APPROACH TO JAUNDICE

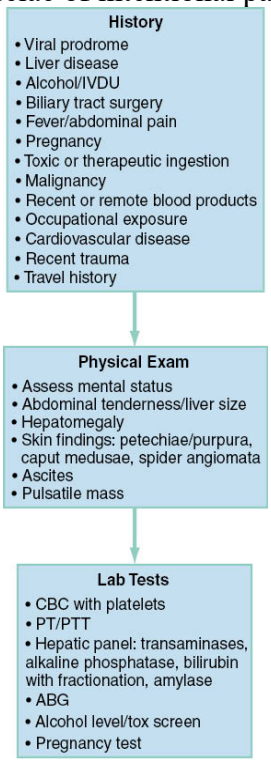
PATHOPHYSIOLOGY:

- Bilirubin is generated from haem products, mostly from RBCs →passively taking into hepatocytes → conjugation →biliary system → Gut → metabolized by colonic bacteria to urobilinogen/stercobilin →stercobilin excreted in stool, urobilinogen reabsorbed
- Jaundice does not become clinically apparent until bilirubin >25
    - It is observed in tissues with HIGH ALBUMIN CONCENTRATIONS (e.g. the eye and skin)
- Occurs in four circumstances when bile metabolism is altered:
    - OVERPRODUCTION of haem products
    - Failure of hepatocyte to take up bilirubin for processing
    - Failure of hepatocyte to conjugate
    - OBSTRUCTION o fbiliary excretion inot the intestine
- Bilirubin that is not bound to albumin can cross the BBB → KERNICTERUS
    - Risk of neurotoxicity ↑d by condition that favour unbound fraction of bilirubin → haemolysis, hypoalbuminaemia, acidaemia, drugs that bind competitively to albumin

PIVOTAL FINDINGS:

HISTORY:

- Can be asymptomatic or non-specific symptoms → pruritus, malaise, nausea
- Jaundice with abdominal pain suggests significant hepatic inflammation
- New onset painless jaundice classical for neoplasm involving head of pancreas
- Personality changes may suggest encephalopathy
- Beware downstream sequelae of intentional paracetamol overdose



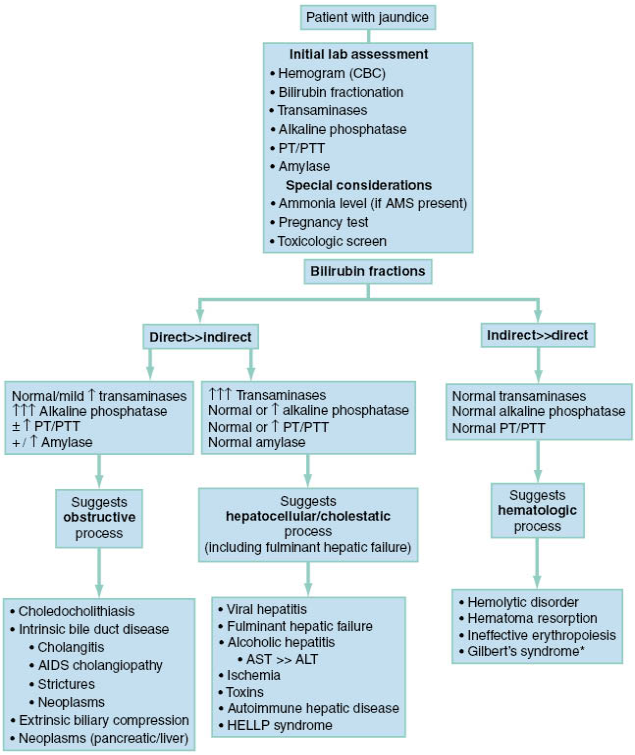
PHYSICAL EXAMINATION:

- Jaundice spreads CAUDALLY, but the level does not accurately estimate serum bilirubin
- Fever with RUQ tenderness suggests cholangitis
- Large/tender liver may represent acute/chronic hepatitis or malignant inflammation
- Presence of splenomegaly suggests haemolysis, malignancy or portal hypertension
- Ascites with abdominal pain/fevers → think SBP
- Features of chronic liver disease → spider angiomas, gynaecomastia, testicular atrophy, caput medusae
- Asterixis → sign of hepatic encephalopathy

Table 25-1 Clinical Stages of Hepatic Encephalopathy

CLINICAL STAGE	INTELLECTUAL FUNCTION	NEUROMUSCULAR FUNCTION
Subclinical	Normal examination findings, but work or driving may be impaired	Subtle changes in psychometric testing
Stage 1	Impaired attention, irritability, depression, or personality changes	Tremor, incoordination, apraxia
Stage 2	Drowsiness, behavioral changes, poor memory, disturbed sleep	Asterixis, slowed or slurred speech, ataxia
Stage 3	Confusion, disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, muscular rigidity
Stage 4	Stupor and coma	Dilated pupils and decerebrate posturing, oculocephalic reflex

ANCILLARY TESTING:



- In presence of abdominal tenderness and ascites, ascitic fluid should be tested for cell count, gram stain, culture and protein

IMAGING:

- Best radiologic study for evaluation of biliary disease controversial:
  - CT if high index of suspicion for malignancy
    - More sensitive than US for locating level of obstruction
  - US → cheaper, less invasive, safe
    - Use for people with most likely benign obstruction
    - If gallstones are present on ultrasound images, a sonographic Murphy sign has a positive predictive value of 90% for acute cholecystitis

DIFFERENTIAL DIAGNOSIS:

- Aim to classify jaundiced patients into critical, emergent and non-emergent categories
- Critically ill if present with → altered level of consciousness, hypotension, fever with abdominal pain or active bleeding
  - Any patient with NEW TRIAD of → jaundice, encephalopathy and coagulopathy is considered to have FULMINANT HEPATIC FAILURE → Require aggressive stabilization, consideration for toxic exposure and admission to ICU/transfer to transplant centre

Table 25-2 Causes of Jaundice Grouped by Level of Urgency

ETIOLOGIC CATEGORY	CRITICAL	EMERGENT	NONEMERGENT
Hepatic	Fulminant hepatic failure Toxin Virus Alcohol Ischemic insult Reye's syndrome	Hepatitis of any etiology with confusion, bleeding, or coagulopathy Wilson's disease* Primary biliary cirrhosis Autoimmune hepatitis Liver transplant rejection Infiltrative liver disease Drug-induced (isoniazid, phenytoin, acetaminophen, ritonavir, halothane, sulfonamides) Toxin ingestion or exposure	Hepatitis with normal mental status, normal vital signs, and no active bleeding
Biliary	Cholangitis	Bile duct obstruction (stone, inflammation, stricture, neoplasm)	
Systemic	Sepsis Heatstroke	Sarcoidosis Amyloidosis Graft-versus-host disease	Post-traumatic hematoma resorption Total parenteral nutrition
Cardiovascular	Obstructing AAA Budd-Chiari syndrome Severe congestive heart failure	Right-sided congestive heart failure Veno-occlusive disease	
Hematologic-oncologic	Transfusion reaction	Hemolytic anemia Massive malignant infiltration Inborn error of metabolism Pancreatic head tumor Metastatic disease	Gilbert's syndrome Physiologic neonatal jaundice
Reproductive	Preclampsia/HELLP syndrome Acute fatty liver of pregnancy	Hyperemesis gravidarum	Cholestasis of pregnancy

EMPIRICAL MANAGEMENT AND DISPOSITION:

- Correct coagulopathy with FFP, anaemia with packed red cells
- If ascites is present → diagnostic paracentesis and treat for SBP if PMN >250/cm3 with third generation cephalosporin
- Lactulose for those considered to have encephalopathy
- On basis of lab values alone, patients with new onset hepatitis should be hospitalized if they have transaminases ≥1000, bilirubin ≥100 or coagulopathy
- For patients with suspected ascending cholangitis → blood cultures, broad spectrum gram negative cover and refer early for decompression with ERCP or cholecystotomy → dramatically improves survival.
- Those with extrahepatic biliary obstruction without cholangitis should still be admitted for ERCP
    - If jaundiced due to malignant obstruction, represents advanced disease with higher morbidity and mortality → drainage has been linked with better oral intake and cardiac function
- In patients with uncomplicated cholecystitis → IV fluids, parenteral analgesia and admission → add IV antibiotics if temp>38.8C, toxic appearance/frank sepsis

SPECIAL POPULATIONS:

- PREGNANCY AND JAUNDICE:
    - JAUNDICE ALWAYS REPRESENTS SERIOUS PATHOLOGY IN PREGNANCY
    - Can occur for all the usual reasons but also some pregnancy-specific conditions:
        - Hyperemesis gravidarum → likely malnutrition-related → IV antiemetics and fluid rehydration
        - Acute fatty liver of pregnancy → third trimester, microvesicular fat → jaundice progressing to fulminant hepatic failure and encephalopathy → PROMPT DELIVERY

- Intrahepatic cholestasis of pregnancy→ idiopathic, occurs early third trimester → manifests with pruritus then jaundice → ↑d risk for preterm delivery and intrauterine foetal demise → cholestyramine for pruritus, vitamin K