Hepatitis D

Hepatitis D virus causes a rare but potentially serious infection of the liver. The complication rate is high and treatment options are limited. The keys to controlling the disease are prevention of hepatitis B infectious through routine as well as targeted use of vaccine, and avoiding situations where the risk for transmission of blood borne pathogens is increased.

**Background**

The hepatitis D virus (HDV), initially known as the delta virus, was first identified in 1977. It is a defective RNA virus that requires the presence of hepatitis B virus (HBV) for replication and infection. Persons infected with hepatitis D virus are always infected with hepatitis B virus. Hepatitis D infection occurs in three forms:

- Acute HBV/HDV coinfection (simultaneous transmission)
- Acute HDV superinfection of a chronic HBV infection
- Chronic HBV/HDV infection

In coinfection, the incubation period of hepatitis D is dependent on the titer of hepatitis B virus and is typically around 13 weeks (ranging 45-160 days). The incubation period for superinfection is approximately two to eight weeks. Symptoms of acute hepatitis D infection range from mild to fulminant hepatitis. Acute HBV/HDV coinfection tends to be more severe than illness due to acute hepatitis B alone. Past studies have shown that hepatitis B cases with fulminant acute symptoms have a much higher prevalence of hepatitis D infection compared to less severe acute hepatitis B cases.
Persons with both chronic hepatitis B and chronic hepatitis D infections tend to have higher morbidity (e.g., more severe liver disease including liver cancer and rapid progression to cirrhosis) and higher mortality compared to persons with chronic hepatitis B infection alone. Persons with coinfection develop chronic hepatitis D less frequently than persons with superinfection. Only two percent of persons with HBV/HDV coinfection develop chronic hepatitis D, whereas 90 percent of persons with chronic hepatitis B superinfected by hepatitis D go on to develop chronic hepatitis D.

**Epidemiology**

Similar to hepatitis B virus, hepatitis D virus is transmitted person-to-person through contact with the blood or other body fluids, including through sharing injection drug equipment or through sexual contact. Vertical transmission from a woman to a baby has been reported, but is rare. Persons who are not immune to hepatitis B as well as persons who have chronic hepatitis B infection are at risk for infection with hepatitis D virus.

Persons who inject drugs, persons who engage in higher-risk sexual activity (e.g., sex work, multiple sexual partners in a short period of time), and persons migrating from high prevalence countries have shown higher prevalence of hepatitis D infection than members of the general population for the same geographic region that do not share these risks. Injection drug use has been an important risk factor for coinfection.

Worldwide, it is estimated that 15 to 20 million people are infected with hepatitis D. High-prevalence areas for hepatitis D include Africa (Central and West Africa), Asia (Central and Northern Asia, Vietnam, Mongolia, Pakistan, Japan, and Chinese Taipei), Pacific Islands (Kiribati, Nauru), Middle East (all countries), Eastern Europe (Eastern Mediterranean regions, Turkey), South America (Amazonian basin), and Greenland. The prevalence of hepatitis D has decreased globally with the expansion of childhood hepatitis B immunization programs, which greatly reduce the number of chronic hepatitis B infections in the target population.

The incidence and prevalence of hepatitis D infection in the United States are unknown because the disease is not nationally notifiable and because testing may not be done consistently to detect cases. Some prevalence studies have shown 1.5-7.2 percent co-infection rate among persons with acute hepatitis B.
Hepatitis D is a reportable condition in this state. Washington Administrative Code (WAC) requires reporting by both healthcare providers and laboratories. Specimen submission to the Washington State Department of Health is required upon request and is encouraged when positive results are obtained. Washington has occasional hepatitis D cases reported. During the past ten years, zero to three cases per year were reported with an average of one per year. In April 2000 a Pierce County outbreak of hepatitis B primarily among persons who inject drugs included 60 reported hepatitis B cases with three deaths. All three persons who died were also infected with hepatitis D virus.

**Figure 1. Reported Hepatitis D Cases by Year, Washington**

![Bar chart showing reported hepatitis D cases by year](image)

**Clinical Aspects**

Clinicians should suspect and test for hepatitis D infection in persons with known hepatitis B infection (acute or chronic) and persons diagnosed with acute hepatitis B of unusual disease severity. Hepatitis D is diagnosed by detecting high titers of anti-HDV, and confirmed by detection of HDV RNA in serum. Although there are commercially available assays, no currently available hepatitis D virus test has been US Food and Drug Administration approved. The Centers for Disease Control and Prevention offers confirmatory testing to public health agencies investigating cases.

In persons with chronic HBV/HDV infection, anti-HDV and HDV RNA persist indefinitely. In persons with coinfection, anti-HDV is detectable during the course of the infection approximately 85 percent of the time. Anti-HDV becomes undetectable after the infection resolves; there is currently no serologic marker that indicates whether a person was previously infected with hepatitis D virus and cleared the infection. The presence of hepatitis B infection (HBsAg, HBV DNA, and/or HBeAg) is also required for the diagnosis of hepatitis D infection. For the diagnosis of acute HBV/HDV coinfection, the presence of IgM anti-HBc and HBsAg is required. For acute superinfection of a chronic hepatitis B case, IgM anti-HBc is negative while HBsAg is usually positive (Table 1).
Table 1. Common serological patterns in hepatitis B/D infections

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<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>IgM anti-HBc</th>
<th>Anti-HDV</th>
<th>HDV RNA</th>
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</thead>
<tbody>
<tr>
<td>Acute HBV/HDV coinfection</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acute HDV superinfection of a chronic HBV carrier</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic HBV/HDV infection</td>
<td>+</td>
<td>-</td>
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Treatment regimen options for hepatitis D infection are limited and of long duration, lasting for a year or longer. Even with extended treatment, sustained virologic response is low. Currently, there is no specific vaccine for preventing infection with hepatitis D virus. The immunity provided by hepatitis B vaccination also provides protection against acquiring hepatitis D infection. Measures to prevent hepatitis B transmission, such as bloodborne pathogen safety measures and harm reduction services (e.g., syringe exchange services), are also effective.

Successfully controlling hepatitis D depends on eliminating susceptibility to hepatitis B. Washington’s universal childhood vaccination program now in place along with targeted vaccination of persons at increased risk of infection are reducing the number of persons susceptible to hepatitis B infection. Each person with hepatitis D infection should be educated about ways to prevent transmission to others, particularly through safe use of injection equipment. Availability of syringe exchange services and drug treatment programs will also support these efforts. Persons with chronic hepatitis B infections need to be informed of the risk of acquiring hepatitis D virus, and should be educated to avoid high-risk parenteral or sexual exposure to reduce the risk of hepatitis D infection.

Resources

- Centers for Disease Control and Prevention. [Guidelines For Viral Hepatitis Surveillance And Case Management](https://www.cdc.gov/hepatitis/guidelines/index.htm)
- Centers for Disease Control and Prevention. [Viral Hepatitis Serology Training](https://www.cdc.gov/hepatitis/Clinicians/serology/index.htm)
- Minnesota Department of Health. [Hepatitis D Infection Fact Sheet (adapted from materials developed by the Centers for Disease Control and Prevention)](https://www.health.state.mn.us/mchp/hepatitis/factsheets/HDV.pdf)
- MMWR: May 18, 2001 / 50(19);388-390, 399. [Hepatitis B Vaccination for Injection Drug Users --- Pierce County, Washington, 2000.](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5019a3.htm)
- World Health Organization, [Hepatitis D Fact Sheet](https://www.who.int/hepatitis/d/patient/en/)