



Chapter 25 - Jaundice

EPISODE CONTENT BASED ON ROSEN'S EMERGENCY MEDICINE (9TH ED.)

Italicized text is quoted directly from Rosen's.

Key Concepts:

1. *Clinical Jaundice is usually not evident until total serum bilirubin rises above 2.5mg/dl (~43 μ mol/L for our Canadian listeners)*
2. *Bile metabolism can be altered when there is overproduction of heme products (hemolysis); failure of hepatocyte to take up, conjugate and excrete bilirubin (hepatocellular dysfunction); or obstruction of biliary excretion into the intestine.*
3. *Unconjugated bilirubin that is not bound to albumin can cross the BBB, causing toxic neurologic effects.*
4. *New onset painless jaundice is the classic presentation for a pancreatic head neoplasm.*
5. *Jaundice is first apparent sublingually, in the conjunctiva, and on the hard palate.*
6. *In cases of unexplained liver injury, a quantitative APAP level may be helpful.*
7. *If the etiology of the ascites is unknown, getting the serum ascites albumin gradient (SAAG) will aid in determining the cause of the ascites and presence of portal hypertension.*
8. *US is the preferred initial modality to evaluate whether or not biliary obstruction is present, whereas CT is preferred if malignant obstruction is suspected, or the entire abdomen needs to be evaluated.*
9. *Elevated direct bilirubin with transaminase elevation is indicative of hepatocellular inflammation or injury.*
10. *Hyperemesis gravidarum can elevate liver enzymes up to 20 times the normal amount, including mildly elevated bilirubin.*
11. *Intrahepatic cholestasis of pregnancy is an idiopathic cause of jaundice that occurs in the third trimester.*



Core Questions

1. Explain broad causes of elevated bilirubin (obstructive, hepatocellular, and hemolysis) and the significance of direct vs. indirect hyperbilirubinemia (Fig 25.1)
2. Explain your approach to the history and physical exam in patients with jaundice (Fig 25.2)
3. List 10 causes of jaundice (Table 25.2)
4. Explain your approach to ancillary testing in patients with jaundice.

Wisecracks

1. What are the stages of hepatic encephalopathy?
2. What is the triad of acute hepatic failure?
3. What is Charcot's triad and Reynold's pentad?
4. What is the "1000s Club" and how do you become a member?

Rosen's in Perspective

Jaundice is one of those ED complaints that is a bit more rare than some of the standard cases we see every shift. However, there is a wide range of causes for jaundice, and an understanding of pathophysiology is key. We have got you covered here at CRACKCast - the next time you walk into a room and your patient is as yellow as Homer Simpson, you will know exactly what to do!

A few points to highlight from those first few Rosen's paragraphs. Jaundice is clinically evident at 2.5mg/dl or about 43 μ mol/L, first seen in tissues with relatively high concentrations of albumin (eyes and skin). Remember that there are 3 categories of bilirubin problems - increased production due to hemolysis, hepatocellular dysfunction causing impaired uptake and conjugation, and obstruction pathologies that prevent bilirubin excretion. When it comes to neurotoxicity, unconjugated bili is the one we worry about - this is not bound to albumin, and can cause encephalopathy and kernicterus.

Core Questions:

[1] Explain broad causes of elevated bilirubin (obstructive, hepatocellular, and hemolysis) and the significance of direct vs. indirect hyperbilirubinemia (Fig 25.1)

Bilirubin is a byproduct of heme breakdown.

This is released into its **unconjugated** form into the circulation and bound to albumin. It is then taken up into the hepatocytes where it is conjugated. **Conjugated** bilirubin is taken up and stored in the hepatocytes, and then subsequently excreted into the intestine.

Direct hyperbilirubinemia = conjugated bilirubin

- **Obstructive causes** to consider:
 - Choledocolithiasis
 - Intrinsic bile duct disease (cholangitis, stricture, neoplasm, extrinsic compression)
 - Extrinsic compression
- **Hepatocellular causes**
 - Viral hepatitis
 - Hepatic failure
 - Alcoholic hepatitis
 - Ischemia
 - Toxins
 - Autoimmune hepatitis
 - HELLP syndrome

Indirect hyperbilirubinemia = unconjugated bilirubin

- **Hematologic causes**
 - Hemolysis
 - Hematoma resorption
 - Ineffective erythropoiesis
 - Gilbert's syndrome

See figure 25.1 for more details.

[2] Explain your approach to the history and physical exam in patients with jaundice (Fig 25.2)



Figure 25.2: Pivotal points in the assessment of the jaundiced patient.

History

- Viral prodrome
- Liver disease
- Alcohol/IVDU
- Biliary surgery
- Fever/abdo pain
- Pregnancy
- Toxic ingestion
- Cancer history
- History of blood products
- Occupational exposure
- CV disease
- Trauma
- Travel history

Exam:

- Mental status
- Abdominal tenderness/HSM
- Skin findings - petechiae/purpura, caput medusae, spider angiomas
- Ascites
- Pulsatile mass

[3] List 10 causes of jaundice (Table 25.2)



Table 25.2: Jaundice: Differential diagnosis of critical and emergent causes

SYSTEM	CRITICAL	EMERGENT	NONEMERGENT
Hepatic	Fulminant hepatic failure; Toxin, Virus, Alcohol, Ischemic insult, Reye's syndrome	Hepatitis of any cause with confusion, bleeding, or coagulopathy	Hepatitis with normal mental status, normal vital signs, and no active bleeding
		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	



Biliary	Cholangitis	Bile duct obstruction (stone, inflammation, stricture, neoplasm)	
Systemic	Sepsis	Sarcoidosis	Post-traumatic hematoma resorption
	Heatstroke	Amyloidosis	Total parenteral nutrition
		Graft-versus-host disease	
Cardiovascular	Obstructing AAA	Right-sided congestive heart failure	
	Budd-Chiari syndrome	Veno-occlusive disease	
	Severe congestive heart failure		
Hematologic-oncologic	Transfusion reaction	Hemolytic anemia	Gilbert's syndrome
		Massive malignant infiltration	Physiologic neonatal jaundice
		Inborn error of metabolism	
		Pancreatic head tumor	
		Metastatic disease	



Reproductive	Preeclampsia or HELLP syndrome	Hyperemesis gravidarum	
	Acute fatty liver of pregnancy		Cholestasis of pregnancy

[4] Explain your approach to ancillary testing in patients with jaundice.

Lab considerations:

Bilirubin:

Conjugated vs. Unconjugated as discussed in previous question

Conjugated - think hepatic causes

Unconjugated - think hemolytic causes (send LDH, haptoglobin, reticulocyte count, peripheral smear, coombs test)

Liver enzymes:

- AST (intracellular, liver, heart, muscle, kidneys, brain, pancreas, lungs, RBC, LBC)
- ALT (specific to **Liver**)
- ALP (liver, bone, placenta, gut)
- GGT - specific to liver, can help confirm that ALP elevation caused by liver

Cholestatic vs. Hepatocellular pattern:

Cholestatic enzymes = ALP/GGT/Bili

Hepatocellular enzymes = AST/ALT

Liver function tests:

Albumin

INR

Imaging - in general, ultrasound is the best place to start assessing for liver/gallbladder/CBD pathology. It can assess for cirrhosis, portal HTN, and ascites as well.



Acute abdomen/undifferentiated sick patient: CT abdo/pelvis is never a bad idea

Wisecracks:

[1] What are the stages of hepatic encephalopathy?

Table 25.1

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

[2] What is the triad of acute hepatic failure?

Jaundice, encephalopathy, coagulopathy INR > 1.5

These can be some of the sickest patients in the hospital. When managing acute hepatic failure, think of the the complications of liver failure and go from there



SCREAM

- **Sepsis** - fluids/antibiotics/source control. Increased susceptibility to bacterial and fungal infections
- **Coagulopathy** - vitamin K, FFP/Platelets if actively bleeding or invasive procedures required. GI bleeds can occur if pt has varices.
- **Renal Failure** - Dialysis if indicated.
 - Hepatorenal syndrome and severe peripheral edema can occur
- **Encephalopathy** - acute setting - ICP management, lactulose/limited protein intake in hospital. Consider intubating and initiating ICP care for grade 3/4 encephalopathy
- **Ascites** (keep SBP on ddx)
- **Metabolic** (hypoglycemia, electrolyte imbalance, acidosis)
 - Hypoglycemia - D10 infusion
 - Acidosis - Bicarb infusion
 - Electrolytes - (hyponatremia, hypokalemia, hypophosphatemia)

- **Detoxification** with NAC if due to acetaminophen ingestion

Get your medicine/GI/ICU colleagues on board for these!

Transfer to a transplant centre may be in the cards for severe disease

[3] What is Charcot's triad and Reynold's pentad?

These triads describe the spectrum of disease seen in ascending cholangitis.

Charcot's Triad

1. Fever
2. RUQ pain
3. Jaundice

Reynold's Pentad

1. Charcot's Triad plus
2. Shock
3. Altered mental status

[4] What is the "1000s Club" and how do you become a member?

There are a few things that will put your ALT/AST in the thousands:

1. Viral hepatitis



2. Ischemic liver (hypotension, hypoxia, sepsis)
3. Drugs/Tox (acetaminophen)
4. Autoimmune hepatitis
5. Gallstone disease (acute bile duct obstruction)
6. Budd Chiari Syndrome (hepatic venous outflow obstruction)
7. Hepatic artery ligation/cealic artery ligation

This is a good list to know. It's not a club you ever want to join.