Hepatitis Training Webinar
August 2nd, 2017

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OREGON HEALTH AUTHORITY
Hepatitis A
Hepatitis A - Serologies

- Anti-HAV, IgM: indicates acute infection.
- Anti-HAV, total (IgM and IgG): marker of past or present infection.
- ALT/AST: useful indicators of liver damage.
Hepatitis A Virus Infection
Typical Serologic Course

- Clinical Illness
- Total anti-HAV
- ALT
- IgM anti-HAV
- Viremia
- HAV in Stool

Weeks After Exposure
Number of Cases of HAV by Year, Oregon, 1997-2016

Oregon: Annual case counts < 100 since 2002; <50 since 2005
>99% reduction from pre-vaccine era

Routine vaccination for high incidence states

Routine vaccination for all kids
Reported Risk Factors (mutually exclusive) for Acute Hepatitis A, Oregon, 2016 (n=17)

- Travel: 39%
- OB related: 8%
- No risk ID: 53%
Hepatitis B
Surface Antigen (HBsAg)

- Protein found on the outer surface of the virus
- Marker of replicating virus, either acute or chronically infected
- Persists indefinitely in chronic infection
- Patient is infectious
- Transient HBsAg positivity has been reported for up to 18 days after vaccination
Acute HBV Infection with Recovery

Typical Serological Course
Core antibody (anti-HBc)

- IgM anti-HBc: indicative of infection in the recent past (<6 months). Best test for acute infection.
  - But no longer part of our acute case definition. Doh!
- Anti-HBc, total (IgG and IgM): marker of past or current infection.
  - Vaccination does not produce anti-HBc.
  - False positive tests can occur in up to 20% of persons tested
Acute HBV Infection with Recovery
Typical Serological Course

Symptoms

Titer

Weeks after Exposure

Titer

HBsAg

IgM anti-HBc

Total anti-HBc

Window phase
Surface Antibody (anti-HBs)

- Antibodies produced against HBsAg as the host recovers from infection
- Produced after either natural infection or immunization (lasts for months after HBIG)
- Indicates immunity
Acute HBV Infection with Recovery

Typical Serological Course

Weeks after Exposure

Titer

Symptoms

Total anti-HBc

HBsAg

IgM anti-HBc

anti-HBs

Window phase
E Antigen (HBeAg) and Antibody (Anti-HBe)

- **HBeAg:**
  - Marker of high infectivity (4X more infectious)

- **HBeAb/anti-HBe:**
  - Indicates loss of HBeAg
  - Seroconversion from e antigen to e antibody is a predictor of long-term clearance of HBV
Acute HBV Infection with Recovery

Typical Serological Course

- **HBeAg**
- **anti-HBe**
- **Total anti-HBc**
- **HBsAg**
- **IgM anti-HBc**
- **anti-HBs**

**Symptoms**

**Window phase**

Weeks after Exposure:

- 0
- 4
- 8
- 12
- 16
- 20
- 24
- 28
- 32
- 36
- 52
- 100

Titer
HBV DNA

- Active replication of virus, patient infectious
- Testing is expensive, rarely obtained during acute infections
- Used to detect chronic infection, viral load may be used to decide whether to initiate treatment
- Detectable in ~50% of carriers. Can be present when HBsAg is undetectable
Chronic HBV Infection
Typical Serological Course

- **Acute (6 months)**
  - HBeAg
  - IgM anti-HBc
  - HBsAg
  - Total anti-HBc

- **Chronic (Years)**
  - anti-HBe
  - HBV DNA

- **Titer**

Weeks after Exposure: 0 4 8 12 16 20 24 28 32 36 52

Years: 0 4 8 12 16 20 24 28 32 36 52
Cases of Acute HBV, Oregon, 2005-2016
Reported Risk Factors (mutually exclusive) for Acute Hepatitis B, Oregon, 2016

- Infusions, transfusions, dialysis and surgery: 5.9%
- Street drugs, needlestick, tattoo, piercing, other blood exposure: 5.9%
- IDU: 5.9%
- Contact Hep B: 5.9%
- MSM: 11.8%
- Multiple Sex Partners: 5.9%
- Potential Healthcare Exposure: 23.5%
- Dental Care: 11.8%
- Other Risk: 11.8%
- No Risk ID/Unknown Risk: 23.5%

*infusions, transfusions, dialysis and surgery
**street drugs, needlestick, tattoo, piercing, other blood exposure
Cases of Chronic HBV in Oregon, 2005-2016
Most common risk factors among chronic HBV Cases, Oregon, 2016
(n=313 interviewed)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign born</td>
<td>189 (60%)</td>
</tr>
<tr>
<td>Multiple sex partners</td>
<td>110 (35%)</td>
</tr>
<tr>
<td>Contact of a case</td>
<td>96 (31%)</td>
</tr>
<tr>
<td>History of transfusion</td>
<td>34 (11%)</td>
</tr>
<tr>
<td>Employed in a medical field</td>
<td>25 (8%)</td>
</tr>
<tr>
<td>Ever STD</td>
<td>24 (8%)</td>
</tr>
<tr>
<td>MSM</td>
<td>18 (6%)</td>
</tr>
</tbody>
</table>
Hepatitis D
Hepatitis D - Serologies

- anti-HDV IgM: indicative of ongoing replication
- Anti-HDV total (IgG and IgM): indicative of chronic or acute infection
- HDV PCR: most sensitive for detecting HDV viremia
Hepatitis C
Hepatitis C - Serologies

- **Anti-HCV EIA**
  - Enzyme immunoassay to measure HCV antibody. Cannot be used to distinguish between recent and past infection.
  - Signal-to-cutoff ratio is used to determine the likelihood that a positive HCV EIA represents a true positive. It is calculated by dividing the optical density value of the sample.
  - Infants born to HCV+ mothers, can have detectible maternal antibodies for up to 18 months

- **PCR**
  - Polymerase chain reaction. Used to measure HCV RNA. There are both qualitative (more sensitive) and quantitative tests.

- **Genotyping**
  - 6 different genotypes. Genotype 1 is the most common in the US, accounting for 70-75% of infections.
2006 Age Distribution of newly reported HCV cases, n=5,463
2015 Age Distribution of newly reported HCV cases, n=5,926
Acute Hepatitis C, Oregon and Nationally, 2007-2015
Hepatitis C Deaths in Oregon and Nationally, 2000-2015
Reported Risk Factors (mutually exclusive) for Acute Hepatitis C, Oregon, 2016

- **IDU**, 62.5%
- Potential Healthcare Exposure, 12.5%
- Multiple Sex Partners, 6.3%
- Other Risk**, 18.8%

*Transfusion, infusions, dialysis and surgery

**street drugs, needlestick, tattoo, piercing, contact of a case, and other blood exposure
Hepatitis E
Serologies – Hepatitis E

- Anti-HEV, IgM: indicates acute infection.
- Anti-HEV, total (IgM and IgG): marker of past infection.
- HEV RNA: detectable by PCR in acute phase feces in ~50% of cases.
Case Studies
Hepatitis B

- 36 year old male IDU tested for hepatitis during follow up for cellulitis. Test results are as follows:
  - + anti-HCV
  - - total anti-HAV
  - - HBsAg
  - - anti-HBs
  - - + total anti-HBc
  - - - IgM anti-HBc

- The patient began injecting drugs at age 23. Does not recall ever having acute HBV infection and does not remember ever receiving HBV vaccine.
Which one of the following most accurately describes the patient’s HBV serology results?

A. A finding of isolated anti-HBc represents past infection with hepatitis B
B. The isolated anti-HBc test has a greater than 95% likelihood of representing a false positive result, and thus the patient should be considered negative for acute or prior HBV infection.
C. A finding of isolated anti-HBc most likely represents a weak response to hepatitis B vaccine, and the patient probably just doesn't remember that he's been vaccinated.
D. Persons with HIV and chronic HCV infection have the lowest prevalence of isolated anti-HBc because they generate enhanced levels of anti-HBs that remain elevated on a long-term basis.
Hepatitis B

- 27-year old woman presents to the urgent care clinic with new onset of nausea and jaundice
- For three years, she has experienced major problems with drug addiction and regularly injects meth
- She usually uses clean needles, but six weeks ago shared needles with a man she found out has HBV infection
- She has never received HBV vaccine
- Two years ago, she tested negative for hepatitis A, B, and C
- Physical examination is normal except for track marks on her arms and visible jaundice.
- Laboratory studies show elevated LFTs, and serology tests for hepatitis A, B, and C viruses are ordered
Which of the following serologic profiles would be most consistent with acute HBV infection?

<table>
<thead>
<tr>
<th>Test</th>
<th>(a) Results</th>
<th>(b) Results</th>
<th>(c) Results</th>
<th>(d) Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Total anti-HBc</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>HBeAg</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Hepatitis C

27 year old female with a history of injection drug use gives birth at 37 weeks. Mom is tested for hepatitis C due to her history of IDU. She has no signs or symptoms of acute viral hepatitis. Results are:

- +anti-HCV
- + RNA PCR
How would you classify this case?

A. Confirmed, acute hepatitis C
B. Presumptive, acute hepatitis C
C. Confirmed, chronic hepatitis C
D. Presumptive, chronic hepatitis C
E. No case
The infant is then tested and she is anti-HCV positive.

What now?

A. Create an acute case
B. Create a presumptive chronic case
C. Create a confirmed chronic case
D. Create a suspect chronic case
E. Call me and get the answer
Hepatitis B

- 40 year old male tested for HBV during his yearly physical
- Case is asymptomatic and LFTs are within normal limits
- Case was born in the United States but mother is from China
- Lab results show:
  - HBsAg Positive
  - Total anti-HBc Positive
- ELRs comes through under Hepatitis B (acute)
How should this case be classified?

A. Presumptive, acute hepatitis B
B. Confirmed, acute hepatitis B
C. Presumptive, chronic hepatitis B
D. Confirmed, chronic hepatitis B
E. No case
For chronic hepatitis B, cases should be positive for one or more:
- Hepatitis B surface e antigen
- Hepatitis B e surface antigen
- Hepatitis B DNA

Results for IgM anti-HBc may not be reported if negative
Hepatitis B Lab Testing

- Some facilities report preliminary test results via ELR.
- If you do not receive confirmatory results, please follow up as the confirmatory testing may have been negative.
- Labs noted to report preliminary results:
  - Providence
  - Biomat Plasma
  - CSL Plasma
  - Talecris Plasma
  - Bloodworks NW
Perinatal Hepatitis B Prevention Program Overview

- Ensure all pregnant women are tested for hepatitis B with each pregnancy
  - In Orpheus this means checking pregnancy status when new labs received for all women of child bearing age [15-45]
  - Some ELRs now indicate if the results are from a prenatal panel (e.g. OB, prenatal)

- Infants born to HBV+ women receive proper preventative treatment (HBIG + vaccine) and testing
  - In Orpheus: add the infant as a contact and track each piece of case management
Updates

Investigative Guidelines (April 2017)

- Expanded case definitions to include HBeAg and HBV DNA
- Added Probable case definition
  - HBV+ infant born to a mother with an unknown status
- New recommendations for infants requiring a second vaccine series
- Added a standard lost to follow-up definition

Orpheus

- Tracking pregnancies that end in miscarriage
- Tracking pregnancies transferred out of state before delivery
  - Both in the pregnancy history box
Perinatal hepatitis B case management activities in Oregon, 1994-2015 birth cohorts. Shown is the number of infants enrolled in case management and the percent of those infants meeting the indicators of successful case management.
Best Practices

- If you need to change an acute case to chronic, may need to copy down risks before changing the disease in Orpheus.
- If new labs are received for an existing acute hepatitis case that suggest chronic infection, create a new chronic hepatitis case for the person.
- When interviewing cases, please try to obtain information on contacts and country of birth.
- Make sure to enter contacts on the contact tab.
- Assess vaccination status by querying ALERT for cases and any contacts elicited.
If you have multiple serology results, it might be a good idea to create a manual lab so you can get an easy snapshot of all of the different results.

For old, out of state cases with a new ELR/Oregon residency:
- Create a new case with the new lab; email the tech team to merge the OLD case to the NEW case.

While not required, LHDs are encouraged to determine reason for testing on chronic hep C cases for persons <30 years of age and to determine if there was a previous negative result (possible asymptomatic seroconverter).
Best Practices con’t

- To transfer a case between counties:
  - Add the new address to the Person Record (not on the Basic tab)
  - On the More tab, add the new county of residences and mark as ‘current’
  - Notify the new county of residences so they can add a new Local Epi

- Check on pregnancy status for females of childbearing age
- The pregnancy field in the demographics section only needs to be answered when a case is first identified and interviewed.
- When an infant contact is created, connect it to the appropriate pregnancy from the Pregnancy History box on the Basic tab
Fin
Questions?
Country of origin for interviewed HBV cases, Oregon 2016

- USA: 60.4%
- Unknown: 26.5%
- Foreign-born: 13.1%

n=313 interviewed
Hepatitis E Virus Infection
Typical Serologic Course

Symptoms

Titer

Virus in stool

ALT

IgG anti-HEV

IgM anti-HEV

Weeks After Exposure

0 1 2 3 4 5 6 7 8 9 10 11 12 13
Acute HCV Infection with Recovery

Typical Serologic Course

- Symptoms +/-
- HCV RNA
- anti-HCV
- ALT

Titer

Time After Exposure

0 1 2 3 4 5 6

0 1 2 3 4

Months

Years

Normal
Risk of Fatal Outcome in Persons Who Develop Hepatitis C Infection

Resolved: 15
Stable: 68
Cirrhosis: 17
Mortality: 4

Resolved 15: 15%
Chronic 85: 80%
Cirrhosis 17: 75%
Mortality 4: 25%

85% of persons develop chronic hepatitis C infection.

 Courtesy of Seeff, LB and Alter, HJ.
Hepatitis A – Clinical Features

- **Incubation period**: Average: 30 days, Range: 15-50 days
- **Clinical illness (jaundice)**:
  - <6 yrs: <10%
  - 6-14 yrs: 40-50%
  - >14 yrs: 70-80%
- **Complications**: Fulminant hepatitis in <1%
- **Chronic sequelae**: None
- **Transmission**: Fecal-oral
Post-exposure prophylaxis

- Vaccine (HAVRIX or VAQTA) is recommended as post-exposure prophylaxis in healthy persons 12 months through 40 years of age.

- Immune globulin (IG) is typically used for post-exposure prophylaxis in persons who are either older than 40 years of age, children younger than 12 months of age, immunocompromised persons, and persons with chronic liver disease.

- Might as well vaccinate at the same time.
Requesting IG

- Contact ACDP Epi on-call for approval with the following information:
  - Number of contacts needing IG
  - Weight and age of each contact eligible for IG
  - Insurance status of each contact.
  - Calculated amount of IG needed
- IG is supplied in 2-mL and 10-mL vials
- IG dosage recommendation: 0.02 mL/kg; IM
- LHDs should bill insurance for IG if the contact has insurance
Hepatitis B – Clinical Features

- **Incubation period**
  - Average: 60-90 days
  - Range: 45-180 days

- **Clinical illness (jaundice)**
  - Mild to severe

- **Complications**
  - Fulminant hepatitis in <1%
  - Cirrhosis, HCC

- **Chronic infection**
  - 10-90% (varies inversely with age)

- **Transmission**
  - Blood, percutaneous and permucosal contact, close personal contact, perinatal.

*Why is HBV infection dangerous?*

- Healthy
- Cirrhosis
- Liver Cancer
<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low/Not Detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood</td>
<td>semen</td>
<td>urine</td>
</tr>
<tr>
<td>open wounds</td>
<td>vaginal fluid</td>
<td>feces</td>
</tr>
<tr>
<td></td>
<td>saliva</td>
<td>sweat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tears</td>
</tr>
<tr>
<td></td>
<td></td>
<td>breast milk</td>
</tr>
</tbody>
</table>
# Post-exposure Prophylaxis for Occupational Exposure to HBV

## Vaccination and antibody response status of exposed workers

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Source HBsAg positive</th>
<th>Source HBsAg negative</th>
<th>Source unknown or not available for testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unvaccinated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B immune globulin (HBIG) x 1 (0.06/mL/kg IM) and initiate HB vaccine series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Previously Vaccinated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Known responder</strong></td>
<td>No treatment</td>
<td>No treatment</td>
<td>No treatment</td>
</tr>
<tr>
<td><strong>Known nonresponder</strong></td>
<td>HBIG x 1 and initiate revaccination or HBIG x 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Response unknown</strong></td>
<td>Test exposed person for anti-HBs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. If adequate, no treatment is necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. If inadequate, administer HBIG x 1 and vaccine booster</td>
<td>No treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test exposed person for anti-HBs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. If adequate, no treatment is necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. If inadequate, administer vaccine booster and recheck titer in 1-2 months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Post-exposure Prophylaxis for Non-Occupational Exposure to HBV

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous (e.g., bite or needlestick) or mucosal exposure to HBsAg-positive blood or body fluids</td>
<td>Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG). HBIG dose is 0.06 mL/kg intramuscularly</td>
</tr>
<tr>
<td>Sex or needle-sharing contact of an HBsAg-positive person</td>
<td>Administer hepatitis B vaccine series</td>
</tr>
<tr>
<td>Victim of sexual assault/abuse by a perpetrator who is HBsAg-positive</td>
<td>Administer hepatitis B vaccine series</td>
</tr>
<tr>
<td>Victim of sexual assault/abuse by a perpetrator with unknown HBsAg status</td>
<td>Administer hepatitis B vaccine series</td>
</tr>
<tr>
<td>Percutaneous (e.g., bite or needlestick) or mucosal exposure to potentially infectious blood or body fluids from a source with unknown HBsAg status</td>
<td>Administer hepatitis B vaccine series</td>
</tr>
</tbody>
</table>
Requesting HBIG

- Contact ACDP Epi on-call for approval with the following information:
  - Number of contacts needing HBIG
  - Weight and age of each contact eligible for HBIG
  - Insurance status of each contact.
- HBIG is supplied in 5-mL vials. HBIG costs >$600 per 5-mL vial, and OHA has a very limited supply.
- HBIG dosage recommendations
  - Adults: 0.06 mL/kg; IM
  - Infants <12 months: 0.5 mL single dose
- LHDs should bill insurance for IG if the contact has insurance
Hepatitis B Serologies
Hepatitis D – Clinical Features

- Incubation period: 2-8 weeks
- Clinical illness (jaundice): Mild to severe. Abrupt onset.
- Chronic sequelae: Superinfection in persons with chronic HBV
- Complications: Children with acute coinfection have higher likelihood of developing chronic infection
- Transmission: Similar to HBV
- Prevention: HBV vaccination
Hepatitis C – Clinical Features

- Incubation period: Average 6-9 weeks, Range 2 weeks – 6 months
- Clinical illness (jaundice): Mild (20-30%)
- Chronic sequelae: 75-85%
- Complications: Cirrhosis, hepatocellular CA
- Transmission: Blood
- Post-exposure prophylaxis/vaccine: None
- Treatment: >90% cured
How it’s Not Spread

- Not spread by sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or casual contact
- People should not be excluded from work, school, play, child-care or other settings on the basis of their HCV infection
Hepatitis E – Clinical Features

- Incubation period: Average 26-42 days, Range 15-64 days
- Clinical illness (jaundice): Similar to HAV
- Complications: 20% case-fatality in pregnant women (3rd trimester)
- Chronic sequelae: Chronic disease among immunocompromised
- Transmission: Fecal-oral
- Vaccine: Yes, but only in China
- Prophylaxis: IG has not been effective
Hepatitis A

- 39 year old female with + anti-HAV IgM reported to LHD
- Has signs and symptoms consistent with hepatitis A and elevated LFTs
- Two household contacts identified
  - 8 year old son; vaccination status is unknown
  - 45 year old spouse; never vaccinated
Prophy - who should get it and how?

Which contact should receive IG?
A. Son
B. Spouse
C. Both
D. Neither

Where do I call to get IG?
A. ACDP – ask for Tasha
B. ACDP – ask for Ann Thomas
C. ACDP – ask for the Epi on-call
D. Immi – ask for Tila
E. Immi – ask for Paul Cieslak
What information does ACDP need with the IG request?

A. Age
B. Height
C. Weight
D. Insurance status
E. Amount IG needed
F. Name of PCP
G. A, C, D, and E
H. A, B, D, E, and F
I. All of the above
Fun Fact

- The weapon I fence with is?
  - Broadsword
  - Foil
  - Epee
  - Sabre