



LIVER FUNCTION TESTS

Megan Chan, Chief Resident

UHCMC 2017



GENERAL APPROACH

- ❖ **Cholestatic**—intrahepatic/extrahepatic biliary obstruction
- ❖ **Hepatocellular**—hepatocyte damage (e.g. viral hepatitis, drugs/toxins, ETOH, ischemia, malignant infiltration)
- ❖ **Isolated hyperbilirubinemia**—e.g. congestive hepatopathy



GUESS THE LFTS

What's the Diagnosis?

Pt with hx of intermittent abdominal pain associated with meals undergoes RUQ US.



GALLBLADDER

<http://radiopaedia.org/articles/cholelithiasis>

CHOLELITHIASIS

If Asymptomatic:

❖ AST

- Normal

❖ ALT

- Normal

❖ Alk Phos

- Normal

❖ T bili

- Normal

If Pass a Stone:

❖ AST

- Elevated

❖ ALT

- Elevated

❖ Alk Phos

- Elevated

❖ T bili

- Normal



<http://radiopaedia.org/articles/cholelithiasis>

What's the diagnosis?

Pt presenting with
RUQ abdominal pain,
fevers/chills, vomiting.
CT scan shown on
right.



<http://radiopaedia.org/images/1780983>

<http://radiopaedia.org/cases/acute-cholecystitis-4>

ACUTE CHOLECYSTITIS

❖ AST

- Normal → Elevated

❖ ALT

- Normal → Elevated

❖ Alk Phos

- Elevated

❖ T bili

- Normal

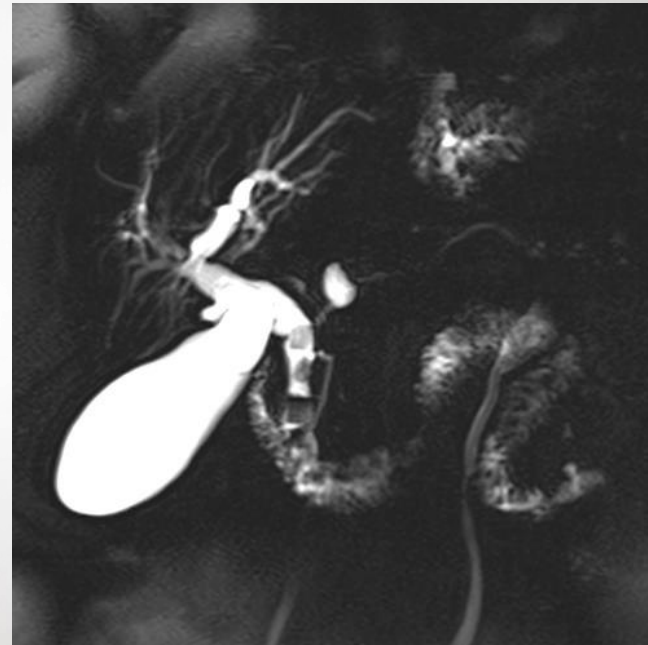


<http://radiopaedia.org/images/1780983>

<http://radiopaedia.org/cases/acute-cholecystitis-4>

What's the diagnosis?

Pt with hx of gallstones
presenting with biliary colic who
undergoes MRCP (shown on
right).



<http://radiopaedia.org/articles/choledocholithiasis>

CHOLEDOCHOLITHIASIS

❖ AST

- Normal → Elevated

❖ ALT

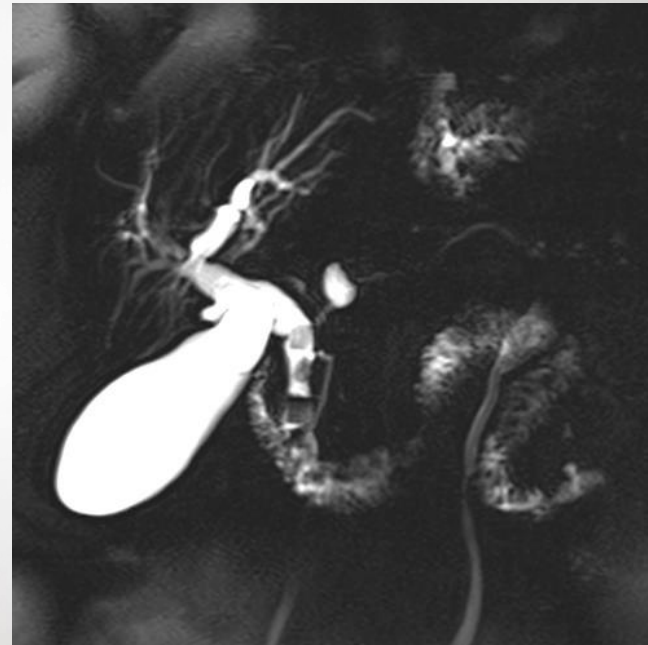
- Normal → Elevated

❖ Alk Phos

- Elevated

❖ T bili

- Elevated



<http://radiopaedia.org/articles/choledocholithiasis>



PRACTICE CASES

CASE 1

46 y/o female presents to your clinic with intermittent RUQ pain and heartburn. Vitals are stable and exam is unremarkable. LFTs are wnl.

What is the next best imaging test to confirm your diagnosis?

RUQ ultrasound
sensitivity and specificity >
95% for stones > 2mm

Pure cholesterol stones are hypodense to bile and calcified gallstones are hyperdense to bile and some gallstones may be isodense to bile and may therefore be missed by CT.

CHOLELITHIASIS

- ❖ Gallstones or sludge in the gallbladder
- ❖ **~10% population, symptomatic in only 25% of cases**
- ❖ 3 types of stones:
 - **Cholesterol stones**—associated with obesity, DM, HLD, OCP use, multiple pregnancies, advanced age, Crohn's disease, ileal resection, cirrhosis, CF
 - **Pigment stones**
 - Black stones—hemolysis, alcoholic cirrhosis
 - Brown stones—biliary tract infection
 - **Mixed stones = 80%**

CHOLELITHIASIS

Pt asks about surgical treatment. What do you tell her?

Only 1-2 % of patients with asymptomatic gallstone disease will develop complications that will require surgery yearly.

4 factors should be considered in evaluation for surgery:

- 1) Symptoms that are severe and frequent enough to necessitate surgery.
- 2) Hx of prior complications of gallstone disease (e.g pancreatitis, acute cholecystitis)
- 3) Presence of anatomic factors that increase the likelihood of complications (e.g. porcelain gallbladder, congenital biliary tract abnormalities)
- 4) Large stones >3cm

Ursodeoxycholic acid can be used to dissolve gallstones. It decreases the cholesterol saturation of bile & allows the dispersion of cholesterol from stones. It is only effective, however, for radiolucent stones <10mm.



CASE 2

55 y/o male with PMHx of recurrent pancreatitis presents to the ED with RUQ abdominal pain and vomiting. Pt is found to be febrile and hypotensive. IV fluids are initiated and the following labs are obtained:
WBC 13,000, AST 25, ALT 30, Alk Phos 450, T bili 1.0, Lipase 20

What is the most likely diagnosis?

CASE 2

55 y/o male with PMHx of recurrent pancreatitis presents to the ED with RUQ abdominal pain and vomiting. Pt is found to be febrile and hypotensive. IV fluids are initiated and the following labs are obtained:
WBC 13,000, AST 25, ALT 30, Alk Phos 450, T bili 1.0, Lipase 20

What is the most likely diagnosis?

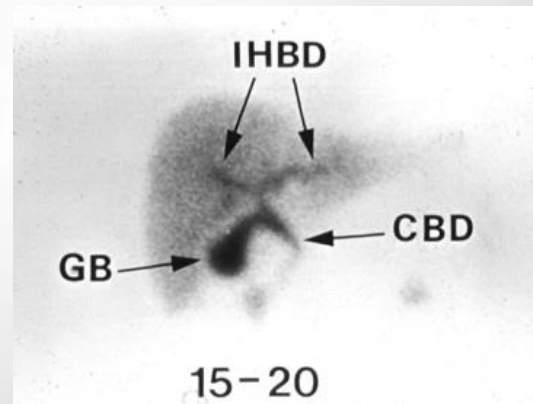
Acute Cholecystitis

❖ You obtain a RUQ ultrasound and the results are inconclusive. What can you order next?

HIDA scan

Diagnosis confirmed if don't visualize gallbladder w/in 4 hours.

97% sensitive, 96% specific.



http://www.stitch.luc.edu/lumen/MedEd/Radiology/curriculum/Procedures/HIDA_scan1.htm

ACUTE CHOLECYSTITIS

- ❖ **Inflammation of gallbladder 2/2 obstruction of cystic duct**
- ❖ Develops in 10% of those with cholelithiasis
- ❖ Clinical features:
 - RUQ tenderness >4-6 hrs \pm rebound
 - **Murphy's sign** = inspiratory arrest during deep palpation of RUQ
 - Low grade fever, leukocytosis, nausea, vomiting, hypoactive bs
- ❖ Diagnosis:
 - **US is test of choice**
 - Distended gallbladder with thickened wall > 5mm, pericholecystic fluid, \pm stones
 - **Sonographic Murphy's sign has higher PPV and NPV than physical exam Murphy's**
 - **HIDA radionuclide scan if US inconclusive**

ACUTE CHOLECYSTITIS

❖ How would you treat this patient?

- **Supportive care:**
 - IV fluids
 - NPO
 - IV abx (Zosyn, Unasyn, 3rd gen cephalosporin + Flagyl)
 - Analgesics
 - Electrolyte replacement
- **Semiurgent Cholecystectomy within 72 hrs** to avoid gangrenous/emphysematous cholecystitis

CASE 3

52 y/o male transferred from an OSH for intermittent abdominal pain and progressive jaundice over the past 2 days. Further history reveals symptoms consistent with biliary colic. Exam shows a patient in mild distress with tenderness in the RUQ and jaundice. Labs are significant for: AST 450, ALT 520, Alk Phos 630, T Bili 4.2

What is the most likely diagnosis ?

CASE 3

52 y/o male transferred from an OSH for intermittent abdominal pain and progressive jaundice over the past 2 days. Further history reveals symptoms consistent with biliary colic. Exam shows a patient in mild distress with tenderness in the RUQ and jaundice. Labs are significant for: AST 450, ALT 520, Alk Phos 630, T Bili 4.2

What is the most likely diagnosis?

Choledocholithiasis

CHOLEDOCHOLITHIASIS

- ❖ **Gallstones within the common bile duct or common hepatic duct, formed in situ or passed from gallbladder**
- ❖ Presentation: asymptomatic (~50%) → biliary colic → ascending cholangitis, obstructive jaundice, acute pancreatitis
- ❖ Definitions of dilated bile duct
 - >6mm + 1mm per decade above 60 y/o
 - >10mm post-cholecystectomy
 - Dilated intrahepatic biliary tree

CHOLEDOCHOLITHIASIS

❖ Diagnostic studies:

- Transabdominal US 13-55% sensitivity¹
- Endoscopic US higher sensitivity and specificity for intraductal stones
- CT w/ contrast 65-88% sensitive²
- CT cholangiography 93% sensitive, 100% specific but difficult to perform³
- **MRCP and ERCP both have sensitivities and specificities approaching 100%**⁴

CHOLEDOCHOLITHIASIS

ERCP



<http://radiopaedia.org/images/2413474>

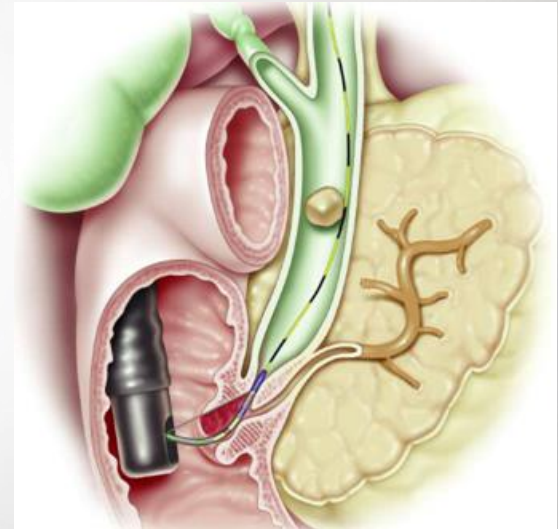
MRCP



http://www.jcdr.net/article_fulltext.asp?issn=0973-709x&year=2013&volume=7&issue=9&page=1941&issn=0973-709x&id=3365

❖ **How would you treat this patient?**

- **Urgent ERCP with sphincterotomy, stone extraction, stent placement**
 - Successful in 90% of patients
 - Complication rates 6-24%⁵, including pancreatitis



<http://patients.gi.org/files/2012/01/ERCP-Figure-2.png>

CASE 4

50 y/o female admitted to the MICU for AMS. Vitals include temp 39, HR 110, BP 90/60, RR 20, sat 96% on RA. Exam reveals a somnolent female with jaundice, scleral icterus, and guarding upon palpation of the RUQ. Labs reveal: WBC 16,000, AST 160, ALT 200, Alk Phos 650, T bili 8.0. Blood cultures are pending.

What is the most likely diagnosis?

CASE 4

50 y/o female admitted to the MICU for AMS. Vitals include temp 39, HR 110, BP 80/60, RR 20, sat 96% on RA. Exam reveals a somnolent female with jaundice, scleral icterus, and guarding upon palpation of the RUQ. Labs reveal: WBC 16,000, AST 160, ALT 200, Alk Phos 650, T bili 8.0. Blood cultures are pending.

What is the most likely diagnosis?

Acute Cholangitis

CHOLANGITIS

❖ Infection of biliary tract 2/2 obstruction → biliary stasis & bacterial overgrowth

- Ecoli & Klebsiella 70%, Enterococcus & Anaerobes (15%)

❖ Choledocholithiasis accounts for 60% of cases

❖ Other causes: pancreatic/biliary neoplasm, strictures, s/p ERCP, choledochal cysts

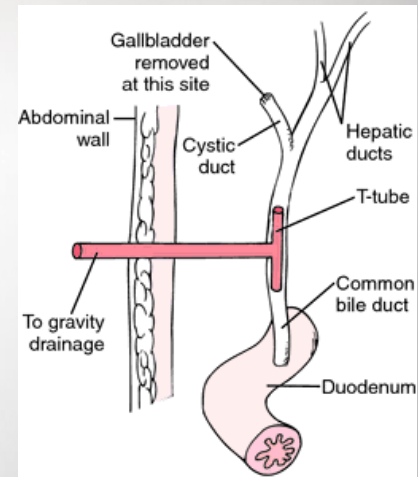
❖ Clinical features:

- **Charcot's Triad:** RUQ pain + Jaundice + Fever
 - Present in 60-79%
- **Reynolds' Pentad:** Charcot's triad + Hypotension + AMS
 - Present in ~15%
- Medical emergency if fever $>40^{\circ}\text{C}$, septic shock, peritoneal signs, or bilirubin > 10

CHOLANGITIS

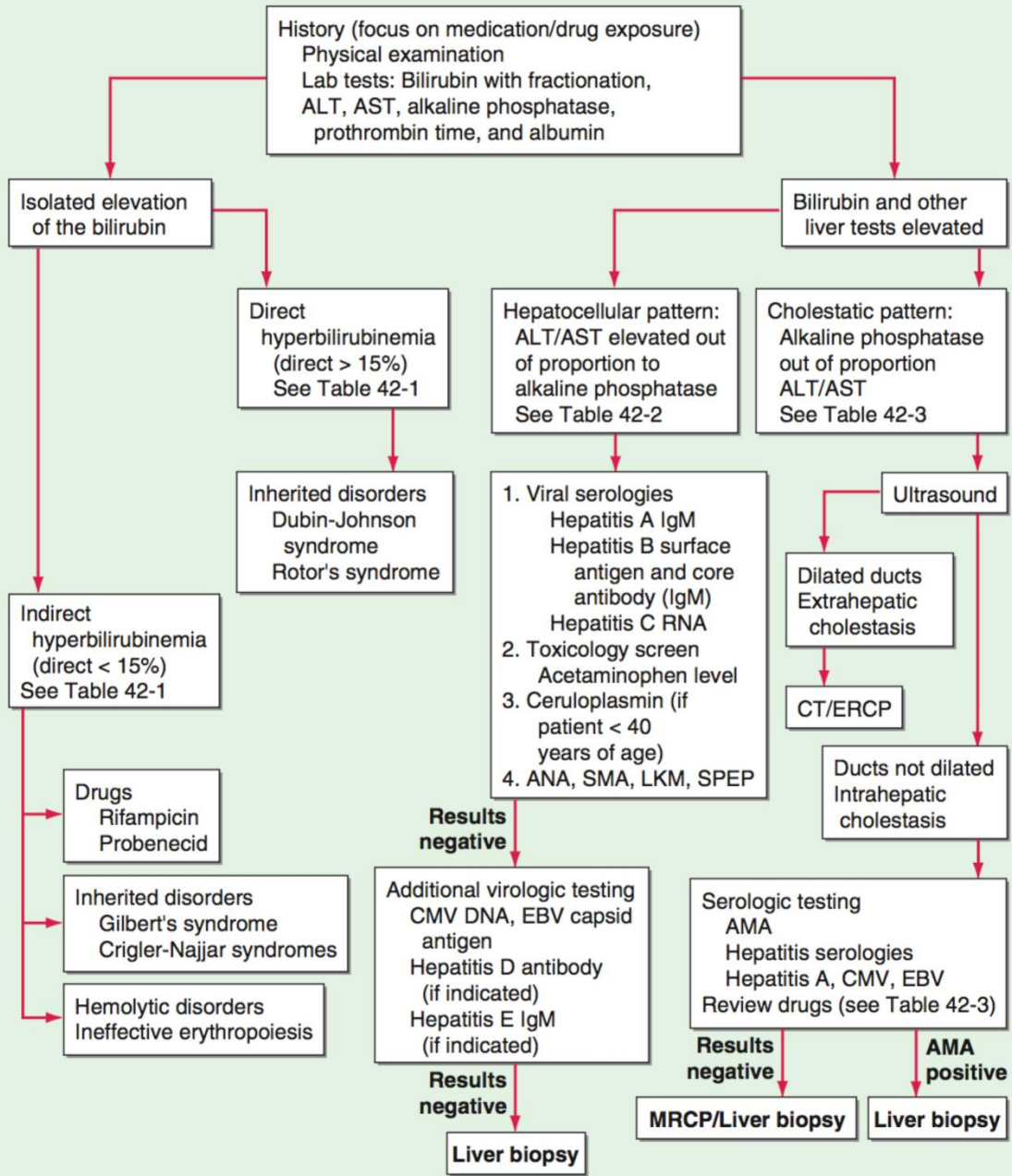
❖ How would you treat this patient?

- **IV abx** (Zosyn, 3rd gen cephalasporin), **IV fluids**
- Interventions:
 - **ERCP sphincterotomy**
 - **PTC** (percutaneous transhepatic cholangiography)
decompression via catheter placement
 - **T-tube insertion** via laparotomy



<http://img.tfd.com/mk/C/X2604-C-47.eps.png>

ALGORITHM FOR PATIENT WITH JAUNDICE



SUMMARY

Cholelithiasis	Cholecystitis	Choledocholithiasis	Cholangitis
Stones in gallbladder	Obstruction of cystic duct → Inflammation	Gallstones in CBD	Infection of biliary tract
Biliary colic	Murphy's sign Fever, ↑ WBC	Biliary colic, jaundice	Charcot's triad, Reynold's pentad
Watchful waiting, Elective surgery	IV abx, cholecystectomy	ERCP, IV abx	ERCP vs PTC vs T-tube, IV abx



GUESS THE LFTS

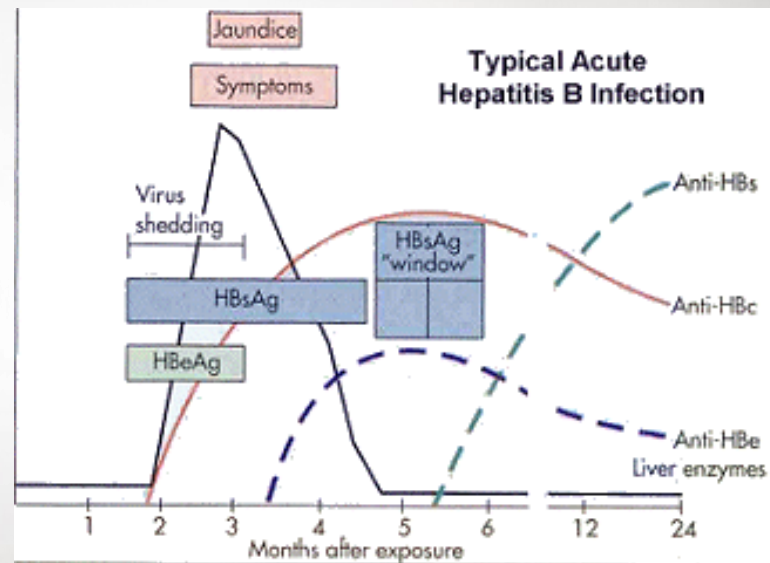


What's the diagnosis?

❖ Pt presents with insidious onset of fatigue, anorexia, nausea, RUQ tenderness. He's also noticed that his urine has been darker for the past couple of days and that his eyes have a yellow hue.

ACUTE HEPATITIS

- ❖ AST
 - **Elevated**
- ❖ ALT
 - **Elevated**
- ❖ Alk Phos
 - **Normal → Elevated**
- ❖ T bili
 - **Normal → Elevated**




<http://www.atsu.edu/faculty/chamberlain/Website/lectures/lecture/hepatit2.htm>

DDX FOR ACUTE HEPATITIS

- ❖ **Shock liver:** AST & ALT >50x ULN
- ❖ **Drugs** (e.g. Tylenol overdose, Isoniazid, Fenofibrate)
- ❖ **Toxins** (e.g. Alcohol, Mushrooms)
- ❖ **Viral** (e.g. Hep A, Hep B, HSV, VZV, CMV, EBV): AST & ALT >25x ULN
- ❖ **Wilson's**
- ❖ **Vascular**—Budd-Chiari
- ❖ **AIH**
- ❖ **NASH:** AST & ALT <4x ULN
- ❖ **HELLP syndrome**

TREATMENT

- ❖ Tylenol toxicity—**N-acetylcysteine**
- ❖ AIH— **Prednisone** 60mg daily (taper)- azathioprine or 6-mercaptopurine
- ❖ Budd-Chiari—**TIPS**
- ❖ Wilson's dz—**Plasma exchange** to remove copper → liver transplant
- ❖ Hep B—**Antiviral therapy**



Causes of mild or moderate increases in AST ALT

Hepatic disease		Nonhepatic disease
ALT predominant (AST/ALT <1)	AST predominant (AST/ALT ≥1)	
Drug-induced liver injury	Alcohol-related hepatitis	Muscle injury (strenuous exercise, myopathy)
Chronic viral hepatitis (HBV, HCV)	Cirrhosis due to viral hepatitis or NAFLD	Adrenal insufficiency
Occupational, toxin-related hepatocellular damage	Wilson disease	Myocardial infarction, heart failure
Autoimmune hepatitis		Anorexia nervosa
NAFLD		Thyroid disease
Genetic disorders <ul style="list-style-type: none">• Wilson disease• Hemochromatosis• Alpha-1 antitrypsin deficiency		Celiac disease
Congestive hepatopathy		Macro AST
Malignant infiltration of the liver		

CIRRHOSIS

❖ AST

- Normal/Elevated

❖ ALT

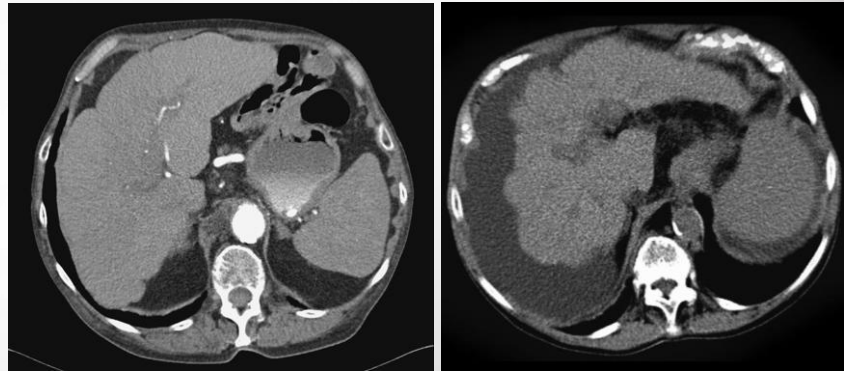
- Normal/Elevated

❖ Alk Phos

- Normal/Elevated

❖ T bili

- Normal/Elevated



<http://radiopaedia.org/cases/cirrhosis>

CIRRHOSIS

❖ As cirrhosis progresses, Total Bili increases because the liver can still conjugate bilirubin but can't excrete it.

- ❖ **MELD-Na Score for 3 month mortality:**
- | | |
|--------------------|------------------------|
| • Total bilirubin | 40 + --71.3% mortality |
| • INR | 30-39– 52.6% mortality |
| • Sodium | 20-29– 19.6% mortality |
| • Serum creatinine | 10-19 – 6.0% mortality |
| • ± Dialysis | <9 – 1.9% mortality |

CHILD PUGH SCORE

❖ Classification to assess severity of liver disease & hepatic functional reserve

Points	1	2	3
Ascites	None	Controlled	Uncontrolled
Bilirubin	<2.0	2.0-3.0	>3.0
Encephalopathy	None	Minimal	Severe
INR	<1.7	1.7-2.2	>2.2
Albumin	>3.5	2.8-3.5	<32.8

Classification	A	B	C
Total points	5-6	7-9	10-15
1-yr survival	100%	81%	45%
2-yr survival	85%	57%	35%

LIVER TRANSPLANT

❖ Evaluate when Child Class B or MELD \geq 10

❖ **Indications:**

- Recurrent/severe encephalopathy
- Refractory ascites
- SBP
- Recurrent variceal bleeding
- Hepatorenal or Hepatopulmonary syndrome
- HCC if no single lesion $>$ 5cm or \leq 3 lesions w/ largest \leq 3 cm
- Fulminant hepatic failure

❖ **Contraindications:**

- Advanced HIV, active substance abuse (ETOH w/in 6 mo), sepsis, extrahepatic malignancy, severe comorbidity (esp cardiopulm), persistent non-compliance

“liver stamp”

- ❖ Liver US with dopplers (for portal vein thrombosis)
- ❖ ANA, Anti smooth muscle Ab (autoimmune)
- ❖ Anti-mitochondrial Ab (primary biliary cirrhosis)
- ❖ Ceruloplasmin (Wilson's)
- ❖ Ferritin + Iron studies w/ TIBC (Hemochromatosis)
- ❖ HepBs Ag, HepBs Ab, HepBc Ab
- ❖ HepC Ab, HepC PCR
- ❖ Alpha-antitrypsin



“liver stamp”

AVERAGE COST?

~\$1,200

CIRRHOSIS ETIOLOGY

❖ Fatty liver diseases

- Alcoholic liver disease
- NASH/NAFLD

❖ Viral hepatitis: Hep B, C, D

❖ Autoimmune

- Autoimmune hepatitis
- Primary biliary cirrhosis
- Primary sclerosing cholangitis

❖ Cardiovascular

- Budd-Chiari syndrome
- Chronic right heart failure

❖ Chronic biliary disease

- Recurrent bacterial cholangitis
- Bile duct stenosis

❖ Storage diseases

- Hemochromatosis
- Wilson disease
- α -1-antitrypsin deficiency

❖ Meds: APAP toxicity, MTX

❖ Cryptogenic 10-15%

DIAGNOSTIC IMAGING

❖ **Ultrasound**

- Surface nodularity: 88% sensitive, 82-95% specific (1)

❖ CT insensitive in early cirrhosis

❖ MRI also insensitive in early cirrhosis, but significant role in assessing small hepatocellular carcinoma (HCC)—develops in 10-25%

❖ **Liver biopsy = gold standard for diagnosis**

TREATMENT

❖ Ascites

- **Furosemide + Spironolactone** with goal negative ~1L/day (~80% effective)
 - Lasix: Aldactone ratio of 2:5 helps maintain K⁺ (Lasix 40mg qday, Aldactone 100mg qday initially)
- **Low-sodium diet** (1-2 g/day)

❖ Refractory Ascites= no response on max doses of Lasix (160mg) & Aldactone (400mg) or ↑ Cr

- **LVP** 4-6L (does not improve mortality)
 - Albumin replacement controversial. AASLD 2009 guidelines recommend if >5L removed, provide 6-8 g/L of albumin 25% (IIA, Grade C)
 - If >5L removed, can have post-paracentesis circulatory dysfxn via RAAS activation
- **TIPS** (↓ ascites in 75%, improves mortality but ↑ HE, 40% need revision for stent stenosis)



Last but not least...

Ascites fluid

The special “LFT”

PARACENTESIS

❖ What tests would you send?

- 4 C's: Cells, Culture, Chemistry, Cytology
- Cell count and differential, gram stain, culture, albumin, total protein, glucose, LDH, cytology
- Optional: amylase, bilirubin, Cr, TG, AFB cx + adenosine deaminase

❖ How do you calculate the SAAG?

- $SAAG = [\text{Serum albumin}] - [\text{Ascites albumin}]$

❖ What does the SAAG indicate?

- If ≥ 1.1 g/dL, portal HTN is very likely (~97% accurate¹)
- If < 1.1 g/dL, portal HTN is unlikely.

Runyon et al. "The serum-ascites albumin gradient is superior to the exudates-transudate concept in the differential diagnosis of ascites."
Annals of Internal Medicine 1992; 117:215-20.

PARACENTESIS

SAAG \geq 1.1

- ❖ Sinusoidal
 - Cirrhosis(81%), SBP
 - Acute hepatitis
 - Extensive malignancy (HCC/mets, 10%)
- ❖ Postsinusoidal
 - R heart failure (3%)
 - Budd-Chiari Syndrome
- ❖ Presinusoidal
 - Portal/splenic vein thrombosis

SAAG $<$ 1.1

- ❖ Peritonitis: TB, ruptured viscus
- ❖ Peritoneal carcinomatosis
- ❖ Pancreatitis
- ❖ Vasculitis
- ❖ Hypoalbuminemia (e.g. nephrotic syndrome)
- ❖ Meigs' syndrome (ovarian tumor)
- ❖ Bowel obstruction/infarction
- ❖ Post-op lymphatic leak

Runyon et al. "The serum-ascites albumin gradient is superior to the exudates-transudate concept in the differential diagnosis of ascites." *Annals of Internal Medicine* 1992; 117:215-20.

THE EXTRAS

- ❖ If the SAAG ≥ 1.1 , how can you tell the difference between cardiac ascites and cirrhosis ascites?
 - **Cirrhosis (AFTP < 2.5) vs Cardiac ascites (AFTP > 2.5)**

- ❖ Does traumatic taps affect your PMN count?
 - **Subtract 1 PMN for every 250 RBC.**

- ❖ How can you tell if a patient has SBP?
 - **Cell count: PMN ≥ 250 cells/ μ L (93% sensitivity, 94% specificity)**

Runyon et al. "The serum-ascites albumin gradient is superior to the exudates-transudate concept in the differential diagnosis of ascites."
Annals of Internal Medicine 1992; 117:215-20.

BACTERIAL PERITONITIS

Type	Ascites Cell Count	Ascites Culture
Sterile	< 250 PMNs	Neg
Spontaneous bacterial peritonitis (SBP)	\geq 250 PMNs	+ (1 organism)
Culture neg neutrocytic ascites (CNNA)	\geq 250 PMNs	Neg
Nonneutrocytic bacterascites (NNBA)	< 250 PMNs	+ (1 organism)
Secondary	\geq 250 PMNs	+ (polymicrobial)
Peritoneal dialysis-associated	\geq 100, PMNs predom	+

WHEN TO TAP/RETAP

- ❖ New ascites
- ❖ Admission of all patients with cirrhotic ascites
- ❖ Deterioration in clinical status
- ❖ Complication of cirrhosis (GI bleed, confusion)
- ❖ Polymicrobial culture or + culture with PMN < 250 (MNB that may be early SBP)
- ❖ Retap 24-48 hrs after treatment started in pts with PMN > 1000 (associated with 88% mortality) or lack of improvement.

REFERENCES

- ❖ Adamek HE, Albert J, Weitz M et-al. A prospective evaluation of magnetic resonance cholangiopancreatography in patients with suspected bile duct obstruction. *Gut*. 1998;43 (5): 680-3.
- ❖ Agabegi SS, Agabegi ED. *Step –Up to Medicine*, 3rd ed. 2013. Lippincott Williams & Wilkins. Philadelphia, PA.
- ❖ Caoili EM, Paulson EK, Heyneman LE et-al. Helical CT cholangiography with three-dimensional volume rendering using an oral biliary contrast agent: feasibility of a novel technique. *AJR Am J Roentgenol*. 2000;174 (2): 487-92.
- ❖ Cronan JJ. US diagnosis of choledocholithiasis: a reappraisal. *Radiology*. 1986;161 (1): 133-4.
- ❖ Guardino JM. *Primo Gastro*. 2008. Lippincott Williams & Wilkins. Philadelphia, PA.
- ❖ Miller FH, Hwang CM, Gabriel H et-al. Contrast-enhanced helical CT of choledocholithiasis. *AJR Am J Roentgenol*. 2003;181 (1): 125-30.
- ❖ Sabatine, MS. *Pocket Medicine*, 4th ed. 2011. Lippincott Williams & Wilkins. Philadelphia, PA.
- ❖ Sugiyama M, Suzuki Y, Abe N et-al. Endoscopic retreatment of recurrent choledocholithiasis after sphincterotomy. *Gut*. 2004;53 (12): 1856-9.
- ❖ Wiener C, Fauci AS, Braunwald E, et al. *Harrison’s Principles of Internal Medicine Self-Assessment & Board Review*, 17th ed. 2008. McGraw Hill. New York, NY.
- ❖ http://medicine.ucsf.edu/education/resed/Chiefs_cover_sheets/SBP,%20cirrhosis,%20empyema.pdf
- ❖ <http://radiopaedia.org>
- ❖ Special thanks to Dr. Caroline Soyka for the inspiration!