

# JAUNDICE

## Differential Diagnosis, Clinical Workup & Emergency Management

*Prehepatic • Hepatic • Cholestatic (Intrahepatic & Extrahepatic)*

### 1. Definition & Classification

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Jaundice is yellow discolouration of the tissues - most easily seen in the skin and sclera - caused by accumulation of bilirubin. Scleral icterus is typically visible before skin discolouration becomes obvious.

The pocketbook classifies jaundice into three mechanistic categories:

- **Prehepatic** - unconjugated hyperbilirubinaemia, usually from haemolysis or a congenital conjugation defect
- **Hepatic** - intrinsic liver (hepatocellular) disease, acute or chronic
- **Cholestatic** - impaired bile flow, either intrahepatic (e.g. drugs, pregnancy) or extrahepatic/obstructive (e.g. gallstones, tumour) - often grouped clinically as "post-hepatic"

### 2. PREHEPATIC JAUNDICE

*Unconjugated hyperbilirubinaemia - normal LFTs otherwise*

#### Causes

##### Congenital defects

- Gilbert's disease (autosomal dominant; reduced hepatocyte uptake of unconjugated bilirubin)
- Crigler-Najjar syndrome (failure of conjugation)

##### Haemolysis - congenital

- Hereditary spherocytosis
- Sickle cell disease
- G6PD deficiency
- Thalassaemia

##### Haemolysis - acquired

- Malaria (common where endemic)
- Incompatible blood transfusion
- Autoimmune haemolysis
- Haemolytic disease of the newborn

##### Other

- Resorption of a large haematoma
- Hypersplenism

#### History pointers

- Family history, racial/ethnic background, current medications, haematuria, prior anaemia
- Gilbert's disease: inherited autosomal dominant; usually incidental, mild, worsens with fasting/illness

#### Examination

- Jaundice often mild ('lemon tinge') rather than deep
- Look for anaemia and splenomegaly

#### Targeted Workup

- FBC with peripheral blood film, reticulocyte count
- LDH raised, haptoglobin low
- Direct antiglobulin (Coombs) test

- Haemoglobin electrophoresis; G6PD assay where indicated
- Urine: **no bilirubin** present (acholuric jaundice) - a key bedside discriminator; urobilinogen normal or raised

### 3. HEPATIC JAUNDICE

*Intrinsic hepatocellular disease - acute or chronic*

#### Causes

##### Acute hepatocellular disease

###### **Infective**

- Viral hepatitis (A, B, C)
- EBV, CMV
- Leptospirosis (and other infections)

###### **Other**

- Drugs, e.g. paracetamol, halothane
- Toxins, e.g. carbon tetrachloride
- Autoimmune hepatitis

##### Chronic hepatocellular disease

- Chronic viral hepatitis; chronic autoimmune hepatitis
- End-stage liver disease: alcohol-related, MASLD/NASH-related cirrhosis, haemochromatosis, Wilson's disease

#### History pointers

- Occupation, travel, alcohol use, sexual history, medications (tablets, injections, anaesthetic agents, drug misuse), industrial solvent exposure
- Prior jaundice episodes; 'flu-like' prodrome; rashes; joint pains

#### Examination

- Tender liver in acute hepatitis
- Signs of chronic liver failure: spider naevi, palmar erythema, leuconychia, clubbing, gynaecomastia, ascites, Dupuytren's contracture, caput medusae, liver flap (asterixis)
- Haematemesis may indicate bleeding oesophageal varices

#### Targeted Workup

- Viral serology: hepatitis A/B/C, CMV, EBV
- Serum copper and ceruloplasmin (both reduced in Wilson's disease)
- Serum alpha-1-antitrypsin (deficiency); iron studies and TIBC (raised iron, TIBC saturation >70% suggests haemochromatosis)
- Leptospirosis complement fixation test, blood cultures, lumbar puncture if leptospirosis is suspected
- Liver biopsy for hepatocellular disease or carcinoma where diagnosis remains unclear

### 4. CHOLESTATIC JAUNDICE

*Intrahepatic cholestasis or extrahepatic (post-hepatic) obstruction*

#### Causes

##### Intrahepatic

- Drugs, e.g. chlorpromazine
- Parenteral nutrition

- Viral hepatitis
- Primary biliary cirrhosis (primary biliary cholangitis)
- Pregnancy (intrahepatic cholestasis of pregnancy)

### Extrahepatic (obstructive)

**In the lumen:** gallstones; infestation (clonorchiasis, schistosomiasis)

**In the wall:** stricture (inflammatory/postoperative), cholangitis, congenital biliary atresia, cholangiocarcinoma, sclerosing cholangitis, choledochal cyst

**Outside the wall:** carcinoma of the head of the pancreas, carcinoma of the ampulla of Vater, malignant porta hepatis lymphadenopathy, chronic pancreatitis, Mirizzi syndrome

### History pointers

- Drug history (e.g. chlorpromazine), foreign travel
- Severe upper-abdominal pain preceding jaundice suggests biliary colic with stone impaction in the common bile duct
- Insidious, painless jaundice raises suspicion of malignancy
- Dark urine, pale stools, pruritus

### Examination

- Hepatomegaly - typically a smooth liver with a firm, 'sharp' edge
- **Courvoisier's law:** in obstructive jaundice, a palpable gallbladder makes gallstones unlikely - think malignancy instead
- Epigastric or other abdominal masses (e.g. pancreatic, gastric, colonic carcinoma with porta hepatis spread)
- Scratch marks from pruritus; recent surgical scars

### Newborn Presentation

- Biliary atresia: deepening jaundice within 2-3 days of birth; liver failure develops over 3-6 months if untreated
- Physiological jaundice: common, due to hepatic immaturity, usually resolves within the first week of life

### Targeted Workup

- **First-line imaging:** ultrasound - gallstones, ductal dilatation, level of obstruction, hepatic secondaries, cirrhosis (may not reveal the underlying cause)
- **ERCP:** perampullary carcinoma, common bile duct stones/tumour/stricture; allows biopsy, brush cytology and stenting
- **PTC:** used if ERCP is unsuccessful
- **MRCP:** bile duct anomalies and stones, non-invasively
- **CT:** staging pancreatic head carcinoma (spread, resectability) and detecting liver secondaries

## 5. General Workup - All Patients

*First-line tests and the classic urine & blood biochemistry pattern*

### First-Line Investigations (every patient)

- **FBC, CRP/ESR, blood film** - Hb low in malignancy/haemolysis; WCC raised in infection (hepatitis, cholangitis); CRP/ESR raised in infection or malignancy; film may show red-cell defects or malaria parasites
- **Reticulocyte count** - raised in haemolysis
- **U&Es** - deranged renal function raises concern for hepatorenal syndrome
- **LFTs** - see biochemistry pattern table below
- **Clotting screen** - PT prolonged with hepatocellular dysfunction

## Urine & Blood Biochemistry Pattern

| Parameter                      | Prehepatic      | Hepatic         | Cholestatic               |
|--------------------------------|-----------------|-----------------|---------------------------|
| Blood - Unconjugated bilirubin | Raised          | Normal / Raised | Normal                    |
| Blood - Conjugated bilirubin   | Normal          | Normal / Raised | Raised                    |
| Blood - Alkaline phosphatase   | Normal          | Normal / Raised | Markedly raised           |
| Blood - Transaminases          | Normal          | Raised          | Normal / Raised           |
| Urine - Bilirubin              | Absent          | Raised          | Raised                    |
| Urine - Urobilinogen           | Normal / Raised | Raised          | Markedly reduced / Absent |

## Clinical Pearls

- **Painless, progressive jaundice** suggests carcinoma of the pancreas, particularly with a palpable gallbladder (Courvoisier's law)
- In **sudden-onset jaundice with fever**, always ask about foreign travel, drug misuse, and sexual history

## 6. EMERGENCY MEDICINE MANAGEMENT

## Red-Flag Presentations

| Clinical finding                                                                         | Concern                                                              | Immediate action                                                                                                                    |
|------------------------------------------------------------------------------------------|----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Fever + RUQ pain + jaundice (Charcot's triad - high specificity, only ~25-50% sensitive) | Acute (ascending) cholangitis                                        | Blood cultures, IV fluids, empirical broad-spectrum antibiotics; urgent biliary drainage (ERCP) per Tokyo Guidelines severity grade |
| Reynolds' pentad: above + hypotension + altered mental status                            | Severe (Grade III) cholangitis / septic shock                        | Sepsis bundle, ICU-level care, emergent biliary decompression                                                                       |
| Altered mental status + jaundice + coagulopathy, no prior liver disease                  | Acute liver failure                                                  | ICU admission; consider N-acetylcysteine in all-cause ALF; monitor for cerebral oedema; early transplant-centre referral            |
| INR > 1.5 with encephalopathy (no pre-existing liver disease)                            | Meets acute liver failure definition; assess King's College Criteria | Urgent transfer to a liver transplant centre                                                                                        |
| Severe pruritus + jaundice in pregnancy (esp. 3rd trimester)                             | Intrahepatic cholestasis of pregnancy; exclude HELLP                 | LFTs, bile acids, platelets, blood pressure; urgent obstetric consultation                                                          |

## General ED Management Principles

- **Stabilise first:** airway, breathing, circulation; IV access; fluid resuscitation as needed
- **Identify obstruction early:** bedside or formal ultrasound guides urgency of surgical/GI referral
- **Treat sepsis promptly** if cholangitis is suspected - start empirical antibiotics per local antibiogram without waiting for imaging if the patient is unstable
- **Correct coagulopathy:** vitamin K; fresh frozen plasma if actively bleeding or pre-procedure

- **Paracetamol toxicity:** check level, treat with N-acetylcysteine per the Rumack-Matthew nomogram if within the treatment window
- **Avoid hepatotoxic drugs** until the underlying cause is clarified
- **Early specialty involvement:** hepatology/GI for hepatic causes; surgery or interventional radiology for obstructive causes; transplant centre for fulminant failure
- **Disposition:** admit for cholangitis, acute liver failure, severe coagulopathy, or haemodynamic instability; stable unconjugated hyperbilirubinaemia (e.g. Gilbert's disease) may be discharged with reassurance and outpatient follow-up