ABIM Review
Hepatobiliary

Danielle Brandman, MD, MAS
Assistant Professor of Medicine
University of California San Francisco

ABIM Certification Exam

Number of Questions

- Liver Disease
- Colonic & Anorectal Disease
- Small Intestinal Disease
- Esophageal Disease
- Pancreatic Disease
- Biliary Tract Disease
- Stomach or Duodenum
- Mouth/Salivary Glands
- GI Complications of HIV
- Undiagnosed GI Hemorrhage
- Miscellaneous
Hepatobiliary Review

- Diagnostic algorithms for cholestatic versus hepatitic pattern of liver test abnormalities
- Viral hepatitis: acute and chronic
- Autoimmune and cholestatic liver diseases
- Fatty liver disease
- Alcoholic liver disease
- Cirrhosis and its complications
- Liver transplantation - indications and contraindications

Case 1

- 30-year-old female with pruritus and fatigue X 3 months
- **Only PMH:** mild ulcerative colitis, stable; No meds
- **P/E:** Sclerae icteric, multiple spider angioma, palmar erythema, hepatomegaly
- **Laboratory tests:** Normal CBC, INR, albumin
  - AST 39 (N<40), ALT 51 (N≤50)
  - Alkaline phosphatase 890 (N<120)
  - Total bilirubin 3.2 (N ≤1.3)
- **Ultrasound abdomen:**
  - Hepatomegaly
  - Mild dilatation of distal left intrahepatic duct and proximal right intrahepatic ducts
  - Normal common bile duct, gallbladder and spleen
Which of the following is the best test to establish the patient’s diagnosis?

1. Blood tests: antimitochondrial antibody, antinuclear antibody, IgG and IgM
2. Blood tests: anti-HCV, HBsAg, anti-HAV IgM
3. Liver biopsy
4. Cholangiogram (ERCP or MRCP)
5. CT scan with pancreatic protocol
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  - Normal common bile duct, gallbladder and spleen

“Cholestatic” Liver Enzyme Pattern
(Elevated alkaline phosphatase ± bilirubin)

- Sources of elevated alkaline phosphatase are almost always LIVER or BONE
  - Note: In pregnancy, placental alkaline phosphatase increases ~2 X ULN starting month 3 of pregnancy
- Work-Up
  - Establish hepatic origin
    • GGT or 5’ nucleotidase or fractionation of alkaline phosphatase if bilirubin is normal
  - Primary differential is intrahepatic versus extrahepatic disease
    • Abdominal imaging is usual “first test”
# Diagnostic Approach for Patient with Cholestatic Enzyme Profile

## Abnormal Biliary Tree
- Stones, Tumors
- Strictures (including PSC)
- Cholangiography
  - ERCP or MRCP

## Normal Biliary Tree
- Primary biliary cirrhosis
- Drugs/toxins
  - e.g., Lymphoma
- Infiltrative
  - Granulomatous
    - e.g., Mycobacterium, sarcoidosis
- AMA, IgM (PBC)
- Liver biopsy

## US Abdomen or CT scan
- Abnormal Biliary Tree
- Normal Biliary Tree

## Clinical presentation
- Fatigue, pruritus, weight loss, fat-soluble vitamin deficiencies, cholangitis
- Fatigue, pruritus, weight loss, fat-soluble vitamin deficiencies

## Demographics
- Men age 30-40
- Middle-aged women

## Concomitant conditions
- Ulcerative colitis (70%)
- Thyroid disease, Sjogren’s syndrome/CREST

## Diagnostic evaluation
<table>
<thead>
<tr>
<th>Labs</th>
<th>Imaging</th>
<th>Liver biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-ANCA</td>
<td>U/S or CT→MRCP or ERCP</td>
<td>Frequently nondiagnostic</td>
</tr>
<tr>
<td>Antimitochondrial Ab, IgM</td>
<td>U/S (normal)</td>
<td>“Florid duct lesion”</td>
</tr>
</tbody>
</table>

## Treatment
- None established
- Liver transplant if decompensated
- Ursodiol (13-15mg/kg)

## Long-term risks
- Cholangiocarcinoma
- Colon cancer
- Cirrhosis, HCC
### Cholestatic Liver Diseases
Nonobstructive, non-PBC/PSC

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Clues</th>
<th>First Order Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-toxicity</td>
<td>History of exposure</td>
<td>Withdrawal</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Lung, lymph node, other systems involvement</td>
<td>Biopsy: non-caseating granulomas; ACE level</td>
</tr>
<tr>
<td>Malignancy: lymphoma</td>
<td>Hepatosplenomegaly, adenopathy, B symptoms</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Infectious</td>
<td>Fever, abnormal abdominal imaging</td>
<td>Cultures other sites, liver biopsy</td>
</tr>
</tbody>
</table>

### Case 2
- A 42-year-old male with 10 day history of fatigue, mild nausea, anorexia and dark urine
- No significant PMH
- Social History:
  - Heterosexual partner, no children.
  - Moderate alcohol and marijuana use, no injection drug use
- Exam: icteric, few cervical nodes, mild right upper quadrant tenderness, no splenomegaly, no asterix
- Labs:
  - WBC 3,200 (50 PMN, 32L, 5M, 4E), normal H/H, plts
  - ALT 1804 U/L, AST 1500 U/L, Total bilirubin 9.5
  - Alk Phos 241, INR 1.1, creatinine 0.8
Case 2

- Anti-HAV IgM positive
- Anti-HCV negative
- HBsAg negative, anti-HBc positive, anti-HBs positive
- ANA 1:80
- Drug/alcohol screen: positive for cannabinoids and alcohol
- Ultrasound: patent portal vein and hepatic veins, heterogenous liver of normal size, no splenomegaly or ascites

Q2

Which of the following is indicated?

1. Vaccinate coworkers
2. Vaccinate partner and household members
3. Refer to transplant center
4. Admit for administration of N-acetyl cysteine
5. Start antiviral therapy for hepatitis B
Q2

Which of the following is indicated?

1. Vaccinate coworkers
2. *Vaccinate partner and household members*
3. Refer to transplant center
4. Admit for administration of N-acetyl cysteine
5. Start antiviral therapy for hepatitis B

“Hepatitic” Pattern of Liver Enzymes Elevation

- ALT and AST elevated
- Distinguishing acute versus chronic hepatitis
  - **Symptoms**
    - Acute: anorexia, nausea, RUQ discomfort, fatigue, flu-like symptoms
    - Chronic: usually asymptomatic, fatigue
  - **Prior history**
    - Acute: no prior history of abnormal liver tests
  - **Severity of ALT elevation**
    - Acute: ALT >500 IU/L
    - Chronic: Usually ≤300 IU/L
### Acute Hepatitis
#### Diagnostic Work-Up

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Work-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs/toxin</td>
<td>Drug/alcohol screen, acetaminophen level, medication history</td>
</tr>
<tr>
<td>Acute viral hepatitis: A, B, C, D, E, HSV, others</td>
<td>HAV IgM, HBsAg, anti-HBcAb IgM, anti-HCV, Monospot, HSV PCR</td>
</tr>
<tr>
<td>Vascular: ischemia or hepatic congestion (Budd-Chiari)</td>
<td>Abdominal ultrasound with dopplers</td>
</tr>
<tr>
<td>Other:</td>
<td>ANA, anti-smooth muscle Ab, IgG Ceruloplasmin</td>
</tr>
<tr>
<td>- Acute fatty liver of pregnancy</td>
<td></td>
</tr>
<tr>
<td>- Autoimmune hepatitis</td>
<td></td>
</tr>
<tr>
<td>- Wilson’s disease</td>
<td></td>
</tr>
</tbody>
</table>

### Acute Hepatitis
#### Management

- **Supportive care**
  - Admit for management of acute hepatitis symptoms: nausea, abdominal pain, etc

- **Consider liver transplantation if:**
  - Develops hepatic encephalopathy or
  - Increasing INR or bilirubin
Acute Hepatitis Management

- **Specific treatment for some causes:**
  - N-acetyl cysteine for acetaminophen toxicity
  - Penicilln G or Silibinin for mushroom poisoning
  - Steroids for autoimmune hepatitis
  - Delivery for acute fatty liver of pregnancy
  - Copper chelating agents for Wilson’s disease
  - Antivirals for hepatitis B

Prevention of HAV

- **General**
  - Hygiene (hand washing)
  - Sanitation (clean water sources)

- **Specific**
  - Hepatitis A vaccination (pre-exposure and post-exposure within 14 days if <40 yrs and healthy)
  - Immune globulin (pre- and post-exposure)
    - **Pre-exposure:** travelers to intermediate and high HAV-endemic regions
    - **Post-exposure:** within 14d to household and sexual contacts if >40 yrs or other medical conditions
Prevention of HAV

- Recommendations For Adult HAV Vaccination
  - Men who have sex with men
  - Injection and non-injection drug users
  - International travelers
  - People with clotting factor disorders
  - Patients with chronic liver disease

Case 3

- 47-year-old asymptomatic female referred for elevated ALT x 6 mos
- PMH: Hypertension on atenolol, diet-controlled DM and hypertriglyceridemia, no other meds, denies alcohol use, no prior blood transfusion, injection drug use
- P/E:
  - Body mass index (BMI) = 35
  - Abdomen: liver edge palpable, no splenomegaly
- Labs:
  - AST 65 (N<40), ALT 75 (N<45)
  - Alkaline phosphatase, total bilirubin, albumin, prothrombin time and CBC normal
Case 3

- Anti-HBc+, HBsAg neg, anti-HBs negative
- Anti-HCV negative
- Autoantibody tests
  - ANA positive 1:80
  - Antimitochondrial antibody negative
  - IgG and IgM normal
- Ferritin and transferrin saturation normal
- Ceruloplasmin normal
- Ultrasound: diffusely hyperechoic liver, otherwise normal, hepatic vessels patent

The most likely diagnosis is:

1. Chronic hepatitis B
2. Non-alcoholic fatty liver disease
3. Drug-induced hepatotoxicity
4. Autoimmune hepatitis
5. Hepatocellular carcinoma
The most likely diagnosis is:

1. Chronic hepatitis B
2. Non-alcoholic fatty liver disease
3. Drug-induced hepatotoxicity
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5. Hepatocellular carcinoma

Chronic “Hepatitis” Pattern
Elevated ALT (and AST)

- Sporadic, isolated ALT elevations need no further w/u
- Persistent (≥6 mos) ALT elevation = chronic liver disease
  - For most chronic liver diseases, ALT <300 U/L
  - ALT slightly > AST or approximately same
  - If AST>ALT = consider alcohol (usually 2:1 ratio)
Hepatitis Liver Enzyme Pattern

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Clues</th>
<th>First Order Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAFLD</td>
<td>Metabolic syndrome</td>
<td>Abdominal imaging to look for fatty liver</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Risk factors: Injection drug use, blood transfusion, occupational</td>
<td>Anti-HCV</td>
</tr>
<tr>
<td>Alcohol, drug-toxicity</td>
<td>History of exposure</td>
<td>Abstinence or removal</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Risk factors: sex, injection drug use, + family hx</td>
<td>HBsAg, anti-HBc</td>
</tr>
<tr>
<td>Autoimmune Hepatitis</td>
<td>Female, other autoimmune conditions</td>
<td>ANA&gt;1:160, anti-smooth muscle Ab &gt;1:40, IgG</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>pseudogout, DM, heart disease, + family history</td>
<td>Transferrin saturation &gt;45%, ferritin &gt;500</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>&lt;40 yrs, neuro or psych sx, hemolytic anemia, pseudogout</td>
<td>Low ceruloplasmin, high 24-hr urine copper</td>
</tr>
</tbody>
</table>

Clues in Evaluating AST/ALT

- AST 65 (N<40), ALT 75 (N<45)
- PMH: **Hypertension** on atenolol, and diet-controlled **DM, hypertriglyceridemia**; no other meds; **denies alcohol use**
- P/E: **BMI = 35**, liver edge palpable, no splenomegaly
- Testing to exclude other causes all negative:
  - anti-HBc+, HBsAg neg, anti-HBs neg = HBV immune
  - ANA positive 1:40 = not autoimmune (titer too low)
- Ultrasound: **diffusely hyperechoic liver**, otherwise normal
NAFLD: Non-Alcoholic Fatty Liver

• Most common causes of chronic liver disease in US
  - Responsible for 14% of liver transplants in 2010 and 2011
• Histology like alcohol but diagnosis requires absence of "significant" alcohol (≤2 drinks per day)
• Associated with the metabolic syndrome
  - Centrally-distributed obesity (waist circumference)
  - Elevated triglycerides (≥150 mg/dl)
  - Hypertension (BP ≥130/85)
  - Diabetes (or insulin resistance)
Causes of NAFLD

**Primary**
- Metabolic syndrome

**Secondary**
- Much less frequent cause but to be considered

**Nutritional**
- Protein calorie malnutrition
- TPN, rapid weight loss
- J-J bypass surgery

**Metabolic/Genetic**
- Lipodystrophy

**Drugs**
- Glucocorticoids, Estrogens, Antiretrovirals
- Calcium channel blockers, Valproic acid, Amiodarone, Tetracycline, Methotrexate

**Others**
- Small bowel bacterial overgrowth
- HIV infection, environmental toxins (e.g. petrochemicals)

Non-Alcoholic Fatty Liver Disease

**Diagnosis**
- **Laboratory Tests**
  - ALT, AST 2-3 X ULN
  - ALT>AST if not cirrhotic
- **Radiology**
  - US: echogenic
  - CT: hypodense
  - MRI: bright on T1
- **Liver Biopsy**
  - Gold standard for diagnosis
  - Distinguishes NAFL from NASH

**Treatment**
- **Treat predisposing conditions**
  - Weight loss (not rapid!)
  - Control of blood sugars
  - Treat lipid disorders
  - Bariatric surgery if obesity plus complications
- **Vitamin E if NASH**
- **Liver transplantation if decompensated cirrhosis**
  - Can recur after transplant
Case 4

• 47-year-old woman, previously healthy, presents with jaundice and fatigue X 3 weeks
• PMH: thyroiditis age 30
• Meds: levothyroxine; no herbs or OTC medications
• SH: No alcohol, injection drug use, new sexual partners or recent travel
• Exam:
  – Icteric, spider angiomata chest, palmar erythema
  – Hepatomegaly, no spleen tip palpable, no asterixis
• Initial laboratory results:
  – ALT 850 U/L, AST 770 U/L, alkaline phosphatase 150 U/L, bilirubin 13.5 mg/dl (indirect 7.7)
  – INR 1.4, albumin 3.2, creatinine 1.1, WBC 5.5, Hgb 11, platelets 150K

Case 4

• Diagnostic tests
  – HAV IgM negative, anti-HCV negative, HBsAg negative, anti-HBc negative, anti-HBs positive
  – ANA 1:640, IgG 3220, anti-smooth muscle antibody 1:40, antimitochondrial antibody negative
  – Ceruloplasmin normal, ferritin 505, transferrin saturation 21%
  – Drug screen negative
• Ultrasound
  – Heterogenous, slightly nodular liver; ascites, spleen size upper limits of normal, hepatic veins and portal veins patent
What is the best treatment for this patient?

1. Referral for liver transplantation
2. Prednisone
3. Tenofovir
4. Phlebotomy
5. Ursodeoxycholic acid
**Autoimmune Hepatitis Diagnosis**

- **Clinical Clues:**
  - Female predominant
  - Presence of other autoimmune diseases
  - Any age
  - Can present acutely
  - Hepatitic pattern of liver tests (ALT>>ALP)

---

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cutoff</th>
<th>Points</th>
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<tbody>
<tr>
<td>Auto-antibodies*</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>ANA or ASMA</td>
<td>≥1:40</td>
<td>1</td>
</tr>
<tr>
<td>ANA or ASMA</td>
<td>≥1:80</td>
<td>2</td>
</tr>
<tr>
<td>LKM</td>
<td>≥1:40</td>
<td>2</td>
</tr>
<tr>
<td>SLA</td>
<td>Positive</td>
<td>2</td>
</tr>
<tr>
<td>IgG</td>
<td>&gt;Upper limit of normal</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1.1 times upper limit of normal</td>
<td>2</td>
</tr>
<tr>
<td>Liver histology</td>
<td>Compatible with AIH</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Typical AIH</td>
<td>2</td>
</tr>
<tr>
<td>Absence of viral hepatitis</td>
<td>Yes</td>
<td>2</td>
</tr>
</tbody>
</table>

*Maximum 2 points total for autoantibodies

≥6: probable AIH, ≥7: definite AIH
Autoimmune Hepatitis

Treatment

• **Indications for treatment:**
  - Elevated AST (≥5 X ULN)
  - Severe histologic disease
  - Symptomatic liver disease

• **Treatment:**
  - Prednisone is first line, alone or with azathioprine
  - Other immunosuppressants if fail to respond
  - Liver transplantation if severe acute or decompensated cirrhosis

Case 5

• 27-year-old heterosexual male referred for evaluation of hepatitis B

• **Labs:**
  - HBsAg +, anti-HBs negative
  - HBeAg negative, HBV DNA 500 IU/mL
  - HIV negative
  - ALT 25, AST 20
  - Normal total bilirubin, prothrombin time and alkaline phosphatase

• Sexually active, single partner, no other risk factors

• **PMH:** Unremarkable and no meds

• **FH:** No known family members with HBV infection, cirrhosis or liver cancer
Q5

Which of the following is indicated in the management of this patient?

1. Testing for anti-HBc IgM to exclude acute HBV
2. Vaccinate for HBV as he lacks anti-HBs
3. Vaccinate sexual and household members for HBV
4. Ultrasound and alpha fetoprotein every 6 months to screen for hepatoma
5. Treatment with HBV antivirals
### Diagnostic Tests for Hepatitis B

<table>
<thead>
<tr>
<th>Test</th>
<th>Acute HBV</th>
<th>Chronic HBV (inactive)</th>
<th>Chronic HBV (active)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HBeAg</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HBV DNA</td>
<td>Elevated</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>ALT</td>
<td>Very elevated</td>
<td>Normal</td>
<td>Elevated</td>
</tr>
</tbody>
</table>

### 2008 CDC Guidelines for HBV Screening

- People born in areas with ≥2% HBsAg prevalence
- People whose parents are from an area with ≥8% HBsAg prevalence
### 2008 CDC Guidelines for HBV Screening

- Persons with behavioral exposures to HBV
  - Injection drug use, men who have sex with men, prisoners
- Pregnant women, infants born to HBsAg+ mothers
- Patients on dialysis
- Persons needing immune-modulatory therapy
  - Chemotherapy, organ transplantation, immunosuppression and biologics for rheumatologic or gastroenterologic disorders
- Persons with elevated ALT/AST of unknown etiology
- Family and household members of HBsAg+ persons
- HIV positive patients

### Indications for HBV Vaccination in Adults

- Men having sex with men (MSM)
- Injection drug users
- Persons with >1 sexual partner last 6 months or recent STD
- Healthcare workers, including laboratory personnel
- Staff/clients of correctional institutes and institutes with mentally handicapped individuals
- Persons with HIV infection
- Persons with chronic liver disease, endstage renal disease
- Travelers to areas where HBV endemic
- Recipients of pooled blood products
- All sexual and household contacts of HBsAg+ persons

MMWR, Adult Immunization Schedule in United States, October 2006
**Surveillance for Hepatocellular Carcinoma**

**Who:**
- Any patient with cirrhosis
- In patients with chronic hepatitis B
  - Asian males ≥40 yrs; Asian females ≥50 years
  - African born ≥20 yrs of age
  - Family history of liver cancer

**How:**
- Abdominal imaging (ultrasound or CT scan) every 6 months
- Alpha fetoprotein (AFP): insufficient alone as screening test
  Can add to imaging but not required

**Chronic HBV Infection**

**Who Should be Treated?**

- Treatment indicated in those with “active” chronic HBV disease
- HBsAg+ with:
  - Elevated ALT/AST (>2 X ULN)
  - Elevated HBV DNA levels (>2000 IU/mL)
- Biopsy not required but can be helpful
  - Presence of moderate necroinflammation in patient with ALT level 1-2 X ULN
- If cirrhosis: all recommended to receive treatment if HBV DNA >2000 IU/mL or ALT elevated
### HBV Treatment in US

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Route and Duration</th>
<th>Patient Population</th>
<th>Preferred Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon alfa-2b</td>
<td>SC, 24 wks</td>
<td>&lt;60 yrs, high ALT, HBeAg+, non-cirrhotic</td>
<td></td>
</tr>
<tr>
<td>Peginterferon alfa-2a</td>
<td>SC, 48 wks</td>
<td>Few comorbidities</td>
<td>X</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Oral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Adefovir dipivoxil)</td>
<td>Longer-term therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entecavir</td>
<td></td>
<td>All patient groups</td>
<td>X</td>
</tr>
<tr>
<td>(Telbivudine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

AASLD Practice Guidelines 2009
HBV Management in Patients Receiving Immunosuppression

- All patients should be tested for HBsAg and anti-HBc
- Patients may experience exacerbation of HBV disease with chemotherapy
- Highest risk group = HBsAg positive
  - Treat HBV during chemotherapy and for 6 months after chemo discontinued
  - Use oral agents e.g. lamivudine, adefovir or entecavir
- Lower risk group = anti-HBc positive only
  - Monitor during chemotherapy and treat if HBV DNA levels increase or becomes HBsAg +

AASLD Practice Guidelines 2009

Case 6

- 38-year-old male with history of injection drug use in his 20s is found to be anti-HCV positive
- PH: otherwise negative
- Meds: none
- Exam: Anicteric, no hepatosplenomegaly
- Labs:
  - CBC normal
  - AST 22 U/L, ALT 27 U/L, bilirubin 0.7 mg/dl
What is the next step in evaluating this patient?

1. HCV RNA test
2. Referral for liver biopsy
3. Obtain abdominal imaging
4. HCV genotype
5. Repeat ALT, AST every 6 months
Hepatitis C

**Diagnosis**
- Screen = anti-HCV
- Confirmatory = HCV RNA by sensitive qualitative assay

**ALT**
- Normal in up to 1/3 of patients
- Usually <200 U/L in chronic infection

**Evaluation**
- Liver function tests, platelet count
- Abdominal imaging
- Stage disease: liver biopsy, FibroSure, Fibroscan
- If considering treatment
  - HCV genotype
  - HCV viral load

**Who Should be Screened for Hepatitis C?**
- Born 1945-1965
- Person with chronically elevated liver enzymes
- All HIV-infected persons
- History of IDU, even if remote and if only once
- History of receiving clotting factors prior to 1987
- History of hemodialysis
- History of blood transfusion or organ transplantation prior to July 1992
- History of percutaneous or mucosal exposure to HCV-infected blood
- Infants born to HCV-positive mothers

MMWR 1998; MMWR 2012
1999 USPHS/IDSA Guidelines
Natural History of Chronic HCV Infection

Risk Factors for Cirrhosis
- Male gender
- Heavy alcohol use
- Older age at time of infection
- Longer duration of disease
- HIV coinfection

Exposure (Acute Phase)
- 15-45%
- 55-85%

Resolved
- 75-95%

Chronic
- 5%-25% over 20-30 years

Stable

Cirrhosis
- 3%/year HCC
- 5%/year decomp

Liver Decompensation Hepatoma
Alter MJ. Semin Liver Dis. 1995
Freeman, Hepatology 2001

Anti-HCV Treatment

All patients with chronic HCV should be considered for antiviral therapy
**Anti-HCV Treatment**

All patients with chronic HCV should be considered for antiviral therapy

**Sofosbuvir = Game Changer**

Other recently approved antiviral drugs: ledipasvir/sofosbuvir, ombitasvir/paritaprevir/ritonavir + dasabuvir
Anti-HCV Treatment

All patients with chronic HCV should be considered for antiviral therapy

Hepatitis C Treatment Options

<table>
<thead>
<tr>
<th></th>
<th>Genotype 1</th>
<th>Genotype 2</th>
<th>Genotype 3</th>
<th>Genotype 4</th>
<th>Genotype 5/6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir + ribavirin</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Ledipasvir/sofosbuvir +/- ribavirin</td>
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<tr>
<td>Ombitasvir/paritaprevir/ritonavir + dasabuvir + ribavirin</td>
<td>X</td>
<td></td>
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<tr>
<td>Simeprevir + sofosbuvir +/- ribavirin</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

AASLD, IDSA, IAS–USA. Recommendations for testing, managing, and treating hepatitis C. 
Case 7

- 54-year-old woman with history of chronic HCV
  - Previously treated with peginterferon and ribavirin but did not respond
- Exam:
  - BP 105/60, HR 72, anicteric, spider angioma
  - No fluid wave, splenomegaly
- Labs:
  - AST 110 U/L, ALT 80 U/L, total bilirubin 1.3 mg/dl
  - INR 1.1, creatinine 1.0 mg/dl, serum albumin 3.4 g/dl
  - Platelet count 97,000, H/H normal
- Abdominal US: nodular liver with no focal lesions, splenomegaly, patent portal and hepatic veins.

Q7

What is the most appropriate next management step?

1. Referral for liver transplantation
2. Referral for upper endoscopy
3. Referral for liver biopsy
4. Urine drug screen
5. Monitoring of liver function tests every 6 months
Q7

What is the most appropriate next management step?

1. Referral for liver transplantation
2. *Referral for upper endoscopy*
3. Referral for liver biopsy
4. Urine drug screen
5. Monitoring of liver function tests every 6 months

Diagnosis of Cirrhosis
(in absence of clinical signs of decompensation)

- **Laboratory clues**
  - AST>ALT
  - Low platelets (<140K)
  - Abnormalities of liver function: INR, albumin or total bilirubin
- **Abdominal imaging**
  - Nodular, small liver
  - Splenomegaly
  - Recanalized umbilical vein, intra-abdominal collaterals
- **Endoscopy**
  - Varices and portal hypertensive gastropathy
- **Biopsy**
Complications of Cirrhosis
Result From Portal HTN or Liver Insufficiency

Primary Prophylaxis for Variceal Bleeding in Patients with Cirrhosis

- If cirrhosis present, screening to look for varices using upper endoscopy is recommended
  - Prophylaxis recommended if varices greater than “small” in size
- Primary prophylaxis options:
  - Non-selective beta blocker (propranolol or nadolol)
  - If intolerant of beta blocker, endoscopic band ligation if varices of medium to large size

AASLD Practice Guidelines 2007
Case 7 (continued)

- 54-year-old woman with HCV cirrhosis returns in 6 months with 1-month history of progressive abdominal distention
- Exam: Ascites, splenomegaly, mild peripheral edema
- Labs:
  - AST 110 U/L, ALT 80 U/L, total bilirubin 2.1 mg/dl
  - INR 1.6, creatinine 1.0 mg/dl, serum albumin 3.3 g/dl
  - MELD score = 14
- Abdominal US: Moderate ascites, nodular liver with no focal lesions, splenomegaly, patent portal and hepatic veins
- Diagnostic paracentesis: albumin 2.0 g/dL, total protein 2.0, WBC 100/mm³

In addition to starting diuretics, which of the following is most appropriate at this time?

1. Referral to interventional radiology for TIPS placement
2. Start prophylaxis for spontaneous bacterial peritonitis
3. Start propranolol for prevention of variceal bleeding
4. Referral for liver transplantation
5. CT scan to look for possible hepatoma
In addition to starting diuretics, which of the following is most appropriate at this time?

1. Referral to interventional radiology for TIPS placement
2. Start prophylaxis for spontaneous bacterial peritonitis
3. Start propranolol for prevention of variceal bleeding
4. Referral for liver transplantation
5. CT scan to look for possible hepatoma
**Ascites**

SAAG: Serum Ascites-Albumin Gradient

<table>
<thead>
<tr>
<th>SAAG ≥1.1 g/dl (high gradient)</th>
<th>SAAG &lt;1.1 g/dl (low gradient)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cirrhosis, any cause</td>
<td>• Peritoneal carcinomatosis</td>
</tr>
<tr>
<td>• Alcoholic hepatitis</td>
<td>• TB peritonitis</td>
</tr>
<tr>
<td>• Fulminant hepatic failure</td>
<td>• Bowel obstruction/infarction</td>
</tr>
<tr>
<td>• Budd-Chiari syndrome</td>
<td>• Biliary ascites</td>
</tr>
<tr>
<td>• Portal vein thrombosis</td>
<td>• Nephrotic syndrome</td>
</tr>
<tr>
<td>• Venoocclusive disease</td>
<td>• Postoperative lymphatic leak</td>
</tr>
<tr>
<td>• Severe right heart failure</td>
<td>• Serositis in connective tissue disease</td>
</tr>
</tbody>
</table>

**Spontaneous Bacterial Peritonitis**

**Definition SBP**
- Positive ascites culture
- Ascitic fluid cell count ≥250 PMN/mm³

**DDX**
- Secondary bacterial peritonitis
  - Clue: polymicrobial, PMN count high (>1000/mm³)
- Partially treated SBP
  - Clue: ascitic fluid count increased but culture negative
**Spontaneous Bacterial Peritonitis**

**Treatment of SBP**
- 3rd gen. cephalosporins or quinolones
- Avoid aminoglycosides!

**Indications for SBP prophylaxis**
- Prior episode of SBP
- Current active GI bleeding
- Ascitic fluid total protein <1.5 g/dl + at least one:
  - Cr ≥1.2, BUN ≥25, serum Na ≤130
  - Child’s C cirrhosis and bilirubin ≥3
- Daily antibiotics preferred to intermittent

---

**Assessing Liver Disease Severity In Patients with Cirrhosis**

<table>
<thead>
<tr>
<th>Components</th>
<th>Child-Pugh Score</th>
<th>Model of Endstage Liver Disease (MELD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>5-15</td>
<td>≥7</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td></td>
<td>≥12</td>
</tr>
<tr>
<td>Albumin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. bilirubin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INR/PT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bilirubin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td></td>
<td></td>
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</tbody>
</table>

Guide for transplant referral ≥7 ≥12
Child’s Score in Cirrhotics
Child-Pugh-Turcotte Score (CPT)

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1-2</td>
<td>Grade 3-4</td>
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<tr>
<td>Total Bilirubin</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt;3.5</td>
<td>2.8-3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>INR</td>
<td>&gt;1.7</td>
<td>1.7-2.3</td>
<td>&gt;2.3</td>
</tr>
</tbody>
</table>

Child’s A = 5-6  Child’s B = 7-9  Child’s C = 10-15

Case 7

• 54-yr-old woman with HCV cirrhosis presents with ascites
  - Diagnostic paracentesis: albumin 1.5 g/dl, WBC 100/mm³
• No history of encephalopathy or variceal bleeding
• Abdominal US: Moderate ascites, nodular liver with no focal lesions, splenomegaly, patent portal and hepatic veins
• Exam:
  - BP 105/60, HR 72, afebrile
  - Ascites, splenomegaly, mild peripheral edema
• Labs: total bilirubin 2.1, INR 1.6, serum albumin 3.3 g/dl

Child-Pugh score = 8 (Child’s B)
Case 8

- 45-yr-old woman presents with jaundice and fever
  - Admits to drinking 6-8 drinks/day (vodka) for past 10 years up until recent DUI and court-mandated rehab; last alcohol 3 days ago
- PMH: otherwise negative and no meds
- PE: BP 100/55, HR 100, T 38.8 icteric, muscle wasting, hepatomegaly, no spleen tip, asterixis present, stools brown, occult blood negative
- Labs:
  - Hgb 11 g/dl, platelet 390K, WBC 13.9 with left shift
  - ALT 35 (N <45), AST 126 (N<40), bilirubin 19.8 mg/dL
  - Cr 1.1 mg/dL, INR 1.8, albumin 2.5 g/dl
- Abdominal US: Enlarged and heterogeneous liver, no bile duct dilatation and gallbladder normal, no ascites
- Cultures negative

Q9

Which are the following are indicated in her management?

1. Referral for liver transplantation
2. Treat with ursodeoxycholic acid
3. Endoscopic retrograde cholangiogram
4. Treat with prednisolone
5. Consult palliative care
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2. Treat with ursodeoxycholic acid
3. Endoscopic retrograde cholangiogram
4. Treat with prednisolone
5. Consult palliative care

Alcoholic Liver Disease

- **Diagnosis**
  - History; underreporting frequent
  - Lab clues: leukocytosis (with left shift), macrocytic anemia, AST>ALT (2:1 or higher) and usually <300 U/L

- **Acute alcoholic hepatitis**
  - Severity assessed using Discriminant Function (DF)
  - DF = 4.6 X (PT seconds - control) + bilirubin (mg/dl)
    - If DF>32, predicts 50% mortality
Alcoholic Liver Disease

• **Treatment**
  – Mainstay is abstinence
  – Liver transplantation a consideration after abstinence established
  – Consider **prednisolone** (or pentoxifylline) if acute alcoholic hepatitis with DF >32, encephalopathy and no GI bleeding, renal dysfunction or infection
    • Assess response to treatment after 7 days with Lille score

Contraindications for Liver Transplantation

• Malignancy
  – Except small (T2) hepatocellular carcinoma
• Systemic infections
• Active drug or alcohol use
• Life limiting co-existing medical conditions
  – Advanced heart, lung or neurologic conditions
• Inability to comply with transplant care
• Inadequate social support
Thank you!

Danielle.Brandman@ucsf.edu