HBV Epidemiology

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Module 1: Screening and Diagnosis
Lesson 1: HBV Epidemiology

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Background

Hepatitis B virus (HBV) is an enveloped, partially double-stranded DNA virus that is transmitted via infected blood and bodily fluids.\[1\] Infection with the hepatitis B virus causes hepatocellular necrosis and inflammation, and chronic infection can lead to liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC).\[2\] In the United States, the estimates for the number of persons living with chronic HBV infection range from 850,000 to 2.2 million persons.\[3,4,5\] Globally, an estimated 257 million people are chronically infected with hepatitis B, making it one of the most prevalent viral infections worldwide and a major public health priority, particularly in highly endemic areas.\[1,6\]
HBV Incidence in the United States

Definition of HBV Incidence

The incidence of HBV infection is defined as the number of new HBV infections in a given population over a given time period. The Centers for Disease Control and Prevention (CDC) uses the 2012 acute hepatitis B case definition to determine the annual reported incidence of HBV infection in the United States.[7,8] This value is commonly presented as an incidence rate, defined as the number of acute HBV cases per 100,000 persons per year.[8] When observing epidemiologic trends over time, incidence rate (number of cases per 100,000 persons per year) is preferred over cumulative incidence (number of new cases in the population), as it standardizes population-based follow-up time and is therefore not impacted by changes in populations or population subgroups.

Method of Estimating HBV Incidence

The severity of symptoms in acute HBV infection varies considerably, and many patients do not seek medical care during acute infection. Furthermore, because many diagnosed cases of acute HBV are not reported to local or federal health departments, the reported cases represent only a fraction of the actual cases of acute HBV occurring within the population in a given year. To better estimate the true incidence of acute HBV, the CDC utilizes complex modeling techniques to account for under-ascertainment and under-reporting of cases.[8] Based on these techniques, the CDC estimates the true number of acute HBV cases in the United States is approximately 6.5-fold greater than the reported cases.[8]

HBV Incidence Trends

In the United States, the incidence of reported acute HBV cases peaked at 26,654 cases in 1985, and subsequently declined throughout the late 1980s, 1990s, and early 2000s, due largely to the implementation and expansion of routine HBV vaccination (Figure 1).[9,10] In more recent years, from 2013 through 2017, there has been fluctuation with a low of 2,791 reported cases of acute hepatitis B in 2014 and a high of 3,407 cases in 2017; after adjusting for under-ascertainment and under-reporting, the estimated number of actual acute hepatitis cases ranged from a low of 18,100 cases in 2014 to a high of 22,100 in 2017 (Figure 2).[8] At the state level, however, considerable variability exists, with West Virginia, Maine, and Kentucky having the highest rates of reported acute hepatitis B cases in 2017 (Figure 3).[8]

HBV Incidence by Groups

From 2002 to 2017, the incidence of reported acute HBV was lowest among children ages 0 to 19 years (incidence rate 0.0/100,000 persons in 2016) and consistently highest among adults 30 to 39 and 40 to 49 years of age (Figure 4).[8,9,10] Since 2001, the incidence rates of acute HBV have been consistently higher for men than for women, with men having an approximately 1.6 times higher incidence rate in 2017 than women (Figure 5).[8] Between 2002 and 2017, the incidence of acute HBV infection fell among nearly all race and ethnic groups, with the exception of non-Hispanic whites whose incidence rates have increased since 2009 (Figure 6).[8] In 2016, non-Hispanic whites had the highest rate of reported acute HBV infection (1.0 per 100,000 person years) among all race and ethnic groups.[8]

Importance of HBV Incidence Data

Although most adults and children over the age of 12 months with acute HBV infection do not have progression to chronic HBV infection, data on the incidence of acute HBV infection provide critical information regarding trends in transmission, identification of outbreaks, and effectiveness of prevention interventions.[1] In particular, data stratified by state, age, gender, race, and risk factor for HBV acquisition can further identify populations at highest risk for acute HBV infection and help guide public health prevention efforts.
**HBV Prevalence in the United States**

**Definition of HBV Prevalence**

The prevalence of hepatitis B infection is defined as the number of persons living with chronic HBV infection in the total population. Although research studies often use HBsAg carrier status as a marker for chronic infection, the CDC defines chronic HBV infection as the presence of HBsAg, HBeAg, or HBV DNA in the absence of IgM antibodies to hepatitis B core antigen (IgM anti-HBc), which are seen in acute infection.[4,11] The HBV prevalence in the United States is impacted by the number of acute HBV infections, the rate of progression from acute to chronic infection, the number of individuals with chronic HBV infection migrating into or out of the country, the number of persons who have spontaneous resolution of HBV or are cured with therapy, and the rate of death among chronically infected individuals.[5]

**HBV Prevalence Estimates**

The estimates for number of persons living with chronic HBV in the United States have varied significantly, ranging from approximately 850,000 to 2.2 million.[3,4,5,12] These estimates equate to a general population prevalence of chronic hepatitis B of 0.3 to 0.7% in the United States.[4,12,13] Most of the prevalence estimates have been based on data collected in National Health and Nutrition Examination Survey (NHANES). Trends in several different studies reporting on NHANES data show that the prevalence rate of chronic HBV infection in the United States remained relatively constant between 1988 and 2016.[4,5,9] It is important to note that NHANES data suffer from several limitations. Specific to HBV infection, NHANES does not sample individuals who are incarcerated or living homeless, and likely under samples foreign-born persons. As such, the estimates presented may underrepresent actual prevalence in some key United States populations.[3,5,14].

**HBV Prevalence by Groups**

Among those living with chronic HBV in the United States, it is not known how many are United States-born versus foreign-born. A meta-analysis estimated that in 2009, 1.32 million foreign-born persons in the United States were living with chronic hepatitis B in comparison to an estimated 300,000 to 600,000 United States-born persons.[3] Of these 1.32 million persons, an estimated 58% immigrated from Asia, 12% from the Caribbean, 11% from Africa, and 7% from Central America (Figure 7).[3] Data from 2007 through 2012 have shown that nearly all persons living with chronic HBV infection in the United States were adults 18 years of age and older.[4] This extremely low rate of HBV in children and adolescents is a result of the widespread implementation of childhood HBV vaccination during the 1990s in the United States. Indeed, the prevalence rate of chronic HBV infection fell significantly among persons less than 20 years of age, from 0.2% in 1988 through 1994 to 0.03% in 2007 through 2012.[5] During 2007 through 2012, the highest chronic HBV infection prevalence rate occurred in non-Hispanic blacks (0.6%) and foreign-born persons (1.1%).[5] More specifically, NHANES estimates for 2011 and 2012 suggested that non-Hispanic Asians accounted for approximately 50% of the cases of chronic HBV infection in the United States (3.1% prevalence within this group), with 93.1% of those cases occurring in foreign-born persons.[5,15]
Awareness of HBV Infection Status

Overall, available data suggest that a minority of persons living with chronic HBV are aware of their HBV infection status.\cite{16,17} One study utilizing 2013 through 2016 NHANES data found that only 33.9\% of those with chronic infection were aware of their HBV status.\cite{16} In addition, this study demonstrated only 11.7\% of persons with a past exposure to HBV, defined by the presence of HbcAb, were aware they had been exposed to HBV.\cite{16} A similar study analyzing 2011 through 2014 NHANES data found that only 26.2\% of persons living with chronic HBV infection and 12.4\% of persons with resolved HBV were aware of their status.\cite{18}
Global HBV Epidemiology

The World Health Organization (WHO) estimates that approximately 257 million people, or 3.5% of the global population, are living with chronic hepatitis B infection, with an estimated 68% living in either the Western Pacific or Africa WHO regions (Figure 8).[6] Globally, most persons living with chronic hepatitis B are adults who acquired HBV before the age of 5 years, prior to the widespread availability of hepatitis B vaccine.[6] In recent years, however, a significant reduction in the rate of chronic HBV infection has occurred among children under the age of 5, owing to the implementation of routine HBV vaccination in infancy.[6] In 2015, an estimated 1.3% of children under the age of 5 years had chronic HBV infection, as compared to 4.7% in the prevaccination era.[6] Although this reduction in childhood infections is expected to lead to a decline in the global HBV epidemic, specific regions are still experiencing high rates of chronic HBV infection in childhood, including the WHO Africa region, where the prevalence for children younger than 5 years of age remains at 3%.[6] Among persons who inject drugs, the global prevalence of HBsAg positivity is estimated to be 8.4%, with East Asia, Southeast Asia, and Eastern Europe having the largest populations of HBsAg-positive persons who inject drugs.[19]

Regional HBV Prevalence Rates

Among the six WHO global regions (Figure 9), the Western Pacific and Africa regions have the highest prevalence rates of chronic HBV infection, followed sequentially by the Southeast Asia region, Eastern Mediterranean region, European region, and region of the Americas (Figure 10).[6] Despite evidence of clear regional trends, the estimates for country level prevalence rates vary considerably, likely due to differences in risk factors, transmission routes, and public health infrastructure.[6,20] Earlier CDC classification defined country-level chronic HBV prevalence rates in three categories: high (8% or greater); intermediate (2 to 7%) and low (less than 2%) (Figure 11). More recent CDC HBV prevalence classification includes five groups: high (8% or greater), intermediate (5 to 7.9%), low intermediate (2 to 4.9%), low (less or equal to 1.9%), and no data (Table 1).[10] A WHO commissioned systemic review and pooled data analysis from 2015 provided the following estimates of HBV prevalence rate ranges within the following WHO regions:[20]

- Africa: 0.5% (Seychelles) to 22.4% (South Sudan)
- Americas: 0.2% (Mexico) to 13.6% (Haiti)
- Eastern Mediterranean: 0.67% (Iraq) to 14.8% (Somalia)
- European: 0.01% (UK, Norway) to 10.3% (Kyrgyzstan)
- Southeast Asia: 0.8% (Nepal) to 6.4% (Thailand)
- Western Pacific: 0.4% (Australia) to 22.7% (Kiribati)

Global Strategy to Eliminate Hepatitis B

In 2016, owing to the high global burden of chronic HBV (and hepatitis C virus [HCV]) infection, the WHO released its first-ever global health sector strategy report on viral hepatitis, which called for the elimination of HBV and HCV by 2030, defined as a 90% reduction in new cases and a 65% reduction in mortality.[21] For hepatitis B, this equates to a reduction in new cases from an estimated 4.7 million in 2015 to 470,000 by 2030 and a reduction in HBV-related deaths from an estimated 884,000 in 2015 to 309,000 by 2030.[22] Prevention of mother-to-child transmission via birth dose vaccination and completion of the 3-dose Hep B vaccine is a key cornerstone of global HBV elimination efforts, but despite relatively high rates of childhood vaccination coverage, major gaps in prevention of mother-to-child transmission exist globally, with at least 20 countries, predominantly in Africa and Southeast Asia, not on track to reach WHO targets by 2030.[21,23] Similarly, major gaps persist in HBV testing and treatment, with an estimated 9% of chronically infected persons diagnosed worldwide and only 8% of those diagnosed on treatment.[6]
Risk Populations and Risk Factors

Overview of Risk Factors for HBV Acquisition

Hepatitis B virus is transmitted via percutaneous or mucous membrane contact with infected blood or bodily fluids.[13] Major risk factors for HBV transmission vary across countries and geographical regions, with perinatal transmission being the most common mode of infection in high prevalence countries and sex and injection drug use being the most common in low prevalence countries.[20,24] Of the 3,218 reports of acute HBV infection submitted to the CDC in 2016, information on risk factors for exposure was included in 1,549 (48.1%) cases.[8] Of these 1,549 cases, 837 (54%) had no risk factors or behaviors identified, whereas 712 (46%) indicated at least one risk exposure in the 6 weeks to 6 months preceding the onset of acute illness, with injection drug use and multiple sex partners being the most commonly reported risk behaviors.[8]

Injection Drug Use

Injection drug use is one of the most common risk factors for acute HBV in the United States.[8,25] In 2016, a history of injection drug use was reported in 34.4% of the 1,371 new cases of acute HBV for which information on injection drug use was available. Similarly, longitudinal CDC data indicate that the proportion of people reporting injection drug use as a risk factor for acute HBV infection increased 114% during the time period 2009 through 2013 in the three state Appalachian region involving Kentucky, Tennessee, and West Virginia.[26] This increase paralleled an increased incidence of acute HBV among white persons aged 30 to 39 years residing in non-urban areas of these three states, likely owing to the ongoing opioid epidemic.[25,26] On a national scale, the prevalence of chronic HBV among persons who inject drugs is poorly defined, with estimates of HBsAg positivity among persons who inject drugs ranging from 3.5 to 20%.[19] More recently, a study utilizing 2001 through 2016 NHANES data reported the prevalence of anti-HBc, which indicates current or prior infection, was 19.7% among persons who inject drugs compared with 4.6% in the general United States population.[27]

Sexual Exposure

In 2016, among CDC case reports of acute HBV that contained information on sexual exposure, 4.2% reported sexual contact with a person confirmed or suspected to have HBV, 8.7% were men who have sex with men (MSM), and 29.7% indicated having at least 2 sex partners in the 2 weeks to 6 months prior to symptom onset.[8] Similar data on acute HBV cases from 7 federally funded surveillance sites indicated sexual exposure (either MSM, multiple sex partners, or other sexual contact) was the likely mode of transmission in over 30% of cases of acute HBV.[25] In addition to MSM and heterosexual persons with multiple sex partners, the World Health Organization also identifies transactional sex workers and their clients as persons at high risk for HBV acquisition.

Infants Born to Mothers with Chronic HBV

Perinatal transmission is the predominant mode of HBV transmission worldwide, particularly in areas with a high HBV prevalence.[15] Although less common, transmission still occurs in low-prevalence areas, and data from the CDC indicate that 800 to 1,000 cases of perinatally acquired HBV occurred yearly from 2000 to 2009 in the United States.[28,29] The rate of HBV transmission from an HBSAg-positive mother to her neonate ranges from 5 to 90% in the absence of maternal antiviral treatment or neonatal immunoprophylaxis, with approximately 90% of perinatal HBV infections becoming chronic.[28,30,31,32,33] In the United States, however, receipt of appropriate birth dose vaccination and hepatitis B immune globulin has been shown to reduce the risk of transmission to 1.1%.[34] The use of antiviral therapy for mothers with high HBV viral loads—in addition to standard immunoprophylaxis—can further reduce the risk of perinatal HBV transmission.[10]

Persons Born Outside of the United States

In the United States, up to 70% of chronic HBV infections occur in foreign-born persons who migrate from
endemic areas, particularly East Asia, Caribbean, and sub-Saharan Africa.\[3,5,15\] Although foreign-born persons constitute the highest number of prevalent cases of chronic HBV in the United States, CDC data indicate that they do not constitute the highest number of incident cases of acute HBV, with rates of acute HBV declining for all races and ethnic groups in the United States from 2001 through 2016, with the exception of non-Hispanic whites.\[8\] In 2016 the incidence rate for acute HBV was highest among non-Hispanic whites and lowest among Asian/Pacific Islanders and Hispanics.\[8\]

**Household Contacts**

In 2016, 663 cases of acute HBV reported to the CDC included information on household contacts. Of these, only 4 (0.6%) reported household contact with a person known or suspected to have HBV.\[8\] In contrast, the CDC estimates that among persons living in the same household as an individual with chronic HBV infection, 16% have evidence of current infection and 45% have evidence of past infection.\[10\] This risk is highest among unvaccinated children and sex partners of persons chronically infected with HBV.\[10,35\]

**Developmentally Disabled Persons in Long-Term Care Facilities**

Hepatitis B outbreaks have been reported in long-term care settings, particularly due to inappropriate infection control practices during routine blood glucose monitoring.\[36,37\] Between 1996 and 2011, 29 such outbreaks were reported to the CDC, 25 of which were related to assisted blood glucose monitoring.\[37\] Prevalence rates for chronic HBV within institutionalized care settings have been reported as high as 20% in the past; although rates have decreased significantly since the implementation of widespread hepatitis B vaccination practices.\[10,38\]

**Correctional Facilities**

The prevalence rate of chronic hepatitis B infection among prisoners in the United States is estimated to be 1.0 to 3.7%, which is considerably higher than the national average.\[39,40\] High prevalence rates in correctional settings are likely due to co-occurring risk factors for HBV among this population, such as injection drug use and multiple sex partners.\[10\] Although most HBV infections are acquired in the community, outbreaks of acute HBV within the correctional setting have been described, and incidence rates have been estimated at 0.82 to 3.8% per year.\[40\]

**Persons at Risk for Occupational Exposure to HBV**

The number of occupational HBV infections among health care workers in the United States has declined dramatically since the implementation of routine HBV vaccination of health care workers and better safety measures.\[10,41\] In 2013, the CDC reported a 98% reduction in the number of acute HBV cases among health care workers from 1983 through 2010, owing largely to routine HBV vaccination and safety improvements in phlebotomy and with injections.\[41\] Similarly, in 2016, of the cases of acute HBV reported to the CDC that included information about occupational exposures, only 7 of 1,364 (0.5%) reported a risk for occupational exposure.\[8\] Despite this very low number of cases, occupational exposure to HBV remains a concern, particularly among nonimmune health care workers, owing to the highly infectious nature of HBV, with seroconversion rates that can exceed 30% after needle stick injury in susceptible hosts who do not receive appropriate prophylaxis.\[41\]

**Persons Receiving Hemodialysis**

The prevalence of chronic HBV among individuals receiving dialysis in the United States declined substantially from the late 1970s through the early 1990s.\[42\] Since 1995, the seroprevalence of HBsAg in the dialysis population has remained stable at 1%, which is currently approximately twice the national average.\[10,42\] In 2016, among 1,079 cases of acute HBV reported to the CDC that included information on dialysis and renal transplantation, only 1 case report designated receipt of either procedure as the cause of HBV infection.\[8\]

**Persons with HCV**
Due to co-occurring modes of transmission, higher rates of HBV infection have been reported in persons infected with hepatitis C virus (HCV), likely due to overlapping risk factors for acquisition of these two hepatitis viruses.\[43\] In a National Veterans Affairs cohort of persons infected with HCV, the prevalence of HBV coinfection was 1.4%. In this same cohort, the prevalence of prior or current HBV infection was 36.6%.\[44\] Similarly, in a large United States cohort of adults with chronic HCV infection from 4 integrated health care systems, 1.1% were positive for either HBsAg and/or HBV DNA.\[45\] Injection drug use is a major shared mode of transmission for HBV and HCV; during the years 2009 through 2013, the incidence of acute hepatitis B infection rose 114% in the Appalachian states of Kentucky, Tennessee, and West Virginia, mainly among white persons aged 30 to 39 who reported a history of injection drug use.\[26\] A concurrent 364% increase in acute HCV infections was seen among young persons in Kentucky, Tennessee, Virginia, and West Virginia between 2006 through 2012, primarily in non-urban areas with a high rate of injection drug use.\[46\]

**Persons with HIV**

Owing to similar modes of transmission, the global prevalence of chronic HBV among persons with HIV is approximately 10%.\[47,48\] In the United States, 2014 surveillance data from 15 states and 2 major cities found that 2% of adults with HIV were coinfected with HBV, while 5.2% of persons with chronic HBV were coinfected with HIV.\[49\] Earlier CDC data from 1998 through 2001 reported a 7.6% prevalence rate of chronic HBV among unvaccinated adults with HIV infection, with the highest incidence rates for acute HBV infection among blacks, persons with alcohol use disorder, persons who had recently injected drugs, and those with a history of AIDS-defining conditions.\[50\]

**Travelers to Countries Where HBV is Endemic**

The risk of HBV acquisition while traveling depends on the prevalence of HBV in the destination country, the duration of travel, the activities undertaken while abroad, and the traveler’s vaccination status.\[51\] In a review of hepatitis B and C epidemiology in international travelers, the estimated monthly incidence of HBV in long-term travelers to endemic countries was 25 to 420 per 100,000 travelers.\[51\]

**Persons with Diabetes**

In the United States, the prevalence of past or present HBV infection is 1.6 times higher among adults with diabetes than adults without diabetes.\[52\] Although recurrent outbreaks of acute HBV related to misuse of blood glucose monitoring devices in institutionalized care settings likely contribute to this higher prevalence, the prevalence remains elevated even in noninstitutionalized persons with diabetes.\[37,52,53\]

**Blood Transfusion**

The risk of acquiring HBV through blood transfusion in the United States is now exceedingly rare. In the United States, all blood donations are screened for HBsAg, anti-HBc, and HBV DNA—a screening process that has led to an exceedingly low risk of HBV transmission through blood transfusions (approximately 1 in 1,000,000).\[54\] Nevertheless, the risk of HBV transmission through blood transfusion is higher in other parts of the world, where screening protocols are not as rigorous.

**Transplant Recipients**

Transmission of hepatitis B has been reported after both solid organ and hematopoietic stem cell transplantation. The risk of transmission is highest for nonimmune liver transplantation recipients who receive an HBsAg negative, anti-HBc positive organ (note the use of HBsAg positive organs is not endorsed by the American Society of Transplant Surgeons).\[55\] The use of antiviral prophylaxis can reduce the risk of HBV acquisition, particularly in susceptible liver transplant recipients, and may be helpful in susceptible non-liver recipients.\[55\]
CDC Case Definition and Reporting

According to the CDC, “a surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance.” Case definitions help public health officials consistently identify and classify cases of a specific disease across different public health jurisdictions. Although case definitions are extremely valuable in epidemiologic surveillance, it is important to note that they are not meant to substitute for diagnostic criteria in the clinical setting; these case definitions for hepatitis B include acute hepatitis B, chronic hepatitis B, and perinatal infection.[7,11,56]

Acute Hepatitis B—2012 Case Definition

The following summarizes the 2012 CDC case definition for acute HBV infection, which divides the case definition into clinical and laboratory criteria.[7] Note that a documented negative hepatitis B surface antigen (HBsAg) laboratory test result within 6 months prior to a positive test (either HBsAg, hepatitis B “e” antigen (HBeAg), or hepatitis B virus nucleic acid testing (HBV NAT) including genotype) result does not require an acute clinical presentation to meet the surveillance case definition.[7]

- **Clinical Description**
  An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g. fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), and either
  - Jaundice, or
  - Elevated serum ALT levels greater than 100 IU/L

- **Laboratory Criteria for Diagnosis**
  - HBsAg positive, AND
  - IgM anti-HBc positive (if done)

- **Case Classification**
  - Confirmed: A case is considered confirmed if it meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis B.

Chronic Hepatitis B—2012 Case Definition

The following summarizes the 2012 CDC case definition for chronic HBV infection, which is based entirely on laboratory criteria.[11]

- **Clinical Description**
  No symptoms are required to meet the case definition. Persons with chronic HBV infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer.

- **Laboratory Criteria for Diagnosis**
  - IgM anti-HBc negative AND a positive result on one of the following tests: HBsAg, HBeAg, or nucleic acid test for hepatitis B virus DNA (including qualitative, quantitative, and genotype testing), OR
  - HBsAg positive or nucleic acid test for HBV DNA positive (including qualitative, quantitative, and genotype testing) or HBeAg positive two times at least 6 months apart (any combination of these tests performed 6 months apart is acceptable).

- **Case Classification**
  - Probable: A person with a single HBsAg positive or HBV DNA positive (including qualitative, quantitative, and genotype testing) or HBeAg positive lab result and does not meet the case definition for acute hepatitis B.
  - Confirmed: A person who meets either of the above laboratory criteria for diagnosis.
  - Comments: Multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a “hepatitis panel.” Testing performed in this manner may lead to seemingly discordant results, e.g., HBsAg-negative AND HBV DNA-
positive. For the purposes of this case definition, any positive result among the three 
laboratory tests mentioned above is acceptable, regardless of other testing results. Negative 
HBeAg results and HBV DNA levels below positive cutoff level do not confirm the absence of 
HBV infection.

**Hepatitis B Perinatal Virus Infection—2017 Case Definition**

The following summarizes the 2017 CDC case definition for perinatal HBV infection.[56]

- **Clinical Criteria**
  In children less than or equal to 24 months, clinical manifestations can range from asymptomatic to 
  fulminant hepatitis.

- **Laboratory Criteria for Diagnosis**
  Laboratory evidence of one or more of the following must be present:
  - Positive HBsAg test (only if at least 4 weeks after last dose of hepatitis B vaccine)
  - Positive HBeAg test
  - Detectable HBV DNA

- **Epidemiologic Linkage**
  Born to a mother known to have HBV infection.

- **Case Classification**
  - Probable: Child born in the United States and positive for HBsAg at ≥1 month of age and ≤24 
    months of age
  - Positive for HBeAg or HBV DNA ≥9 months of age and ≤24 months of age, but for whom the 
    mother’s hepatitis B status is unknown (i.e. epidemiologic link not present).
  - Confirmed: Child born in the United States to a mother with HBV infection and the child tests 
    positive for HBsAg at ≥1 month of age and ≤24 months of age
  - Positive for HBeAg or HBV DNA ≥9 months of age and ≤24 months of age.
  - Comments: Infants born to mothers with HBV infection should receive hepatitis B immune 
    globulin (HBIG) and the first dose of hepatitis B vaccine within 12 hours of birth, followed by 
    the second and third doses of hepatitis B vaccine at 1 and 6 months of age, respectively. 
    Testing for HBsAg and anti-HBsAg is recommended 1 to 2 months following completion of the 
    vaccine series, but not earlier than 9 months of age. If the mother is known to not be infected 
    with HBV, refer to the case definition for acute hepatitis B.
HBV Disease Burden

Global HBV-Related Deaths

In 2015, viral hepatitis led to 1.34 million deaths worldwide and 884,000 (66%) of these were due to hepatitis B.[6] More recent data from the Institute for Health Metrics and Evaluation estimated that in 2017, deaths due to viral hepatitis outnumbered those of tuberculosis, HIV, and malaria, with deaths from viral hepatitis projected to exceed the combined mortality of tuberculosis, HIV, and malaria by 2040 (Figure 12).[22,57]. Globally, the majority of deaths due to HBV are from complications of cirrhosis and hepatocellular carcinoma, with a small minority from acute infection.[6]

HBV-Related Deaths in United States

In the United States, the mortality rate from HBV ranged from 0.5 to 0.52 deaths per 100,000 population between 2012 and 2014. In 2017, the HBV-related mortality rate was 0.46 deaths per 100,000 population, with a total of 1,727 HBV-related deaths.[8] The HBV-related mortality rates correlated closely with age—the highest rates occurred in persons 75 years of age and older (1.43 per 100,000) and the lowest in persons younger than age 35 year of age (0.02 per 100,000) (Figure 13).[8] In addition, death rates were highest in Asian/Pacific Islanders and blacks (Figure 14).[8] Further, HBV-related mortality in 2016 was three times higher among men (0.69 per 100,000) than women (0.23 per 100,000).[8] Data evaluating overall and cause-specific death rates among a large United States-based cohort of persons with chronic HBV found that on average, individuals with chronic HBV died 14 years younger than the general United States population (59.8 vs. 73.9 years). In this same study, a further increased risk of death was seen among those with chronic HBV who also had one of the following conditions: diabetes, history of alcohol use disorder, coinfection with HCV, coinfection with HIV, hepatocellular carcinoma, history of liver transplantation, or history of treatment for chronic HBV.[58]
Summary Points

- Globally, an estimated 257 million people, or 3.5% of the world’s population, are living with chronic HBV infection. Of these 257 million, an estimated 68% are in the WHO-defined Africa and Western Pacific regions.
- In 2016 the WHO released its first-ever global health sector strategy report on viral hepatitis, which called for the elimination of HBV and HCV by 2030, defined as a 90% reduction in new cases and a 65% reduction in mortality.
- Globally, perinatal transmission remains the predominant mode of HBV transmission.
- In 2017, there were an estimated 2.4 million persons living with chronic hepatitis B in the United States, which equates to 0.8% of the population. Prevalence is highest among foreign-born persons and adults 18 years of age and older.
- In the United States, the incidence of acute HBV increased from 2001 through 2016 among adults 30 years of age and older, despite consistent reductions in incidence for adults ages 20 to 29 years and children ages 0 to 19 years.
- Injection drug use and sexual exposure are the major risk factors for HBV acquisition in the United States, with injection drug use playing an increasingly important role in transmission as a result of the ongoing opioid epidemic.
- In 2015, HBV was responsible for an estimated 884,000 deaths worldwide.
- In the United States there were approximately 1,700 HBV-related deaths reported in 2016, yielding a mortality rate of 0.45 deaths per 100,000 population.
- Persons with chronic HBV in the United States die, on average, 14 years younger than persons in the general population.
- The CDC has established uniform case definitions for acute HBV, chronic HBV, and HBV perinatal infection to assist with public health reporting.
Citations


References


  [PubMed Abstract] -

  [PubMed Abstract] -

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Figures

Figure 1 Acute Hepatitis B: Number of Reported Cased — United States, 1966-2017

**Figure 2 Acute Hepatitis B: Reported and Estimated Cases — United States, 2013-2017**

This graphic shows the actual number of acute hepatitis B cases submitted to CDC and the estimated number of acute hepatitis B cases. The number of estimated cases of acute hepatitis B was determined by multiplying the number of reported cases by a factor that adjusted for under-ascertainment and under-reporting.

Figure 3 Acute Hepatitis B: 10 States with Highest Rates of Reported Cases — United States, 2017

Figure 4 Acute Hepatitis B: Rates of Reported Cases, by Age Group — United States, 2002-2017

Figure 5 Acute Hepatitis B: Rates of Reported Cases, by Sex — United States, 2002-2017

Figure 6 Acute Hepatitis B: Rates of Reported Cased, by Race/Ethnicity — United States, 2002–2017

Figure 7 Foreign-Born Populations Living in the United States with Chronic Hepatitis B, 2009

These estimates are based on random effects meta-analysis by world region of origin. Overall, approximately 58% of the foreign-born persons living in the United States with chronic hepatitis B migrated from Asia and 11% from Africa.

Figure 8 Chronic HBV: Global Prevalence Estimates, 2015

Figure 9 World Health Organization Regions

WHO Member States are grouped into six regions. Each region has a regional office. The map shows the WHO regions.

Source: WHO Regional Offices
Figure 10 Chronic HBV: Global Prevalence Rate Estimates by WHO Regions, 2015

Figure 11 Chronic HBV: Global Prevalence Rate Estimates

Source: Centers for Disease Control and Prevention
Figure 12 Worldwide Deaths from Chronic Viral Hepatitis as Compared with Deaths from Tuberculosis, Human Immunodeficiency Virus (HIV) Infection, and Malaria.

Figure 13 HBV-Related Death Rate, by Age Group — United States, 2017

Figure 14 HBV-Related Death Rate, by Race/Ethnicity — United States, 2017

This graphic shows the death rate with hepatitis B listed as a cause of death among United States residents in 2017.

Table 1.

**Global Prevalence of Chronic HBV Infection, by Country**

<table>
<thead>
<tr>
<th>Prevalence Category</th>
<th>Country</th>
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<tbody>
<tr>
<td><strong>High</strong> (≥8%)</td>
<td>Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Congo, Côte d’Ivoire, Djibouti, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Haiti, Kiribati, Kyrgyzstan, Laos, Liberia, Malawi, Mali, Mauritania, Mongolia, Mozambique, Namibia, Nauru, Niger, Nigeria, Niue, Papua New Guinea, Senegal, Sierra Leone, Solomon Islands, Somalia, South Sudan, Sudan, Swaziland, Togo, Tonga, Uganda, Vanuatu, Vietnam, Yemen, and Zimbabwe.</td>
</tr>
<tr>
<td><strong>Intermediate</strong> (5.0-7.9%)</td>
<td>Albania, Bhutan, Cape Verde, China, Democratic Republic of the Congo, Ethiopia, Kazakhstan, Kenya, Marshall Islands, Moldova, Oman, Romania, Rwanda, Samoa, South Africa, Tajikistan, Tanzania, Thailand, Tunisia, Tuvalu, Uzbekistan, and Zambia.</td>
</tr>
<tr>
<td><strong>Low Intermediate</strong> (2.0-4.9%)</td>
<td>Algeria, Azerbaijan, Bangladesh, Belarus, Belize, Brunei Darussalam, Bulgaria, Cambodia, Colombia, Cyprus, Dominican Republic, Ecuador, Eritrea, Federated States of Micronesia, Fiji, Georgia, Italy, Jamaica, Kosovo, Libya, Madagascar, Myanmar, New Zealand, Pakistan, Palau, Philippines, Peru, Russia, Saudi Arabia, Singapore, South Korea, Sri Lanka, Suriname, Syria, Tahiti, and Turkey.</td>
</tr>
<tr>
<td><strong>Low</strong> (≤1.9%)</td>
<td>Afghanistan, Argentina, Australia, Austria, Bahrain, Barbados, Belgium, Bolivia,</td>
</tr>
<tr>
<td>Prevalence Category</td>
<td>Country</td>
</tr>
<tr>
<td>---------------------</td>
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</tr>
<tr>
<td>Bosnia and Herzegovina, Brazil, Canada, Chile, Costa Rica, Croatia, Cuba, Czech Republic, Denmark, Egypt, France, Germany, Greece, Guatemala, Hungary, Iceland, India, Indonesia, Iran, Iraq, Ireland, Israel, Japan, Jordan, Kuwait, Lebanon, Lithuania, Malaysia, Mexico, Morocco, Nepal, Netherlands, Nicaragua, Norway, Palestine, Panama, Poland, Portugal, Qatar, Serbia, Seychelles, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, United Kingdom, United Arab Emirates, United States of America, and Venezuela.</td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td>Andorra, Antigua and Barbuda, Armenia, The Bahamas, Botswana, Chad, Comoros, Cook Islands, Dominica, El Salvador, Finland, Grenada, Guinea-Bissau, Guyana, Honduras, Latvia, Lesotho, Lithuania, Luxembourg, Macedonia, Maldives, Malta, Mauritius, Monaco, Montenegro, North Korea, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, San Marino, Sao Tome and Principe, Timor-Leste, Trinidad and Tobago, Turkmenistan, and Uruguay.</td>
</tr>
</tbody>
</table>

**NOTE:** This table is based on data from the Centers for Disease Control and Prevention (CDC)

**Source:**
