HEPATITIS

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Hepatitis

- An inflammatory process of the liver
  - Usually presents with elevated liver enzymes
  - Can be infectious or non-infectious
    - Infectious = A, B, C....
    - Non-infectious = medications, ETOH
- Most common are Hepatitis A, B, and C
  - D, E, G......
- Can be acute or chronic
- Prognosis varies by type
Liver Enzymes:

- **Theoretically**, a measure of the severity of hepatocellular injury or inflammation.

- **ALT** = ALANINE AMINOTRANSFERASE
  - Not uncommon to see only ALT elevated and not impressive, especially in chronic infection.
  - More specific to the liver than AST.
  - Circulatory half-life 37-57 hours.
  - Normal range 10-40 IU/L.

- **AST** = ASPARTATE AMINOTRANFERASE
  - Circulatory half-life 12-24 hours.
  - Normal range 10-34 IU/L.

**TAKE HOME**: SMALL ELEVATION DESERVES INVESTIGATION.
CDC Statistics for 2012

- Estimated 3,050 new cases of HAV
  - Most acquired outside US by adult travelers
- Estimated 18,760 new cases of acute HBV
  - Chronic HBV estimated at 700,000 – 1.4 million of US population
  - 1/2 of chronic HBV are Asian or Asian-American born to HBV infected mothers in the US
- Estimated 21,870 new cases of acute HCV
  - 75% increase from 2010 to 2012
  - 20% of all new cases in Tennessee, West Virginia, and Kentucky
  - 75-85% of newly infected persons develop chronic infection

Hepatitis A

- Transmitted via fecal-oral route
  - 50% international travelers
  - Male-male sexual activity
  - Food and water borne
  - Injection drug use
  - Sexual/household contact

- VACCINE AVAILABLE
  - Not a live virus
  - Two injections at 0 and 6 months

Who needs Hepatitis A Vaccine?

- All children at age 1 year
- Foreign travelers, esp with high rates of HAV
- Men who have sex with men
- Illegal drug users (injection and non)
- Persons with clotting-factor disorders
- Persons with chronic liver disease (including HBV, HCV)
- Caregivers of adoptees from countries with high rates of HAV
Hepatitis A Serology

- Hepatitis A Antibody (Anti-HAV antibody)
  - Positive only indicates exposure
  - Does not differentiate between past or current infection
- IgG \(G=Gone\)
  - Positive indicates past infection
  - Indicates immunity
  - Will be positive for years
- IgM
  - Positive indicates current infection
  - Will be positive at symptom onset and for months later

HEPATITIS B
Hepatitis B

- DNA Virus
- Transmitted through blood/body fluids
  - Commonly sexually transmitted
  - Sharing drug paraphernalia
  - Perinatal transmission
  - Close household contacts
- Chronic infection risk decreases with increasing age

- VACCINE AVAILABLE
  - Not a live virus
  - Series of three injections at 0, 1 and 6 months

Source:

Who needs HBV vaccine

- All infants at birth and children not previously vaccinated
- Sex partners of infected persons
- Persons with multiple sex partners
- Men who have sex with men
- Injection drug users
- Household contacts of infected persons
- Healthcare/public safety/emergency personnel
- Persons with chronic liver disease, ESRD, or HIV
- Unvaccinated with diabetes, ages 19-59
Hepatitis B Serology
Understanding the markers......

- **HBsAg**: Hepatitis B Surface antigen - protein on surface of HBV produced in response to infection. Positive during *acute or chronic infection*

- **anti-HBs**: Hepatitis B Surface antibody – antibody on surface of HBV produced in response to infection. *Indicates immunity* from either illness or vaccination.

- **anti-HBc**: Hepatitis B core antibody – appears at onset of symptoms of acute hepatitis, persists for life. Indicates *prior or current HBV infection*.

- **IgM anti-HBc**: IgM antibody to hepatitis B core antigen – M=misery - presence indicates *acute infection* (or recent <6 months)

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<th>anti-HBc</th>
<th>anti-HBs</th>
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<td>negative</td>
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<td>positive</td>
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<td>Immune due to natural infection</td>
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<td>negative</td>
<td>negative</td>
<td>positive</td>
<td>Immune due to Hepatitis B <em>vaccination</em></td>
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Immune due to natural infection or vaccination?

### Natural Infection
- HBsAG negative – (HBV surface antigen) - not currently infected
- anti-HBc positive – (HBV core antibody) – antibodies have developed due to current or recent infection
- anti-HBs positive – (HBV surface antibody) – appears at onset of acute HBV and persists for life = immunity

### Vaccination
- HBsAG negative – (HBV surface antigen) - not currently infected
- anti-HBc negative – (HBV core antibody) – no current or recent infection
- Anti-HBs positive (HBV surface antibody) – appears at onset of acute HBV and persists for life = immunity

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Acute or Chronic Infection?

### Acute
- HBsAg positive – (HBV surface antigen) – currently infected
- anti-HBc positive – (HBV core antibody) – antibodies have developed to current or recent infection
- IgM anti-HBc positive – (antibody to HBV core antigen) – Indicates acute infection (M = misery)
- anti-HBs negative – (HBV surface antibody) – no recovery or immunity

### Chronic
- HBsAg positive – (HBV surface antigen) – currently infected
- anti-HBc positive – (HBV core antibody) – antibodies have developed to current or recent infection
- IgM anti-HBc negative – (antibody to HBV core antigen) – NOT an acute infection (no misery)
- anti-HBs negative – (HBV surface antibody) – no recovery or immunity
Time to pull it all together.......
Hepatitis C

- RNA Virus
- Found primarily in blood
- Usually asymptomatic
- Transmitted primarily through injection drug use
- Other modes of transmission:
  - Blood transfusions prior to 1992
  - Needlestick injuries
  - Sexual contact (infrequent)
  - Sharing person items
  - Perinatal
- 75-85% become chronic

Source: cdc.gov/hepatitis/HCV/HCVfaq.htm#section1

Why Hepatitis C is BAD NEWS

- Most common bloodborne infection in the US
  - 2.7 – 3.9 million chronically infected
- #1 reason for liver transplant in the US
- Average time to seroconversion (anti-HCV) is 8-9 weeks
- Infection most prevalent in those born between 1945-1965
- 75-85% develop chronic infection
- 60-70% develop chronic liver disease
- 5-20% develop cirrhosis
- 1-5% will die from liver cancer or cirrhosis
THE NEW FACE OF HCV INFECTION

- Young persons
- White
- Non-urban areas
- History of injection drug use
- Previously used opioid agonists

Source: cdc.gov/hepatitis/Statistics/2012Surveillance/Commentary.htm

CDC Testing Recommendations for Hepatitis C

- BABY BOOMERS 1945-1965 regardless of risk factors
- Injection drug users (current or past)
- Persons who:
  - Received blood transfusion prior to 1992
  - Received clotting factor before 1987
  - Ever on hemodialysis
  - Persistently elevated ALT
  - HIV+
  - Are at increased risk for exposure (healthcare, EMS, public safety)
  - Born to HCV-positive mothers (risk of transmission low)
Hepatitis C diagnostic testing:

- If anti-HCV screening test positive, then
- HCV recombinant immunoblot assay (HCV RIBA)
  - OR
  - **HCV-RNA** by PCR (not as sensitive to low level viremia)
    - "Viral load"
- Genotyping

END OF HEPATITIS PART 1
Hepatitis Part 2

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Chief Complaint:

- **If symptomatic**, may present with a few of these or many of these:
  - Jaundice **
  - Itching
  - Scleral icterus
  - Malaise
  - Myalgia
  - Fatigue
  - Nausea
  - Anorexia
  - Aversion to cigarette smoking
Less common complaints:

- Arthritis-like symptoms
- Skin rash
- Diarrhea
- Low-grade fever
- RUQ tenderness
- Dark colored urine **
  - You have to ASK
- Acholic stools **
  - You have to ASK

Differential Diagnoses:

- Viral illness
  - Symptoms non-specific
- Non-infectious cause of hepatitis
  - Medication
    - Statins, Acetaminophen, OCP, Phenytoin, Dilantin, Isoniazid
    - AST>ALT
  - ETOH induced
    - AST>ALT – usually 2X
SUBJECTIVE:

▲ Complaints will generally be vague – easy to miss!
▲ Many patients do NOT complain of jaundice or icterus

Review of Systems:

▲ General: fatigue, malaise, +/- fever
▲ HEENT: scleral icterus
▲ GI: nausea, occasionally vomiting, diarrhea, possibly RUQ tenderness, anorexia, acholic stools
▲ Skin: pruritis
▲ Urinary: “Coke” colored urine
## History

### Medical
- Allergies
- Medications:
  - Statins
  - Acetaminophen
  - OTC and herbs
- Vaccinations
- Blood/blood products
- Recent illness?
  - EBV, varicella zoster...

### Family
- Household exposures with known disease
- Similar illness in family members (food-borne?)

### Social
- Injection drug use
- ETOH use/abuse
- Sexual partners
- Any STIs?
- Travel history
- Child care center

## Physical Examination:

- Skin, mucous membranes, sclera
- Abdominal exam
  - Liver size and tenderness
  - Splenomegaly
Diagnostic testing:

*Hepatitis panel ~ If positive, THEN commonly:*
- Hepatitis D if Hepatitis B +
- AST and ALT
- CBC
- Platelet count
- Prothrombin time
- Total bilirubin – typically →
- Alkaline phosphatase

- HIV

Plan/Management:

### Hepatitis A
- Reportable disease
- Supportive care:
  - Rest, fluids, diet, no ETOH, avoid acetaminophen
  - Usually complete recovery
- Counseling:
  - Transmission
  - Risk factors

### Hepatitis B
- Reportable disease
- Supportive care (acute)
- 95% complete recovery
- Counseling:
  - Transmission
  - Risk factors
- Hepatitis A vaccination
- REFERRAL FOR CHRONIC INFECTION
  - Anti-viral drugs

### Hepatitis C
- Reportable disease
- Supportive care (acute)
  - Only 20% symptomatic
- Counseling:
  - Transmission
  - Risk factors
- Hepatitis A & B vaccination
- REFERRAL***
**HCV Pharmacologic Treatment:**

- **Pegylated Interferon** – long acting form of Interferon
- **Ribavirin** – Used only in combination with Interferon
- **Boceprevir** (Victrelis) – protease inhibitor **Both used in combination**
- **Telaprevir** (Incivek) – protease inhibitor
- **Semprevir (Olysio)** – once-daily protease inhibitor**
  - Combination with Interferon/Riba
  - **Shorter treatment**
  - **Better cure rate**
- **Sofosbuvir** (Sovaldi) – polymerase inhibitor
  - Genotypes 1, 2, 3, and 4

**Source:** American Liver Foundation

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**HCV Plan/Management (cont)**

- **REFERRAL**
- **Viral genotyping**
  - at least 6 genotypes
  - 1a – 50-60% in US
  - 1b – 15-20% - most severe symptoms, poorest response to Interferon therapy
- **LIVER BIOPSY** **GOLD STANDARD**
Post-exposure Prophylaxis (Adults)

**Hepatitis A**
Single dose of single-antigen hepatitis A vaccine or immune globulin (IG) within 2 weeks of exposure

**Hepatitis B**
Hepatitis B vaccine asap, preferably within 24 hours of exposure

**Hepatitis C**
Prophylaxis with immune globulin is not effective

Premature Infants born to HBsAg + mothers:
- HBIG + single-antigen HBV within 12 hours of birth
  - Dose NOT counted as part of series
- Regular series of HBV vaccination
- Test for HBsAg and antibody to HBsAg 1-2 months after completion of series

**Term Infants:**
- HBIG + HBV within 12 hours
- Dose 2 at one month, dose 3 at 6 months
- Retest at 9-15 months of age
Followup

- Depends on potential for chronicity
  - B & C – refer for monitoring for chronic infection
  - Alpha-fetoprotein (AFP) – marker for hepatic tumor growth