The Skeleton

- Acute Liver Diseases
- Chronic Liver diseases
- Cirrhosis and Portal Hypertension
- Liver Neoplasms
- Liver Transplantation
Nomenclature of Liver Disease

- **Acute Liver Diseases:**
  - Acute Hepatitis: Hepatitic, Cholestatic, or Mixed
  - Acute Liver Failure: Jaundice, Encephalopathy, Coagulopathy

- **Chronic Liver Diseases:**
  - Chronic inflammation with/without fibrosis
  - Cirrhosis (stage 4 fibrosis)
  - Liver Neoplasms

- **Acute on top of Chronic Liver Diseases**
Acute Liver Diseases

- Acute Hepatitis: New onset rise in LCTs with or without symptoms with no signs of ALF

- Acute Liver Failure (ALF): Acute Liver injury with Jaundice, Encephalopathy, and Coagulopathy.
A 38 YOF with no known history of CLD presents with progressive fatigue over the last 3 weeks. No evidence of AMS. Her LCT revealed ALT of 670, AST 500, AP 175, and TB of 2.4 with direct of 2. INR is normal at 1.0. Old record revealed normal LCT 2 months ago.

What is the cause of this abnormal LCTs?

- 1- Hepatocellular inflammatory process
- 2- Intrahepatic bile duct disease
- 3- Extrahepatic bile duct obstruction
- 4- Any of the above
Question

- A 45 YOF presents with Fever, RUQ pain over the last 2 days with progressive course. She vomited 3 times over the last 12 hours. She is known to have Metabolic syndrome with DM and obesity. Her LCT showed ALT of 67, AST 69, AP 430, and TB of 3.1 with direct of 2.5. The likely cause of her abnormal LCT is:
  - 1-Acute HBV infection
  - 2-AIH flare
  - 3-NASH
  - 4-Acute cholangitis
Acute Hepatitis

- Acute rise in transaminases (AST & ALT) and/or AP
- The clinical course ranges from asymptomatic disease to ALF
- Look at the pattern:
- Three Patterns for abnormal LCTs
  - Hepatitic: AST and ALT elevation >>> AP elevation
  - Cholestatic: AP elevation >> AST and ALT elevation
  - Infiltrative: Mixed
  - Bilirubin: Does not help much!
Causes of Acute Hepatitic Hepatitis

- Alcoholic hepatitis
- Acute ischemic hepatitis
- Viral Hepatitis: Hepatotrophic and non-hepatotrophic
- Drug-induced: Acetaminophen, ABx...
- Autoimmune hepatitis flare
- Wilson disease
- Others (acute BCS, VOD, HELLP,...)
Acute Cholestatic Hepatitis

- Extrahepatic BD obstruction (U/S is a good start)
- Acute cholangitis/cholecystitis
- Drug and toxins associated with cholestasis
- Liver allograft rejection
- Infectious hepatobiliary diseases seen in patients with AIDS
- Note that PBC does not present acutely
Question

- A 42 YOM with history of IVDU and ETOH dependence presents with Jaundice and abdominal distension. No AMS. His LCTs showed ALT of 85, AST 305, AP 148, TB 5.6 and PT of 18 with INR of 1.4. His acute hepatitis panel is unremarkable. The likely cause of his abnormal LCT is:

- 1-Acute hepatitis B
- 2-Acute alcoholic hepatitis
- 3-Wilson disease flare
- 4-Tylenol toxicity
Acute Alcoholic Hepatitis

- Usual symptoms +/- AMS
- Not necessarily still an active drinker!
- HSM, Spider angiomatosis, Palmer erythema, +/- Asterixis
- AST >> ALT but less than 400 → if more → think of concomitant process as Tylenol, acute viral hepatitis, Rhabdo, or others
Acute Alcoholic Hepatitis

- MDF = 4.6 (patient’s PT - control PT) + Total bilirubin
- If > 32 → Increased short term mortality with 1-month mortality of 30%-50%
- Steroid if MDF > 32 or with AMS if no CIs
- Rule out infection, GI bleeding, HRS
- Nutrition (1.2 gm/kg/day protein & 35-40 Kcal/Kg/day)
- Thiamine and Folate
A 78 YOM with ischemic cardiomyopathy presents with hypotension and AKI. His LCT revealed AST 2300, ALT 3200, AP 230, and TB of 0.8. He was put on pressors. Next day his LCT showed AST 1200, ALT 1500. The likely cause of his abnormal LCT is

- Tylenol overdose
- Acute ischemic hepatitis
- AIH flare
- Acute cholecystitis
Acute Ischemic Hepatitis

- Acute rise in AST and ALT followed by rapid decline with Resuscitation
- Hemodynamic instability (Shock)
- Cocaine or Amphetamine
- Long acting Niacin
- Always rule out other relevant causes
- Supportive management
A 26 YOM came back from a summer camp in Mexico 2 weeks ago. He started having fatigue and RUQ discomfort over the last few days. His urine became dark yellow. On Exam, he has jaundice. No asterixis. Acute hepatitis A is suspected. What test should you order?

- HAV-IgG
- HAV-IgM
- HAV PCR
Acute Viral Hepatitis (HAV & HEV)

- Outbreak or a recent travel
- IP is 2-6 weeks for HAV and 2-9 weeks for HEV
- Fecal-oral route
- Jaundice, tender hepatomegaly
- Positive Anti HAV IgM (stays for 3-6 months)
- Positive Anti HEV IgM (Need to do PCR)
- Supportive measures
- Might lead to ALF (< 1%)
- Case Fatality of HAV is about 0.3%
- Case fatality of HEV in pregnant women is 10%-20%
- Chronic HEV infection leading to cirrhosis could happen in immunosuppressed patients
Acute HBV infection

- DNA virus
- Transmitted by blood, IVDU, sexual route, and vertical
- About 2 million Americans are infected (Asians)
- IP is 4-24 weeks
- Non-specific symptoms
- Arthritis or urticaria in few patients
- HBsAg is the landmark except in the window phase with positive HBc-IgM
- Supportive therapy except in certain cases (ALF)
- Chronicity risk is based on route of infection:
  - 5-10% with horizontal route
  - 90% with vertical route
Natural History of HBV Infection

Early Childhood > 95% Immune Tolerance

HBeAg- Chronic Hepatitis B

HCC

HBeAg+ Chronic Hepatitis B

Inactive Carrier < 5%

Adulthood

<table>
<thead>
<tr>
<th>HBs Ag</th>
<th>HBe Ag</th>
<th>IgM anti-HBc</th>
<th>Total anti-HBc</th>
<th>Anti-HBs</th>
<th>Anti-HBe</th>
<th>HBV DNA</th>
<th>Interpretation</th>
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<td>+++</td>
<td>HBeAg+ chronic hepatitis</td>
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<td>±</td>
<td>Inactive carrier state</td>
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<td>-</td>
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<td>+</td>
<td>±</td>
<td>-</td>
<td>-</td>
<td>Resolved hepatitis B</td>
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</table>
A 31 YOM with history of IVDU was referred to you for elevated LCT (ALT 200, AST 159). His HBV markers showed HBsAg +, HBc-IgM -, anti-HBc total +, HBV DNA 2,000,000 IU/ml. HBe Ag -. His HCV antibody is negative. The likely stage of his HBV infection is:

• 1-Inactive carrier
• 2-Acute HBV infection
• 3-Chronic Hepatitis B
• 4-Resolved HBV infection
Herpes viruses

- **EBV:**
  - 80-90% of cases of IM have mildly elevated liver enzymes
  - Frank Jaundice in 5%
  - IgM VCA

- **CMV:**
  - Usually in Immunocompromized patients
  - Scattered microscopic granulomas

- **HSV:**
  - Immunocompromized patients
  - Very ill with fever and markedly elevated transaminases
  - Mortality is high

- **VZV:**
  - Lymphoproliferative disorders
  - Disseminated disease
  - Rarely fatal
Drug induced liver injury (DILI)

- The most common mechanism is idiosyncratic reaction
- That reaction usually occurs during the first 6 months of intake and very unlikely to occur after one year of intake but it does occur (as with Nevarapine)
- ABx, NSAIDs, Anti-convulsants, and herbal meds
- If you suspect DILI, D/C all meds except the essential ones that have no alternatives.
- Use steroid with hypersensitivity reaction (Associated rash, Eosinophils in the blood with or without increased AEC, or with Eosinophils in the liver biopsy)
- Urso is sometimes used with cholestatic hepatitis
- May lead to ALF
Acetaminophen induced Hepatitis

- Dose dependant injury
- The most common form is acute injury 2/2 mega dose (> 10 gram/day) but smaller doses could do it especially in ETOH and patients with CLD.
- The time of ingestion is important for the nomogram, but it is often unknown exactly.
- If the time is well known: give Charcol if within 4 hours of it and give NAC even if the ingestion was 2-3 days ago!!
NAC

- Indication In acute toxicity: In approved, suspected or even unknown cases → Negative or low blood level in cases of unclear time frame does not rule out Tylenol overdose and NAC is needed; so think thrice before saying “NAC is not needed”!!

- 2-Indication in chronic use:
  - Having hepatitis picture as with RUQ tenderness and/or ↑ ALT regardless the level
  - Level > 20 mcg/mL
  - Level > 10 mcg/mL in susceptible patients as above

- How to give it: IV is recommended in a lot of situations not just AMS with no NGT, these situations include also ileus, persistent hypotension, persistent N/V, and GI bleeding.
Question

- A 56 YOF presents with progressive fatigue and jaundice. LCT showed AST of 700, ALT 850, TB of 6 and INR of 1.4. ANA and SMA were highly positive. Which one of the following is incorrect?

  - IgG is usually high
  - The typical liver biopsy finding is lymphoid aggregates
  - Prednisone is the first line of therapy
  - Prognosis of this patient is poor without therapy
AIH

- Relatively common
- Treatable, otherwise dangerous (40% mortality within 6 months if severe)
- Types:

<table>
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<tr>
<th></th>
<th>AIH-I</th>
<th>AIH-II</th>
<th>AIH-III</th>
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<tbody>
<tr>
<td>Age</td>
<td>Bimodal: 16-30 &amp; &gt;50</td>
<td>2-14</td>
<td>20-40</td>
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<tr>
<td>Abs</td>
<td>ANA, ASMA</td>
<td>LKM-1</td>
<td>SLA/LP</td>
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<tr>
<td>Prevalence in USA</td>
<td>80%</td>
<td>4%</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>Extrahepatic dz</td>
<td>40%</td>
<td>35%</td>
<td>58%</td>
</tr>
<tr>
<td>Progression to cirrhosis</td>
<td>45%</td>
<td>82%</td>
<td>75%</td>
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</tbody>
</table>
AIH, Auto-Antibodies

- Elevated IgG
- **ANA**: non-specific and of no specific pattern for AIH
- **ASM**: more sensitive and specific
- **Anti-actin Ab**:
  - A subtype of ASM
  - Highly specific to AIH
- Liver Biopsy: Lymphoplasmacytic infiltrate, Eosinophils, Interface hepatitis, necrosis
- Treat with Prednisone +/- AZA
Acute Wilsonian Hepatitis

- Rare (1:30,000)
- Young patient with non-specific symptoms
- Elevated AST and ALT
- If AP (IU/L):T. Bili (mg/dL) is < 2 → Highly suspect it
- Coombs-negative hemolysis
- Low or low normal Ceruloplasmin
- KFR in 50% of patients but in 95% of those with Neuro manifestations
- lunulae ceruleae: Bluish discoloration at the base of fingernails
- Liver Transplantation
Acute Liver Failure (ALF)

- Rapid onset of encephalopathy (HE) along with a marked decline in hepatic synthetic function within 28 days.
- Hepatic function measured by INR, bilirubin, Factor V levels

Clinical triad:

- Jaundice
- Coagulopathy
- HE
Lines of Management of ALF

- Look for the cause and treat as feasible
- Assess the need & candidacy for OLT at LT Center

General therapeutic measures
- ICU
- Look for, prevent, and treat infection aggressively
- Monitor blood glucose closely
- GI prophylaxis, Avoid increasing ICP, Nutrition....

Specific therapeutic Measures:
- Management of Coagulopathy
- Management of Brain edema
Chronic Liver Diseases
Natural history of chronic liver disease

- Increasing liver fibrosis
  - Steatohepatitis
  - HBV & HCV Hepatitis
  - Autoimmune Hepatitis
  - Biliary liver disease
  - Metabolic/Hereditary Liver Disease
  - Others

- Jaundice
- Encephalopathy
- Variceal bleeding
- Ascites

- Liver Transplantation

- HCC

- Death

- Decompensated Cirrhosis

- 2%-7%/Y

- Death

- Compensated Cirrhosis

- 5%-7%/Y

- Death

- Chronic Liver Disease
HCV

- RNA virus
- About 4 million Americans are infected
- The Natural History:

```
20 percent  Acute infection  80 percent
Recovery  Persistence

30 percent stable chronic hepatitis 40 percent variable progression 30 percent severe progression
```
Question

A 27 YOM who actively uses IV heroin. He presents with fatigue and abnormal LCTs. What is the best test to rule out HCV infection in this person?

- 1-HCV RIBA
- 2-HCV Antibody
- 3-HCV PCR
- 4-HCV Genotype
Whom should you screen, regardless LCT

- IVDU: In the recent or remote past even once
- Hemophiliacs who received clotting factor concentrates before 1987
- Blood transfusion/ organ transplant before July 1992
- Patients on HD
- HIV patients
- Children born to HCV-infected mothers
- Sexual partners of HCV-infected patients
- Elevated liver enzymes
- Others: Occupational exposure, ?Tattoo, Snorting cocaine
- Persons born in 1945-1965
HCV serology

- Not for acute HCV infection

- May give false negative results in patients with AIDS or in hemodialysis

- False positive results in those with AIH

- Always confirm positive ones with qualitative PCR testing
Recombinant Immunoblot Assay (RIBA)

- RIBA-2 has the same antigens as EIA-2 $\rightarrow$ not more sensitive

- 2/3 or 3/3 $\rightarrow$ positive test

- RIBA is more technically demanding than EIA
HCV RNA by PCR

- Two weeks after infection
- The lower limit for Qualitative one is 50 IU/mL
- For Quantitative one:
  - 10-43 IU/mL → detected but below the limit of Quantitation
  - > 43 IU/mL → Will give the number
HCV Genotypes

- **Genotype 1:**
  - The most common in the US (75%)
  - Was the least responsive to therapy (48 weeks) (about 45-50%)
  - Now it is better with Direct Antiviral Agents

- **Genotype 2 & 3:**
  - About 20%
  - More responsive to therapy (12-24 weeks)

- **Genotype 4:**

- **Genotype 5:**

- **Genotype 6:**
Interpretation of HCV Laboratory Tests

- **If anti-HCV positive and HCV RNA positive**
  - Acute or chronic HCV infection depending on clinical context

- **If anti-HCV positive and HCV RNA negative**
  - Resolution of HCV; acute HCV infection during period of low-level viremia; False positive anti-HCV

- **If anti-HCV negative and HCV RNA positive**
  - Early acute HCV infection; chronic HCV infection in setting of immunosuppression; false-positive HCV RNA test

- **If anti-HCV negative and HCV RNA negative**
  - Absence of HCV infection
## Oral regimens for GT1a

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velpatasvir/Sofosbuvir</td>
<td>12 weeks</td>
<td>Treatment-naïve or treatment-exp with/ without compensated cirrhosis</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>12 weeks</td>
<td>Treatment naïve with or without comp cirrhosis, treatment exp (PEG/RBV +/- PI) without comp cirrhosis</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>24 weeks</td>
<td>Treatment exp (PEG/RBV +/- PI) without comp cirrhosis</td>
</tr>
<tr>
<td>Elbasvir/Grozoprevir</td>
<td>12 weeks</td>
<td>Treatment naïve or PEG/RBV-exp without baseline NS5A polymorphisms; with/without comp cirrhosis</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir + RBV</td>
<td>16 weeks</td>
<td>Treatment naïve or PEG/RBV-exp with baseline NS5A polymorphisms</td>
</tr>
<tr>
<td>Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + RBV</td>
<td>12 weeks</td>
<td>Without comp cirrhosis</td>
</tr>
<tr>
<td>Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + RBV</td>
<td>24 weeks</td>
<td>With comp cirrhosis</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td>12 weeks</td>
<td>No comp cirrhosis</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir + RBV</td>
<td>12 weeks</td>
<td>Comp cirrhosis</td>
</tr>
<tr>
<td>Simeprevir + Sofosbuvir</td>
<td>12 weeks</td>
<td>No comp cirrhosis</td>
</tr>
<tr>
<td>Simeprevir + Sofosbuvir + RBV</td>
<td>24 weeks</td>
<td>Comp cirrhosis</td>
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## Oral Regimens for GT1b

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Caveats</th>
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<td>Velpatasvir/ Sofosbuvir</td>
<td>12 weeks</td>
<td>Treatment naïve or treatment experienced with/without comp cirrhosis</td>
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<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>12 weeks</td>
<td>Treatment naïve with or without comp cirrhosis; treatment exp (PEG/RBV +/-) without comp cirrhosis</td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>24 weeks</td>
<td>Treatment- exp (PEG/RBV +/- PI) without comp cirrhosis</td>
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<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>12 weeks</td>
<td>Treatment naïve or PEG/RBV; with/without comp cirrhosis</td>
</tr>
<tr>
<td>Elbasvir/ Grazoprevir + RBV</td>
<td>12 weeks</td>
<td>PEG/RBV/PI experienced; with or without comp cirrhosis</td>
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<tr>
<td>Ombitasvir/ Paritrepervir/ Ritonavir + Dasabuvir</td>
<td>12 weeks</td>
<td>With or without comp cirrhosis</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td>12 weeks</td>
<td>No cirrhosis</td>
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<tr>
<td>Daclatasvir + Sofosbuvir + RBV</td>
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<tr>
<td>Simeprevir + Sofosbuvir</td>
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<td>Simeprevir + Sofosbuvir</td>
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## Oral Regimens for Non-GT1 patients

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<th>Duration</th>
<th>Population</th>
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<tr>
<td>GT2</td>
<td>Velpatasvir/ Sofosbuvir</td>
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<td></td>
<td>Sofosbuvir + RBV</td>
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<tr>
<td>GT3</td>
<td>Velpatasvir/ Sofosbuvir</td>
<td>12 weeks</td>
<td>No cirrhosis or comp cirrhosis</td>
</tr>
<tr>
<td>GT3</td>
<td>Daclatasvir + Sofosbuvir</td>
<td>12 weeks</td>
<td>No cirrhosis or comp cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir + Sofosbuvir + RBV</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>GT4</td>
<td>Ledipasvir/ Sofobuvir</td>
<td>24 weeks</td>
<td>No cirrhosis or comp cirrhosis</td>
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<td></td>
<td>Velpatasvir/ Sofosbuvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GT4</td>
<td>Ombitasvir/ Paritaprevir/ Ritonavir + RBV</td>
<td>12 weeks</td>
<td>No cirrhosis</td>
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<tr>
<td>GT4</td>
<td>Elbasvir/ Grazoprevir</td>
<td>12 weeks</td>
<td>Treatment naïve with/without cirrhosis</td>
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<td></td>
<td>Elbasvir/ Grazoprevir + RBV</td>
<td></td>
<td>Treatment exp with/without cirrhosis</td>
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<td>GT5</td>
<td>Ledipasvir/ Sofobuvir</td>
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<td>No cirrhosis or comp cirrhosis</td>
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<td>GT6</td>
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<td>12 weeks</td>
<td>No cirrhosis or comp cirrhosis</td>
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<td>Velpatasvir/ Sofosbuvir</td>
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# Oral Regimens for Decompensated Cirrhotic

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<thead>
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<th>GT</th>
<th>Regimen</th>
<th>Duration</th>
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<tr>
<td>GT 1-6</td>
<td>Velpatasvir/ Sofosbuvir + RBV</td>
<td>12 weeks</td>
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<tr>
<td>GT 1 or 3</td>
<td>Daclatasvir + Sofosbuvir + RBV</td>
<td>12 weeks</td>
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<tr>
<td>GT 1</td>
<td>Ledipasvir/ Sofosbuvir + RBV</td>
<td>12 weeks</td>
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</table>
Chronic HCV therapy

- **Genotype 1 and 4:**
  - Sofosbuvir / Ledipasvir for 12 weeks or
  - Three DAA (ombitasvir, paritaprevir/ritonavir with dasabuvir)
  - No more Telaprevir or Boceprevir

- **Genotype 2:** Ribavirin + Sofosbuvir for 12 weeks

- **Genotype 3:** Ribavirin + Sofosbuvir for 24 weeks
HBV, Whom should you screen

- Immigrants and adopted children
- Households of HBs Ag positive patients
- Sexual contacts of HBs Ag positive patients
- Persons who have ever injected drug
- Persons with multiple sexual partners or Hx of STD
- Men who have sex with men
- Inmates of correctional facilities
- Individuals with chronically elevated ALT or AST
- Individuals infected with HCV or HIV
- Patients undergoing renal dialysis
- All pregnant women
What should we order with positive risk factor screening of HBV infection

- **Hepatitis B surface antigen:**
  - The cardinal sign of current HBV infection
  - False negative is very rare

- **Hepatitis B surface antibody:**
  - Positive in remote infection or with immunization

- **Hepatitis B core Antibody (IgM)**
  - Positive in acute infection

- **Hepatitis B core Antibody (Total)**
  - Positive in current or remote infection but NOT with immunization

- **Hepatitis B DNA**

- **Hepatitis B e antigen and antibody**
# Chronic HBV infection

<table>
<thead>
<tr>
<th>Phase/Character</th>
<th>HBeAg</th>
<th>Anti-HBe</th>
<th>HBV DNA</th>
<th>ALT</th>
<th>Liver biopsy findings</th>
</tr>
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<tbody>
<tr>
<td><strong>Immune Tolerance</strong></td>
<td>Positive</td>
<td>Negative</td>
<td>++++</td>
<td>Normal</td>
<td>Normal or nonspecific</td>
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<tr>
<td><strong>Immune Clearance</strong></td>
<td>Positive</td>
<td>Negative</td>
<td>+++</td>
<td>Elevated</td>
<td>Chronic hepatitis (++)</td>
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<tr>
<td><strong>Inactive Carrier</strong></td>
<td>Negative</td>
<td>Positive</td>
<td>-/+</td>
<td>Normal</td>
<td>Non-significant hepatitis (usually)</td>
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<td><strong>Reactivation</strong></td>
<td>Negative or Positive</td>
<td>Positive or Negative</td>
<td>++</td>
<td>Elevated</td>
<td>Chronic hepatitis (+++ )</td>
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</table>
The Natural History of CHB

Acute HBV infection

Perinatal
- Resolved infection (~10%)
- Chronic infection (~90%)

Early Childhood
- Resolved infection (20-50%)
- Chronic infection (50-80%)

Adult
- Resolved infection (~95%)
- Chronic infection (~5%)

Reactivation phase (HBeAg+ chronic hepatitis)

Immune tolerance phase
- Immune tolerance phase (~85%)
- Pre-core/core mutation (~15%)
- Spontaneous HBsAg loss (0.5-2%/year)

Inactive carrier phase
- (10-20%/year)
- (4-20% with ≥ 1 sero-reversion)
- (2.6%/year)

Spontaneous HBsAg loss

Decompensation 5%/year

Cirrhosis
- Cirrhosis 2.5-3%/year

HCC

# HBV Therapy

## Table 1: Common indications for antiviral therapy in patients with chronic hepatitis B virus (HBV) infection

<table>
<thead>
<tr>
<th>Category</th>
<th>Indications for Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HBV e antigen positivity</strong></td>
<td>Persistent alanine aminotransferase (ALT) elevation with HBV DNA $&gt; 2 \times 10^4$ IU/mL, or</td>
</tr>
<tr>
<td></td>
<td>Significant liver injury (necroinflammation or fibrosis) on liver biopsy, or</td>
</tr>
<tr>
<td></td>
<td>Icteric ALT flare, or</td>
</tr>
<tr>
<td></td>
<td>Recurrent hepatitis flares with failed seroconversion</td>
</tr>
<tr>
<td><strong>HBV e antigen negativity</strong></td>
<td>Persistent ALT elevation with HBV DNA $&gt; 2 \times 10^3$ IU/mL, or</td>
</tr>
<tr>
<td></td>
<td>Significant liver injury (necroinflammation or fibrosis) on liver biopsy</td>
</tr>
<tr>
<td><strong>Compensated cirrhosis</strong></td>
<td>HBV DNA level $&gt; 2 \times 10^3$ IU/mL</td>
</tr>
<tr>
<td></td>
<td>Consider therapy even with lower HBV DNA levels if ALT is elevated</td>
</tr>
<tr>
<td>** Decompensated cirrhosis**</td>
<td>Any detectable HBV DNA; refer to a liver transplantation center</td>
</tr>
</tbody>
</table>

# Approved agents for treating hepatitis B virus infection

<table>
<thead>
<tr>
<th></th>
<th>INTERFERONS</th>
<th>NUCLEOSIDE/NUCLEOTIDE ANALOGUES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>INF ALFA-2B (INTRON-A)</td>
<td>PEG IFN ALFA-2A (PEGASYS)</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>5 MU/day or 10 MU 3 times weekly</td>
<td>180 μg/week</td>
</tr>
<tr>
<td><strong>Renal dose adjustment</strong></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>Subcutaneous</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td><strong>Duration in chronic hepatitis e antigen-positive</strong></td>
<td>4–6 months</td>
<td>1 year</td>
</tr>
<tr>
<td><strong>Duration in chronic hepatitis e antigen-negative</strong></td>
<td>1 year</td>
<td>1 year</td>
</tr>
<tr>
<td><strong>Black-box warnings</strong></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Drug resistance</strong></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Pregnancy risk category</strong></td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>
A 57 YOF with DM, HPL, and hypothyroidism presents for chronically abnormal LCT with ALT 2-4 times ULN, AST of 2-3 times ULN, and normal AP. Her Abdominal U/S showed increased echogenicity of the liver. W/U for viral and autoimmune CLD was negative. Liver biopsy revealed Steatosis along with ballooning degeneration, and moderate fibrosis. What is the likely diagnosis?

- AIH
- NASH
- Simple steatosis
- PBC
NAFLD

- Very common (About 23%)
- No alcohol
- Metabolic Syndrome
- Clusters (Low thyroid/Low Pituitary/OSA/PCO)
- AST:ALT ratio → not very helpful
- U/S: Good to do, but not very sensitive
- Rule out concomitant disease
- Liver biopsy: Steatosis versus NASH (steatosis+ significant inflammation+ hepatocytes Ballooning +/- fibrosis)
- Counsel your patient and treat MS aggressively
The Suggested Natural History of NAFLD

Simple Steatosis

Majority

Stable

NASH

25%-35%

Fibrosis Progression

9%-20%

Cirrhosis

10%/7 yrs

Liver cancer

65%-75%

Stable or with Regression

22%-33%

Death or OLT

50%/7 yrs

Liver failure
Hereditary Hemochromatosis (HH)

- In white people with Nordic or Celtic ancestry, the prevalence of HFE-related HH is 0.5%.
- But over all in whites, it is 1:300
- HH is classified broadly into 2 groups:
  
  1. **HFE-related HH (about 90%)**:
     - C282Y/C282Y → 85-90 %
     - C282Y/H63D (compound heterozygote) → 5 %
     - Others → including mis-sense mutations as S65C
  2. **Non-HFE-related HH (about 10%)**:
     - Hemojuvelin mutations (AR)
     - Hepcidin mutations (AR)
     - Ferroportin mutations (AD)
     - Others
## Stages of HH

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Parenchymal iron</th>
<th>Organ damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insignificant iron accumulation</td>
<td>0-20</td>
<td>0-5 gram</td>
<td>No</td>
</tr>
<tr>
<td>Iron overload with no organ damage</td>
<td>20-40</td>
<td>10-20</td>
<td>No</td>
</tr>
<tr>
<td>Iron overload with organ damage</td>
<td>&gt; 40</td>
<td>&gt; 20</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Diagnosis of HH/1-Iron studies

- Get the three; iron, TIBC, and ferritin (Not necessarily fasting)

<table>
<thead>
<tr>
<th>TS %</th>
<th>Sensitivity for HH</th>
<th>Specificity for HH</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% for Female 60 % for Male</td>
<td>92%</td>
<td>93%</td>
</tr>
<tr>
<td>45%</td>
<td>99%</td>
<td>44%, the other 56% are with NASH, ETOH, CHC, or C282Y/normal</td>
</tr>
</tbody>
</table>
Diagnosis of HH/HFE gene testing

- All patients with abnormal iron studies (TS ≥ 45%)
- First degree relatives (at age of 20 years or more) of patients with C282Y/H63D mutations
- The result could be:
  1-wt/wt (normal)
  2-H63D/wt
  3-H63D/H63D
  4-C282Y/wt
  5-C282Y/H63D
  6-C282Y/C282Y
A 48 YOF presents with fatigue and pruritus over the last 8 months. Her LCT revealed AST of 56, ALT 66, AP 480, and TB of 0.8. Which of the following will confirm the diagnosis of this patient disease?

- ANA
- SMA
- AMA
- Iron studies
Primary Biliary Cholangitis (PBC)

- Autoimmune disease affecting the small IHBD
- Usually female
- Genetic predisposition and environmental triggers
- A progressive disease of variable rate
- Fatigue, pruritus, Sicca syndrome
- Diagnosis: At least two of the followings:
  - Biochemical evidence of cholestasis
  - Positive AMA (90%-95%) → In negative cases → Positive ANA/ASMA
  - Biopsy showing Interlobular duct injury
Primary Biliary Cholangitis (PBC)

- Portal HTN even in pre-cirrhotic phase
- Osteoporosis with RR of 4.4
- Elevated cholesterol with HDL elevation
- Fat-soluble vitamin deficiency (ADEK)
- Urso
- Liver Transplantation in advanced stage
Question

- A 48 YOM with PMH of UC presents with fatigue and pruritus over the last 8 months. His LCT revealed AST of 56, ALT 66, AP 480, and TB of 0.8. AMA is negative. Which of the following will confirm the diagnosis of this patient disease?
  - ANA
  - SMA
  - Iron studies
  - ERCP
Primary Sclerosing Cholangitis (PSC)

- A male disease
- About 65% of patients with PSC have IBD
- 4% of patients with IBD (UC>CD) have PSC
- The mean time of diagnosis to death or LT is 10-12 years
- Cholangiocarcinoma (CC) occurs in about 10% with annual incidence of 1%-1.5%
- Accuracy of ERCP is 91% Vs 88% for MRCP
Cirrhosis and Portal hypertension
Natural history of chronic liver disease

- Increasing liver fibrosis
  - Steatohepatitis
  - HBV & HCV Hepatitis
  - Autoimmune Hepatitis
  - Biliary liver disease
  - Metabolic/Hereditary Liver Disease
  - Others

- Jaundice
- Encephalopathy
- Variceal bleeding
- Ascites

- Decompensated Cirrhosis
  - HCC
- Liver Transplantation
- Death

- Compensated Cirrhosis
  - Death

- Chronic Liver Disease
  - 2%-7%/Y
  - 5%-7%/Y
Liver Cirrhosis

- Stage 4 fibrosis (bridging fibrosis and regeneration nodules)
- Liver Biopsy is Not always needed
Skin signs of Chronic Liver Disease
Grading of Cirrhosis

- Child-Pugh score
- Cirrhosis Stages
- MELD score
### Child-Pugh Score

<table>
<thead>
<tr>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Encephalopathy</strong></td>
<td>None</td>
<td>Grade 1-2</td>
<td>Grade 3-4</td>
</tr>
<tr>
<td><strong>Ascites</strong></td>
<td>Absent</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Bilirubin (mg/dL):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In all except PBC</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>In PBC</td>
<td>1-4</td>
<td>4-10</td>
<td>&gt;10</td>
</tr>
<tr>
<td><strong>Albumin (g/dL)</strong></td>
<td>&gt;3.5</td>
<td>2.8-3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td><strong>PT/INR:</strong></td>
<td>&lt;4</td>
<td>4-6</td>
<td>&gt;6</td>
</tr>
<tr>
<td>Seconds over control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7-2.3</td>
<td>&gt;2.3</td>
</tr>
</tbody>
</table>
Child-Pugh Score

- Child A: 5-6 with 90% survival at 5 year
- Child B: 7-9 with 80% survival at 5 year
- Child C: 10-15 with 60% survival at 1 year
<table>
<thead>
<tr>
<th>Stage</th>
<th>Characters</th>
<th>1-Year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>No varices or ascites</td>
<td>1%</td>
</tr>
<tr>
<td>Stage II</td>
<td>Non-bleeding Varices</td>
<td>3%</td>
</tr>
<tr>
<td>Stage III</td>
<td>Ascites</td>
<td>20%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Variceal bleeding +/- Ascites</td>
<td>57%</td>
</tr>
</tbody>
</table>
MELD (Model for End Stage Liver Disease)

- Approved for organ allocation in February 2002
- Was initially studied to predict mortality after TIPS
- \[ \text{MELD} = 3.8[\ln \text{serum bilirubin (mg/dL)}] + 11.2[\ln \text{INR}] + 9.6[\ln \text{serum creatinine (mg/dL)}] + 6.4 \]
- The lowest is 6 and the highest is 40
- It predicts the 3 month mortality
Complications of Cirrhosis

- Portal Hypertension
  - Ascites
  - Esophageal and Gastric Varices
  - Hepatorenal Syndrome
  - Pulmonary Complications (HH, HPS, PPHTN)
  - Hypersplenism

- Coagulopathy

- Encephalopathy

- ? Cardiomyopathy

- Hepatocellular Carcinoma

- Malnutrition
A 58 YOM with HCV cirrhosis presents with progressive abdominal distension. U/S reveals ascites. The key underlying pathophysiological process(es) of ascites is/are:

- 1-Splanchnic vasodilation
- 2-Splanchnic vasoconstriction
- 3-Renal vasodilation
- 4-Renal vasoconstriction
- 1 and 4
- 2 and 3
Approach to Ascites...Easy!

- Do Paracentesis
- Get Cell count with diff always to rule out SBP
- Get ascitic albumin and protein
- Get Serum Ascitic Albumin Gradient (SAAG)
- If $\geq 1.1 \rightarrow$ Portal Hypertension:
  - If Protein $> 2.5 \rightarrow$ Think more of cardiac ascites
  - If protein $< 2.5\text{gm/dl} \rightarrow$ Think more of cirrhotic ascites
- If $< 1.1 \rightarrow$ Others (Cancer, TB, Renal, Thyroid...
Ascites Management

- Salt not fluid restriction
- NO NSAIDs
- Diuretics especially Spironolactone and maximize with monitoring
- Paracentesis:
  - Always for any inpatient if feasible
  - Get Cell count in a purple-top tube
  - No limit but give Albumin if ≥ 5 Liters or even less with renal insufficiency
- Transjugular Intrahepatic Portosystemic Shunt (TIPS)
Spontaneous Bacterial Peritonitis

- No specific or sensitive symptom or sign
- Ascitic fluid analysis is the only way
- PMNLs > 250 cells/cc and/or Positive Culture
- Ascitic fluid culture in BC tubes (80% Vs 50%)
- The usual MOs are E. coli (43%), Klebsiella (11%), Pneumococci (9%), and others
- Treat with 3rd GCS and add Albumin if TB > 4, Creatinine > 1, or BUN > 30 → ↓ HRS & short term Mortality
- Indefinite secondary prophylaxis if ascites exists
Variceal Bleeding

- Despite every thing we have, the current mortality of EV bleeding is at least 20% at 6 weeks and the immediate mortality from uncontrolled bleeding is 50%.
- Variceal bleeding ceases spontaneously in 40-50% of cases & in 80% by active therapy if done in the 1st 24h.
- With acute variceal bleeding:
  - ICU + Airway protection + good IV lineSSS with IVF
  - Octreotide IV (50 ug loading dose then 50 ug/hour for 3-5 d)
  - Keep Hb around 8 gm/dL and do not replace all lost blood (increase rebleeding risk and the mortality if you give more)
  - Ceftriaxone 1 gm IV daily for ≤ 7 days
  - EGD within 12 hours
  - Platelet and/or FFP transfusion if needed
  - Alert IR for possible TIPS
Hepatic Encephalopathy (HE)

- HE-A for ALF-related; B for Bypass (shunt) without intrinsic liver disease; and C for cirrhosis-related HE

- Regarding B and C:
  - Minimal HE: with 2 or more abnormal psychomotor tests (Digit symbol test, Block design test, Number connection test A and B)
  - Episodic HE: Spontaneous, precipitated, or recurrent (2 or more within 1 year)
  - Persistent HE (> 28 days): Mild (grade I and II), Severe (grade III and IV), and treatment-dependent
HE, Lines of Management

- Make sure of Diagnosis (No alternatives or Concomitant problems)
- Look for and treat the Predisposing Factors
- Specific Therapy
Make sure of Diagnosis

- Cirrhotic patients are not immune to other causes of AMS
- Gradual Onset
- Presence of precipitating factors
- Asterixis
- Non focal Neuro exam
- Ammonia level is not helpful
- Get CT head in the following scenarios:
  - Severe HE (grade III or IV)
  - Focal Neurological examination
  - Head trauma is suspected or confirmed
  - Absence of recovery/improvement with standard treatment
Specific Therapy

- **Lactulose/Krystalose:**
  - Still first line and cheap
  - Has side effects as Diarrhea that may ↑ Serum Na and Ileus
  - Get 3-4 semisolid BM daily

- **Rifaximin:**
  - Good Medicine with less side effects
  - Expensive but may be cost-effective

- **Neomycin:**
  - Rarely used now
  - 4% get absorbed → may lead to renal or Oto toxicity

- **Flagyl:**
  - Do not give it for long duration as it may lead to neuropathy

- **Others:**
  - Do not restrict protein intake completely
  - Compliance
Management of HRS

- Avoid Nephrotoxic drugs and diuretics
- Liver Transplantation Evaluation
- HRS-I:
  - Albumin
  - Vasoconstrictors (Octreotide & Midodrine)
  - Terlipressin/Noradrenaline
  - RRT if OLT candidate
- HRS-II
  - LVP with Albumin
  - ? TIPS
  - ? Vasoconstrictors (Octreotide & Midodrine)
Liver Neoplasms
A 29 YOF presents with RUQ discomfort. Her U/S revealed a liver lesion of 6 cm. She has been taking OCP over the last 5 years. Triphasic CT showed heterogenous enhancement with no central scarring or venous washout. AFP is normal.

The likely diagnosis in this patient is:

- 1-HCC
- 2-Adenoma
- 3-FNH
- 4-Hemangioma
# Adenoma & Focal nodular hyperplasia (FNH)

<table>
<thead>
<tr>
<th>Sex</th>
<th><strong>FNH</strong></th>
<th><strong>Adenoma</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Usually female</td>
<td>The same</td>
</tr>
<tr>
<td>Multiple lesions</td>
<td>About 30%</td>
<td>About 20%, called liver adenomatosis if &gt; 4 lesions</td>
</tr>
<tr>
<td><strong>Relation to OCP/Pregnancy</strong></td>
<td>Not clear</td>
<td>Very clear except with liver adenomatosis which has less strong association</td>
</tr>
<tr>
<td>Symptoms/Malignant transformation/Bleeding</td>
<td>Rare</td>
<td>Occasionally</td>
</tr>
<tr>
<td><strong>Findings on 3 phases CT/MRI:</strong></td>
<td>Homogenous Present (not always)</td>
<td>Heterogeneous Absent</td>
</tr>
<tr>
<td>-Arterial enhancement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Central arterial scar</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Resection</strong></td>
<td>If symptomatic or of uncertain diagnosis</td>
<td>Large (&gt;4.5cm), Symptomatic, OR With complications</td>
</tr>
</tbody>
</table>
Question

- A 58 YOM with HCV/ETOH cirrhosis presents with new onset ascites. Abdominal U/S showed a 4.5 cm mass in the liver. Triphasic CT showed the lesion with arterial enhancement and venous washout. AFP is normal. The most likely diagnosis is:
  - 1-Regeneration nodule
  - 2-Adenoma
  - 3-HCC
  - 4-Hemangioma
Hepatocellular Carcinoma (HCC)

- Increasing incidence and mortality
- The 3\textsuperscript{rd} most lethal cancer in the world
- Usually on top of cirrhotic liver from any cause with an annual incidence of 2-8%
- Chronic hepatitis B is an important exception
- Do U/S and AFP every 6 months to screen
- AFP sensitivity is 60\% at a level of 20 ng/mL
- If the screening is positive $\rightarrow$ Triphasic CT/MRI
- Liver mass biopsy is RARELY needed
Hepatocellular Carcinoma (HCC)

- Liver Resection: Small focal mass with no metastasis or portal HTN
- Liver Transplantation:
  - Milan Criteria:
    - One lesion $\leq 5$ cm OR 2-3 Lesions $\leq 3$ cm
    - No metastasis or Portal vein thrombosis
  - 5-year survival is $> 70\%$
- Percutaneous ablation (RFA, PEI)
- Trans Arterial Chemoembolization (TACE)
- Sorafenib in advanced stage
A Question

- A 45 YOF presents with RUQ discomfort. Her U/S revealed a liver lesion of 6 cm. No OCP. U/S revealed a well-demarcated homogeneous hyperechoic mass. MRI then showed Enhanced lesion more prominent in the delayed phase with centripetal pattern.

- The likely diagnosis in this patient is:
  - 1-HCC
  - 2-Adenoma
  - 3-FNH
  - 4-Hemangioma
Question

- A 57 YOM with Hx of UC presented with jaundice, weight loss for the last 6 weeks. His bilirubin was 6.2 with direct of 5. Triphasic CT showed Perihilar liver mass and IHBD dilatation with beaded appearance. His CA19-9 is 490 U/mL. The most likely diagnosis is:

  - PSC complicated with cholangiocarcinoma
  - PSC
  - PSC complicated with cholangitis
  - Cholangiocarcinoma
Orthotopic Liver Transplantation

- The same anatomic place
- The 1-year survival is now about 90% from 30% Forty years ago
- Refer patients with Child score > B7, MELD > 10, or with significant complication of Cirrhosis
- Extensive evaluation
- MELD score is used for allocation
- Demand is >>> the available livers → Living donor Liver Transplantation
Questions???
A 58 y.o. man with cirrhosis presents for ongoing management. Clinical exam reveals a soft protuberant abdomen with flank dullness. His laboratory tests are as follows: Na+: 134 mmol/L, K+: 3.8 mmol/L, Cl-: 98 mmol/L, BUN: 14 mg/dL, Cr: 1.14 mg/dL. You advise restricting dietary sodium intake to 2 grams daily, and start furosemide 20 mgs and spironolactone 50 mgs by orally. 3 weeks later, he returns and complains of worsening ascites. He has gained 10 lbs. His abdominal exam reveals more ascites than before. His repeat laboratory tests reveal:

- Na+: 124 mmol/L, K+: 4.2 mmol/L, Cl-: 97 mmol/L, BUN: 19 mg/dL, Cr: 1.27 mg/dL.

**Which of the following is the best plan for outpatient treatment of this patient's hyponatremia?**

- A. Increasing dietary salt intake.
- B. Increasing diuretics
- C. Restricting fluid intake.
- D. Starting tolvaptan (V2 receptor antagonist)
A 52 year old man is referred for elevated liver enzymes found on routine physical. He currently drinks at least 6 ounces of distilled alcohol per day. His physical exam is normal, apart from a body mass index of 29 kg/meters squared. Review of his laboratory work reveals:

- Hematocrit 38%, MCV 104 fL, Platelet count 162,000 K/uL, AST 148 U/L, ALT 34 U/L, alkaline phosphatase 113 U/L, total bilirubin 1.2 mg/dL, Ferritin 548 ng/ml (reference range 20-300). Serological markers for hepatitis A, B and C viruses are absent.

- An ultrasound of the abdomen shows an enlarged liver consistent with “fatty liver” but no nodularity and no splenomegaly.

Which of the following statements accurately describes this patient’s clinical state?

- A. The AST:ALT ratio is suggestive of alcoholic liver disease
- B. His platelet count makes a diagnosis of alcoholic liver disease unlikely.
- C. Absence of physical signs makes a diagnosis of alcoholic liver disease unlikely.
- D. The serum ferritin is suggestive of alcoholic liver disease
What statement is correct regarding renal failure requiring hemodialysis arising in patients awaiting liver transplantation?

- A. is most commonly attributable to Hepatitis C infection
- B. is always an indication for simultaneous liver-kidney transplantation
- C. may improve after liver transplantation in patients who require short-term hemodialysis
- D. is a contra-indication to liver transplantation
10. An elderly alcoholic man presents with an upper GI bleed. He also complains of chronic diarrhea. Physical exam is notable for bi-temporal wasting and ascites. His neurological exam is unremarkable. In addition, an erythematous, scaly, vesiculopustular rash is noted on his face and legs. He is stabilized, including upper endoscopy.

Which of the following serology tests is most likely to explain his symptoms and clinical signs:

- A. zinc
- B. 25-hydroxycholecalciferol
- C. thyroid stimulating hormone (TSH)
- D. Vitamin A
A 56 year old Caucasian male with cirrhosis of the liver due to hepatitis C undergoes upper endoscopy. You identify that patient has grade II esophageal varices with no red wale signs. The patient has no history of asthma or DM.

As primary prevention of esophageal variceal hemorrhage, which of the following treatments is indicated?

A. Nadolol
B. Isosorbide mononitrate
C. Losartan
D. Metoprolol
A 48 yo woman is referred for elevated liver tests over the last several months. The abnormality was discovered when she attended her primary care physician on account of ‘tiredness’. She has no other symptoms. The patient does not drink alcohol. She takes no medicines or supplements. She has a cousin with ulcerative colitis, but no first degree relatives have inflammatory bowel disease.

Investigations: AST 184 U/L, ALT 235 U/L Alk phos 260 U/L Total Bilirubin 1.9 mg/dL ANA 1:160, Anti smooth muscle antibody: negative, Anti mitochondrial antibody: negative Serum IgG: normal HBsAg: negative Anti HBs: positive Anti HBc: negative Anti HC: negative

Which of the following is the best next step?

- A. Start corticosteroids
- B. Liver biopsy
- C. Start ursodeoxycholic acid
- D. colonoscopy
A 16 year old young woman and her parents meet with you to discuss discontinuation of immunomodulatory medication as a treatment for autoimmune hepatitis type I. She presented with fatigue and elevated aminotransferases at age 10 years. Her ANA and SMA antibody titers were greater than 1:80 and a liver biopsy showed interface hepatitis with periportal hepatitis. An MRCP was normal and screening for Wilson Disease was negative. She was begun on treatment with prednisone 2 mg/kg/day and rapidly achieved biochemical and clinical remission. She has been on prednisone 5 mg daily for 4 years and her liver tests have been normal. Vital signs and physical exam: Anicteric healthy appearing 16 year old young woman  BP 105/60  HR 75  Temperature 37°C  No signs of portal hypertension

Diagnostic tests: Hgb: 14  AST 32 ALT 23 GGT 27  Albumin 4.2  ANA titer < 1:10  IgG level normal  Total Bilirubin: 0.7  INR 1.1  Platelets 282000

Which of the following is the next best step before discontinuation of immunomodulatory medications?

A. Monitor liver tests for additional 12 months on present therapy
B. MRCP
C. Change to every other day treatment with corticosteroids
D. Immunomodulatory medications should not be discontinued
E. Liver biopsy
A 17 year-old woman presents to her primary care physician for a routine visit as part of her preparation to enter university. She has no complaints. She is an excellent student and has had no recent change in her cognitive abilities or mental health. She is an athlete, competing successfully in the state tennis championships. She experienced menarche at age 13, since when her menstrual cycle has been irregular. Her last period was 5 months ago, which her pediatrician attributed to the stress of maintaining her studies, while applying for college and training for tennis. She denies drinking alcohol, smoking cigarettes or using illicit drugs. She is not sexually active. She takes no prescription medicines, nutritional supplements or herbal remedies. There is no family history of liver disease, or inherited disorders.

On examination, she is a healthy female whose height is 173 cms/ 5’8”, weight 67.8kg (145 lbs); body mass index is 22 kg/m2. Apart from a few scattered spider angiomata on her upper torso, her physical exam is normal. Examination of the eyes shows normal blue irises and absence of scleral icterus or pigmented corneal rings.

Her laboratory tests results are as follows: Hb: 12.4 g/dL WBC: 5.6 K/uL Platelets: 231 K/uL AST: 267 U/L ALT: 280 U/L Alkaline phosphatase: 244 U/L LDH: 68 U/L Total/Direct bilirubin: 0.7/0.3 mg/dL Total protein 9.1 g/dL Serum Albumin: 3.5 g/dL

Which of the following tests is most likely to assist in establishing the diagnosis in this patient?

- A. Human chorionic gonadotropin (hCG)
- B. Anti-mitochondrial antibody
- C. Ceruloplasmin
- D. Anti-nuclear antibody (ANA) and Anti-smooth muscle autoantibody (ASMA)
A patient presents to you for management of PBC and asks you to describe any factors that may be associated with the development of the disease.

Which of the following best describes a factor or factors associated with PBC?

A. Onset of abnormal liver chemistry tests in childhood (age <18 years).
B. More common in men than women
C. HLA gene loci
D. Watery eyes
E. Irritable bowel syndrome.
A 36 yo Asian man presents for advice on screening on HCC. He was discovered to be infected with hepatitis B virus at age 8 years, when his mother was diagnosed with hepatocellular carcinoma (HCC). He does not smoke or drink. His BMI is 25 Kg/meter squared. He has never received treatment.

His test results are as follows: T.Bil 0.8 mg/dL AST: 23 U/L ALT: 17 U/L Alkaline phosphatase 77 U/L Platelets: 293 K/uL HBeAg negative, HBeAb positive, HBV DNA 60,000 IU/ml, HBV Genotype C. Liver biopsy: inflammatory grade 1, fibrosis stage 2. Liver ultrasound shows a smooth surface to the liver, with normal echotexture.

What statement regarding screening for HCC best describes his situation?

A. He should start semi-annual screening now on account of the presence of liver fibrosis.
B. He should start semi-annual screening if he becomes HBeAg positive, HBeAb negative
C. He should start semi-annual screening when he becomes 40 yo.
D. He should start semi-annual screening now because he has a family history of HCC.
Which of the following statements most accurately reflects the AASLD guidelines regarding surveillance for hepatocellular cancer (HCC)? The AASLD guidelines recommend surveillance for HCC for:

A. all patients with cirrhosis, who could be treated if diagnosed with HCC, but not for liver disorders in the absence of cirrhosis.

B. all patients with cirrhosis, who could be treated if diagnosed with HCC, as well as some patients with chronic hepatitis B infection, even in the absence of cirrhosis.

C. all patients with cirrhosis, who could be treated if diagnosed with HCC and all patients with chronic viral hepatitis (hepatitis B, D and C) irrespective of the presence of cirrhosis.

D. all patients with compensated cirrhosis, but not patients with decompensation such as ascites, or a history of variceal hemorrhage.
A 55-year-old man is evaluated during a routine examination. He feels well other than mild knee pain. He drinks six to eight cans of beer per night. He has no personal history of liver disease, but his older brother was recently diagnosed with hereditary hemochromatosis.

On physical examination, vital signs are normal; BMI is 24. He is tanned on sun-exposed body surfaces. Cardiac examination is normal. Abdominal examination reveals hepatomegaly. Bilateral bony hypertrophy of the knees is noted.

Laboratory studies: Alanine aminotransferase 70 U/L, Aspartate aminotransferase 160 U/L

Ferritin 592 ng/mL (592 µg/L) Transferrin saturation 40%

Genetic testing for hemochromatosis reveals heterozygosity for C282Y. Abdominal ultrasound reveals a change in liver echotexture consistent with fatty changes.

Which of the following is the most appropriate treatment?

• Administer deferoxamine
• Perform phlebotomy
• Repeat serum iron tests now
• Stop alcohol intake
A 68-year-old man is evaluated for new-onset ascites with lower-extremity edema. Symptoms have increased gradually over the past 4 weeks. He has consumed three alcoholic beverages per day for many years. His medical history is notable for coronary artery bypass graft surgery 8 months ago and dyslipidemia. His medications are low-dose aspirin, atorvastatin, and metoprolol. On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 122/84 mm Hg, pulse rate is 64/min, and respiration rate is 16/min; BMI is 28. Cardiac examination reveals an elevated jugular venous pressure, a normal S₁ and S₂, and no murmurs. Pulmonary examination findings are normal. Abdominal examination reveals hepatomegaly, distention, dullness to percussion over the flanks, and a positive fluid wave. There is 2+ pitting edema of the lower extremities. Laboratory studies reveal a serum albumin level of 3.5 g/dL (35 g/L). Other studies, including serum alanine aminotransferase and aspartate aminotransferase levels, are normal. Paracentesis reveals a total nucleated cell count of 120/µL with 30% polymorphonucleocytes. Ascitic fluid albumin level is 2.3 g/dL (23 g/L) and total protein is 3.5 g/dL (35 g/L).

Which of the following is the most likely cause of this patient's ascites?

- Alcoholic cirrhosis
- Non Alcoholic cirrhosis
- TB peritonitis
- Constrictive Pericarditis
A 56-year-old woman is hospitalized for new-onset confusion. She has a history of decompensated hepatitis B cirrhosis with chronic ascites. Her medications are spironolactone, furosemide, lactulose, and entecavir. On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 118/62 mm Hg, pulse rate is 88/min, and respiration rate is 20/min; BMI is 23. She is disoriented to time and date. Asterixis is noted. The abdomen is moderately distended with ascites. Laboratory studies reveal a serum bilirubin level of 2.9 mg/dL (49.6 µmol/L), a serum creatinine level of 1.3 mg/dL (114.9 µmol/L), and a blood urea nitrogen level of 34 mg/dL (12.1 mmol/L). Diagnostic paracentesis reveals a nucleated cell count of 820/µL with 70% polymorphonuclear leukocytes. Gram stain and culture results are pending.

Which of the following is the most appropriate treatment?

- Cefotaxime
- Cefotaxime and normal saline
- Cefotaxime and Albumin
- Norfloxacin
A 28-year-old man is evaluated in follow-up for elevated liver chemistry test results, which were performed to assess a 3-month history of fatigue. He has no history of liver disease and has not had abdominal pain or fever. His medical history is significant for a 3-year history of diarrhea.

On physical examination, vital signs are normal; BMI is 24. Spider angiomata and jaundice are absent. Abdominal examination reveals hepatomegaly but no splenomegaly or ascites.

Laboratory studies:

- Alanine aminotransferase 75 U/L, Aspartate aminotransferase 87 U/L, Alkaline phosphatase 456 U/L, Total bilirubin 1.2 mg/dL (20.5 µmol/L), Direct bilirubin 0.4 mg/dL (6.8 µmol/L), Abdominal CT shows a thickened extrahepatic bile duct but no intrahepatic biliary dilatation and no hepatic or pancreatic mass. Magnetic resonance cholangiopancreatography reveals changes consistent with primary sclerosing cholangitis.

Which of the following is the most appropriate next step in management?

- ERCP
- Colonoscopy
- Liver biopsy
- IgG4