Interpretation of Viral Hepatitis Serology

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Learning Objective

• Given serologic markers, diagnose acute or chronic viral hepatitis
Viral Hepatitis: Clinical Presentation

- Spectrum: Asymptomatic → fulminant
- Nonspecific signs and symptoms
- Elevated liver enzymes
- Impaired liver function (typically only mild)
Acute Hepatitis: Probably NOT Viral

- Very high LAE’s: >5000
- Low LAE’s: <300
- High bilirubin on initial presentation
- High fever
# Acute vs. Chronic Viral Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong></td>
<td>&lt; 6 months</td>
<td>&gt; 6 months</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Spontaneous resolution</td>
<td>Unlikely to clear on its own</td>
</tr>
<tr>
<td><strong>Permanent Liver Damage</strong></td>
<td>None</td>
<td>Likely</td>
</tr>
</tbody>
</table>
Viral Hepatitis

- Hepatitis A – HAV
- Hepatitis B – HBV
- Hepatitis C – HCV
- Hepatitis D – HDV
- Hepatitis E – HEV
A

Is for Acute

• Always Acute
• Never Chronic
• Fecal-Oral transmission
Is for **Blood** (& sex)

- Transmitted by:
  - Inoculation with infected blood
  - Sexual contact
- Endemic in Southeast Asia and Africa
C is for Chronic

- Almost always chronic
  - 80% become chronic
  - 20% clear the infection on their own
- Rarely acute symptoms
Getting on the same page

- Ag = antigen

- Ab = antibody
- Anti-__ __ = antibody

- IgM
  - Acute marker

- IgG
  - Chronic marker
  - Previous exposure

- Total
  - Measures both IgG and IgM forms of the antibody
Hepatitis A
Hepatitis A – Serology

• Hepatitis A **ANTIBODY**
• **Anti-HAV-IgM**
  – First antibody to appear
  – Denotes acute disease
• **Anti-HAV total**
  – Includes both IgM and IgG fractions
  – May indicate acute disease or past exposure
• The IgM **must** be positive to diagnose acute hepatitis A!
HAV: Serologic Detection

• Anti-HAV IgM: 1 week - 6 mos
• Anti-HAV IgG: detectable for life
Hepatitis A – Summary

• Acute disease only
• Anti-HAV-IgM establishes the diagnosis of acute disease
• Anti-HAV (total) with a negative IgM fraction indicates immunity
Hepatitis B
Hepatitis B in Adults

Acute Hepatitis B

Resolved Infection

95%

Chronic Infection

5%

Chronic Hepatitis

Asymptomatic Carrier

Chronic Hepatitis

Cirrhosis

Hepatocellular carcinoma
Hepatitis B Virus Structure

- HBsAg
- HBcAg
- HBeAg

42nm

(HBsAb)
(HBcAb)
(HBeAb)

https://commons.wikimedia.org/wiki/File:Hepatitis_B_virus_v2.svg
HBsAg

http://depts.washington.edu/hepstudy
HBcAg

http://depts.washington.edu/hepstudy
To dig to the center, start on the surface, then dig through the earth to reach the core.

Adapted from: Theriot, BL. Clinical Laboratory Science Review. Creative Educators.
HBV: Detection and Diagnosis

Surface: HBsAg
Earth: HBeAg
Core: HBcAb

Adapted from: Theriot, BL. Clinical Laboratory Science Review. Creative Educators.
HBV: Detection and Diagnosis

Core: HBcAb
Earth: HBeAb
Surface: HBsAb

Adapted from: Theriot, BL. Clinical Laboratory Science Review. Creative Educators.
Hepatitis B that resolves

HBsAb -> HBsAg

HBeAb -> HBeAg

HBcAb

HBsAb
Chronic Hepatitis B

- HBsAg
- HBeAg
- HBcAb

Road Closed
The 3 question approach to diagnosis:

- **Acute Hepatitis B**
  - 95%Resolved Infection
  - 5%Chronic Infection

- **Resolved Infection**
- **Chronic Infection**
- **Chronic Hepatitis Asymptomatic Carrier**
- **Chronic Hepatitis**
Question # 1

1. Does the patient have hepatitis B?
   ✓ Check HBsAg

   • HBsAg (-) – NO 😊
   • HBsAg (+) – YES 😞

   What should be your next question?
2. Is the infection acute or chronic?

- Check HBcAb-IgM
  - HBcAb-IgM (+)
    - Acute hepatitis
    - Recheck serology in 6 months
  - HBcAb-IgM (-)
    - Chronic hepatitis

What should be your next question?
3. Is the patient viremic?
   ✅ Check HBeAg
   - HBeAg (-)
     – Carrier, low viremia
     – Observe every six months
   - HBeAg (+)
     – Highly infectious
     – Referral to GI for further evaluation
Hepatitis B – Serology

HBsAg
Hepatitis B Surface Antigen

Without it, there is NO hepatitis B infection!
Hepatitis B – Serology

• Acute hepatitis B
  – HBsAg (+)
  – HBcAb – IgM (+)

• Hepatitis B core Antibody – IgM fraction
  – Must be positive in acute infection
  – Must be negative in chronic infection
HBV: Serologic Detection

- HBcAb IgM: clinical onset - 6 months
- HBcAb IgG: persists indefinitely
Hepatitis B – Serology

HBeAg
Hepatitis B Early Antigen
Indicates replicating virus
# Chronic Hepatitis B

<table>
<thead>
<tr>
<th>Carrier</th>
<th>Viremic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low infectivity</td>
<td>Very infectious</td>
</tr>
<tr>
<td>• HBsAg (+)</td>
<td>• HBsAg (+)</td>
</tr>
<tr>
<td>• HBeAg (-)</td>
<td>• HBeAg (+)</td>
</tr>
<tr>
<td>• HBeAb (+)</td>
<td>• HBeAb (-)</td>
</tr>
<tr>
<td>• ALT normal</td>
<td>• ALT elevated</td>
</tr>
</tbody>
</table>

Chronic Hepatitis B
- HBsAg (+) > 6 months
- HBcAb-IgM (-)
Hepatitis B – Serology

HBsAb
Hepatitis B Surface Antibody

Indicates immunity in absence of HBsAg,
Only positive marker after vaccination
Hepatitis B – Serology

• Prior Immunization
  – HBsAb (+) only

• Prior Infection
  – HBsAb (+)
  – HBcAb (+) (total)
Hepatitis B – Review

- Check HBsAg
  - POS? Check HBcAb - IgM
    - POS? Acute
      - Check HBsAb in 6 months
        - POS? Immune
  - NEG? Chronic
    - NEG? Carrier
      - NEG? Chronic
        - POS? Viremic
          - NEG? Chronic
            - NEG? Carrier
              - NEG? DONE

Department of PA Studies  A.T. Still University  ATSU
A “core window” exists between disappearance of antigen (HBsAg) and appearance of antibody (HBsAb).

HBcAb-IgM may be the only detectable marker during the “core window”
Hepatitis B – Summary

• Does the patient have HBV?
  • HBsAg
• Acute or chronic?
  • HBcAb-IgM
• Carrier or active infection?
  • HBeAg
• Immunity?
  • HBsAb
<table>
<thead>
<tr>
<th>Marker</th>
<th>Acute</th>
<th>Chronic</th>
<th>Carrier</th>
<th>Resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>HBsAb</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>HBcAb</td>
<td>+ IgM</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IgG/Total</td>
<td></td>
<td>IgG/Total</td>
</tr>
<tr>
<td>HBeAg</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HBeAb</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>+/-</td>
</tr>
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</table>
Hepatitis C
Hepatitis C – Overview

• Initial infection **usually asymptomatic**
  – <20% will have mild nonspecific symptoms
  – Transmission: blood inoculation
  – >80% develop chronic hepatitis

• Serologic tests do not definitively distinguish acute from chronic
Hepatitis C – Serology

• Hepatitis C ANTIBODY
• *Anti-HCV*
  – Best initial diagnostic test
  – Accurate & sensitive in high risk patients
    • Elevated AST & ALT
    • History of blood transfusion
    • History of IVDU
• Positive test indicates infection until proven otherwise!
Hepatitis C – Serology

• HCV-RNA
  – Detects actual viral particles – *viral load/viremia*
  – Used to:
    • Confirm infection
    • Monitor therapy
  – Negative HCV-RNA with a positive antibody most likely indicates resolution

• **Important:** *Viral load does not correlate with severity of disease*
Hepatitis C – Summary

• Usually chronic at the time of diagnosis
• **Anti-HCV is the best initial test**
• Positive Anti-HCV and elevated LAE’s usually confirm diagnosis – refer for treatment
• HCV-RNA detects viremia
Serologic Evaluation

**Acute Hepatitis Panel**

1. Anti-HAV, IgM fraction
2. HBsAg
3. HBcAb, IgM fraction
4. Anti-HCV

A B C
## Serologic Evaluation

### Acute Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>HBcAb-IgM</th>
<th>Anti-HAV-IgM</th>
<th>Anti-HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute A</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Acute B</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Acute C</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
# Serologic Evaluation

## Chronic Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>Anti-HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B</strong></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>&gt; 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
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References


