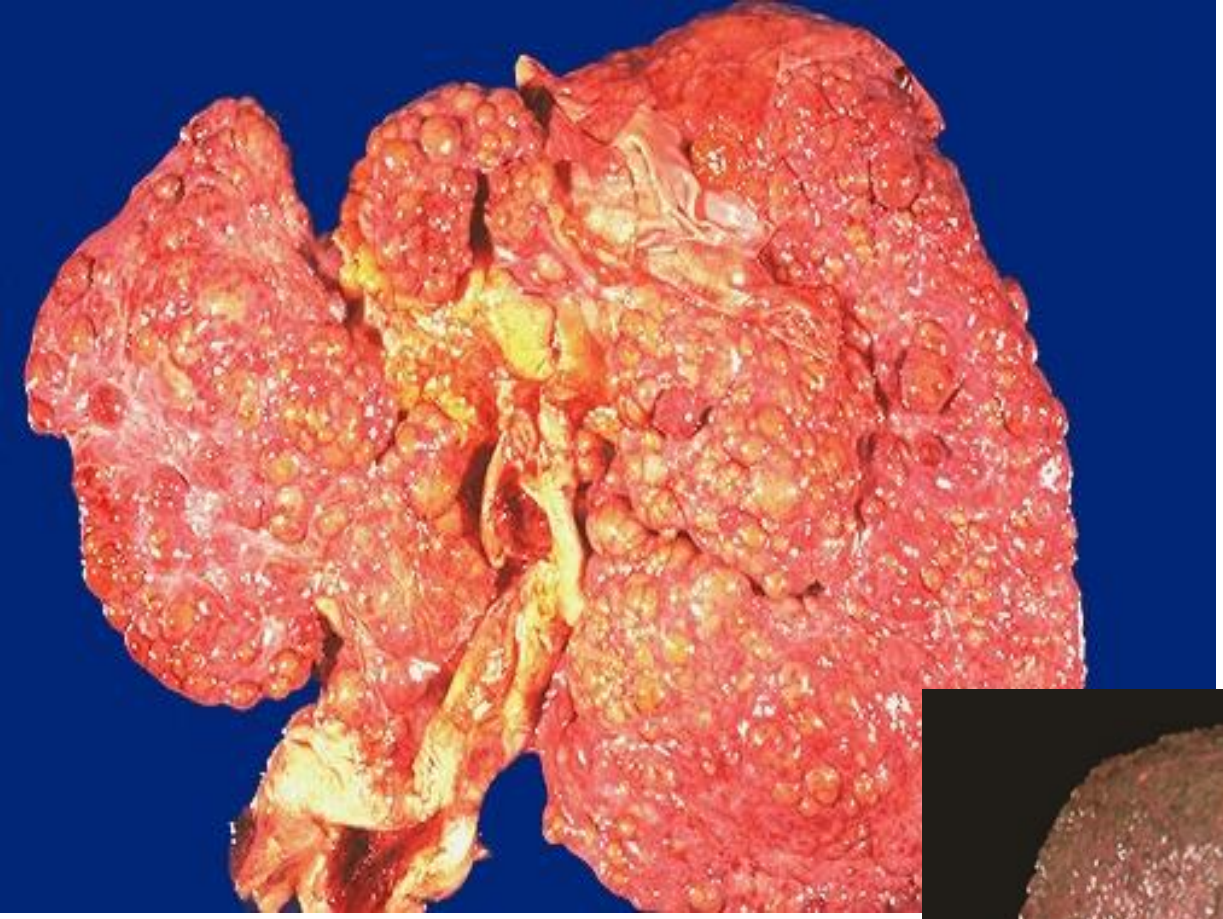
- Liver weight 1400 - 1600gm.

- Parenchyma - liver cells (hepatocytes) trabeculae 1 cell thick in adults.
  - Kupffer cells in sinusoids are phagocytes.
  - hepatic stellate cells in space of Disse, store vitamin A, transform into collagen-producing myofibroblasts, regulate blood flow in sinusoids.
  - liver-associated lymphocytes.

- Biliary drainage system - canaliculi (in centre of liver cell plates).
  - canals of Hering & cholangioles.
  - intra-hepatic bile ducts.
  - extra-hepatic bile ducts.

- Vasculature - portal vein supplies 70% of the blood flow.
  - hepatic artery supplies 30% of the blood flow.
  - sinusoids lined by fenestrated endothelium.
  - hepatic venules, hepatic veins drain into the IVC.

- The liver is important for - metabolism of carbohydrate, protein,lipids.
  - protein synthesis, albumin, coagulation factors, complement factors etc.
  - storage of iron, copper, vitamins A,D,B12.
  - detoxification/drug metabolism.
  - bile production.



CIRRHOSIS

- **Pathogenesis.**

  Liver injury results in chronic inflammation and activation of Kupffer cell, and other endogenous liver cells with the production of cytokines. These, together with disruption of the extracellular matrix activates hepatic stellate cells (HSC). Toxins may activate HSCs. These transform into myofibroblasts which produce collagen and constrict sinusoids.

  Collagen in the space of Disse leads to “capillarisation” of the sinusoids and loss of endothelial fenestrations, hindering exchange of solutes.

  New vascular channels in fibrous bands link inflow of blood (venous & arterial) with outflow (hepatic venules) thus by- passing parenchyma.

  Existing vascular channels and biliary channels may be obliterated.

  The results are internal vascular shunts and portal hypertension.

The hepatocytes in the regenerative nodules may appear normal microscopically but are unable to adequately fulfill their functions. Function will be further reduced if there is continuing liver cell damage.

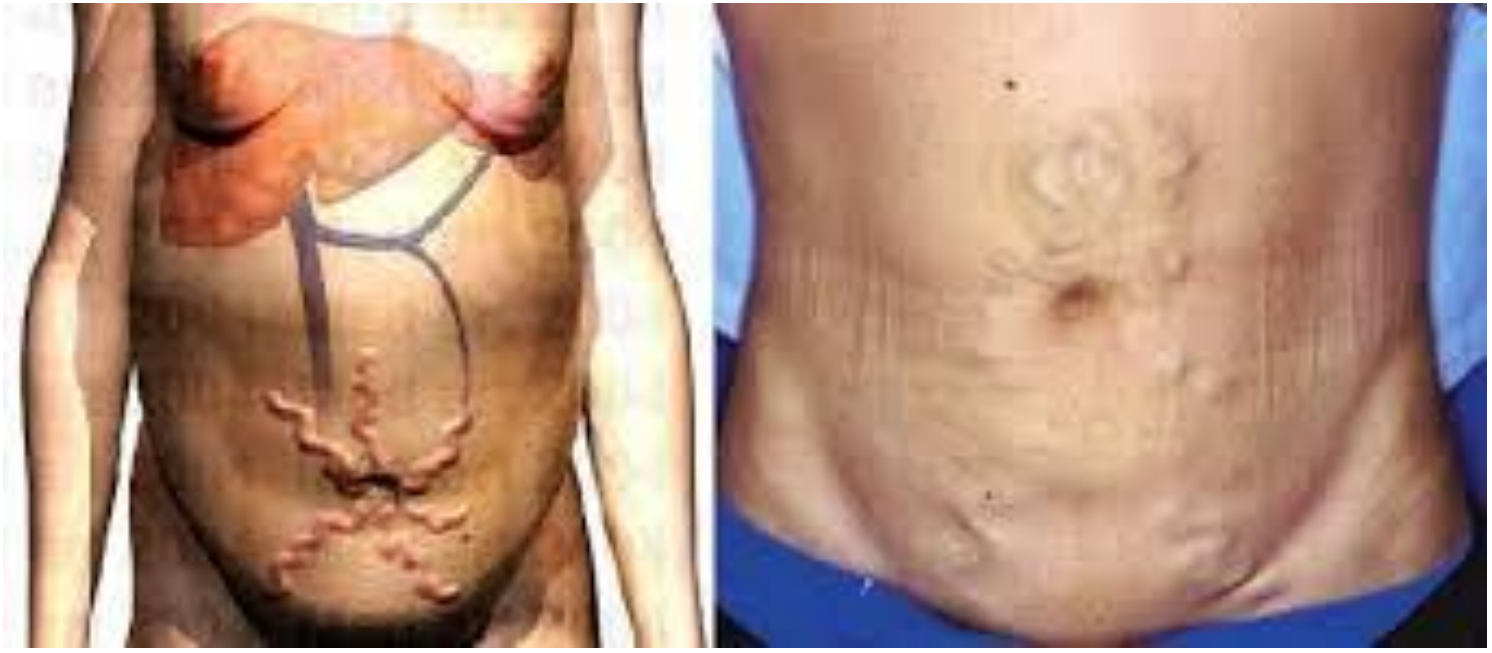
- **Infections.** Viral hepatitis.
- **Toxins and drugs.** Alcohol.
  Therapeutic drugs.
- **Autoimmune.** Hepatitis.
  Primary biliary cirrhosis.
- **Metabolic.** Haemochromatosis.
  Wilson disease.
  Alpha-1-antitrypsin deficiency.
  Glycogen storage disease and many others.
- **Biliary obstruction.** Congenital atresia.
  Sclerosing cholangitis.
- **Hepatic outflow obstruction.**
- **Cryptogenic.**

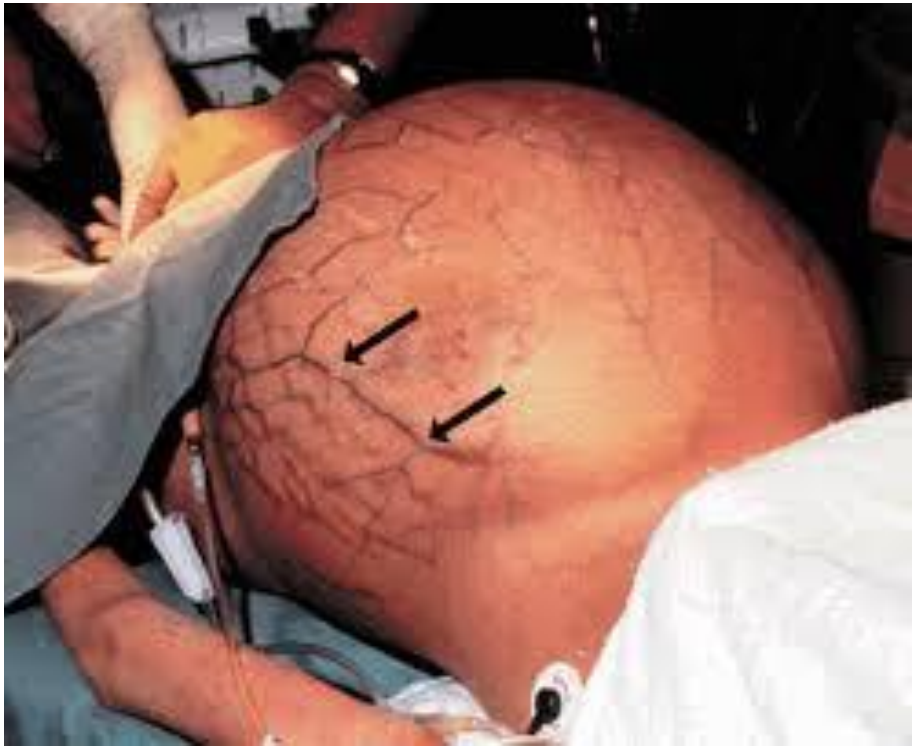
CLINICAL FEATURES

- Cirrhosis may be asymptomatic.
- When symptomatic, the features are nonspecific - weakness, fatigue, weight loss, anorexia, nausea, gaseous abdominal distension, upper abdominal discomfort.
- The liver may be enlarged, hard and irregular or smaller than normal.
- At this stage the patient is said to have compensated cirrhosis.
- Decompensated cirrhosis manifests as signs of liver failure or complications of portal hypertension. Deterioration in liver function can be an indication of the development of hepatocellular carcinoma.
- Death is usually due to one of these 3 conditions.

COMPLICATIONS OF CIRRHOSIS

- **Liver failure.**
- **Portal hypertension.** Portal venous pressure >10mmHg. Splenomegaly - hypersplenism leading to thrombocytopenia.
- Portal-systemic shunts where portal venous system anastomoses with the systemic venous system. Lower end of oesophagus leading to oesophageal varices and risk of massive GIT haemorrhage. Periumbilical ("caput medusae"), lower rectum (haemorrhoids), posterior abdominal wall. Ascites, ie excess fluid in the peritoneal cavity. A transudate (<3gm/dL protein),straw coloured or pale green, a few mononuclear cells. Risk of spontaneous infection when polymorphs predominate. Is due to aldosterone-induced retention of Na & water, low oncotic pressure (low albumin), and portal hypertension. Excess hepatic lymph and intestinal fluid leakage also contributes to ascites.
- **Hepatocellular carcinoma.**





Hepatocellular carcinoma

Investigation of liver diseases.

Biochemical - enzymes, proteins, bilirubin.

Haematological - coagulation factors among others.

Immunological - antibodies (viruses, autoimmune).

Imaging - ultrasound, CT, MRI, ERCP, MRCP.

Liver biopsy - percutaneous needle biopsy, transjugular biopsy, wedge biopsy at laparoscopy or open surgery.

Useful in providing information as to the aetiology and severity of the liver disease, ruling out the presence of other concomitant disease, monitoring response to therapy.

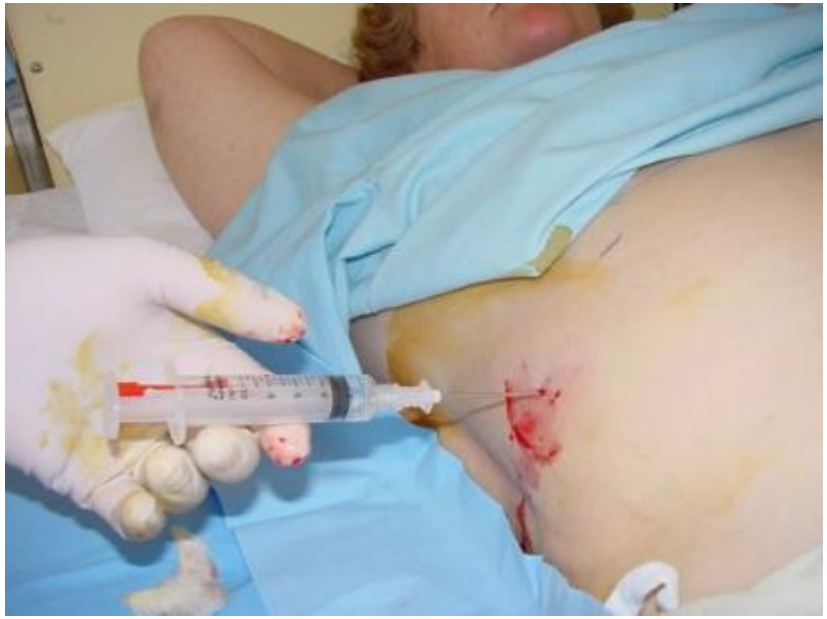
Focal lesions (tumors) require US or CT guidance

Diagnosis

- Physical examination - enlarged, tender liver
- Elevated serum alpha fetoprotein (normally : 40mg/l)
- Elevated liver enzymes (ALT, AST, Alpha-1 antitrypsin, serum bilirubin, urine bilirubin...)

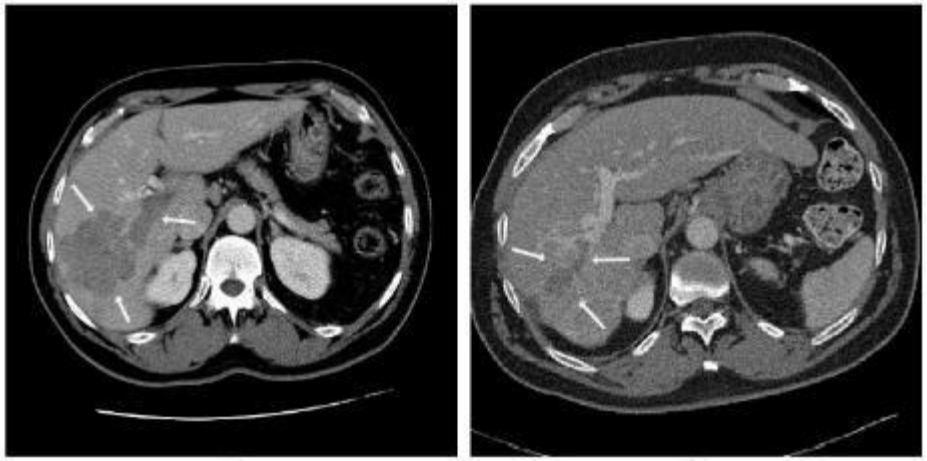
Biopsy

- Definitive diagnosis of hepatocellular carcinoma



Diagnosis

- CT

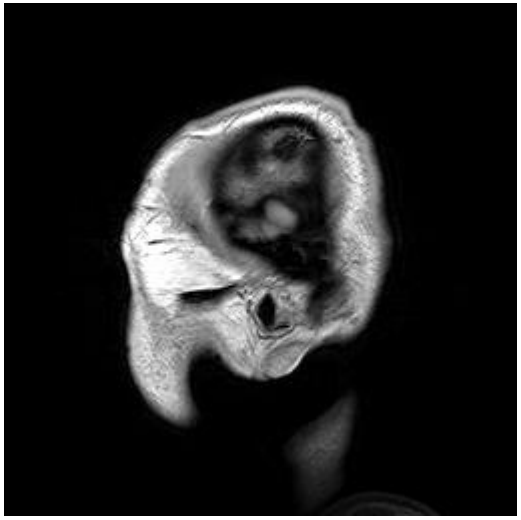


(a) (b)

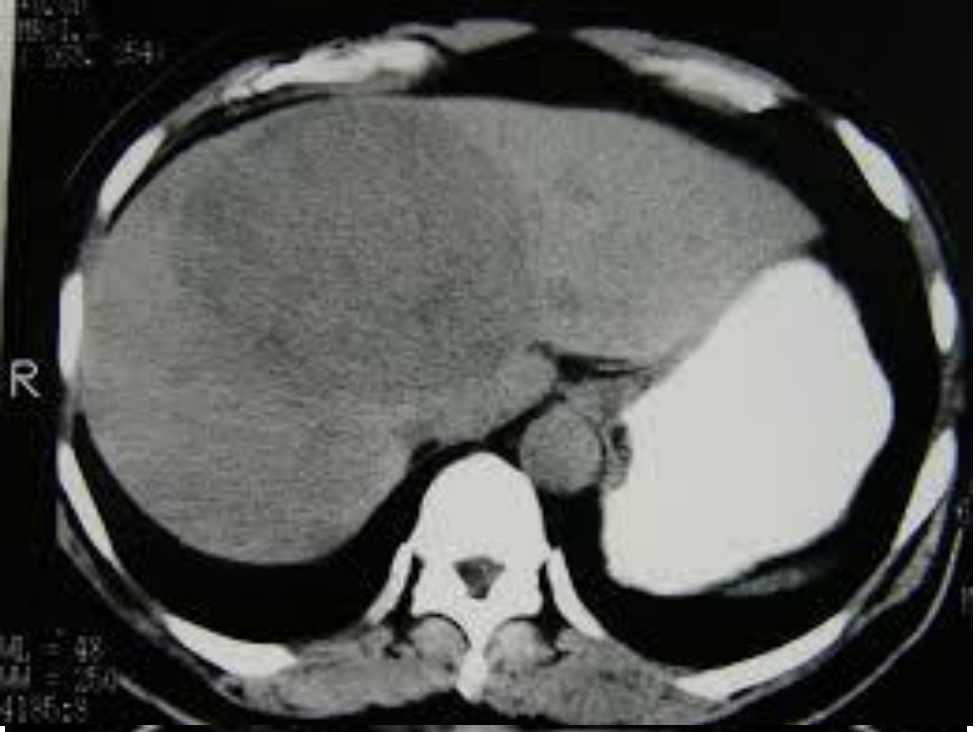
CT

- **Computed tomography -** medical imaging method employing tomography (imaging by sections or sectioning)
- Large series of two-dimensional X-ray images taken around a single axis of rotation, computer integration
- Iodine dye through vein for better visualisation (allergy)

MRI



- **Magnetic resonance imaging**
- The body - mainly composed of water molecules
- Electromagnetic field causes protons to absorb some of its energy
- Scanner detects release of proton energy (tumor tissue releases different frequency)
- Greater contrast than CT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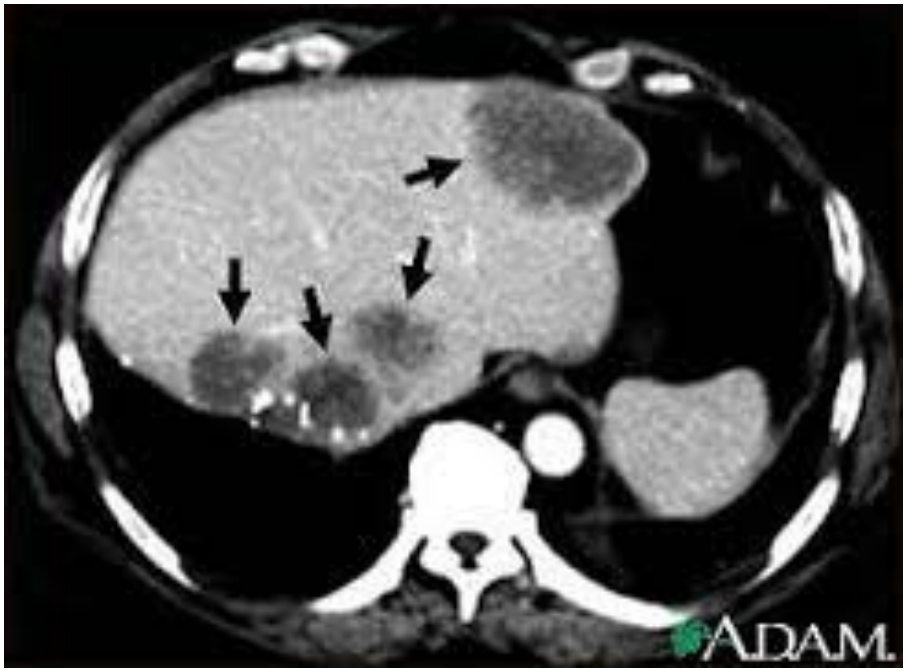
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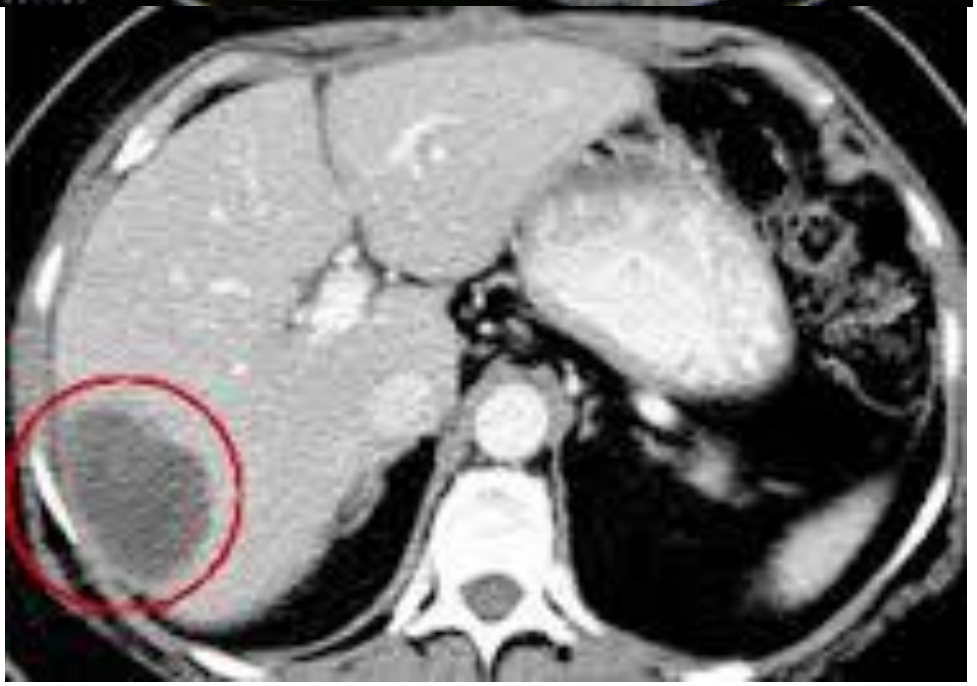
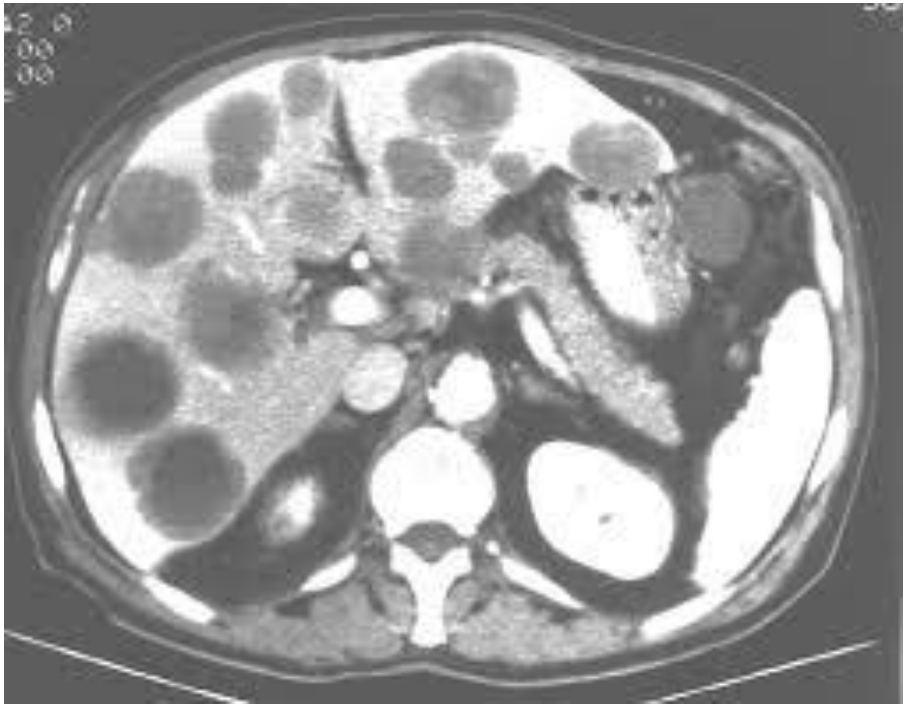
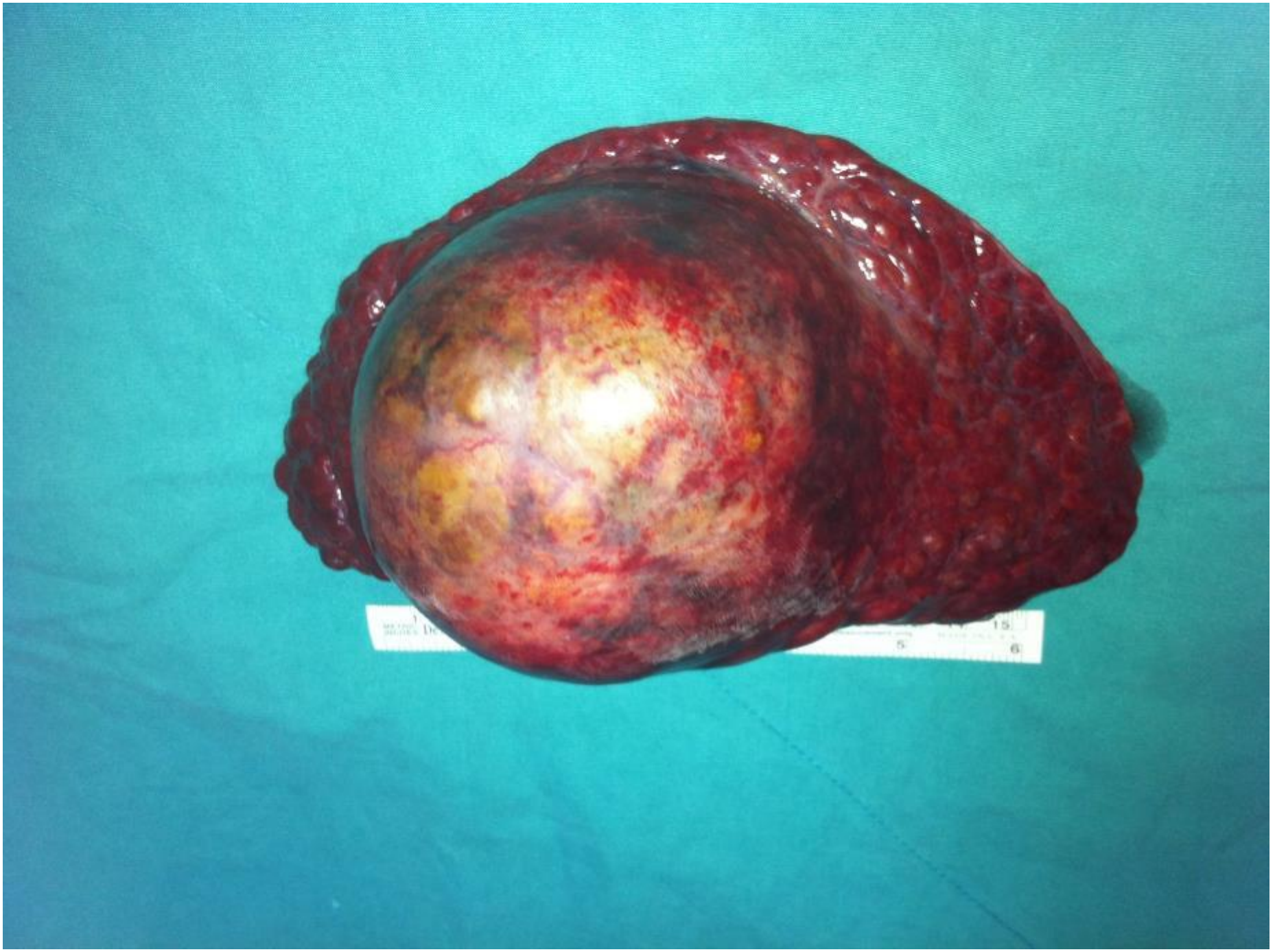
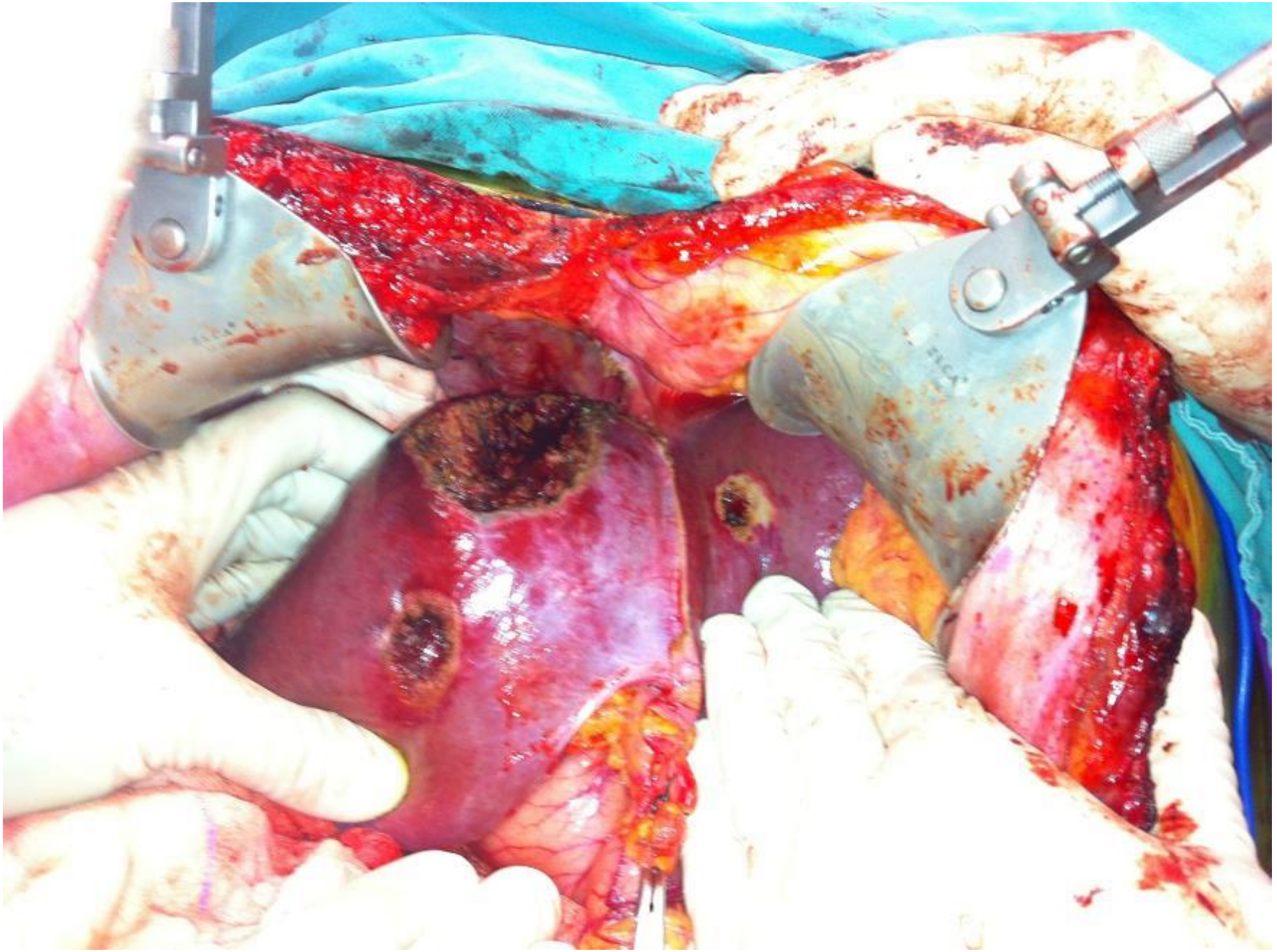
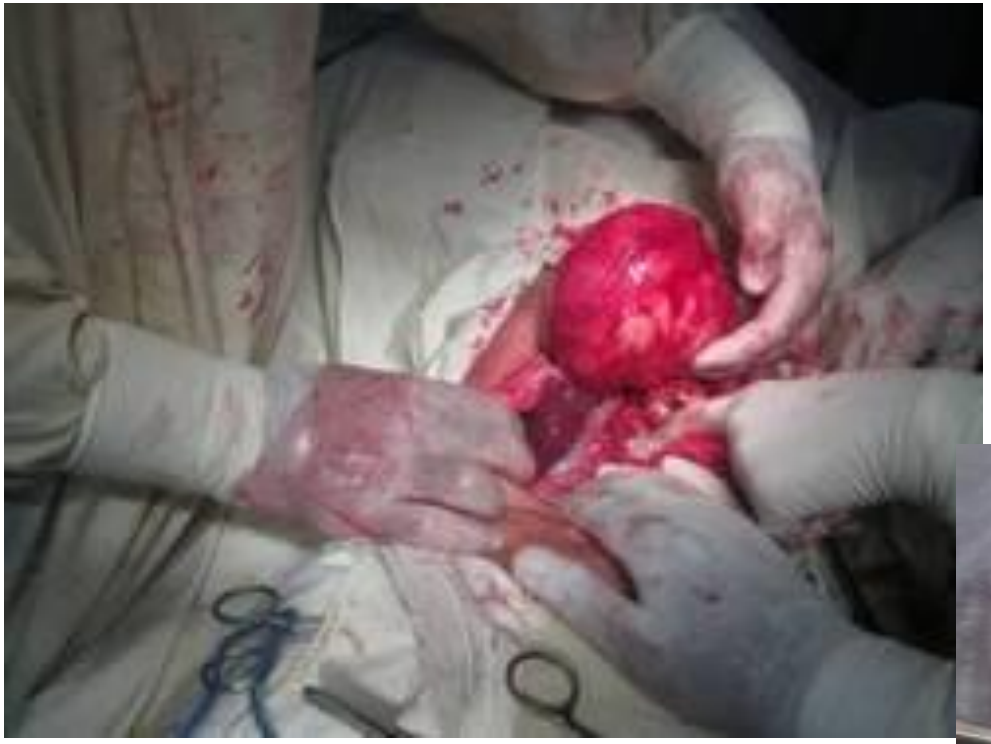


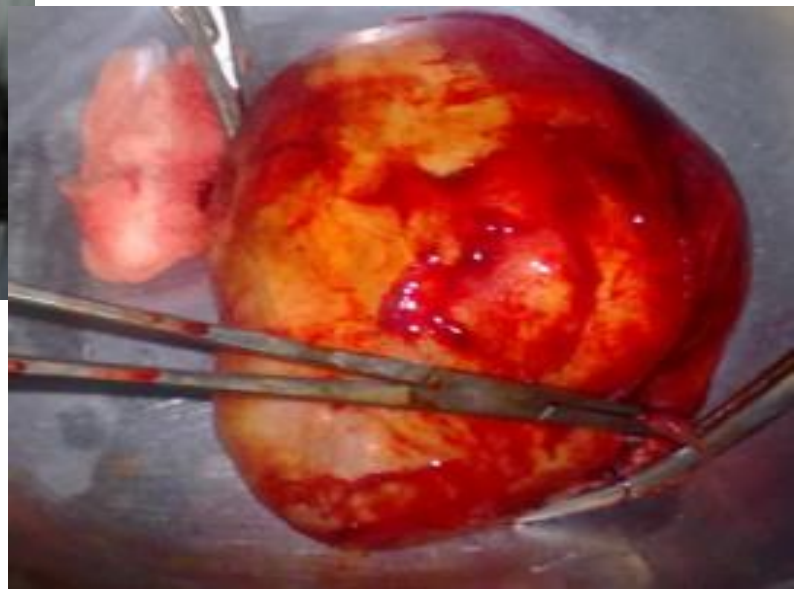






Hydatid Disease

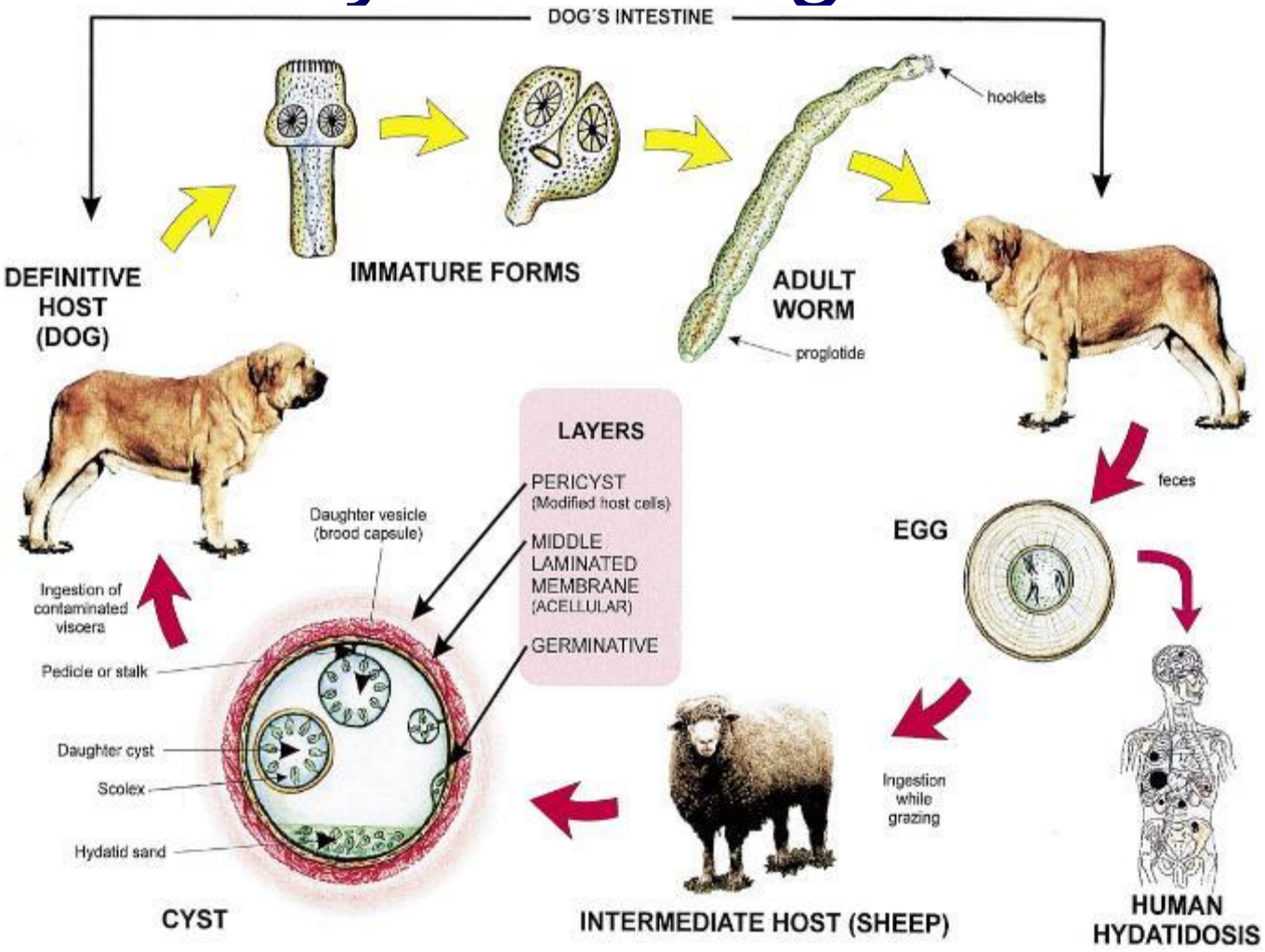




Introduction:

- Hydatid disease is a worldwide zoonosis produced by the larval stage of the *Echinococcus* tapeworm .
- The two main types of hydatid disease are caused by *E granulosus* and *E multilocularis.*
- *E granulosus* is commonly seen in the great grazing regions of the world—particularly the Mediterranean region, Africa, South America, the Middle East, Australia, and New Zealand—and is the most frequently encountered type of hydatid disease in humans.

Life Cycle of E *granulosus*



Hydatid Cyst Structure

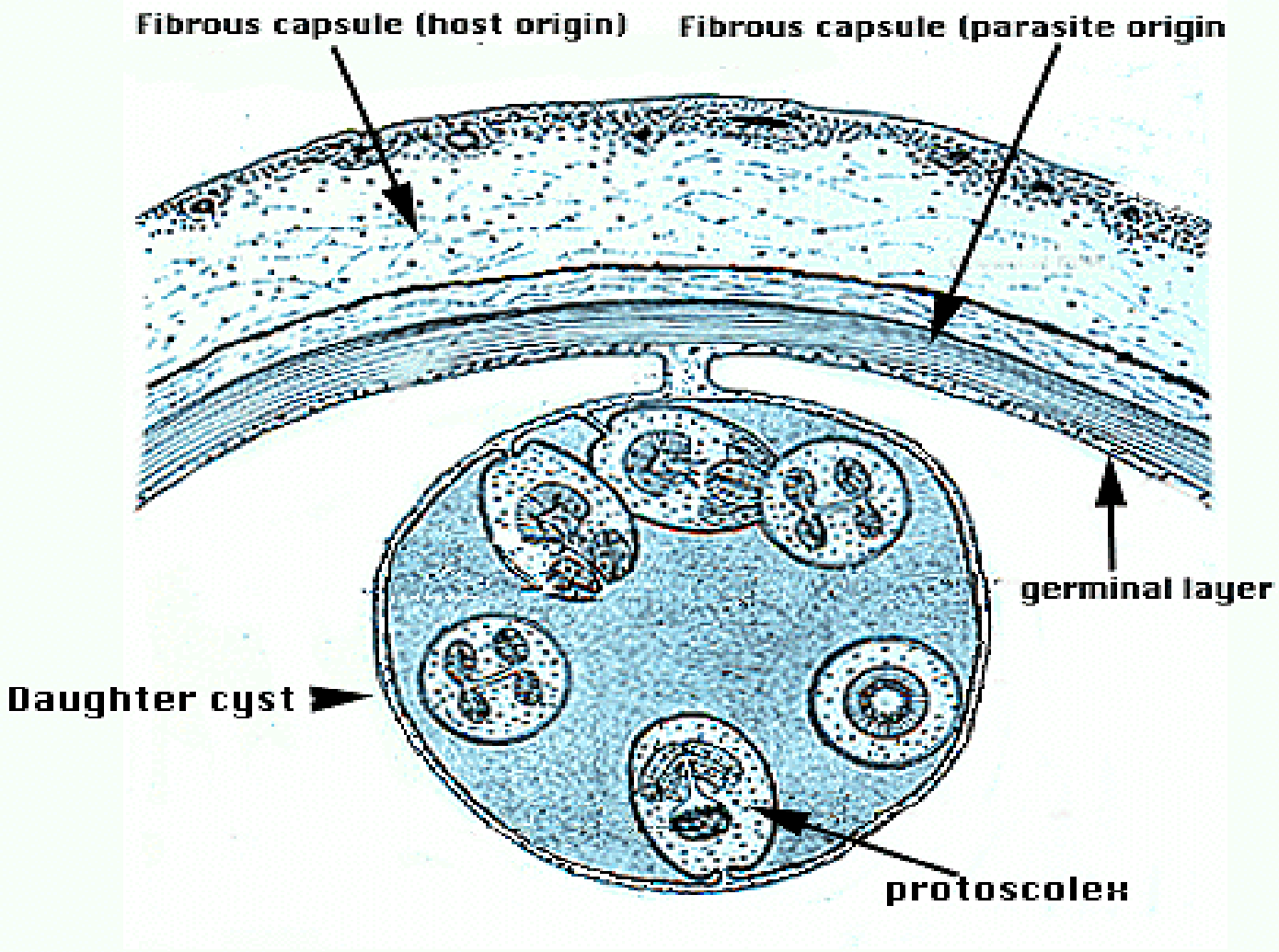
- The hydatid cyst has three layers:

(*a*) the outer pericyst, composed of modified host cells that form a dense and fibrous protective zone;

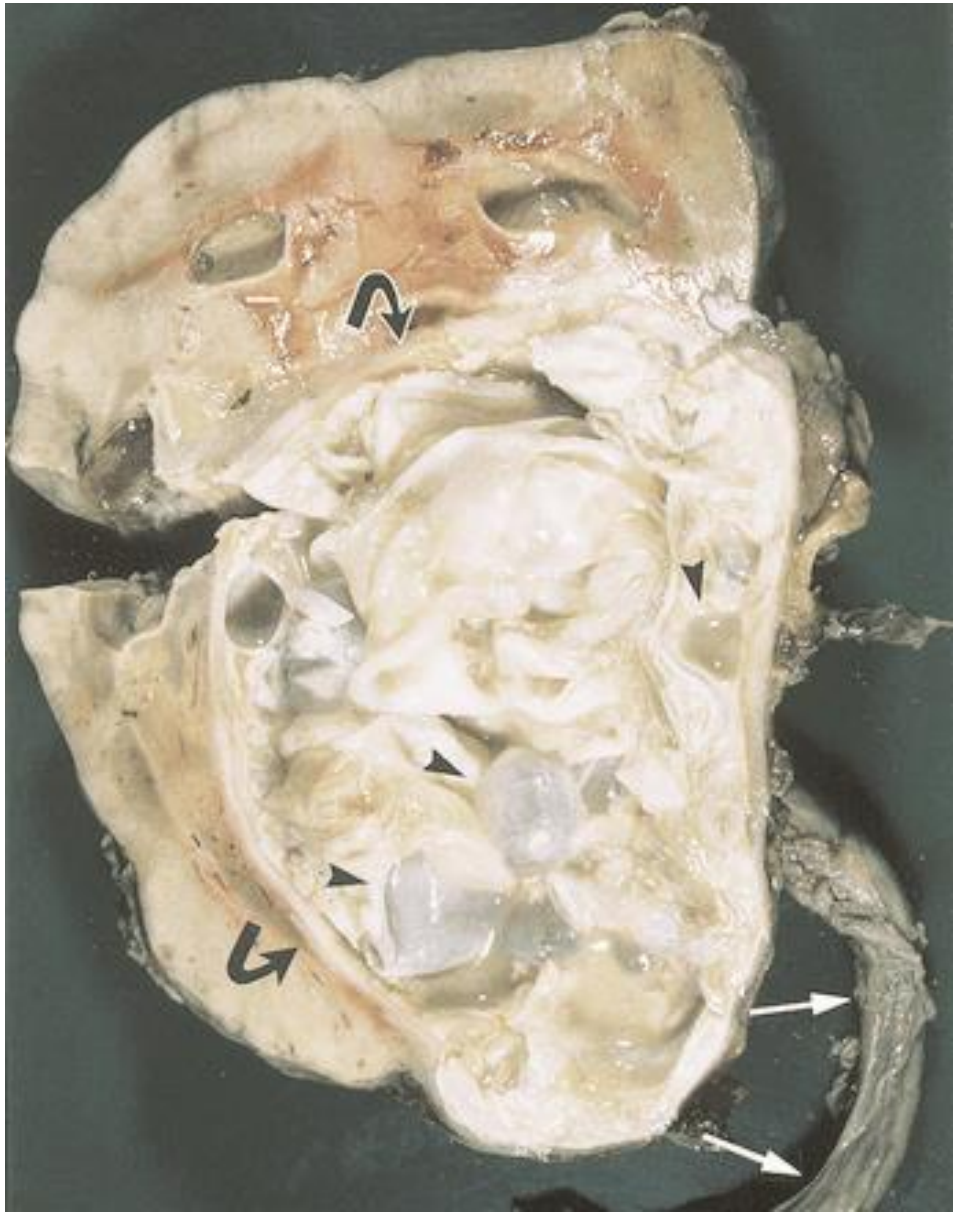
(*b*) the middle laminated membrane, which is acellular and allows the passage of nutrients;

(*c*) the inner germinal layer, where the scolices (the larval stage of the parasite) and the laminated membrane are produced.

- Daughter vesicles (brood capsules) are small spheres that contain the protoscolices and are formed from rests of the germinal layer. Before becoming daughter cysts, these daughter vesicles are attached by a pedicle to the germinal layer of the mother cyst. At gross examination, the vesicles resemble a bunch of grapes.



Hydatid cyst



Hydatid Disease in Humans

Hydatid disease involves the liver in approximately 75% of cases, the lung in 15%, and other anatomic locations in 10%

Clinical presentation :

The clinical features are highly variable. The spectrum of symptoms depends on the following:

- Involved organs
- Size of cysts and their sites within the affected organ or organs
- Interaction between the expanding cysts and adjacent organ structures, particularly bile ducts and the vascular system of the liver
- Symptoms due to pressure usually take a long time to manifest, except when they occur in the brain .
- Most symptomatic cysts are larger than 5 cm in diameter.
- Bacterial infection of cysts and spread of protoscolices and larval material into bile ducts or blood vessels
- Immunologic reactions such as asthma, anaphylaxis, or membranous nephropathy secondary to release of antigenic material

Hepatic Disease

- The right lobe is the most frequently involved portion of the liver.

- Once in the human liver, cysts grow to 1 cm during the first 6 months and 2–3 cm annually thereafter, depending on host tissue resistance.

Clinical presentation of liver disease:

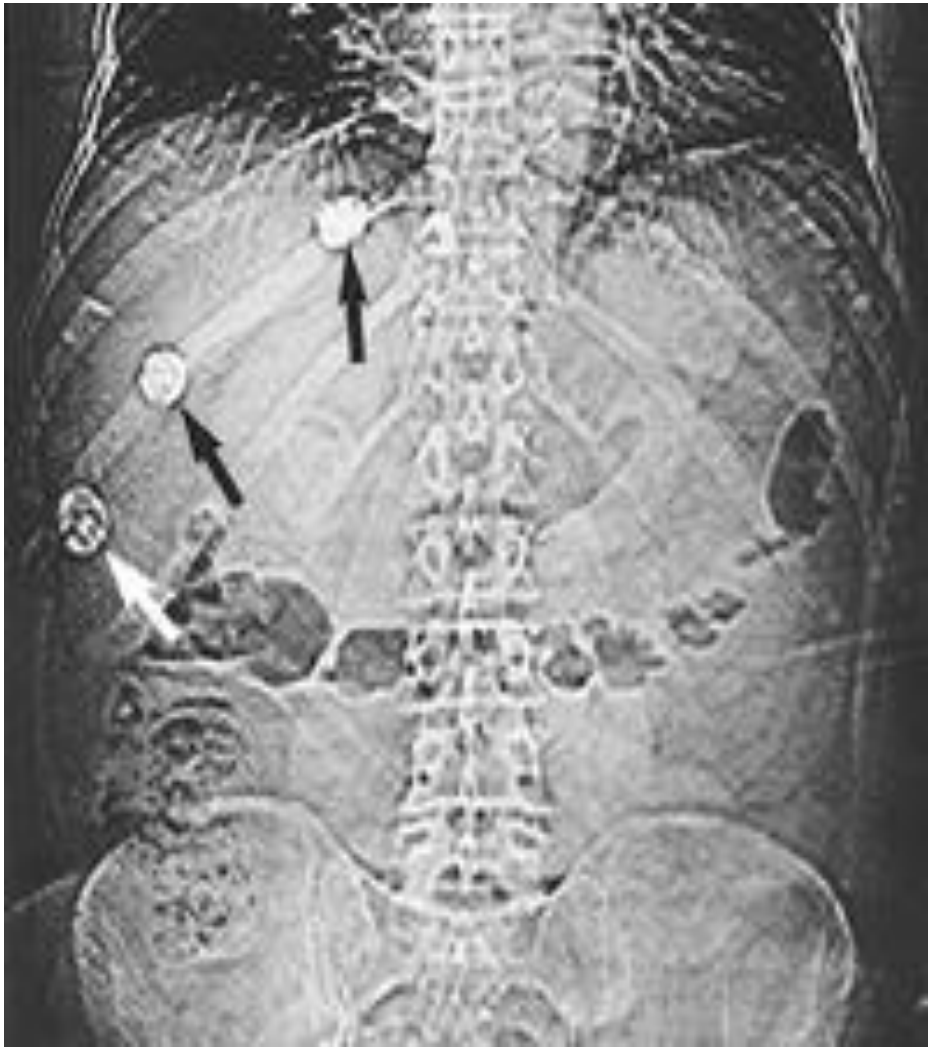
Presenting Sign or Symptom
Abdominal pain and/or tenderness
Abdominal mass
History of fever
History of jaundice
Pruritis, rash, or urticaria
Anaphylaxis
Asymptomatic

Work Up

- Generally, routine laboratory tests do not show specific results.
- In patients with rupture of the cyst in the biliary tree, marked and transient elevation of cholestatic enzyme levels occurs, often in association with hyperamylasemia and eosinophilia (as many as 60%).
- Indirect hemagglutination test and enzyme-linked immunosorbent assay are the most widely used methods for detection of anti-Echinococcus antibodies (immunoglobulin G [IgG]).These tests give false positive results in cases of schistosomiasis and nematode infestations that is why they are not specific for diagnosing hydatidosis.

Imaging Studies:

- Plain radiography
- Ultrasound examination
- CT scaning
- MRI



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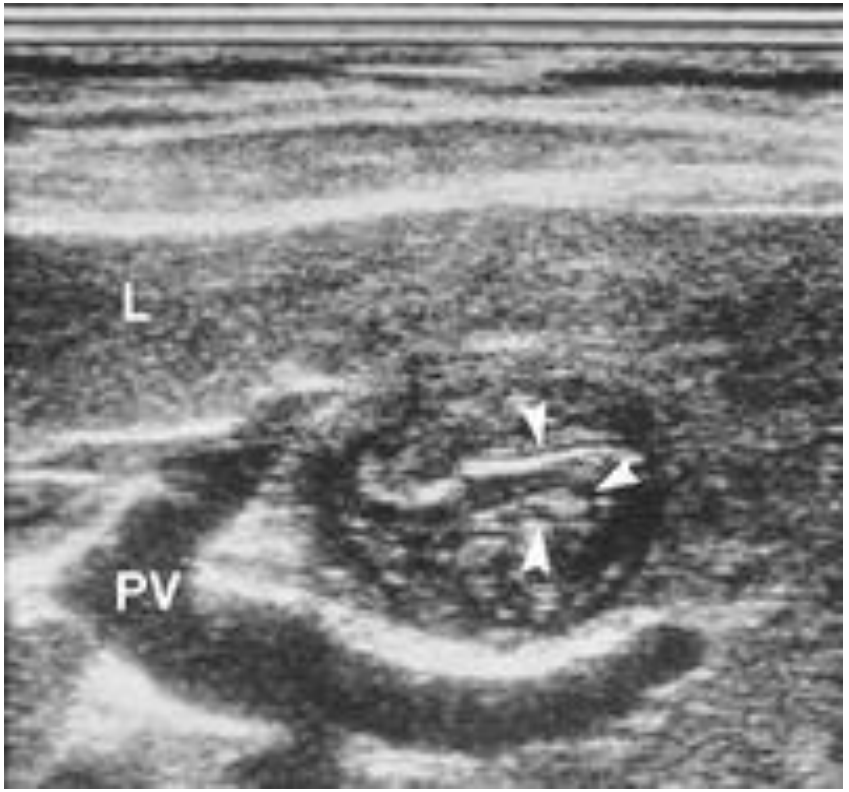
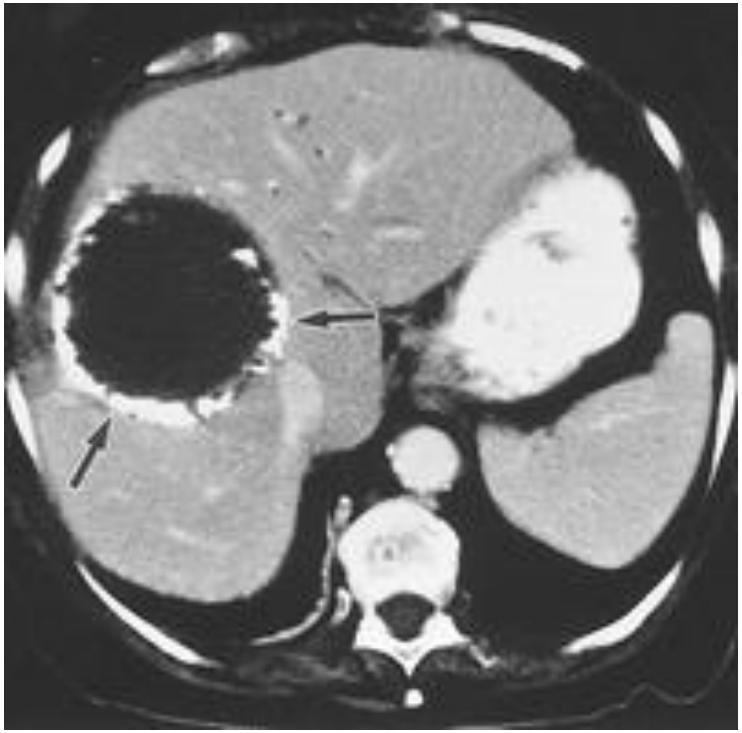


B

Table 1: Sonographic classification of hydatid cysts

Gharbi Type	WHO Type	Cyst Morphology
I	CE 1	Unilocular anechoic lesion with double line sign
III	CE 2	Multiseptated rosette like honeycomb cyst
II	CE 3A	Cyst with detached membranes (water-lily sign)
III	CE 3B	Cyst with daughter cysts in solid matrix
IV	CE 4	Cyst with hetrogenous hypoechoic/ hyperechoic contents. No daughter cysts
V	CE 5	Solid plus calcified wall



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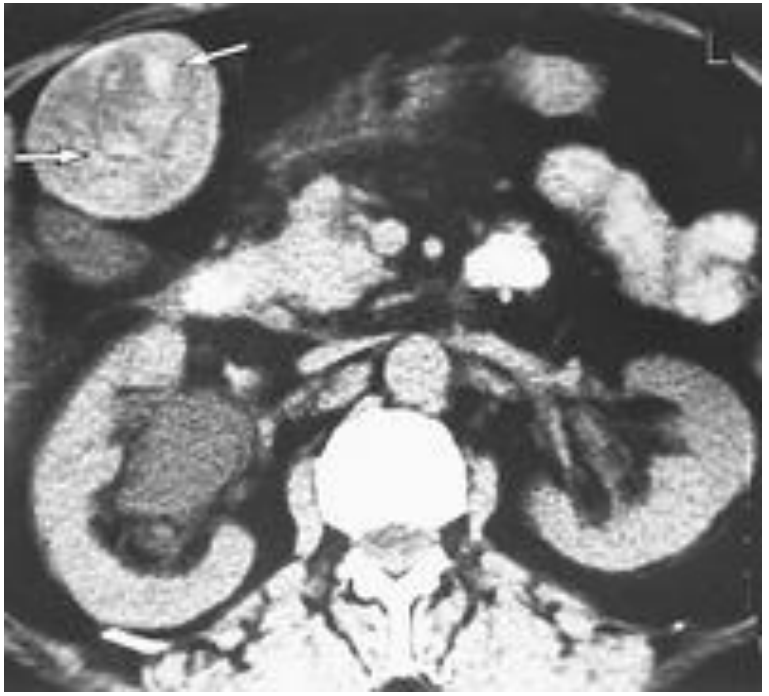

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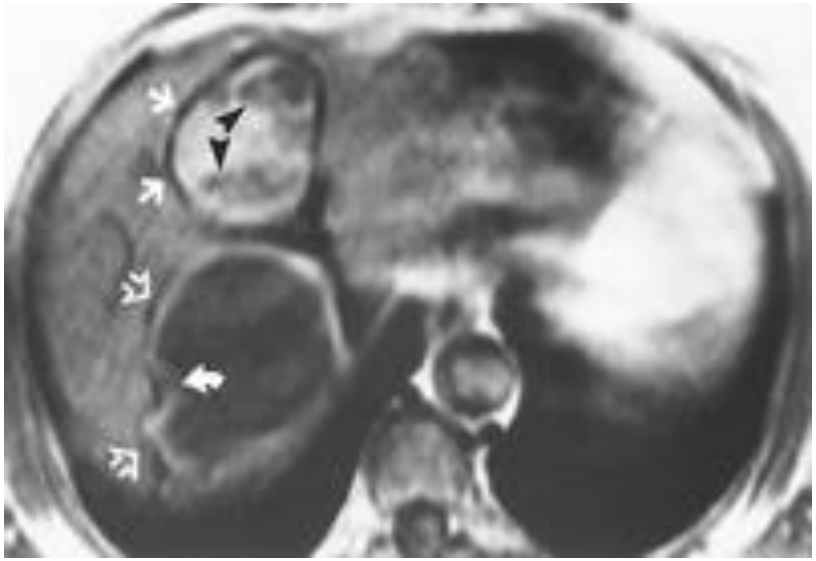

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Bile duct and GB cancer

Bile duct Cancer

- Average age 60 years
- Ulcerative colitis is a common associated condition
- Subtypes: (1) periductal infiltrating, (2) papillary or intraductal, and (3) mass forming-nodular
- Location: 85% extrahepatic

Risk Factors

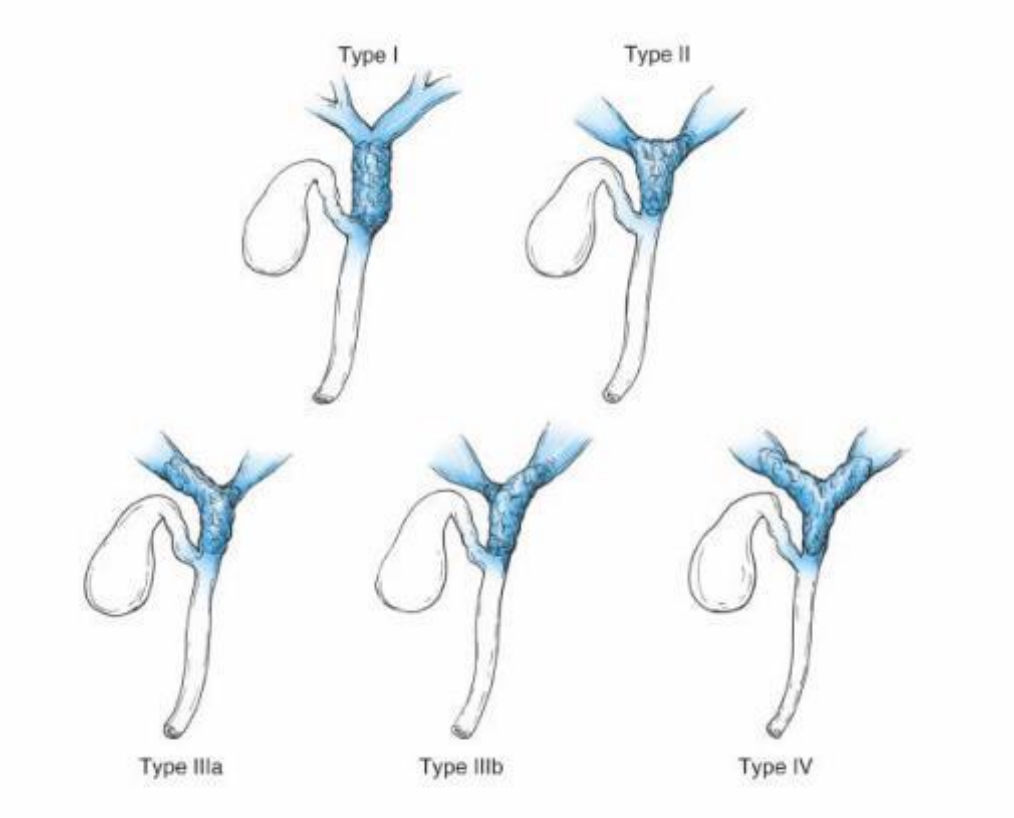
Definite risk factors

- Primary sclerosing cholangitis (1% per year)
- Liver fluke infection (*Opisthorchis viverrini*)
- Hepatolithiasis (10%)
- Biliary malformation (10% choledochal cysts, Caroli's)

Probable risk factors

- Hepatitis C
- Cirrhosis T
- oxins (dioxin, polyvinyl chloride)
- Biliary-enteric drainage procedures

Staging



Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE, Schwartz SI: *Schwartz's Principles of Surgery*, 8th Edition: http://www.accessmedicine.com

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Presentation

- Obstructive jaundice
- Cholangitis (10%)
- Palpable mass
- Liver cirrhosis
- Cachexia

Diagnosis

- Blood work

- CA19-9: Its sensitivity and specificity for detection of CCA in PSC are 79% and 98%, respectively, at a cutoff value of 129 U/mL.

Imaging (US, CT, MRI/MRCP, ERCP, PTC, EUS, PET/CT)

GB cancer

- Predominantly in the elderly
- Incidentally diagnosed at an early stage after cholecystectomy for cholelithiasis (1%)
- Approximately 90% of patients have gallstones.
- The 20-year risk of developing cancer

Risk Factors

Larger stones (3 cm) tenfold increased risk

- The risk is higher in patients with symptomatic pts

Polypoid lesions, particularly in polyps >10mm

The calcified "porcelain" gallbladder (20%)

- selective mucosal calcification (7%)

Choledochal cysts have an increased risk of developing cancer anywhere in the biliary tree, but the incidence is highest in the gallbladder.

Other Risk Factors

- Anomalous pancreatobiliary duct junction
- Obesity and pregnancy
- Chronic inflammatory bowel disease
- Polyposis coli
- Mirizzi syndrome
- Bacterial and Salmonella infections
- Industrial exposure to carcinogens
- Familial tendency

Presentation

- Abdominal discomfort, right upper quadrant pain, nausea, and vomiting.
- Jaundice, weight loss, anorexia, ascites, and mass
- Blood work
- Imaging (UD, CT, MRI/MRCP, ERCP, PTC, PET/CT)

JAUNDICE AND CHOLESTASIS

- **Jaundice (or icterus)** - yellow discolouration of the skin, sclerae and mucous membranes due to excess plasma bilirubin (hyperbilirubinemia).

- Jaundice appears when plasma bilirubin exceeds 50umol/l. (Normal 3 - 17umol/l)

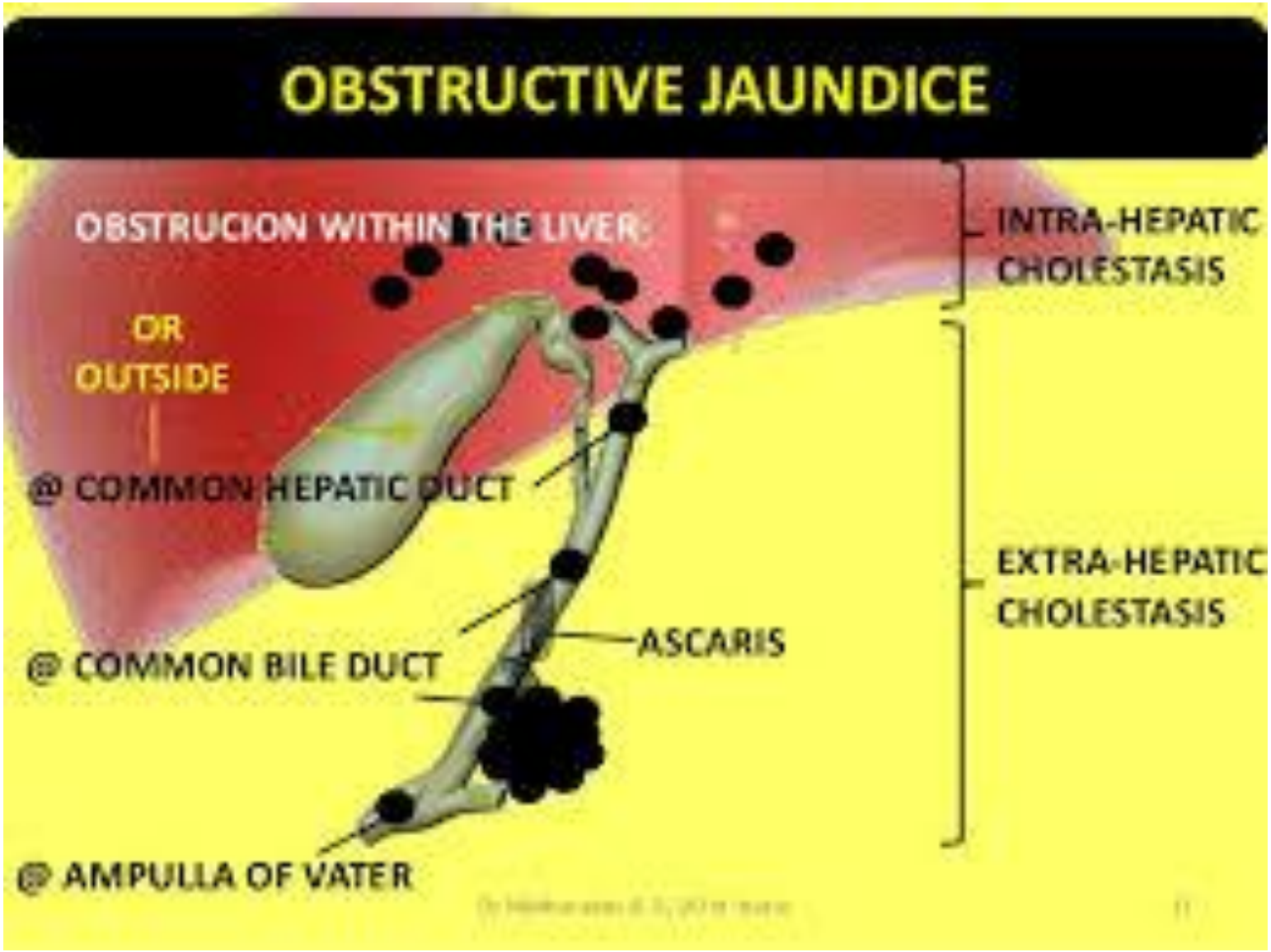
  Liver disease is not the only cause of jaundice and many patients with significant liver disease do not have jaundice (are anicteric).

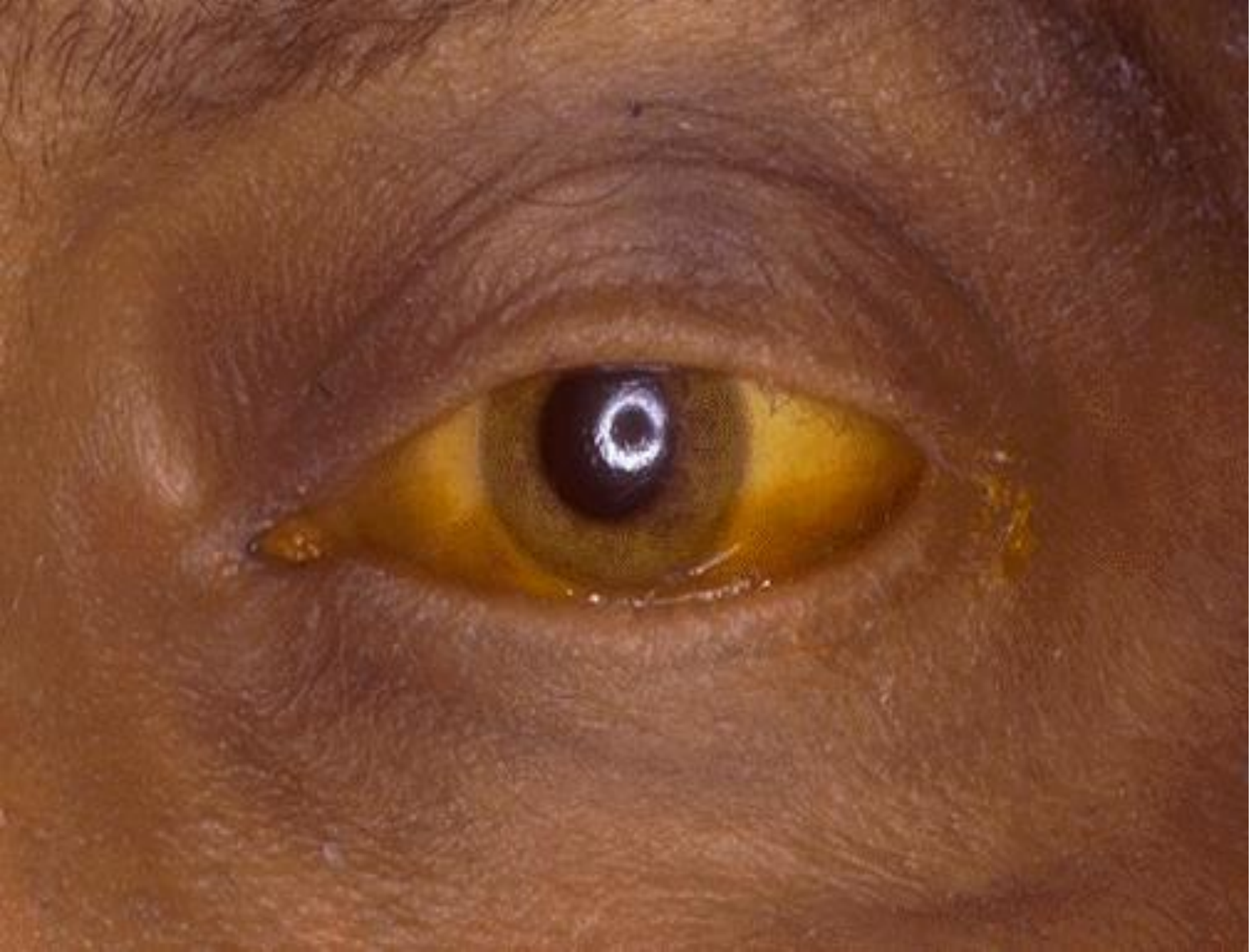
- **Cholestasis** - arrest of bile flow. A failure of adequate amounts of bile to reach the duodenum - due to interference anywhere from liver cell microsomes to the duodenum.

MECHANISMS AND CLASSIFICATION OF JAUNDICE

- **Mechanisms** - Increased bilirubin production.
  - Decreased uptake by hepatocytes.
  - Impaired conjugation.
  - Impaired excretion - intrahepatic
  - extrahepatic.
- **Classification.**

  Pre-hepatic - haemolysis most important of several causes. Unconjugated bilirubin insoluble in water, not excreted in urine. Risk of brain damage in neonates (kernicterus); pigment gallstones in adults. **Hepatic** - eg hepatitis,intra-hepatic bile duct damage, congenital hyperbilirubinemias eg Gilbert's syndrome. Mainly conjugated (except Gilbert's syndrome) so soluble in water resulting in dark urine. **Post-hepatic** - obstruction to extra-hepatic bile ducts by gallstone, stricture, tumour, or congenital biliary atresia. Conjugated bilirubin.


OBSTRUCTIVE JAUNDICE
OBSTRUCION WITHIN THE LIVER
OR
OUTSIDE
@ COMMON HEPATIC DUCT
@ COMMON BILE DUCT
ASCARIS
@ AMPULLA OF VATER
INTRA-HEPATIC
CHOLESTASIS
EXTRA-HEPATIC
CHOLESTASIS

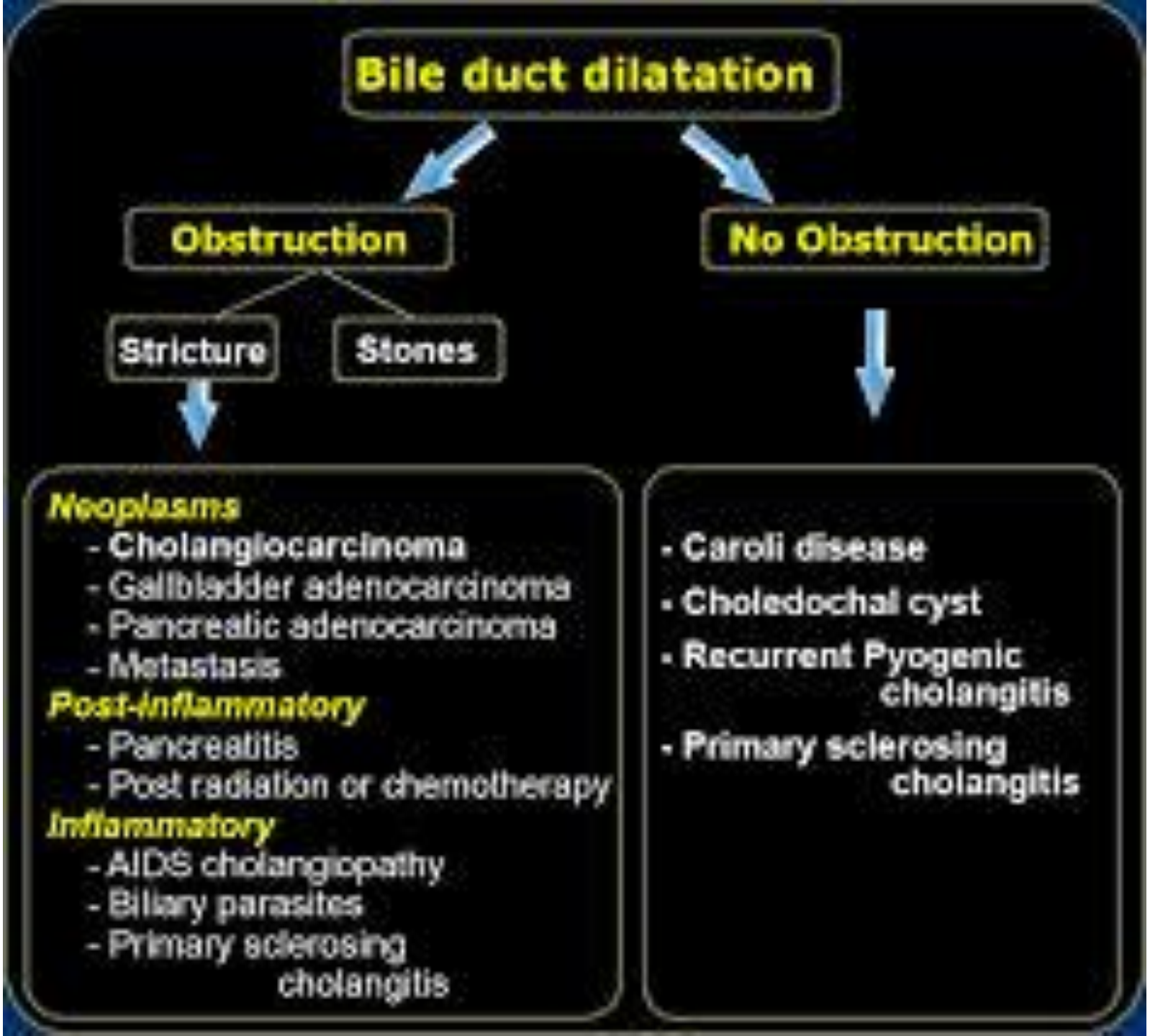


- In cases of hepatic jaundice, when there is predominantly hepatocyte damage, the patient is often very symptomatic and raised serum transaminases are the predominant biochemical finding. This is sometimes called “hepatocellular jaundice.”

- In cases where there is biliary obstruction, whether intra- or extra-hepatic, the patient has what is called “cholestatic jaundice” with pruritis, dark urine and pale stools, and with time may develop skin xanthelasmas and steatorrhoea. Serum alkaline phosphatase is raised.

- Mixed patterns occur.

- Distinction between intra-hepatic and extra-hepatic obstruction requires imaging. This should be done urgently and the obstruction relieved where at all possible.


Bile duct dilatation
Obstruction
No Obstruction
Stricture
Stones
Neoplasms
- Cholangiocarcinoma
- Gallbladder adenocarcinoma
- Pancreatic adenocarcinoma
- Metastasis
Post-inflammatory
- Pancreatitis
- Post radiation or chemotherapy
Inflammatory
- AIDS cholangiopathy
- Biliary parasites
- Primary sclerosing cholangitis
- Caroli disease
- Choledochal cyst
- Recurrent Pyogenic cholangitis
- Primary sclerosing cholangitis