Alopecia

Alopecia classified into:

- ***Non-cicatricial Alopecia*** **:** No clinical sign of tissue inflammation, scarring, or atrophy of skin .
- ***Cicatricial alopecia*** **:** Evidence of tissue destruction such as inflammation, atrophy, and scarring is apparent.

Classification of acquired alopecia

Can occur **globally** or **focally** : (Causes of hair loss)

Diffuse (global) hair loss

Non-scarring

1- **Failure of follicle production**
2- **Hair shaft abnormality**
3- **Abnormality of cycling (shedding)**
- Telogen effluvium
- Anagen effluvium
- Loose anagen syndrome
- Alopecia areata

Focal (patchy, localized) hair loss

Non-scarring

3- Production decline :
- Triangular alopecia
- Pattern hair loss (androgenetic alopecia)

4- Hair breakage :
- Trichotillomania
- Traction alopecia
- Infection (tinea capitis)
- Primary or acquired hair shaft abnormality

5- Unruly hair.

6- Abnormality of cycling :
- Alopecia areata
- Secondary syphilis (alopecia areolaris) ("moth-eaten" appearance in beard or scalp).

Scarring (cicatricial) alopecia

1- Lymphocytic :
- Chronical cutaneous (discoid) lupus erythematosus
- Lichen planopilaris (LPP)
- Classic pseudopelade of Brocq
- Central centrifugal cicatricial alopecia
- Alopecia mucinosa
- Kertosis folliclaris spinulosa decalvans

2- Neutrophilic :
- Folliculitis decalvans
- Dissecting folliculitis (cellulitis)

3- Mixed :
- Folliculitis keloidalis
- Folliculitis necrotica
- Erosive pustular dermatosis

4- Non-specific :
- Trauma.
- Chemical or physical burn.
- Surgical wound
- Neoplasm (Basal cell carcinoma ,Squamous cell carcinoma)

Scarring (cicatricial) alopecia

- Primary cicatricial alopecia (PCA) results from damage or destruction of the hair follicles stem cells by:
  - Inflammatory (usually noninfectious) processes
  - Infection: e.g., "kerion" tinea capitis, necrotizing herpes zoster
  - Other pathologic processes: surgical scar, primary or metastatic neoplasm.
- Manifestations: Effacement of follicular orifices in a patchy or focal distribution, usually in scalp or beard.
- The end result is effacement of follicular orifices & replacement of the follicular structure by fibrous tissue.
- Scarring is irreversible. Therapies are ineffective.

TELOGEN EFFLUVIUM

- Telogen effluvium (TE) is the transient increased shedding of normal club (telogen) hairs from resting scalp follicles.
- Secondary to accelerated shift of anagen (growth phase) into catagen and telogen (resting phase)
- Results in increased daily hair loss and, if severe, diffuse thinning of scalp hair.

Etiology:

A reaction pattern to a variety of physical or mental stressors :

- **Endocrine :**
  1- Hypo- or hyperthyroidism ;
  2- postpartum ;
  3- discontinuation or changing type of estrogen containing drugs
- **Nutritional:**
  1- Deficiency: biotin, zinc, iron, essential fatty acid
  2- Rapid weight loss,
  3- caloric or protein deprivation,
  4- excessive vitamin A ingestion
- **Physical stress :**
  1- Febrile illnesses,
  2- catabolic illnesses (e.g., malignancy, chronic infection),
  3- major surgery,
  4- major trauma,
  5- acute or chronic psychological stress
- **Psychological stress :**
  1- Anxiety,
  2- depression,
  3- bipolar disorder
- **Intoxication :** Thallium, mercury, arsenic
- **Drugs :**
  1- Antimitotic agents (dose dependent): cancer chemotherapy, benzimidazoles.
  2- Antihypertensives: captopril
  3- Anticoagulants
  4- CNS drugs: lithium, valproic acid
  5- Cholesterol-lowering drugs
  6- Colchicine
  7- Cytostatic drugs
  8- Interferon
  9- Penicillamine
  10- Retinoids: vitamin A excess, retinoids (isotretinoin, acitretin, indinavir)
  11- Selective serotonin reuptake inhibitors
  12- Inflammatory scalp disease: Seborrheic dermatitis, erythroderma
- **Idiopathic :**
  No obvious cause is apparent in a significant number of cases.

ANAGEN EFFLUVIUM

- **Etiology:** See below
- **Onset** is usually rapid & extensive.
- **Pathogenesis:** Occurs after any insult to hair follicle that impairs its mitotic/metabolic activity. Rapid growth arrest or damage to anagen hairs that skip catagen and telogen phases and are shed.
- More common and severe with combination chemotherapy than with the use of a single drug. Severity is generally dose dependent.
- **Manifestations:**
  Scalp hair : loss is diffuse, extensive; also: eyebrows/lashes, beard, etc.
  Nails: show transverse banding or ridging.
- Regrowth is usually rapid after discontinuation of Chemotherapy

Etiology:

Anagen cycle disrupted causing varying degrees of hair follicle dystrophy :

- **Radiation therapy to head .**
- **Alkylating agents:**
  busulfan, carboplatin, carmustine, BCNU, chlorambucil, cisplatin, dacarbazine, estramustine, fotemustine, ifosamide, lomustine, mechlorethamine, nitrogen mustard, melphalan, oxaliplatin, procarbazine, streptozocin, temozolomide, thiotepa.
- **Intoxications:**
  mercury, boric acid, thallium, colchicine.
- **Severe protein malnutrition.**

Alopecia areata

- A localized loss of hair in round or oval areas with no apparent inflammation of the skin. Most common on scalp.
- Nonscarring; hair follicle intact; hair can regrow.
- **Clinical findings:** Hair loss ranging from solitary patch to complete loss of all terminal hair.
- **Prognosis:** good for limited involvement. Poor for extensive hair loss.
- **Management:** intralesional triamcinolone effective for limited number of lesions.

PATHOGENESIS

- **Chronic organ-specific autoimmune disease,** mediated by autoreactive T cells affecting hair follicles and nails.
- **Associated autoimmune disorders:** Autoimmune thyroid disease in adults.
- Follicular damage occurs in **anagen** followed by → rapid transformation to **catagen** and to → **telogen**; then to → **dystrophic anagen status**.
  While the disease is active, follicles unable to progress beyond early anagen and do not develop normal hair.

CLINICAL MANIFESTATIONS

Age: Any age , but peak between 20 – 50 years

Sex : affect both sexes.

Duration of Hair Loss
Gradual over weeks to months.

Skin Symptoms
Disfiguring bald patch.

Associated Findings
- Autoimmune thyroiditis.
- Down syndrome.
- Autoimmune polyendocrinopathy-candidiasis–ectodermal dysplasia syndrome.

Skin Findings
- Usually none.
- Possibly minimal erythema in area of hair loss.

Hair

Round patches of hair loss.
- Single or multiple. May coalesce.
- It's often **sharply defined.**
- **Normal-appearing skin** with follicular openings present .
- **"Exclamation mark" hairs** (Fig. 32-8) : Diagnostic broken- off stubby hairs (distal ends are broader than proximal ends) seen at margins of hair loss areas.
- **Scattered, discrete areas of alopecia** (Fig. 32-9) or **Confluent with total loss of scalp hair** (Fig. 32-10), or **generalized loss of body hair (including vellus hair).**
  Diffuse AA of scalp (noncircumscribed) gives the appearance of thinned hair; can be difficult to differentiate from pattern hair loss of telogen effluvium, hair loss with thyroid disease.
- With regrowth of hair, **new hairs** are fine, often white or gray.

Sites of Predilection
- Scalp (most commonly)
- Any hair-bearing area : Beard, eyebrows, eyelashes, pubic hair.
  - **Alopecia areata (AA):** Solitary or multiple areas of hair loss.
  - **AA totalis (AAT):** Total loss of terminal scalp hair.
  - **AA universalis (AAU):** Total loss of all terminal body & scalp hair.
  - **Ophiasis:** Bandlike pattern of hair loss over periphery of scalp .

Nails
- Fine pitting ("hammered brass") of dorsal nail plate.
- mottled lunula,
- trachyonychia (rough nails),
- onychomadesis (separation of nail from matrix).

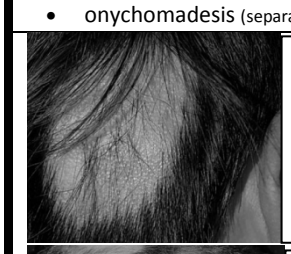


FIGURE 32-8
Solitary lesion
The short, broken-off hair shafts (so-called exclamation point hair) appear as very short stubs emerging from the

FIGURE 32-9
multiple, extensive lesions
Multiple, confluent, involved sites on the scalp with "exclamation point hairs."

FIGURE 32-10
AA totalis

DIFFERENTIAL DIAGNOSIS

Nonscarring Alopecia :
- White-patch tinea capitis,
- Trichotillomania,
- Early scarring alopecia,
- Pattern hair loss,
- Secondary syphilis (alopecia areolaris) ("moth-eaten" appearance)

LABORATORY EXAMINATIONS

- **Serology** :
  1- ANA (to rule out SLE);
  2- rapid plasma reagin (RPR) test (to rule out secondary syphilis).
- **KOH Preparation:** Rule out tinea capitis.
- **Dermatopathology :**
  Acute lesions show :
  - peribulbar, perivascular, and outer root sheath mononuclear cell infiltrate of T cells and macrophages;
  - follicular dystrophy with abnormal pigmentation and matrix degeneration.

MANAGEMENT

No curative treatment is currently available. Treatment for AA is unsatisfactory.

Treatment directed at inflammatory infiltrate and growth inhibitor factors produced by inflammation.

1- General measures :
- **Psychological support (very important).**
- Persons with extensive scalp involvement such as AAT may prefer to wear a wig or hairpiece.
- Makeup applied to eyebrows is helpful. Eyebrows can be tattooed.

2- Glucocorticoids
- **Glucocorticoids *Topical*** :
  Superpotent agents not usually effective.
- ***Intralesional Injection*** :
  Few and small lesions of AA can be treated with intralesional triamcinolone acetonide, 3–7 mg/mL, which can be very effective temporarily.
- ***Systemic Glucocorticoids :***
  May induce regrowth, but AA recurs on discontinuation; risks of long-term therapy therefore preclude their use.

3- Systemic Cyclosporine
Induces regrowth, but AA recurs when drug is discontinued.

4- Induction of Allergic Contact Dermatitis -
By Dinitrochlorobenzene (DNCP) , but local discomfort due to allergic contact dermatitis and swelling of regional lymph nodes poses a problem.

5- Oral PUVA (Photochemotherapy) :
Entire body must be exposed,
in that the therapy is believed to be a form of systemic immune suppression.

- **Patchy alopecia :**
  - Intralesional corticosteroids : Up to 2 mL injected/session and repeated at intervals.
  - Potent topical steroid (1-2×/day).
  - Topical anthralin (0.1%-2.0% once daily) : Wash off after 10-20 min, steadily increase contact duration, switch to higher dose if no significant irritation.
  - Minoxidil lotion (5%) twice daily.
- **Extensive or rapidly progressive alopecia.**
  - Contact immunotherapy.
  - Systemic corticosteroids. Benefits are uncertain and must be weighed against risk of systemic corticosteroid therapy.
  - Wig or hairpiece.
- **Alopecia totalis/universalis**
  - Contact immunotherapy.
  - Topical/systemic steroids.
  - Wig or hairpiece.

COURSE

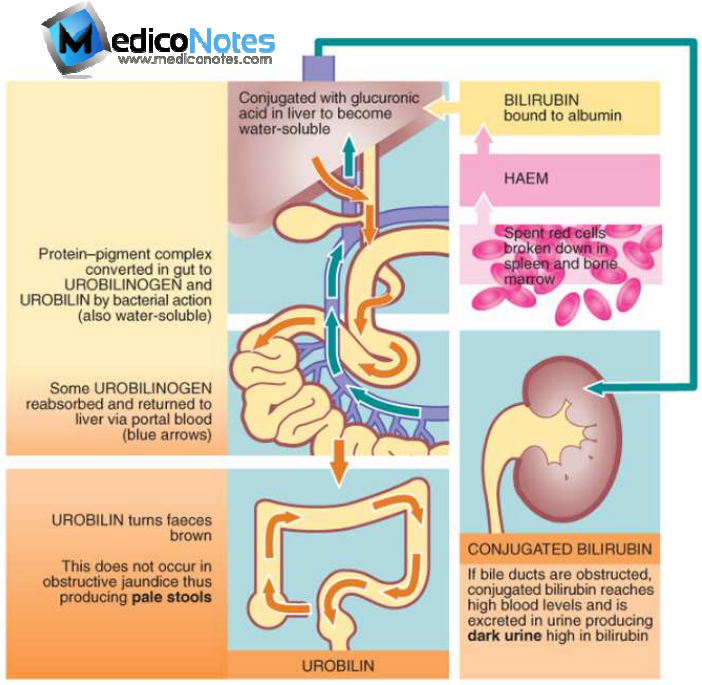
- Spontaneous remission is common in patchy AA but is less so with AAT or AAU.
- Poor prognosis associated with onset in childhood, loss of body hair, nail involvement, atopy, family history of AA.
- If occurring after puberty, 80% regrow hair. With extensive AA, AAT, AAU, <10% recover spontaneously.
- Recurrences of AA, however, are frequent.
- Systemic glucocorticoids or cyclosporine can induce remission of AA but do not alter the course.

Approach to a jaundiced patient

THE NORMAL ENTEROHEPATIC CIRCULATION

- The **haem** component of spent red cells is normally broken down to bilirubin (mainly in the spleen and bone marrow), bound to albumin and transported to the liver. *This relatively stable protein-pigment complex is insoluble in water and is not excreted in the urine.*
- In the liver, the complex is split and the bilirubin conjugated with glucuronic acid which makes it water-soluble, before it is excreted into the bile canaliculi. *The normal concentration of both conjugated and unconjugated bilirubin in the blood is very low.*
- Bacterial action in the bowel converts conjugated bilirubin into colourless **urobilinogen** & pigmented **urobilin** which gives the brown colour to normal faeces.
- Some urobilinogen is reabsorbed, passing to the liver in the portal blood, and is then re-excreted in the bile. The entire process is called an **enterohepatic circulation**. A small amount of urobilinogen escapes into the systemic circulation and is excreted in the urine, *colouring it yellow*.

➔ **Bile acids** (**salts**) are synthesised in the liver from cholesterol-based precursors. These are excreted in bile to the duodenum and facilitate lipid digestion and absorption in the small intestine. About 95% of the bile acids are reabsorbed in the distal ileum and returned to the liver via the portal vein, only to be re-excreted in the bile →Thus both bilirubin and bile acids are involved in enterohepatic circulations.



PATHOPHYSIOLOGY OF OBSTRUCTIVE JAUNDICE

<u>If biliary outflow becomes obstructed :</u>

- Conjugated bilirubin is dammed back in liver from where it enters bloodstream and causes a gradual rise in plasma bilirubin.
- Once the plasma bilirubin level exceeds about 30 µmol/L, jaundice should be clinically detectable. Above 60 µmol/L, jaundice is obvious.

- **<u>Urine:</u>** Conjugated bilirubin, being water-soluble, is excreted in the urine, turning it **dark urine.**
- **<u>Feces:</u>** Diminished or absent excretion of bile into the bowel → less urobilin → causing **pale faeces**.
  Diminshed bile acids → **defective fat absorption**
  The two combine to give the stool a characteristic *'putty' colour.*
- <u>Skin:</u> Biliary obstruction also dams back bile acids, which raises their blood concentration leading to→ deposition in skin – causing **intense itching.**

➔ A consequence of poor dietary fat absorption is **malabsorption of vitamin K** → leading to decreased hepatic synthesis of clotting factors (prothrombin) .

- Impairment of blood clotting is not so great as to cause spontaneous haemorrhage or bruising but there is a significant risk of haemorrhage during surgery.
- Thus the patient's coagulation profile must be checked before any invasive procedure.
- The coagulopathy is corrected with parenteral vitamin K or, in the case of an urgent procedure, fresh frozen plasma.

Approach to a jaundiced patient

History-taking

➔ Change in colour of urine and stools, i.e. **dark urine & pale stools .**

- **<u>Gall stone disease</u>,** Enquiry about :
  - **E**pisodes of pain typical of gallstone disease,
  - **P**revious episodes of obstructive jaundice which resolved spontaneously,
  - **P**revious attacks of acute pancreatitis also suggest gallstone disease.
- **<u>Iatrogenic:</u> P**revious biliary tract surgery.
- **<u>Drug history:</u>** e.g : oral contraceptive pill-potential for intrahepatic cholestasis
- **<u>Risk factors for viral hepatitis:</u>** blood product transfusion, intravenous drug abuse, tattoos, shellfish ingestion, sexual exposure.
- **<u>Alcohol intake:</u>** if excessive, predisposes to pancreatitis & cirrhosis
- **<u>Symptoms suggestive of malignancy:</u>** anorexia, weight loss & non-specific upper GIT disturbance is common in carcinoma of the pancreas
- **<u>History of inflammatory bowel disease</u>**: predisposes to **sclerosing cholangitis** (rare).

Examination

<u>General examination:</u>

- **Jaundice :** is first detectable in the sclera of the eye.
- **Scratch marks :** In some cases of obstructive jaundice, the patient develops generalised itching (pruritus) and scratch marks
- **Stigmata of liver disease:** such as : spider naevi and liver 'flap', are only found when jaundice is caused by primary liver disease
- Enlarged left supraclavicular node (Virchow's node) or periumbilical nodule (Sister Mary Joseph's nodule) suggests an : **abdominal malignancy.**
- Jugular venous distention, a sign of right-sided heart failure, suggests : **hepatic congestion .**

<u>Local Abdominal Examination:</u> Abdomen should be examined for :

1- **Ascites:** Ascites in the presence of jaundice suggests either : 1- cirrhosis or 2- malignancy with peritoneal spread.

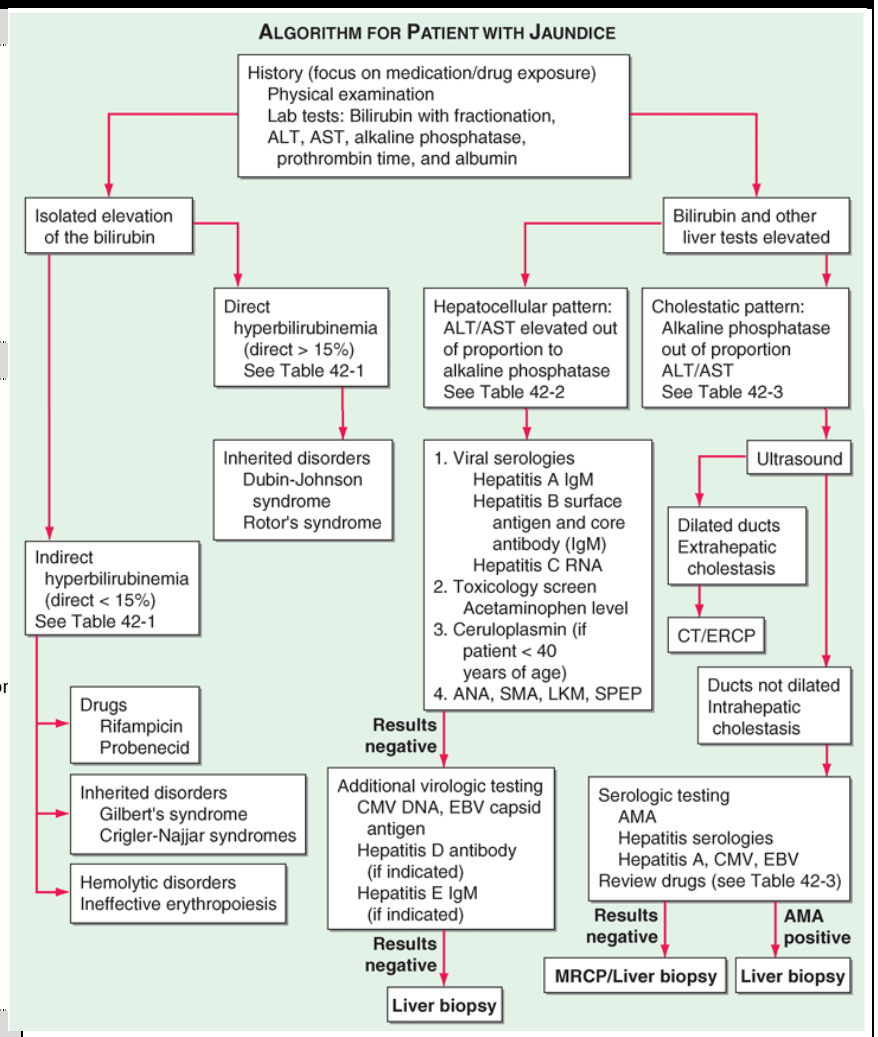
2- **Enlarged liver or spleen :**
   - An enlarged nodular liver may be caused by primary or secondary malignancy.
   - Splenomegaly & hepatomegaly is an important sign of chronic parenchymal liver disease (usually cirrhosis) & indicates portal hypertension

3- **Abnormal masses :** Obvious abdominal mass suggests malignancy.

4- **Palpable gall bladder** :
   - **Courvoisier's 'law'** : states that obstructive jaundice in the presence of a palpable gall bladder is not due to stone (and is therefore likely to be caused by tumour) :
     - In gall stone: - Gallstones cause chronic inflammation leading to: fibrosis of the gall bladder, which **prevents its distension**.
       - Intermittent stone obstruction leads to : thickening of the gall bladder wall, which **prevents its distension.**
     - In malignancy:
       - Progressive obstruction occurs over a short period and the gall bladder distends easily.

5- **Rectal Examination :** Pale stool is characteristic of obstructive jaundice.

➔ The urine should be inspected : - dark yellow or orange from the presence of conjugated bilirubin, and
- froths when shaken due to the detergent effect of bile acids.



Approach to investigation of jaundice , step by step as follows:

Laboratory :

1- <u>Urine tests :</u> Presence of substantial quantities of bilirubin in the urine which is established by: 1- clinic al or 2- bedside dipstick urine tests

2- <u>Blood tests</u> : →

A) Enzyme tests : To differentiate between : a **hepatocellular process** <u>&</u> **cholestatic process**

- <u>Patients with a hepatocellular process</u> : have a disproportionate rise in the aminotransferases compared to the ALP.
- <u>Patients with a cholestatic process</u>: have a disproportionate rise in the ALP compared to the aminotransferases.
- *The bilirubin can be prominently elevated in both hepatocellular & cholestatic conditions →, therefore, is not necessarily in differentiating.*

B) Assessment of liver function : All jaundiced patients should have additional blood tests, to assess liver function :

1- **Albumin level: -** Low albumin level suggests a chronic process such as cirrhosis or cancer.
   - Normal albumin level is suggestive of a more acute process such as viral hepatitis or choledocholithiasis

2- **Prothrombin time:**
   - An elevated prothrombin time indicates either 1- Vitamin K deficiency ,due to prolonged jaundice & malabsorption of vitamin K <u>or</u> 2- Significant hepatocellular dysfunction.

The failure of the prothrombin time to correct with parenteral administration of vitamin K indicates severe hepatocellular injury.

➔ **<u>By liver function tests , Obstructive jaundice is characterised by :</u>**
1- Elevated level of plasma bilirubin, predominantly in the conjugated form.
2- There is marked elevation of plasma ALP , which is derived from bile canaliculi.
3- The transaminases, derived from hepatocytes, are usually only mildly elevated

- When pattern of the liver tests suggests a **cholestatic disorder**, the next step is to determine whether it's :
  - Intra- hepatic cholestasis or
  - Extra-hepatic cholestasis.
- Distinguishing intrahepatic from extrahepatic cholestasis may be difficult. History, physical examination, and laboratory tests are often not helpful.
- The next appropriate test is an **ultrasound**.

Imaging :

A) <u>Hepatobiliary ultrasonography</u>, shows :

1- U/S can detect dilation of the intra- and extrahepatic biliary tree :
   Absence of biliary dilatation suggests: **intrahepatic cholestasis** / while Presence of biliary dilatation indicates: **extrahepatic cholestasis.**
2- Liver secondaries
3- Gall bladder abnormalities including stones.

➔ Although ultrasonography may indicate extrahepatic cholestasis, **it rarely identifies the site or cause of obstruction**.
➔ The distal common bile duct is a particularly difficult area to visualize by ultrasound because of overlying bowel gas.

Appropriate next tests include: CT, & ERCP.

B) <u>CT scanning</u> : CT scanning & MRCP are better than ultrasonography for :

1- Assessing the head of the pancreas and
2- Assessment distal common bile duct for a- choledocholithiasis , particularly when the ducts are not dilated b- small carcinoma .

C) <u>Endoscopy-diagnostic & therapeutic</u>

- **If ultrasound demonstrates dilated ducts→<u>ERCP</u>** is frequently next investigation (gold standard for identifying & ttt choledocholithiasis).
- **IF** ERCP failed → Percutaneous Transhepatic Cholangiopancreatography (PTC).

D) <u>Liver biopsy :</u>

- **If bile ducts are not dilated** (intrahepatic cholestasis)→ **1- Serologic testing** <u>in combination with</u> 2- **Percutaneous liver biopsy**

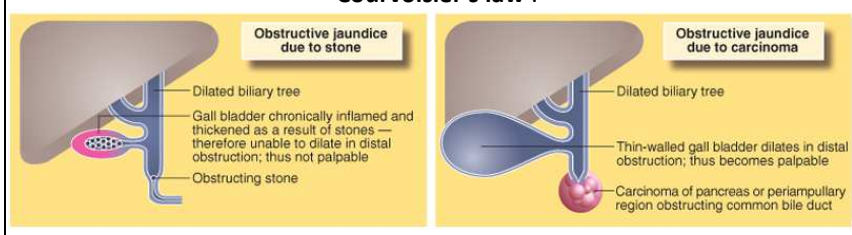
E) <u>Laparoscopy</u>, indications :

1- In patients unsuitable for percutaneous biopsy, or
2- Those who require visualisation of other organs,

- Laparoscopy may be used to visualise the liver directly and to obtain biopsy specimens from suspicious areas.

Occasionally, a firm diagnosis cannot be made before operation → abdominal exploration and frozen section histology + opportunity for treatment at the same time.

Courvoisier's law :



Conditions causing obstructive jaundice :