Reviewed By Tarfa Alsharidi

MED439 KING SAUD UNIVERSITY

# Approach to Management of Chronic Liver Disease

**Objectives** (regarding the Blueprint) **:**

1. List the common causes of liver cirrhosis in Saudi Arabia
2. List the complications of advanced liver disease.
3. To be able to identify patients with hepatic encephalopathy to understand the key elements in the management.
4. To be able to interpret the results of the ascetic tap to be able to diagnose the spontaneous bacterial peritonitis (SBP)
5. To understand the key points in the management SBP


**439 Team Leader:**

Nourah Alklaib

**439 Team Member:**

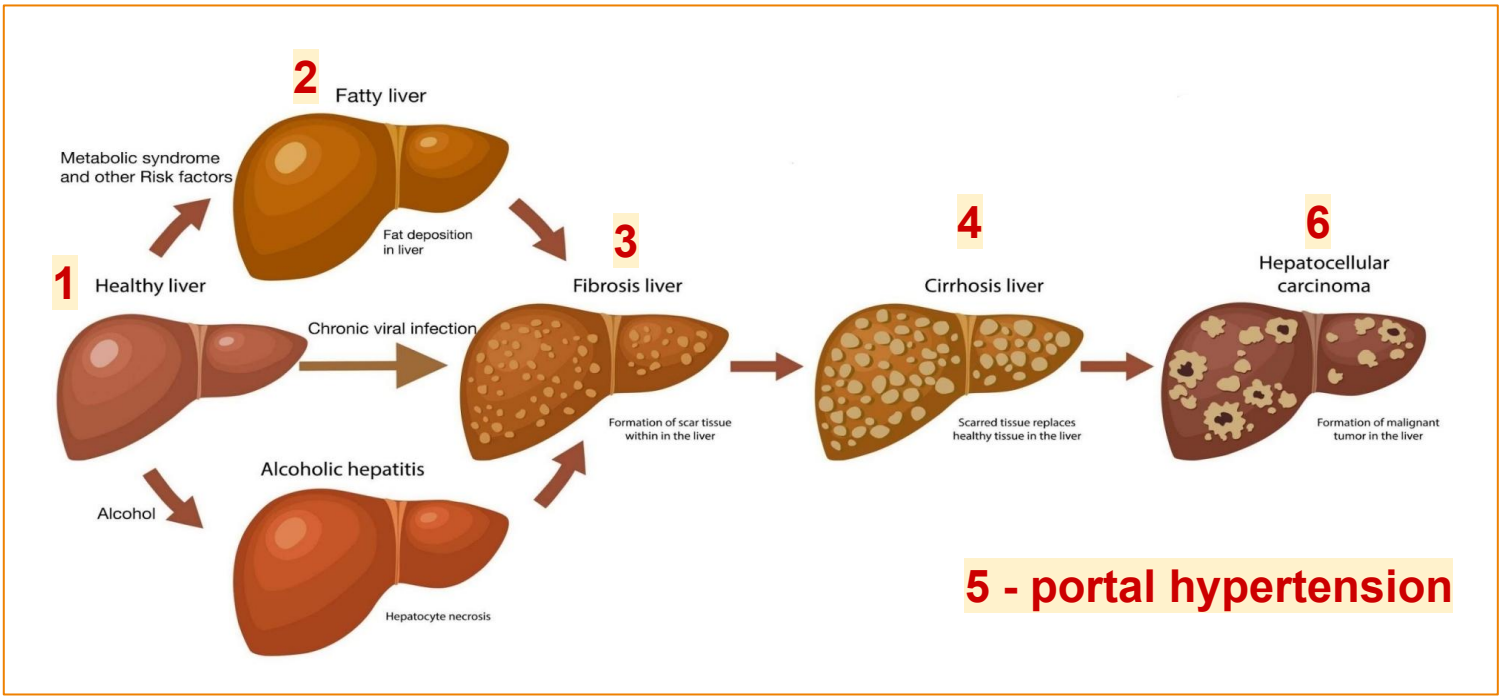
Shaden Fahad


**Editing File**

Color Index

- Slides / Reference Book
- Doctor notes
- OnlineMeded / Amboss
- Important
- Extra

## Stages of Liver Disease :




## What are the most common causes of cirrhosis?

**Most common causes of cirrhosis are:**

- Chronic viral hepatitis (hepatitis B and hepatitis C)[1]
- Alcoholic liver disease[2]
- **Nonalcoholic fatty liver disease**[2]
- Hemochromatosis

**Other causes :**

- Infections : Hepatitis B, Hepatitis C, Schistosomiasis
- Toxins: Alcohol, Herbal
- Metabolic: Hemochromatosis, Wilson's, Alpha-1 Antitrypsin deficiency, Amyloidosis, NASH
- Autoimmune: Autoimmune Hepatitis, PSC, PBC
- Vascular: Budd-Chiari Syndrome
- Cardiac: Heart Failure[3] (Congestive hepatopathy)

**The commonest causes of liver cirrhosis is Saudi Arabia were:**
Hepatitis C virus (HCV) in 73.3% of patients tested for it and hepatitis B virus (HBV) in 23.2%. Complications related to the procedures were exceedingly low.

1- In the past it was first common cause, but now with vaccine it is second common cause.
2- Most common cause.
3- Especially right side heart failure.

## History taking:[1]

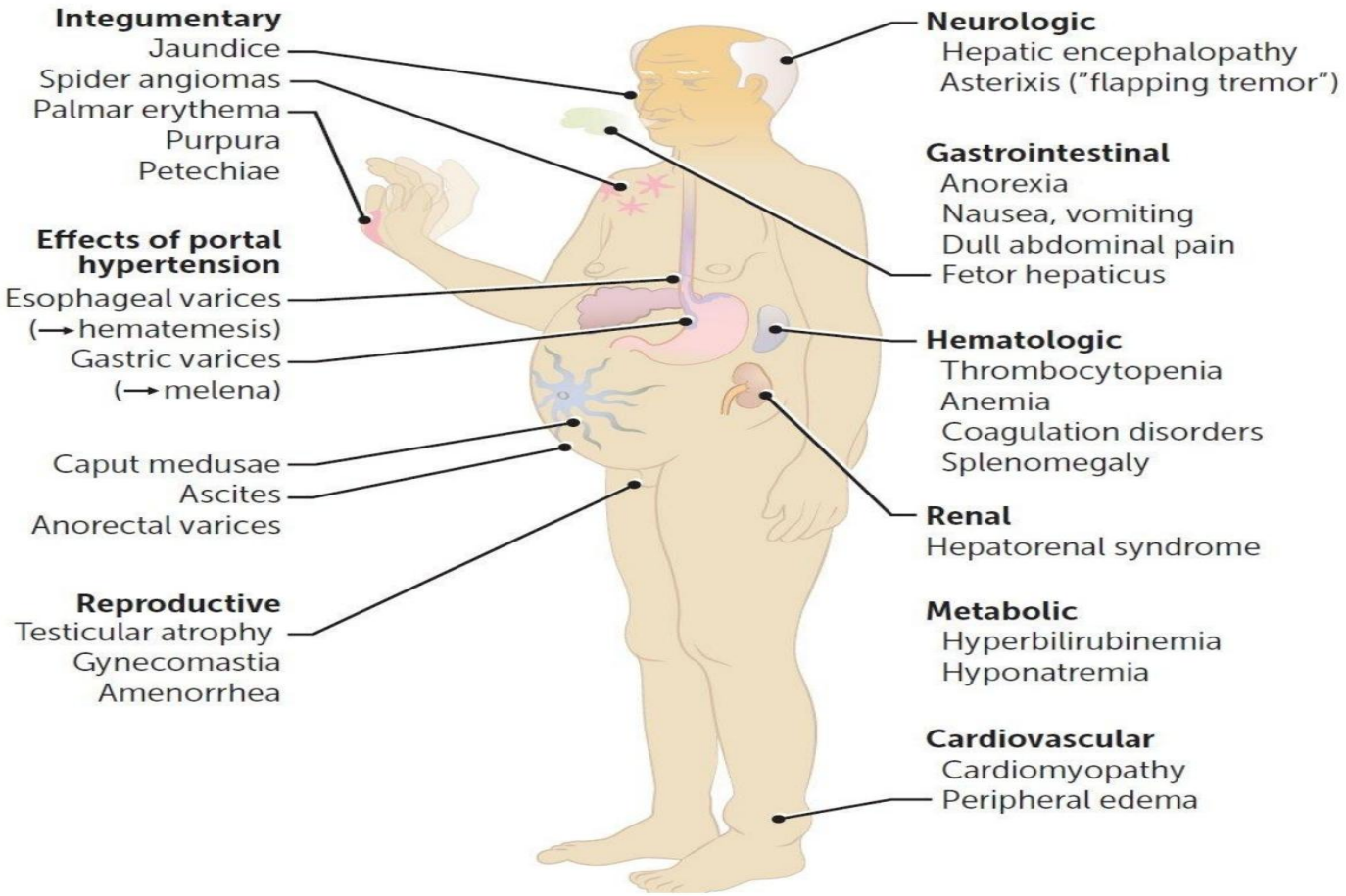
| Liver condition | Symptoms and signs and history hints |
|---|---|
| Alcoholic liver disease | History of alcohol abuse (duration, type and amount) |
| Chronic hepatitis B and C [2] | IV drug use, sexual contact, tattoos and remote blood transfusion, family history, vertical transmission . |
| Primary sclerosing cholangitis (PSC) | Strong association with inflammatory bowel disease |
| Hereditary hemochromatosis | Family history of cirrhosis |
| Wilson disease | Family or personal history of cirrhosis at a young age,<br>neurologic or psychiatric symptoms |
| Alpha-1 antitrypsin deficiency | Family or personal history of cirrhosis at a young age |
| Nonalcoholic fatty liver disease (NAFLD) | History of diabetes mellitus , metabolic syndrome or hyperlipidemia. |
| Autoimmune hepatitis | Associated with common autoimmune disorders, e.g.<br>autoimmune thyroiditis, rheumatoid arthritis, type 1<br>diabetes mellitus, ulcerative colitis, celiac disease, SLE |
| Congestive hepatopathy | History of right-sided heart failure, constrictive<br>pericarditis, mitral stenosis, tricuspid regurgitation,<br>cor pulmonale, cardiomyopathy |

1- Usually they present with ascites, jaundice and upper GI bleeding.
2- But not hepatitis A, as it fecal-oral transmission.

## Symptoms of CLD :

• Can be compensated or decompensated cirrhosis
• Can be asymptomatic[1] or symptomatic cirrhosis
• Symptoms of cirrhosis include: anorexia, weight loss, weakness, fatigue, muscle cramps, lower limb edema, diarrhea, easy bruisability, jaundice or pruritus
• Patients with decompensated cirrhosis may present with jaundice, pruritus, signs of upper gastrointestinal bleeding (hematemesis, melena, hematochezia), abdominal distension from ascites, or confusion due to hepatic encephalopathy.
• In women, amenorrhea or irregular menstrual bleeding.
• In men with cirrhosis may develop hypogonadism (impotence, infertility, loss of sexual drive, and testicular atrophy)

## Clinical manifestations of Cirrhosis?




1- Mostly asymptomatic, 80% of them diagnosed incidentally.

# Important Diagnostic Tests in Common Liver Diseases :

| Disease | Diagnostic Test |
|---|---|
| Hepatitis A (acute)[1] | Anti-HAV IgM |
| Hepatitis B ( acute) | HBsAg and anti-HBc IgM |
| Hepatitis B ( chronic) | HBsAg and HBeAg and/or HBV DNA. (To screen for Chronic HBV, check HBsAg) |
| Hepatitis C | Anti-HCV Ab and HCV RNA. (To screen for Chronic HCV, check Anti-HCV Ab) |
| Autoimmune hepatitis | ANA or ASMA, anti-LKM-ab, elevated IgG levels, and compatible histology |
| Primary biliary cholangitis | AMA, elevated IgM levels, and compatible histology |
| Primary sclerosing cholangitis | P-ANCA, cholangiography MRCP or ERCP |
| **Nonalcoholic steatohepatitis** | Ultrasound or CT evidence of fatty liver and **compatible histology** |
| α1 Antitrypsin disease | Reduced α-1 antitrypsin levels |
| Wilson's disease | Decreased serum ceruloplasmin, increased **urinary copper**, increased hepatic copper level |
| **Hemochromatosis** | Elevated **iron** saturation and **serum ferritin**; genetic testing for HFE gene mutations |
| Hepatocellular cancer | Elevated α-fetoprotein, radiological imaging |

1- Self-limiting, does not cause chronicity.

# Investigations

## Lab Test :

- Moderately elevated **aminotransferases** (often with an AST:ALT ratio >1)
- Elevated ALP (2 to 3 times the ULN)
- Hyperbilirubinemia
- Thrombocytopenia
- Leukopenia/neutropenia
- Anemia
- Low serum albumin
- Prolonged PT/elevated **INR**
- Hyponatremia
- Elevated serum creatinine

## Radiology ( US, CT ) :

- Small, nodular liver and shrunk liver.
- Ascites
- Hepatocellular carcinoma
- Portal/splenic/superior mesenteric vein thrombosis
- Portosystemic collaterals

## Diagnostic Confirmation :

**To confirm and support the clinical and radiologic manifestations if needed:**

•Invasive:

Biopsy (histopathology) (high risk of bleeding )

•Noninvasive tests

Elastography (e.g **fibroscan**)

## What is the course of cirrhosis?

- **Compensated Cirrhosis :**Cirrhosis without symptoms Usually, incidental finding.
- **Decompensated Cirrhosis :**Cirrhosis with symptoms (Any of the following):

1. Ascites
2. Bleeding Varices
3. Hepatic Encephalopathy
4. Jaundice

# Severity & Prognosis of CLD

## How to assess severity & prognosis of CLD ?

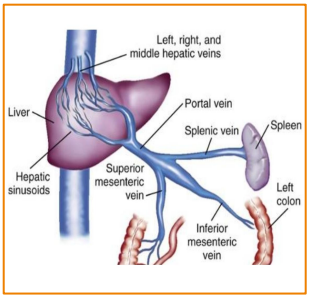
- **Child–Pugh[1] classification**
- **MELD2 score (model for end-stage liver disease)**

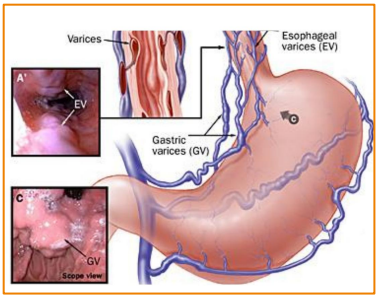
| **Child–Pugh classification** | |
|---|---|
| **5 variables of Child–Pugh classification?**<br>**Bake Another Pie At Eleven** | **Classes of Child–Pugh classification** |
| Bilirubin | class A (well-compensated disease) |
| Albumin | |
| PT (or INR) | class B (significant functional compromise) |
| Ascites | |
| Encephalopathy | class C (decompensated disease) |

1-To know if compensated or decompensated
2- Guide us for who is candidate for liver transplantation

# Common complications of Cirrhosis[1]

- Variceal hemorrhage
- Ascites
  - Spontaneous bacterial peritonitis
  - Hepatic hydrothorax
  - Hepatorenal syndrome
- Hepatocellular carcinoma (HCC)
- Hepatic encephalopathy
- Pulmonary
  - Hepatopulmonary syndrome
  - Portopulmonary hypertension

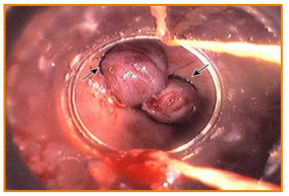


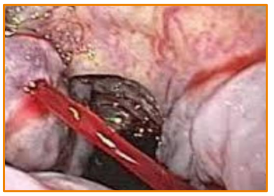




**portal hypertension** causes porto-caval shunting (hemorrhoids, caput medusa, esophageal varices) and transudation of fluid (ankle edema and ascites). Ascites is exacerbated by a ↓ protein production (hypoalbuminemia, Total protein ↓). Estrogen is degraded and converted to testosterone while estrogen excess produces gynecomastia, palmar erythema, and spider angioma. Finally, the liver controls ammonium metabolism. Excess ammonium can cause asterixis (flapping tremor) and encephalopathy. Get an Ultrasound (1st, to identify cirrhosis), a CT /MRI to evaluate nodules or masses, and finally a biopsy (best) to confirm the diagnosis and etiology. Acute hepatitis causes an elevation of liver enzymes. A cirrhotic liver is burned out; the AST/ALT will be low or smoldering just above elevated.

## Management Variceal Bleeding :

1. Endoscopic treatment
2. Octereotide
3. Antibiotics ( to prevent bacterimea)





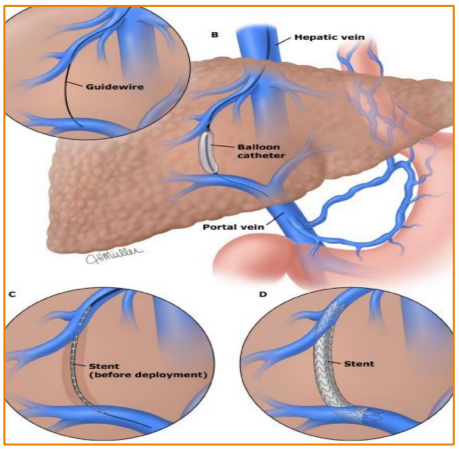
## What if endoscopic therapy fails?

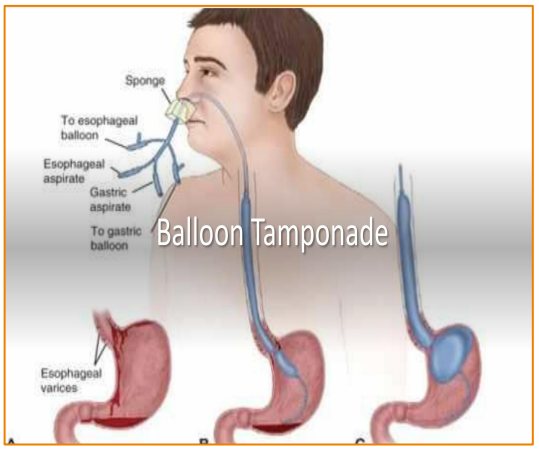
- TIPS (Transjugular Intrahepatic Portosystemic Shunt)
- Balloon Tamponade
- Surgery

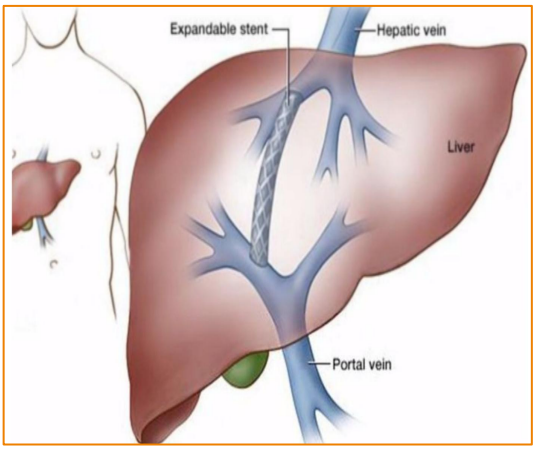
## When is TIPS also indicated?

- TIPS is indicated in:

1. Refractory Ascites
2. Uncontrolled variceal bleeding (Esophageal, Gastric)

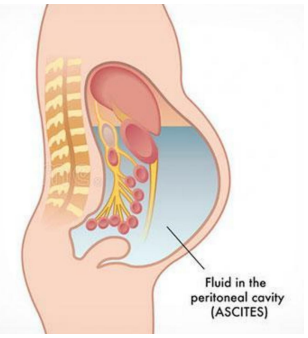


# Ascites

- Accumulation of fluid within the peritoneal cavity
- 1500 ml of fluid must be present before flank dullness is detected.
- Shifting dullness
- If no flank dullness is present less likely ascites (< 10%).
- Ascites causes:
- 85% of due to cirrhosis
- 15% other causes




## Rule of thumb: Any ascites needs to be tapped (when possible) to determine the cause of ascites :

**Ascitic Fluid Analysis :**

1. Cell count and differential
2. Albumin ( low albumin)
3. Total protein

Other optional tests: glucose, LDH, Gram stain,cultures and amylase…etc.

**How to evaluate the cause of ascites? Imp in osce**

1- Measure SAAG (Serum Albumin-Ascetic Gradient)
2- SAAG = Serum Albumin – Ascetic Albumin

| SAAG ≥ 1.1 g/dl<br>PORTAL HYPERTENSION | SAAG <1.1 g/dl<br>NON-PORTAL HYPERTENSION |
|---|---|
| Chronic Liver disease | Nephrotic syndrome |
| Budd-Chiari Syndrome | Peritoneal Tuberculosis |
| Congestive heart failure | Pancreatitis |
| | Peritoneal carcinomatosis |

| Protein ≥ 2.5 g/dl | Protein <2.5 g/dl | Protein ≥ 2.5 g/dl | Protein <2.5g/dl |
|---|---|---|---|
| Congestive heart failure | Chronic Liver disease | Pancreatitis<br>TB | Nephrotic Syndrome |
| Budd-Chiari Syndrome | | Cancinomatosis | |

## How do we treat ascites?

1. Salt Restriction (< 2g/day)
2. Diuretics (Furosemide and Spironolactone)
3. Paracenthesis +/- albumin
4. TIPS
5. Treat underlying cause.

# Spontaneous Bacterial Peritonitis (SBP)[1] :

### How do we diagnose SBP?

- Ascitic fluid polymorphonuclear leukocyte (PMN) (neutrophils) count ≥ 250 cells/mm3
- Usually one organism (gram negatives) - E-coli or klebsiella
- If multiple organisms think of secondary peritonitis

### How to treat SBP?

1. Antibiotics ( Treat with ceftriaxone for double coverage (fluoroquinolone if allergy) and prophylax with fluoroquinolone.)
2. Albumin

# Hepatic encephalopathy (HE)

### What is Hepatic encephalopathy (HE)?

- HE is a **REVIRSABLE** syndrome of impaired brain function occurring in patients with advanced liver disease
- HE is characterized by cognitive deficits, altered mental status, asterixis, and cirrhosis and impaired neuromuscular function (ranges from disorientation & asterixis to coma) is treated with lactulose.

### Common precipitants of HE :

- Drugs (benzodiazepines, narcotics or alcohol)
- Increased ammonia production, absorption or entry into the brain (excess dietary intake of protein, GI bleeding, infection, electrolyte disturbances such as hypoK, constipation or metabolic alkalosis)
- Dehydration (e.g. vomiting, diarrhea, hemorrhage or diuretics)
- Vascular occlusion (i.e. hepatic or portal vein thrombosis)
- Hepatocellular carcinoma (HCC)

## Summary:

| Hepatic Encephalopathy | SBP |
|---|---|
| Path: Ammonium | Path: Strep Gram Neg Rods |
| Pt: AMS , Asterixis | Pt: Asx, Fever, Abdo Pain |
| Dx: Clinical | Dx: Paracentesis > 250 Polys |
| Tx: Lactulose ,Rifaximin, Zinc | Tx: Ceftriaxone |
| | PPx: FQ or TMP-SMX if SBP or TP < 1.0 |

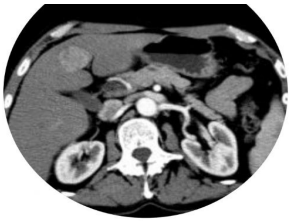
1- One of the complications of portal hypertension, if not treated lead to sepsis and death.

## Treatment of HE :

- **IDENTIFY and TREAT precipitating factors for HE**
- **Lactulose is the first choice (or rifaximin: non-absorbable antibiotic)**

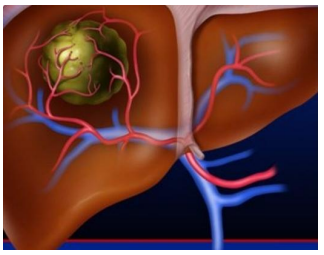
### Tests to diagnose HCC :

- Blood tests (AFP)
- Radiology (most important)
- Biopsy (not routinely done)



### Treatment options for HCC :

- Surgical (resection or liver transplantation)
- Ablation
- Embolization of.
- Chemotherapy
- Palliative



**Liver transplantation is the DEFINITIVE treatment for patients with cirrhosis**

## Summary & important points :

- Determine the cause of CLD and treat if possible, Prevent further insult (Vaccinations, avoid hepatotoxic medications & Alcohol), Prevent and treat complications.
- Most common complications of CLD are: Variceal bleeding, Ascites, Hepatic encephalopathy, HCC.
- Assess severity using Child-Pugh classification (5 variables: Bilirubin, PT(or INR), Albumin,Ascites, Encephalopathy), OR MELD
- SBP is diagnosed when neutrophils (not total WBC) count in ascitic fluid is ≥ 250 cells/mm3 and treated with antibiotics and albumin
- Treat precipitants of HE and give Lactulose
- Screen for HCC with liver imaging every 6 months (in patient with cirrhosis)
- Liver transplantation is the definitive treatment for patients with cirrhosis

# Lecture Quiz

**Q1: A 56-year-old chronic alcoholic has a 1-year history of ascites. He is admitted with a 2-day history of diffuse abdominal pain and fever. Examination reveals scleral icterus, spider angiomas, a distended abdomen with shifting dullness, and diffuse abdominal tenderness. Paracentesis reveals slightly cloudy ascitic fluid with an ascitic fluid PMN cell count of 1000/μL. Which of the following statements about treatment is true?**

A- Antibiotic therapy is unnecessary if the ascitic fluid culture is negative for bacteria.

B- The addition of albumin to antibiotic therapy improves survival.

C- Repeated paracenteses are required to assess the response to antibiotic treatment.

D- After treatment of this acute episode, a second episode of spontaneous bacterial peritonitis would be unlikely.

**Q2: A 70-year-old man presents with a complaint of fatigue. There is no history of alcohol abuse or liver disease; the patient is taking no medications. Scleral icterus is noted on physical examination; the liver and spleen are nonpalpable. The patient has a normocytic, normochromic anemia. Urinalysis shows bilirubinuria with absent urine urobilinogen. Serum bilirubin is 12 mg/dL, with 9.8 mg/dL direct-reacting fraction. Aspartate aminotransferase (AST) and alanine transaminase (ALT) are normal, and alkaline phosphatase (ALP) is 300 U/L (three times normal). Which of the following is the best next step in evaluation of this patient's jaundice?**

A- Ultrasound or CT scan of the abdomen.

B- Viral hepatitis profile.

C- Reticulocyte count.

D- Antimitochondrial antibody.

**Q3: A 47-year-old man presents complaining of weight gain, on examination there is an abdominal distension with a fluid thrill. Which of following is not a cause of ascites secondary to venous hypertension?**

A- Congestive heart failure.

B- Cirrhosis.

C- Budd–Chiari syndrome.

D- Nephrotic syndrome.

Answer: Q1:B | Q2:A | Q3:D