Hepatitis B
by Alex Ho

Disease:
Hepatitis is an inflammation of the liver. Hepatitis B is an infectious liver disease caused by hepatitis B virus (HBV), an etiologic agent. Without treatment, the infection can progress to liver cancer, liver failure, or cirrhosis and eventually death unless people receive liver transplant. Hepatitis B infection is 50-100 times more infectious than HIV (1).

Transmission:
Hepatitis B virus is transmitted through contact with infected blood or body fluids, such as semen or vaginal fluids. The virus does not spread through food, water, air, breastfeeding, kissing, or shared eating utensils.

Examples of exposure:
- Unprotected sex with infected person
- In contact with blood, open sores, needles, or body fluids at work
- Being born from infected mother
- Sharing needles for drug use with infected person
- Getting tattooed or pierced with unsterilized tools
- Sharing household items: razor, toothbrush, or nail clippers (2,3)

Reservoirs:
Humans

General characteristics of HBV:
Hepatitis B virus belongs to the family of Hepadnaviridae and consists of a core particle surrounded by an envelope. The core particle is made up of partially double-stranded DNA, DNA polymerase capable of reverse transcriptase, and core antigen (HBcAg). The envelope consists of surface antigen (HBsAg). The diameter of the virion is 30-42 nm. Three different particles are found in the serum of infected people (4,5).

Infectious particle:
-Dane particle: largest particle, complete virion, and capable of replicating.

Noninfectious particles:
-Spherical particle: half the size of Dane particle and unassembled without nucleic acids.
-Filamentous particle: tubular shape, same diameter as spherical particle but 10 times as long, and unassembled without nucleic acids (4,5).

Hepatitis B virus replicates in the liver and its presence triggers an immune response leading to inflammation of the liver as the liver tries to fight off the infection (6).

Key tests for identification:
Blood test is the serological test used to identify HBV and the stage (acute or chronic) of the infection. The result is broken down into 5 categories as listed below.

<table>
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<tr>
<th>Tests</th>
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<th>Interpretation</th>
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</thead>
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<tr>
<td>HBsAg</td>
<td>negative</td>
<td>Susceptible</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td>Immune due to natural infection</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
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</tr>
<tr>
<td>anti-HBc</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td>Immune due to Hepatitis B vaccination</td>
</tr>
<tr>
<td>HBsAg</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td>Acutely infected</td>
</tr>
<tr>
<td>HBsAg</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>negative</td>
<td>Chronically infected</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1:** Results of liver blood test provided by CDC (3).

- **HBsAg**: hepatitis B surface antigen. Presence indicates infection.
- **anti-HBs**: antibody to hepatitis B surface antigen. Presence indicates immunity due to natural infection or vaccination.
- **anti-HBc**: antibody to hepatitis B core antigen. Presence indicates previous or ongoing infection. Persists for life.
- **IgM anti-HBc**: IgM antibody to Hepatitis B core antigen. Presence indicates acute infection (less than 6 months).

**Signs and symptoms of disease:**
Hepatitis B infection can often be misdiagnosed as having flu since the signs and symptoms are similar such as fever, fatigue, loss of appetite, nausea, and vomiting. Important clues in diagnosis are jaundice (yellowing of the skin and eyes), dark urine and pale stools, distaste for cigarettes, abdominal pain, and joint pain (3,7).

Incubation period of the hepatitis B virus is 6-24 weeks. The virus can be detected within 1-2 months after infection. Damage to liver is caused by the immune response destroying the infected cells. In acute infection, patients are sometimes symptomatic and the symptoms can either resolve within 6 months or progress to chronic infection. However, in chronic infection,
the majority are asymptomatic, infectious carriers for as long as 20-30 years resulting in unnoticed transmission and progression to liver cancer, liver failure, or cirrhosis and possibly death without treatment (6-8).

**Historical information:**
Dr. Baruch Blumberg and his colleagues discovered hepatitis B virus in 1967. The virus causes inflammation of the liver; thus, the word hepatitis (hepat/o- = liver and -itis = inflammation) and the letter B (B = Blumberg) were chosen. In 1969, Dr. Blumberg and Dr. Irving Millman invented the first vaccine (9).

Dr. Blumberg and his colleagues were originally looking for genetic differences associated with a disease in hemophiliacs. Through the use of the blood samples collected and the newly developed blood test in matching antibodies with antigens, the team made a unique discovery. The “Australian antigen” found in the blood sample of an Australian aborigine matched up with the antibody from NY hemophiliac. This specific antigen of the virus was later confirmed as the cause of hepatitis B infection (9).

**Virulence factors:**
HBV was originally known to produce three different proteins or antigens called HBsAg (surface), HBcAg (core), and HBeAg (envelope). Its virulence factor is due to the fact that it can hide surface antigen (HBsAg) from the immune system, thereby leading to or maintaining chronic infection (6).

New discovery of a special X protein (HBx) was published in January 2008 by Dr. Dina Kremsdorf and her associates. After a partial hepatectomy or injury, the liver is able to slowly regenerate. However, this X protein produced by HBV inhibits liver regeneration; thereby, exacerbating the infection (10).

**Control/treatment:**
For acute infection, there is no treatment since the symptoms will resolve within 6 months or less. Immunity due to natural infection can develop over time. Possible home treatment to alleviate symptoms can include eating balanced diet, staying hydrated, and avoiding heavy workload and alcohol (7,8,11).

For chronic infection, some people can be treated with interferons and antiviral drugs to slow the progression of cirrhosis and improve long-term survival. Liver transplant is another possible option for people with severe liver damage or liver failure (7,12).

**Interferons:** interferon alfa-2b and pegylated interferon alfa-2a

**Antiviral drugs (nucleoside reverse transcriptase inhibitors = NRTIs):** adefovir, entecavir, lamivudine, telbivudine, and tenofovir.

Liver cancer is fatal and most people die within months of diagnosis. However, surgery and chemotherapy can prolong life for up to a few years.
Infected people should be educated about hepatitis B infection and its transmission and be advised to engage in safe sex and injection and not to donate organs or blood.

**Prevention/vaccine:**
Hepatitis B vaccine provides the best protection against HBV for at least 20 years. The vaccine has been available on the market since 1982. Vaccination is given as a 3-dose injection with second and third doses administered at 1 and 6 months respectively after the first dose. There are 5 vaccines currently licensed in US (3).

**Single-antigen vaccine:**
- ENGERIX-B®
- RECOMBIVAX HB®

**Combination vaccines:**
- COMVAX®: Combined Hepatitis B-Haemophilus influenzae type b (Hib) conjugate vaccine (Age: 6 weeks-71 months)
- PEDIARIX®: Combined Hepatitis B, diphtheria, tetanus, acellular pertussis (DTaP), and inactivated poliovirus (IPV) vaccine (Age: 6 weeks-7 years)
- TWINRIX®: Combined Hepatitis A and Hepatitis B vaccine (Age: 18 years or older)

® = Recombinant

Infants receive both Hepatitis B vaccine and Hepatitis B immune globulin (HBIG) within 12 hours of birth. People exposed to HBV are given both also within 24 hours to prevent infection (3).

**Local cases or outbreaks:**
**Texas:**
- Only acute hepatitis B is reported. Reported incidence was 170 in 2012.
- Approximately 1,200 children are born to HBsAg-positive women annually. In 2006, only 553 cases were reported (11).

**US:**
- 80,000 people are infected annually.
- 1.25 million people are chronically infected.
- About 5,000 people die annually from hepatitis B and its related complications (13).

**Hepatitis B cases provided by CDC below (3,14):**

<table>
<thead>
<tr>
<th>Reported Acute (New) Cases of Hepatitis B Virus (HBV)</th>
<th>Estimated Actual New Cases of HBV (range) in 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005 2006 2007 2008 2009 2010 2011</td>
<td>2011 (estimated)</td>
</tr>
<tr>
<td>5,4944,7584,5194,0333,3743,3502,890</td>
<td>18,800(7,400-86,200)</td>
</tr>
</tbody>
</table>
Global cases or outbreaks:

England’s jails:
- Number of chronically infected prisoners rises from 22 in 2010 to 109 in 2013 (15).

Chronically infected by region:
- 5-10% of population in sub-Saharan Africa and East Asia.
- 2-5% of population in Middle East and Indian subcontinent.
- <1% of population in western Europe and North America (8).

Worldwide:
- 1/3 of world’s population has been infected (5% are chronic carriers with 25% of these carriers having liver cancer or cirrhosis).
- More than 1 million people die annually (8).

References:


