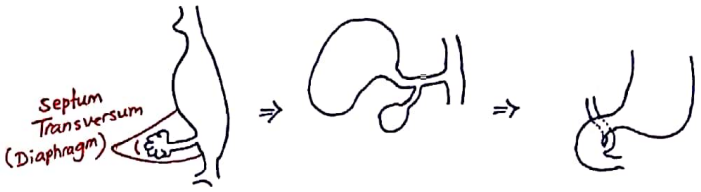
# GallBladder

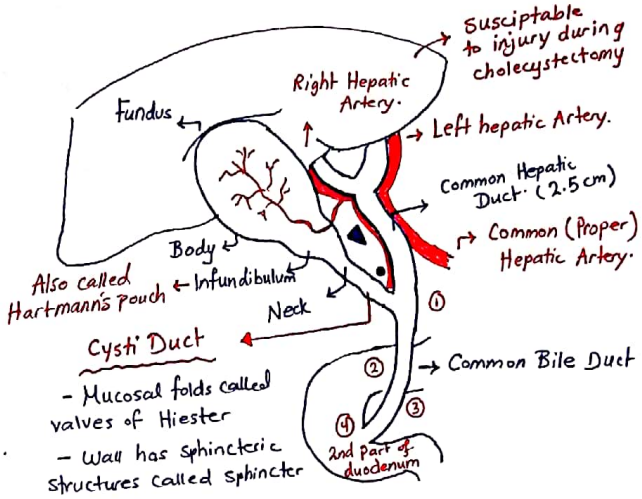
## * Embryology :-

- Early in the 4th week, the caudal part of foregut develop a diverticulum " Hepatic Diverticulum" in its Ventral wall → The diverticulum enlarges to form " Choledochus" & divides into 2 parts :
  1) Large Cranial Part " Hepatic Primordium".
  2) Small Caudal Part " Biliary Apparatus"
- As the Duodenum rotates, the Bile duct carried into the dorsal aspect of duodenum.
- Bile synthesis starts around week 12.




## * Anatomy :-

- GB lies at the Junction of Right & Left lobes of the liver.
- Composed of : 1) Fundus 2) Body 3) Infundibulum 4) Neck.
- Contain mucosal indentations called Crypts of Luschka.
- GB is 7.5-12 cm, Capacity: 25-30mL, Cystic Duct is 3cm long & 1-3 mm in diameter, CBD is 7 cm Long & 4-8mm in diameter.




- Mucosal folds called valves of Hiester
- Wall has sphincteric structures called sphincter of Lutkens.

- Common Bile Duct:
- Divided into 4 parts:
  1. supraduodenal part.
  2. Retroduodenal part.
  3. Infraduodenal part => lies in a groove on posterior aspect of the pancreas.
  4. Intraduodenal part => surrounded by sphincter of oddi & opens into Ampulla of vater.

**Calot's Triangle** → Safe Triangle for cholecystectomy.

- cystic Artery or Inferior Border of liver (superiorly)
- Common Hepatic Duct (Medially)
- Cystic Duct (Inferiorly)

- Blood Supply :-
  - Celiac Trunk → Common Hepatic Artery → Proper hepatic → Right Hepatic Artery + Left Hepatic Artery.
  - Right Gastric
  - Gastroduodenal → Lower part of CBD*
  - Cystic Artery → Cystic Duct, Common Hepatic Duct, Upper Part of CBD*
- Lymphatics :-
  - Sentinel LN called "Cystic LN of Lund" - lie at the junction between cystic duct & Common Hepatic Duct - → Hilum of Liver → Celiac LNs.
  - * Submucosal & subserosal Lymphatics of GB also connect to subcapsular LN of liver → Mets into Liver in GB cancers.

* CBD has weak Blood supply so any problem will lead to strictures.

* Ducts of luschka drains bile directly from liver to Gallbladder (could be the site of Bile leak)

## * physiology :-

- GB Functions:
  1. Stores Bile secreted from Liver. (Reservoir) - Liver excrete bile in a rate of 40mL/hour -
  2. Concentrates Bile (Mucosa absorbs NaCL & HCO3)
  3. Secrete Mucous (20mL/day)
  4. Release Bile => 500-800 cc/day. => After feeding (fat, Protein, HCL) → cholecystokinin hormone released from duodenal mucosal cells → Contraction of GB & relaxation of sphincter of oddi & slows Gastric emptying.

* Trypsin & chemotrypsin Inhibit cholecystokinin.

- Bile Composition:
  1. Water 97%.
  2. Bile Salts (Chenodeoxycholic, deoxycholic, cholic, lithocolic acid)
  3. phospholipid (lecithin)
  4. Bilirubin (mostly conjugated & small % unconjugated)
  5. Cholestrole.

95%. → Bile salts are reabsorped in Terminal Ileum (Enterohepatic Circulation) => if patient has Crohn's, ileal resection → depleted Bile Acid Pool → supersaturated Bile with Cholesterole → Gallstones formation.

## * Radiological Investigations of Biliary tract:

### ① Plain Abdominal x-ray:

1- GB stones seen only in 10% because they are mostly Bilirubin unlike Renal stones which contain Calcium.

2- Calcified GB "Porcelin Gallbladder" → Indication for Cholecystectomy because there's 25% risk for malignant transformation.

3- Gas in Gallbladder & its wall → Emphysematous cholecystitis → Caused by C. perferinges after surgical Anastomosis or Endoscopic sphincrotomy (Emergency due to Risk of perforation) & its more common in DM.

### ② Ultrasound: "Gold standard & initial imaging of choice"

- Can detect stones in GB "Acoustic Shadow", size of GB & upper 2/3 of CBD (lower third behind gaseous duodenum), wall thickness signs of inflammation.
- Disadvantages: 1- distended Bowel, 2- Obese patients, 3- operator dependant. → Obscured GB.
- Endoscopic US: - More Accurate if pt. is obese. - Visualize GB & CBD.

### ③ CT scan:

- Modality of choice in staging cancers (in Liver, Pancreas, GB, CBD) & LNs & used in complications (perforated GB, liver Abcsess)

### ④ MRCP: "Only Diagnostic"

- Non-Invasive, depend on fluid-filling defect in Biliary tree.
- Used if suspected CBD stone (show whole CBD) or if US doesn't show GBS.
- Also used for liver, Pancreatic masses.

### ⑤ HIDA scan: "Dimethyl Iminodiacetic acid"

Non-visualized GB suggest Acute cholecystitis.
Contracted GB suggest chronic cholecystitis

- Isotope administration to check the function of gallbladder. (storage & release)
- Image of choice for Bile leak post cholecystectomy.

### ⑥ ERCP: "Diagnostic & Therapeutic"

Complications: 1. Bleeding 2. Perforation 3. Pancreatitis

- Endoscope → cholangiography →
  1) Confirm site of stone → Sphincrotomy → Balloon Dilation & stone removal
  2) If there's stricture → Brush cytology / Bile Aspiration to exclude cholangio carcinoma. ↳ Stent.

### ⑦ PTC (Percutaneous Transhepatic Cholangiography)

- Only used if ERCP failed, & there's intrahepatic Biliary Dilation.
- Stent insertion.

### ⑧ Intraoperative Cholangiography:

- Enter from cystic Duct & inject a dye → stones are seen.

### ⑨ Choledochoscopy

**US Signs of Acute Cholecystitis**
1. Distended Gallbladder
2. Thickened GB wall (>3mm)
3. Pericholecystic fluid.
4. Gallstones. (Acoustic shadow)
5. +ve murphy's sign.

## Gallbladder Stones

### * Types of Gallstones

- 80% are cholestrole in USA
- 80% are pigmented in Asia.

1. **Cholestrole (non-pigmented)** (most common, not seen on x-ray) ⇒ - 99% pure cholestrole. - Ca salt, Bile Acid & phospholipid. ⇒ 1. Supersaturated Bile (Depleted Bile Acid pool as in Ileal resection, crohn's Disease), Hyperlipidemia (Not hypercholesterolemia) 2. Bile stasis
2. **Pigmented**
   - **Black** ⇒ - formed from Ca-Bilirubinate (Radiopaque on x-ray) ⇒ Occur when there's too much extravascular Hemolysis & Bilirubin production (sickle cell or in liver Cirrhosis or spherocytosis)
   - **Brown** ⇒ - Occur in infected Bile, foreign body (stent), parasitic infections (Ascaris Lumbricoids, Clonorchis senensis) ⇒ Deconjugation of Bilirubin by bacterial B-glucoronidase → Percipitation of insoluble UC Bilirubin.
3. **Mixed**

### * Gallstones formation Risk factors:

1- 5 Fs: 1. female 2. fourty 3. fat 4. fertile (Estrogen) 5. fair (caucassian)

2- Impaired GB function: 1. Emptying 2. Absorption 3. excretion.

3- Cholestrole Nucleating factors: 1. Mucous 2. Glycoprotein 3. infection.

4- Enterohepatic circulation Defect: 1. Ileal resection 2. Crohn's 3. Bowel transit time.

**DDx of Acute Cholecystitis**
1. Acute Appendicitis.
2. Perforated PU.
3. lower lobe pneumonia
4. MI
5. Acute Pyelonephritis
6. Acute Pancreatitis

### * Gallstones Complications: (80% of GS are Asymptomatic)

1. Biliary colick (Only Pain) - Intermittent -
2. Acute cholecystitis (Continuous Pain + fever + Elevated WBC) ↳ pericholecystic fluid on US.
3. Empyema (Complete obstruction → Bacterial outgrowth → Abscess)
4. Mucocele (GB neck obstruction with no infection)
5. Perforation ↔ Localized → In liver or Omentum. / diffuse
6. CBD stone → Cholangitis (Pain + fever + Jaundice)
7. Acute Pancreatitis
8. Gallstone Ileus → Cholangioenteric fistula formation. (Intestinal Obstruction)

## * Lab Investigation & preperation for surgery:

1. CBC ( WBC ) & exclude Anemia.
2. Liver function Test , coagulation screen ( PT )
3. Renal function Test ( High Bilirubin damage the kidney, also the patient may be dehydrated )
4. CXR & ECG ( if > 45 or medically Indicated )
5. DVT Prophylaxis
6. Abx prophylaxis
7. Informed consent

## - Complications of cholecystectomy:

- Occur in 10-15% & operative mortality is < 1%.
- factors ↑ the risk: 1) Age 2) Comorbidities 3) Acute Presentation.
- Serious complications of lapchole. fall into: ↳ Access Complication.
  ↳ Bile Duct injury (.5%)

* Jaundice post-op → need urgent investigation
  → Resuscitation → US ( looking for intra or extrahepatic duct dilation)
  → ERCP or MRCP → Remove obstructing stone.
  ↳ CBD injury → Reconstruction surgery. or choledochojejunostomy.

* Small Bile leaks resolves alone.
* leakage could lead to Biloma (Bile accumulation intraperitoneally) → Put PTC (external drain) / ERCP ( stent placement)

## Cholecystectomy

1- Patient should be supine in Reverse Trendelberg Position ( Head Above feet, 30° )
2- Pneumoperitoneum → closed (veres needle) / open (sub-umbilical)
3- Initial Port placement ( Camera port)
4- Other ports ( subxiphoid, Right subcostal)
5- Define Calot triangle & clip Cystic Artery & Duct.
6- Seperate GB from liver bed & remove via umbilical port.
↳ Could be laparoscopic or open by Kocher Incision ( Right Subcostal Incision)

## Cholangio Carcinoma

- Rare, but incidence is increasing, equally affect males & females
- Most patients present with Abnormal LFT or painless Jaundice ( Advanced Presentation)
- CT scan needed for staging.
- Adjuvant chemotherapy has limited role.
* If it occur at the junction of right & left hepatic ducts its called Klatskin Tumor.
- Most common location is proximal Bile ducts ( Perihilar)

- If proximal Ca. → Resection + Roux-eny + unilateral liver lobectomy
- If distal → whipple procedure.

→ Palliative care only.
→ complete surgical resection in only 10%.
→ Poor prognosis ( 90% dead in 1st year due to Biliary sepsis or liver failure)

### Aim for staging

1. Detect Local disease.
2. Detect liver mets, peritoneal seeding, LNs

## Gallbladder Cancer

- Very rare, more in women (4:1)
- Most patients present with advanced disease
- Poor prognosis - median survival 6 months.
- 10% only surgically feasible, remainder only palliative.
- 90% of Gallbladder Ca. are Adenocarcinoma, most common site at the fundus.

## # Gallbladder Polyp:

- Don't form Acoustic Shadow.
- Should do cholecystectomy if ≥ 1cm. ( 1st order CT to R/o invasion then do the surgery).

## * Acute Acalculous cholecystitis :

→ Cholecystitis without Gallstones

→ Pathogenesis: Biliary stasis (maybe due to abscense of cholecystokinin) → Sludge.

→ Risk factors:
1. ICU patients
2. long postoperative period
3. Trauma
4. TPN / Prolonged fasting.

→ Diagnosed by → US
HIDA scan → non-filling gallbladder

→ Management → cholecystectomy (if pt. is stable)
cholecystostomy (if unstable)

## * Cholangitis :

→ Bacterial infection in Biliary tract from obstruction.

→ Causes:
1. Most common is choledocholethiasis (CBD stone)
2. Stricture.
3. Ampullary ca.
4. Pancreatic pseudocyst.
5. foreign Body (stent)

→ Charcot's triad → Pain, fever, Jaundice
, Reynold's pentad → charcots triad + Altered mental status, shock.

→ Organisms → Gram -ve (E.coli, Klebsiella), Pseudomonas. (Most common)
Gram +ve (Enterococci are the most common)
Anaerobes (B.fragilis)
fungi (candida) - less frequent.

→ Diagnosis → US / ERCP.

→ Management → NPO, IVF, IV Abx, cholecystectomy.

## * Sclerosing cholangitis :

→ Hardening & strictures In (Intra & extrahepatic ducts) that lead into inflammation of Bile ducts.

→ Etiology: Unknown, Genetic, Autoimmune. → ANCA, ANA, ACL

→ Risk factors:
1. Male
2. Age 30-40
3. family history of PSC
4. Having (Ulcerative Colitis) (7% will have PSC)

early colectomy in UC doesn't prevent PSC ←

→ Presentation: As in Obstructive Jaundice. & in advanced stage Hepatomegally.

→ Diagnosis:
1. ↑ ALP
2. ERCP → shows beads on string.
3. AST & ALT may be elevated if liver become to be Cirrhotic.

→ Complications → Obstructive Jaundice
Cholangitis
Cholangiocarcinoma (10%)
Cirrhosis → Bile backflow into the liver

→ Management → Hepatoenteric Anastomosis & resection of extrahepatic ducts
Balloon dilation
Liver Transplant.

## * Gall stone Ileus :

→ Small Bowel Obstruction from Large stone >2.5 cm that made fistula between GB & duodenum

→ The most common site of Obstruction is Ileocecal valve (Terminal ileum)

→ Riglers Triad → Air in hepatic bile duct
SBO obstruction with Air-fluid levels.
Gallstone in Ileocecal valve

→ Management: → Enterotomy (opening the Bowel wall from Above the obstruction because above it the bowel will be distended) & remore the stone.
↳ Then do Interval Cholecystectomy (Delayed)

# Obstructive Jaundice

## ① History:

1. Pain ⇒ Site, Onset → Acute (hours-days), character (colicky), Associated symptoms → N/v, Diarrhea/steatorrhea, Relation to food (↑ with fatty food), Itching → Bile salt in SC.
   - Chronic (months) → Contraction of hollow viscous organ against an obstruction.
   - Timing → Contineous / Intermittent.
   - Constitutional Sx → Anorexia, fatigue, weight loss. → 10% weight loss in short period indicates Ca.
   - Stool (clay) & urin (tea) color. ↓ Due to CB. Because Urobilinogen ha no color.
   - Stercobilinogen ↩
2. PMHx ⇒ HTN, DM → Immunocompromised & ↑ Risk for infections. Silent cholecystitis → diminished sensation → Late presentation (Gangrene)
3. Past surgical hx
4. Alcohol → Pancreatitis. Hepatitis. Liver cirrhosis.
5. Smoking.

Charcot's triad
1. Pain
2. Jaundice
3. fever

## ② Physical Examination:

↱ Become clinically visible if Bilirubin > 2.5 mg/dL.

- General exam: Yellow discoloration of skin & mucous membrane sclera, cachexia, (first site to see Jaundice is under the tongue.)
- Vitals: fever (↑ Temp.),
- Abdominal exam:
  - Murphy Sign → Cessation of breath during Inspiration as the tip of inflammed GB touch examiner hand or the prope.
  - Mass or Ascites.
  - Liver span
  - Palpable mass in RUQ. ⇒ Courvoisier Sign - Painless distention seen in pancreatic head Tumors or cholangiocarcinoma
  - Collateral / distended veins → Portal HTN

* Boas Sign: Refered Right subscapular pain of Biliary colick.

## ③ Differential Diagnosis:

1) Biliary stones
2) Malignancy. (Most common Ca that cause obstructive Jaundice is pancreatic Tumors)

## ④ Investigation:

1) CBC → ↑ WBC → stones
   ↓ Anemia → Ca. until Proven otherwise.
2) LFT
3) KFT (Diarrhea & vomiting - dehydration - & high Bilirubin are toxic to the kidney)
4) Urine Analysis

- Imaging:

1) US → Stones, calcification, Pericholecystic fluid.
2) CT scan → may show Double Duct Sign - Dilation in CBD & Pancreatic duct - which indicate pancreatic head Ca or Ampullary Tumor, stricture from ulcer in duodenum.
3) MRCP → See the whole CBD.

## 5) Treatment:

1. NPO
2. IV fluids & electrolyte balance (mainly K+)
3. Analgesia, Antipyretics.
4. Antibiotics
5. Antiemetics
6. Cholestramine (Anti-itching)

- Then According to cause:
  ERCP, Surgery, Chemo or Radiotherapy.

# Gallstones are clinical dx (hx & PE) + ultrasound.

## Causes of Obstructive Jaundice

**Extrinsic**
1. Pancreatic tumor
2. Ampullary tumor
3. Duodenal Tumor
4. Portal Lymphadenopathy.

**Intraluminal**
1. GS
2. Schistosomiasis
3. Ascaris / clonorchus

**Intrinsic**
1. cholangiocarcinoma
2. sclerosing cholangitis
3. strictures → post op. / postradiation / post inflammatory
4. Mirrizzi Syndrome.
   ↳ GBS in neck with CHD obstruction

# Bilirubin cycle :

- RBC Breakdown after 120 days.

Proteins → A.A

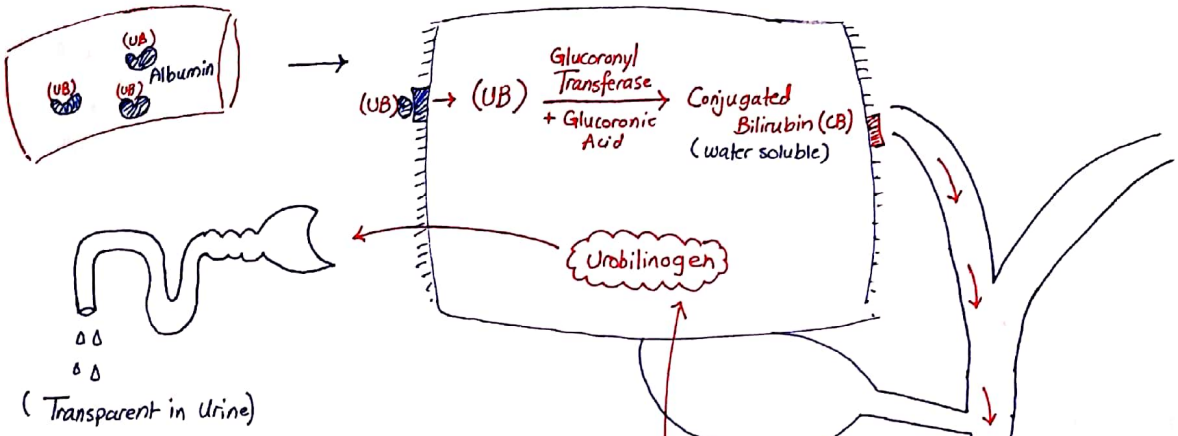
Hemoglobin → Heme → (Heme Oxygenase) → Biliviridin → (Biliviridin Reductase) → Unconjugated Bilirubin (UB) (water Insoluble)

Heme → Globin → A.A.

Heme → $Fe^{+}$ + Apoferritin → Ferritin → Hemosiderin ...

Membrane → lipid → FFA
Membrane → protein → A.A

In the Spleen




| Jaundice | Prehepatic | Hepatic | Posthepatic |
|---|---|---|---|
| Total Bilirubin | ↑ | ↑ | ↑ |
| Direct Bilirubin | Normal | ↑ | ↑↑↑ |
| Alkalin phosphatase (from Bile duct epithelium) | Normal | ↑ | ↑↑↑ |
| ALT & AST | Normal | ↑↑↑ | ↑ |
| Gamma GT | Normal | ↑ | ↑↑↑ |
| Urine Bilirubin (Direct) | Abscent | Present (Deep yellow) | ↑ (tea colored urin) |
| Urine Urobilinogen | ↑ | Present | Markdly decreased or Abscent. |
| Fecal stercobilinogen | ↑ (Dark brown) | Minimally ↓ (Pale stool) | Markdly Decreased or abscent (clay) |
| Fecal fat level | Normal | ↑ | ↑ |
| Pruritis | Abscent | Minimal | Marked |
| Palpable Organs | Spleen | liver, spleen | Gall bladder |




→ - Cause is unknown
- Accummulation of Bile Acids in skin or release of endogenous opiods.
- Treatment: 1. Antihistamine (chlorpheniramine)
2. Bile salt chelating agent (Cholestyramine)

# Jaundice

- **Definition:** - yellow Discoloration of sclera, mucous membrane & skin.
  - Appears clinically if total Bilirubin become > 2 mg/dL (34.2 mmol/L) - without clinical Appearance its called hypobilirubinemia.

## # DDx of yellowish pigment Disposition:

1) Hypercarotinemia.
2) Drugs like Rifampicin & Quinidine.

↳ In these cases the skin only involved & sclera & Mucous membrane shows no icteric pigmentation.

## # Clinical Assessment:

### [1] History:

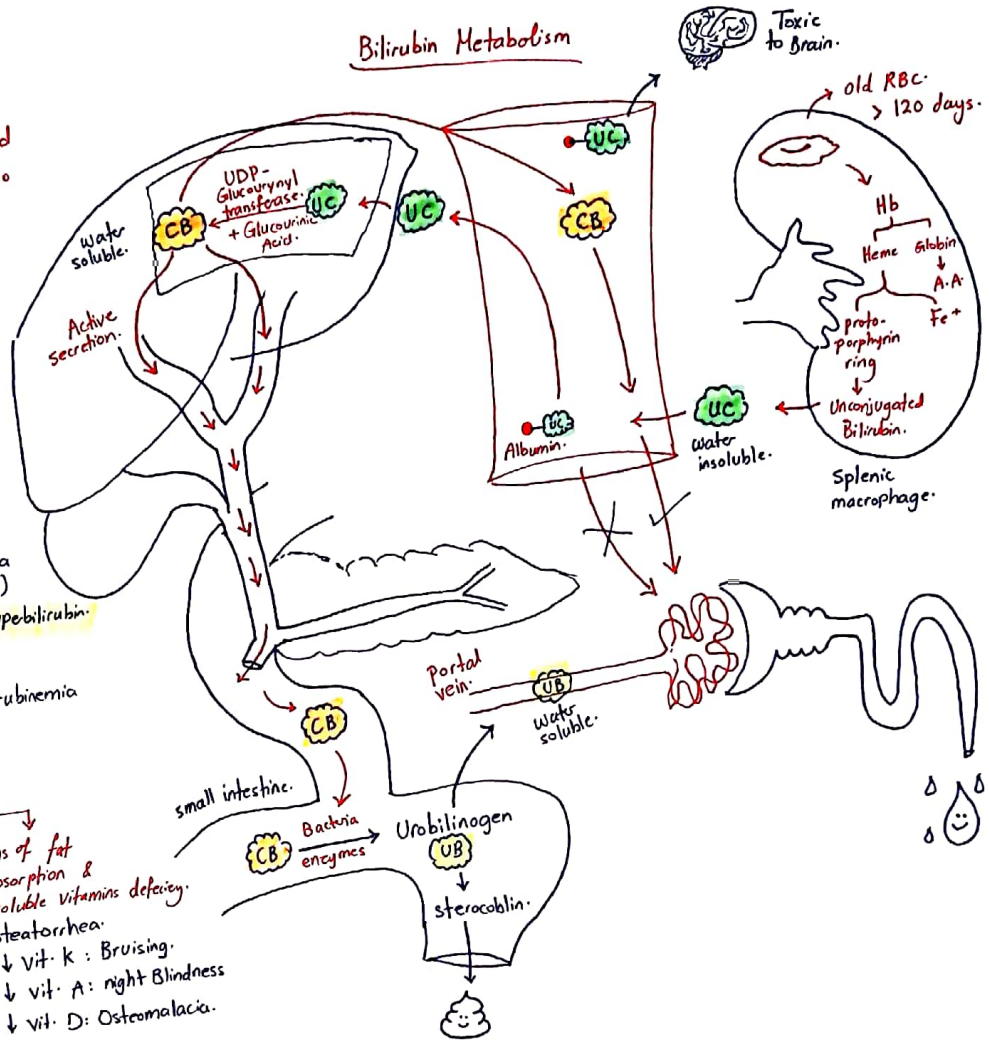
1- Skin Discoloration.
2- Itching (Bile salt Deposition)
3- Fever (to differentiate Between it & cholangitis), Also pain.
4- Color of Urine → Dark → conjugated hyperbilirubinemia (post-hepatic)
→ Normal → Unconjugated Hyperbilirubin (hepatic).
5- Color of stool → Normal
→ pale → Conjugated hyperbilirubinemia (Obstructive).
6- Weight loss & Appetite to exclude malignancy.

**Cholestatic Syndrome**

signs of Conjugated hyperbilirubenemia.
1- Dark urin.
2- pale stool.
3- itching.
4- Jaundice.

signs of fat malabsorption & fat soluble vitamins defeciey.
1- steatorrhea.
2- ↓ Vit. K : Bruising.
3- ↓ vit. A: night Blindness
4- ↓ vit. D: Osteomalacia.

## Bilirubin Metabolism




### [2] Physical Exam:

1- sclera & mucous membrane exam (at day light).
2- Tattoos (viral hepatitis)
3- scratch mark (itching).
4- UQ tenderness (+ve murphy's sign)
5- Ascites.

### [3] Lab Tests:

[1] CBC → ↑ WBC in cholangitis, Hb.
[2] Amylase.
[3] liver function test:
1- liver enzymes: ALT, AST, ALP, GGT
2- Bilirubin (Tota & direct) → ↑ indirect → Pre-hepatic.
↑ direct → post-hepatic.
↑ direct & indirect → Hepatic
3- Albumin & PT (vit. K dependant coagulation).

### [4] Radiological Tests:

[1] US (cheap, Available, sensitive)
[2] CT scan.
[3] ERCP (Dx & Rx)
[4] MRCP.
[5] PTC.

## liver function Test

[1] Aminotransferase: - ALT → specific for liver. - AST → heart, skeletal muscle, Kidney, Brain.
[1] AST: ALT > 2:1 → Alcoholic hepatitis.
[2] AST, ALT (low hundreds) → Acute Alcoholic hep → ALT < 300, AST < 500
→ chronic viral hep.
[3] AST, ALT (moderately elevated) → Acute viral hep.
[4] AST, ALT > 10,000 → Hepatic necrosis (Ischemia, Acitamenophen toxicity
- Asymptomatic ↑ in ALT & AST: Autoimmune hep., Hep. B, Hep. C, Drugs, Ethanol, Fatty liver, Growths (Tumor), Hemodynamic Disorder (CHF) & Iron (Hemochromatosis), Wilson, AAT defeciency.

[2] ALP (found Also in bone, Gut, Placenta):
↳ ↑ ALP indicate Bile flow Obstruction:
- if very high (>10-folds) → extrahepatic.
- if elevated → ↑ GGT → hepatic # GGT used to confirm that high ALP due to hepatic origin.
→ normal GGT → Pregnancy or Bone Disease.

[3] Bilirubin.
[4] GGT
[5] Albumin. → ↓ in chronic liver D., nephrotic syndrome, malnutrition
[6] PT/INR → ↓ in Advanced liver Disease.

# Causes of Obstructive Jaundice

## [1] Prehepatic (normal LFTs)

- Increased Production → Hemolysis / Blood transfusion / Large Hematoma Resorption → Unconjugated Bilirubinemia.
- decreased excretion:
  - Others (Inhireted) → Dubin-Johnson, Rotor Syndrome → Conjugated hyperbilirubinemia.
  - Impaired Conjugation (Unconjugated Bilirubinemia):
    - Gilbert syndrome
    - Crigglar-Najjar syndrome (Type 1 → Complete Absence of UDP-GT; Type 2 → ↓ Activity of UDP-GT)
    - Neonatal Jaundice.
    - Familial Unconjugated hyperbilirubenemia).

## [2] Hepatic (↓ transport & excretion).

A- Hepatitis (Viral, Autoimmune, Drugs).
B- pregnancy, OCP.
C- Infiltration (Amyloidosis)
D- Cirrhosis.
E- Post-operative intrahepatic cholestasis.
F- Idiopathic hepatic Jaundice.
G- Infantile cholestatic syndrome.
H- TPN

## [3] Post-Hepatic (Conjugated Hyperbilirubinemia).

1. Cholangiocarcinoma.
2. Sclerosing cholangitis
3. Papilloma of Bile duct
4. Iatrogenic Bile duct injury.