18 year-old with jaundice

- 18 y/o presents with 5d of headache, fever, diarrhea, vomiting, chest pain
- PMH – Open fractures of all R metatarsals with pins x 3mo
- SH – home tattoos; lives with parents and pregnant girlfriend; dogs and rats; swam in freshwater dam 1 wk before symptom onset; cuts grass; multiple tick bites; Maryland

18 year-old with jaundice, con’ t

- T 39.4; BP 118/62 (then on pressors); P 91; 97% RA
- Icteric, non-injected, no murmurs
- Diffuse petechial rash; purple macules on ankle
- WBC 11,740 (92.4 P, 0.8B, 2% L); Hb 14.2; Plt 47,000
- Creatinine 0.9-3.4; CRP 10.1; Tbil 4.1 (direct 3.7); ALT/AST 26/53; CK 887
- HIV Ab neg; SARS-CoV-2 PCR neg; Monospot - neg

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18 year old with jaundice

The cause of his illness is:
A. Acute hepatitis A
B. Babesia microti
C. Tularemia
D. Leptospira icterohaemorrhagiae
E. HSV

Leptospirosis

1. Exposure to fresh water (eg rafting in Hawaii/Costa Rico or triathlon) OR rats (Baltimore)

2. Bilirubin fold change > ALT

3. Biphasic possible and systemic findings (conjunctival suffusion, kidney, skin, muscle, lungs, liver)
   - ddx: liver (ALT) and muscle (CPK): lepto, flu, adeno, EBV, HIV, malaria, Rickettsia/Ehrlichiosis, tularemia, TSS, coxsackie, vasculitis

4. Diagnosis:
   - PCR most useful (urine pos longer)
   - serology late
Acute Hepatitis in Uganda

- 42 year old female has malaise and RUQ pain; she just returned from 2 months working at an IDP camp in north Uganda. She endorses tick and other ‘bug’ bites and swam in the Nile. 1st HAV vaccine 2 days before departure. Prior HBV vaccine series.
- Exam shows no fever, vitals are normal. RUQ tender. Mild icteric. ALT 1245 IU/ml; Hb 13.4 g/dl; TB 3.2 mg/dl; WBC 3.2k nl differential.

Acute hepatitis in Uganda

Which test result is most likely positive?
A. Ebola PCR
B. IgM anti-HEV
C. IgM anti-HAV
D. Schistosomiasis “liver” antigen
E. 16S RNA for Rickettsial organism

1. Vaccination works vs immune globulin to prevent hepatitis A up to 14d after exposure

<table>
<thead>
<tr>
<th>End Points</th>
<th>Per-Protocol Population</th>
<th>Modified Immune Globulin Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Vaccine Group</td>
<td>Control Group</td>
</tr>
<tr>
<td>Primary</td>
<td>25 (3.5)</td>
<td>24 (3.5)</td>
</tr>
<tr>
<td>Secondary</td>
<td>25 (3.5)</td>
<td>24 (3.5)</td>
</tr>
</tbody>
</table>

Victor NEJM 2007

2. There are HEV outbreaks, eg. North-Ugandan IDP Camp

3. Hepatitis E: Epidemiologic Clues

- Outbreaks – contaminated water in Asia/Africa
- Sporadic - undercooked meat (BOAR, deer, etc)
- Overseas travel typical
- USA: endemic rare, genotype 3, IgG serology positive far more than can be explained by cases - can be hard to interpret
4. Hepatitis E: Clinical Clues

- Fatalities in pregnant women
- Can be chronic in transplant (rarely in HIV)
- GBS and neurologic manifestations (vs other hep viruses); pancreatitis
- Diagnosis: RNA PCR; IgM anti-HEV
- Treatment: ribavirin for chronic
- Vaccine: not USA (not boards)

Acute Hepatitis at ID Week

- 42 year old homeless male approaches a group of ID fellows while attending ID Week in San Diego.
- One fellow noticed jaundice and suggested he seek medical testing. With what diagnosis was the fellow most concerned?

1. Hepatitis A: Key Epidemiologic Clues – People, Places and Foods

Homelessness and Hepatitis A—San Diego County, 2016–2018

1. Hepatitis A: Key Epidemiologic Clues – People, Places and Foods

Outbreak of Hepatitis A in Hawaii linked to raw scallops

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2. Hepatitis A: Key Clinical Clues

- There are outbreaks all over the world
- The most common cause of acute hepatitis in USA
- Clinical syndrome
  - fulminant on HCV
  - relapsing: symptoms/jaundice recur <12 mo

3. Vaccination to Prevent Hepatitis A

- Pre-exposure: vaccinate
  - HOW: Inactivated vaccines USA (HAVRIX, VAQTA) (TWINRIX)
  - WHOM: HCV or HBV positive persons/chronic liver disease/homeless/MSM/PWID/Travelers/HIV pos/adoptive exposure
  - All children 1-18 yrs receive hepatitis A vaccine (since 2006)

- Post-exposure: vaccinate (and possibly IG)
  - Unless >40 years or immunosuppressed then IG is “preferred”
  - Close exposure (sex or IDU partner) not casual (eg office worker)

Acute Viral Hepatitis B Clues

- Most linked to sex, drugs, nosocomial
  - Nosocomial (fingerstick devices, etc)
  - Most transmissible (HBV>HCV>HIV)
- Clinical
  - Acute immune complex disease possible
  - Diagnose: IgM anti-core, HBsAg and HBV DNA
  - New infection vs reactivation (both can be IgM pos)

More on HBV

- See lecture on chronic hepatitis for prevention, HIV coinfection, and treatment

Acute Viral Hepatitis Delta will be with HBV

- HDV
  - HBV coinfection
    - Fulminant with acute HBV
  - HBV superinfection
    - Acute hepatitis in someone with chronic HBV
  - Test for HDV RNA (antibodies for routine screen)

Acute Viral Hepatitis C clues

- HCV
  - IDU link (hepatitis in Appalachia)
  - HIV pos MSM
  - Acute RNA pos but AB neg or pos
  - 60-80% persist: more in men, HIV pos, African ancestry, INFL4 gene intact

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**OL3 - Online Only Lectures - Acute Hepatitis**

*Speaker: David Thomas, MD*

### Hepatitis in a pilot

- 70 y/o pilot presents with 1 week of fever, diarrhea and sweats, then “collapses”
- Tooth extraction 1 month before, E. Shore of Maryland and extensive travel, chelation “treatment”
- T 38.1, 135/70, 85, 18, 97% on 2L; few small nodes, petechial rash on legs, neuro- WNL

### Pilot Case History, con’t

- Hct 33%, WBC 1.4 K (81% P 10% L), Plt 15,000
- Creat 2.8
- AST 495, ALT 159, Alk Phos 47, alb 2.6, TBR 0.8
- CPK 8477
- CXR: infiltrate LLL

### What agent caused this illness?

A. Leptospira icterohaemorrhagiae  
B. Hepatitis A  
C. EBV  
D. Ehrlichia chaffeensis  
E. Hepatitis G (GB virus C)

---

### Hepatitis with bacterial infections

1. Think Rickettsia/Ehrlichia with exposure, low PMN, modest ALT, and especially low platelets

---

### Hepatitis with bacterial infections

2. Coxiella burnetti and spirochetes (syphilis and lepto) also in ddx with liver, lung, renal, skin, CNS disease but tend to be cholestatic vs Rickettsia/Ehrlichia
Hepatitis with bacterial infections

3. Hepatitis F or G are always WRONG answers

Hepatitis with travel to developing country

There is a broad differential

Hepatitis with travel

Especially remember dengue (below), Chickungunya, or Zika

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Present</th>
<th>Random</th>
<th>Normal</th>
<th>Aver</th>
<th>Max</th>
<th>Hyper</th>
<th>min. + 3SD (ALT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.8%</td>
<td>1.2%</td>
<td>5%</td>
<td>11%</td>
<td>1%</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>0.04%</td>
<td>0.07%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.5%</td>
<td>1%</td>
<td>3%</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>0.03%</td>
<td>0.05%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1%</td>
<td>3%</td>
<td>6%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>25%</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>0.5%</td>
<td>1%</td>
<td>2%</td>
<td>3%</td>
<td>5%</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.4%</td>
<td>0.6%</td>
<td>1%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>0.02%</td>
<td>0.03%</td>
<td>0.05%</td>
<td>0.07%</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Hepatitis in Pregnancy

What is the best diagnosis?

A. HELLP
B. Acute fatty liver of pregnancy
C. Atypical DRESS from cefalexin
D. HSV infection
E. HEV

What is the best diagnosis?

A. HELLP
B. Acute fatty liver of pregnancy
C. HAV infection
D. HSV infection
E. HEV

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Hepatitis in pregnancy

1. Rule out HSV
   ~50% have mucocutaneous lesions
   High mortality without acyclovir

Hepatitis in pregnancy

2. HELLP
   – HTN and can occur post partum
   – Fibrinogen high vs. sepsis and AFLP

3. AFLP – severe and low glucose, inc INR, low fibrinogen (Swansea criteria)

Fulminant hepatitis

- 65 year old man with hx of jaundice. 2 weeks before finished amoxicillin/clavulanate acid for sinusitis. Hx of HTN on HCTZ and rosuvastatin. ETOH: 2 drinks per day.
- TB24; ALT 162 U/L; AST 97 U/L ALK P 235 U/L. IgM anti-HAV neg; IgM anti-HBc neg; HCV RNA neg. RUQ US neg.

Fulminant Hepatitis

Which of the following is the most likely cause of hepatitis:
A. toxicity from amox/clav
B. alcohol
C. porphyria flare
D. leptospirosis
E. statin

Fulminant Hepatitis

Which of the following is the most likely cause of hepatitis:
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D. leptospirosis
E. statin

Drug related liver toxicity

Amoxicillin/clavulanate is most common

- Cholestatic or mixed
- Often AFTER stopping
- 1/2500 Rx
- DRB1*1501
- clavulanate-amoxicillin

**Acute Hepatitis Summary**

- Acute A: vaccine effective
- HEV: chronic in transplant and/or boar
- HIV: acute HCV in MSM
- Low plt: Ehrlichial or rickettsial
- Find the lepto case (jaundice>hepatitis)

**Case 6. Hepatitis in Pregnancy**

- 24yo 33 wks gestation with nausea and vomiting and RUQ pain. Taking acetaminophen 1gm q6; has dog and bird; recent visit to mom in NC.
- T 37.2; BP 158/110; 2/6 SEM; RUQ tender; no rash.
- Plt 103K; Hct 26; WBC 6.6 10%/l; PMN 82%; G 85; creat 0.6; ALT 225; AST 559; TB 1.4; CRP 15.8; PT WNL; fibrinogen NL.

**Case 4: Tired and jaundiced**

- 27 year old male presents with fatigue and dark urine. Hx recent sexual exposures with other men.
- No fever, vitals normal. Mild icteric. ALT 1945 IU/ml; AST 1239 IU/ml; TB 4.2 mg/dl; WBC 3.2k nl diff.
- Total HAV pos; HAV IgM neg; HCV RNA neg; IgM anti-HBc pos; HBsAg pos; RPR neg; HIV 4th gen neg
- Ptr was tested and is HBsAg and anti-HBs neg

**Hepatitis in 2020: SARS-CoV-2**

Table 2. Laboratory and radiographic findings of patients with COVID

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (median)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate dehydrogenase (LDH)</td>
<td>432 (235)</td>
<td>152-1265</td>
</tr>
<tr>
<td>Creatine kinase (CK)</td>
<td>223 (179)</td>
<td>52-2800</td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>6.6 (3.9)</td>
<td>0.0-19.0</td>
</tr>
<tr>
<td>Procalcitonin (PCT)</td>
<td>3.0 (2.0)</td>
<td>0.0-33.0</td>
</tr>
<tr>
<td>Platelets (PLT)</td>
<td>128 (105)</td>
<td>68-420</td>
</tr>
<tr>
<td>Red blood cell count (RBC)</td>
<td>4.4 (4.2)</td>
<td>3.6-5.5</td>
</tr>
<tr>
<td>Hemoglobin (Hb)</td>
<td>12.9 (12.5)</td>
<td>10.5-15.0</td>
</tr>
<tr>
<td>Hematocrit (Hct)</td>
<td>40.2 (39.5)</td>
<td>34.0-47.0</td>
</tr>
<tr>
<td>White blood cell count (WBC)</td>
<td>9.4 (6.9)</td>
<td>4.0-12.5</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>60.2 (49.6)</td>
<td>38.0-74.0</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>22.7 (18.9)</td>
<td>16.0-44.0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>10.7 (8.8)</td>
<td>5.0-12.5</td>
</tr>
</tbody>
</table>

**Case 7.**

- 24yo 33 wks gestation with nausea and vomiting and RUQ pain. Taking acetaminophen 1gm q6; has dog and bird; recent visit to mom in NC.
- T 37.2; BP 158/110; 2/6 SEM; RUQ tender; no rash.
- Plt 103K; Hct 26; WBC 6.6 10%/l; PMN 82%; G 85; creat 0.6; ALT 225; AST 559; TB 1.4; CRP 15.8; PT WNL; fibrinogen NL.

Thanks and good luck on the test!

Questions:

Dave Thomas
—dthomas@jhmi.edu
Question #4
Which is easiest to justify medically?
A. Repeat HBsAg and anti-HBs testing for partner
B. HBIG and HBV vaccine for partner
C. HBV vaccine for partner
D. Entecavir 0.5 mg/d for patient
E. TAF for partner

Diagnose acute HBV infection with IgM anti-HBc

2. No treatment indicated for acute HBV (unless fulminant)

3. Prevention by vaccine +/- HBIG
   - HBsAg and anti-HBs screening of partners
   - Tools: HBIG and/or HBV vaccine (USA)
     - Engerix, Recombivax, Heplisav-B, Pediarix, Twinrix
   - Post-exposure:
     - Vaccinated and anti-HBs >10 ever, done*
     - No hx vaccine and/or anti-HBs >10, HBIG and vaccinate

*may be exception for patients with immunosuppression like HIV or dialysis

3. Prevention by vaccine +/- HBIG con’t
   - Pre-exposure:
     - no vaccine hx – vaccinate
     - Vaccine hx no testing – test for anti-HBs, boost or revaccinate if neg, retest anti-HBs

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Acute hepatitis in HIV

46 y/o HIV pos male, CD4+ lymphocyte 235/ml³, HIV RNA undetect; HBsAg pos; no symptoms on TDF/FTC/RAL. Liver enzymes increased from ALT of 46 to 1041 IU/L. TB was 2.3. He has a long history of various ART regimens. He is sexually active with other men.

Acute hepatitis in HIV

Which of the following is the most likely cause of hepatitis:

A. toxicity from the RAL
B. acute HCV infection
C. IRIS
D. resistant HBV
E. HDV