Screening for Viral Hepatitis During the Domestic Medical Examination of Newly Arrived Refugees

US Department of Health and Human Services
Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases
Division of Global Migration and Quarantine

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Key Points

- Hepatitis B
    - All newly arriving refugees who were born in or have lived in countries with intermediate (2% to 7%) or high (≥ 8%) prevalence of chronic HBV infection should be tested for HBV infection, including HBsAg, HBsAb, and HBcAb. Those who do not have hepatitis B infection should be offered hepatitis B vaccination series according to the ACIP-recommended schedule.
    - Clinicians should consider further evaluation and management for people whose serologic testing indicates prior HBV infection. In this case, hepatitis B vaccination should not be given.
- Hepatitis C
    - Routinely screen refugees born between 1945 and 1965 and those with risk factors.
    - It is reasonable to screen all adults (≥ 18 years of age) who originated from or have lived in countries with high moderate (2% to 5%) or high (≥ 5%) HCV infection prevalence.
    - HCV screening is not routinely recommended for children < 18 years old, unless they have risk factors. Children born to HCV-positive mothers may be tested before 18 months of age. However, a child's HCV antibody result may be falsely positive due to passively acquired maternal antibody. In such cases, the child should be tested for HCV RNA [1].
- Routine screening for hepatitis D infection is not recommended.
- Routine screening for hepatitis A infection is not recommended.
- Routine screening for hepatitis E infection is not recommended.

Background

Hepatitis is inflammation of the liver. Hepatitis may result from a number of infectious and noninfectious causes. Many viral infections can cause liver inflammation, but the term **viral hepatitis** is usually reserved for infections with one of the five hepatotropic viruses (viruses known to target the human liver): hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV).

Infections caused by these viruses vary in their epidemiologic features and natural history, including incubation period, routes of transmission, geographic and demographic distribution, patterns of clinical disease, and propensity for becoming chronic. Therefore, strategies for prevention and approaches to clinical management vary.

Each of the five types of viral hepatitis may cause illness during acute infection (2 weeks to 6 months following exposure). Although acute viral hepatitis can be severe or fatal, it is often asymptomatic. Acute infections caused by HBV and HCV commonly become chronic, persisting for decades and often silently damaging the liver. Chronic HBV and HCV infections result in a high disease burden and are leading causes of cirrhosis (late-stage scarring of the liver) and hepatocellular carcinoma (liver cancer) in the United States and globally. As chronic HBV and HCV are frequently asymptomatic and refugees often come from settings where these viruses are endemic, it is important to consider these infections during the domestic medical screening for newly arrived refugees.

Only those infected with HBV can become infected with hepatitis D virus (HDV). Chronic HBV/HDV co-infections are more likely to progress to advanced liver disease than infection with HBV alone, and increase the risk for development of hepatocellular carcinoma. HAV and HEV cause predominantly acute hepatitis and are the leading causes of symptomatic viral hepatitis infections globally. Although HAV has never been reported to cause chronic infection, there are rare reports of chronic HEV infection, particularly in immunosuppressed people.

For additional information, see the CDC Viral Hepatitis website.

Medical Screening

Overseas Pre-Departure Screening and Vaccination

Refugees from participating overseas sites may be eligible to receive up to two doses of hepatitis B vaccine before resettlement in the United States through the Vaccination Program for US-bound Refugees. Eligible refugees who choose to participate in the voluntary vaccination program are first screened for HBV infection by testing for the presence of hepatitis B surface antigen (HBsAg). Refugees positive for HBsAg do not receive hepatitis B vaccination overseas, and are counseled about the infection and how to prevent transmission. Refugees negative for HBsAg receive up to two hepatitis B vaccine doses overseas, if due. HBsAg results are documented on each refugee's overseas medical records (DS-3026 Medical History Form's remarks section). Vaccines received overseas through this program are documented on the DS-

3025 (Vaccination Documentation Worksheet). These records are available to state health departments through the Electronic Disease Notification (EDN) system.

Household contacts of HBsAg-positive people who test negative for HBsAg may be given a third dose of hepatitis B vaccine overseas, in order to complete the series, if time allows. Because the third dose may be given close to the time of departure, providers should be aware that HBsAg results may be falsely positive during the first month after vaccination. *CDC advises waiting at least 30 days after hepatitis B vaccination before testing.*

Summary of Post-Arrival Screening and Evaluation for Viral Hepatitis

Consider the following viral hepatitides during the post-arrival medical examination:

- Hepatitis B
- Hepatitis C
- Hepatitis A

A complete evaluation for viral hepatitides includes a thorough medical history, review of overseas screening results, physical examination, and testing.

The following summarizes the currently recommended testing. For additional recommendations, see below.

- **Hepatitis B**
  All newly arriving refugees (including infants and children regardless of vaccination history) who were born in or have lived in countries with intermediate (2% to 7%) or high (≥ 8%) prevalence of chronic HBV infection should be tested for HBV infection.
    - Review overseas records (pre-departure testing for HBV infection and hepatitis B vaccination are increasingly common among arriving refugee populations).
      - If hepatitis B virus infection was diagnosed overseas (HBsAg-positive), additional evaluation and treatment options or referral to a specialist is recommended.
      - If overseas HBsAg was negative, and the vaccination series has been initiated, the series should be completed according to the ACIP schedule.
      - If overseas HBsAg was negative, and the refugee has a record of completing the vaccination series before arrival, no further testing or vaccination is necessary.*
      - If overseas HBsAg was negative and no doses of vaccine were received, the refugee, regardless of age, should be offered either vaccination or serologic testing for immunity (Table 1).

- If overseas screening was not documented, the refugee should be screened for hepatitis B serologic markers, including HBsAg, HBsAb, and HBcAb. If HBsAg is negative, the refugee should be offered vaccination.

Notes:
*In refugees with high risk of future exposure (e.g., with household contacts who are HBsAg-positive or other high-risk situations), it is reasonable to check serology for evidence of immunity (Table 1).

Table 1. Hepatitis B Serologic Marker Interpretation

Serologic Marker				Interpretation
	HBsAg[a]	**anti-HBc[b]**	**anti-HBs[c]**	
Test Results	-	-	-	Never infected and susceptible to infection
	+	+	-	HBV infection[d]
	-	+	+	Immune following natural infection
	-	-	+	Immune due to hepatitis B vaccination. **Refugees who are partially vaccinated should complete the series irrespective of anti-HBs results**.
	-	+	-	Interpretation unclear; four possibilities: 1. Resolved infection (most common in regions with intermediate or high endemicity) 2. False-positive anti-HBc, thus susceptible 3. Chronic infection with low level viral load 4. Resolving acute infection

[a]HBsAg=hepatitis B surface antigen; [b]anti-HBc=total antibody to hepatitis B core antigen; [c]anti-HBs=total antibody to hepatitis B surface antigen (Note: anti-HBs ≥ 10 mIU/mL is only considered a correlate of protection after completion of the HBV vaccine series-does not apply to people with evidence of past or current infection); [d]May be acute or chronic infection, requires further testing to differentiate.

- **Hepatitis C**
  - Hepatitis C Virus (HCV) Infection
    - Routinely screen refugees born between 1945 and 1965 and those with risk factors.
    - Risk factors include but are not limited to:

        - Injection drug use
        - Receipt of clotting factor concentrates
        - Receipt of blood transfusions or solid organs
        - Known exposure to HCV (such as needlesticks involving HCV-positive blood)
        - HIV infection
        - Signs or symptoms of liver disease (e.g., abnormal liver enzyme tests, jaundice, abdominal pain or swelling, fatigue)
        - Household contacts with hepatitis C
        - Traditional/unregulated tattoos or history of FGM/C (data are limited)
      - It is reasonable to screen all adults (≥ 18 years of age) who originated from or have lived in countries with high moderate (2% to 5%) or high (≥ 5%) HCV infection prevalence.
    - HCV screening is not routinely recommended for children < 18 years old, unless they have risk factors. Children born to HCV-positive mothers may be tested before 18 months of age, however, in these cases, a child's HCV antibody testing result may be falsely positive from passively acquired maternal antibody. In such cases, the child should be tested for HCV RNA [1]. It is reasonable to screen all children who are from or have lived in regions with high moderate (2% to < 5%) or high (≥ 5%) prevalence.

- **Hepatitis A**
    - *Routine testing for active HAV infection* is *not recommended*. When vaccination against hepatitis A is indicated per ACIP for a specific refugee, checking for pre-existing immunity may be cost-effective. People with signs or symptoms of disease (jaundice, abdominal pain, vomiting, elevated liver enzymes) should be evaluated for acute HAV infection by testing for immunoglobulin M antibody to HAV (anti-HAV IgM). Additionally, people presenting with signs or symptoms of HAV infection, should also be tested for HBV and HCV. Acute HBV and acute HCV often present similarly to HAV.

The most current information on viral hepatitis, including treatment and laboratory guidelines, is available at the CDC Viral Hepatitis website.

Clinical Presentations and Diagnostic Testing for Specific Viral Hepatitides

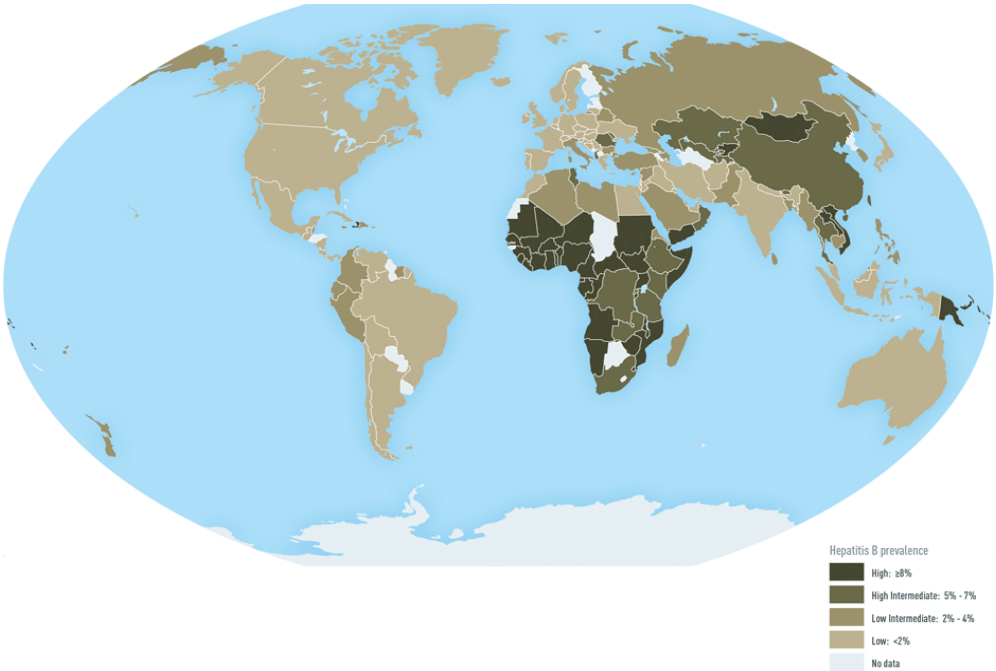
Chronic Viral Hepatitis

Hepatitis B Virus (HBV)

Background

Chronic hepatitis B virus (HBV) infection, defined as hepatitis B surface antigen (HBsAg) positivity for at least 6 months, is a major cause of preventable morbidity and mortality, with as many as 2.2 million cases in the United States, and **more than 786,000 deaths per year worldwide** [2-5]. The **overwhelming majority of these deaths occur in resource-limited countries**. In 2015, an estimated 257 million people were living with chronic HBV infection worldwide. Approximately 45% of the world's population lives in areas of high endemicity, where the prevalence of chronic HBV infection is ≥ 8% and the lifetime risk of acquiring HBV infection is > 60%. Another 43% live in areas of intermediate endemicity, where the HBsAg prevalence is 2% to 7% and the lifetime risk of infection is 20% to 60%. The remaining 12% live in areas of low endemicity, where the HBsAg prevalence is < 2% and the lifetime risk of infection is < 20%. In countries endemic for HBV, perinatal transmission is the leading cause of chronic HBV infection, with perinatal transmission causing 90% of chronic HBV infections [6]. Most refugees arriving in the United States come from countries of intermediate or high HBV endemicity (Figure 1).

Figure 1: Prevalence of Hepatitis B Virus Infection (2014)



Source: CDC Health Information for International Travel (Yellow Book) 2018

People with chronic HBV infection are at risk for developing HBV-related chronic liver disease, including cirrhosis and hepatocellular carcinoma, and extrahepatic manifestations, such as glomerulonephritis.

Although usually asymptomatic, people with chronic HBV infection may transmit the infection to others. Common modes of HBV transmission include perinatal exposure, sexual contact, and needle sharing. Transmission may also occur within households. More details on prevention of and screening for HBV are available on the CDC Division of Viral Hepatitis website. The domestic medical examination is an opportunity to identify HBV-infection in resettling refugees to decrease morbidity and mortality, and prevent transmission to family members and other close contacts. Translated patient education materials are also available on the CDC Division of Viral Hepatitis website.

Epidemiology of HBV Infection in Refugees

HBV infection prevalence and transmission patterns vary markedly among countries and populations (Figure 1). In general, prevalence of chronic HBV infection in migrant populations reflects rates in the region of birth. Many refugees arrive from countries with intermediate (2% to 7%) or high (≥ 8%) prevalence. Areas of intermediate endemicity include much of Asia; parts of Latin America, particularly the Amazon Basin; South Pacific islands; and sub-Saharan Africa. Areas of high endemicity include much of West Africa, select countries in sub-Saharan Africa, and parts of South East Asia. The CDC's Refugee Health Profiles provide current information about select refugee groups resettling in the United States, including epidemiologic information on viral hepatitis in refugees.

In highly endemic regions where routine immunization has not been implemented, new infections occur predominantly among infants and young children, often a result from perinatal or household transmission. The sequelae of chronic HBV infection vary by age at time of infection. Acquisition during infancy or childhood is associated with a higher likelihood of progression to chronic infection and hepatocellular carcinoma. Without early diagnosis and management, 25% of people who become chronically infected as infants and 15% of people who become chronically infected at an older age die of cirrhosis, hepatocellular carcinoma, or end-stage liver disease [7].

Testing for HBV Infection

Most refugees resettling to the United States originate from or have lived in countries with intermediate or high hepatitis B endemicity. The serologic patterns of HBV infection are complex, and a complete discussion is beyond the scope of this document. Briefly, antigens and antibodies associated with HBV infection include HBV surface antigen (HBsAg) and antibody to HBsAg (anti-HBs), HBV core antigen (HBcAg) and antibody to HBcAg (anti-HBc), and HBV e-antigen (HBeAg) and antibody to HBeAg (anti-HBe). At least one serologic marker is present during each phase of HBV infection. The serologic markers most widely used in diagnosis of acute, resolving, or chronic HBV infection are HBsAg, total and IgM anti-HBc, and anti-HBs [8]. Table 2 outlines the typical interpretation of HBV serology.

HBeAg is a secreted product of the nucleocapsid gene of HBV that is found in serum during acute and chronic hepatitis B infection. Its presence indicates that the virus is replicating, and that the infected person typically has high levels of HBV. Anti-HBe is produced by the immune system temporarily during acute HBV infection or consistently during or after a burst in viral replication. Spontaneous conversion from HBeAg to anti-HBe (known as seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV. HBeAg and anti-HBe should be checked only if the initial screening for HBV infection is positive. For more information on HBV and interpretation of hepatitis B serologic markers, please refer to the CDC Hepatitis B FAQs for Health Professionals website.

Table 2. Expanded Hepatitis B Serologic Marker Interpretation and Initial Management

Serologic Marker					Interpretation (I) & Initial Management (M)
	HBsAg[a]	**anti-HBc[b]**	**IgM anti-HBc[c]**	**anti-HBs[d]**	
Test Results	-	-	-	-	**I:** Never infected and susceptible to infection **M:** Recommend hepatitis B vaccination series
	+	+	-	-	**I:** Chronic HBV infection **M:** Obtain additional testing including HBV DNA, HBeAg, anti-HBe, and ALT, **AND** refer to hepatology; provide patient counseling related to chronic HBV infection
	-	+	-	+	**I:** Immune[e] following natural infection **M:** No additional vaccination needed for HBV, even if series initiated pre-departure
	+	+	+	-	**I:** Acute HBV infection **M:** Obtain additional testing including HBV DNA, HBeAg, anti-HBe, and ALT **AND** refer to hepatology
	-	-	-	+	**I:** Immune[e] due to hepatitis B vaccination **M:** Review
	-	+	-	-	**I:** Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible

					3. Chronic infection with low viral load 4. Resolving acute infection **M:** Consider administering hepatitis B vaccine and rechecking screening labs[f]

[a]HBsAg=hepatitis B surface antigen; [b]anti-HBc=total antibody to hepatitis B core antigen; [c]IgM anti-HBc=IgM antibody to hepatitis B core antigen; [d]anti-HBs=total antibody to hepatitis B surface antigen; [e]Refugees who are partially vaccinated should complete the series, except if they are positive for anti-HBc AND anti-HBs and, thus, considered immune by infection; [f]Refugees with an isolated anti-HBc may have an undetectable infection and may be at risk of disease with immunosuppression.

No medication is available for acute HBV infection; treatment is supportive. There are several antiviral medications for people diagnosed with chronic HBV infection. People with chronic HBV infection need regular monitoring to prevent liver damage or hepatocellular carcinoma. Practice guidelines for the treatment of chronic hepatitis B are available from the American Association for the Study of Liver Diseases (AASLD).

Screening Recommendations for Chronic HBV Infection in Refugees

Adults

During the domestic medical examination, all newly arriving adult refugees who were born in or have lived in countries with intermediate (2% to 7%) or high (≥ 8%) prevalence of chronic HBV infection should be tested for HBV infection (Figure 2). Additionally, all adults ≥ 18 years of age who were born or have lived in countries where the rate of chronic HBV infection is < 2% should be tested as above if they belong to one of the following high-risk groups:

- Men who have sex with men
- People with multiple sex partners or a history of sexual exploitation
- People with a history of injection drug use
- People living with HIV
- Household contacts of people with chronic HBV infection
- Subpopulations with known prevalence rates ≥ 2% (e.g., indigenous populations, ethnic minorities)
- Hemodialysis patients
- People who have received whole blood or blood product transfusions before migration
- People with elevated liver enzymes of unknown etiology
- People with medical conditions that require immunosuppressive therapy
- Pregnant women

  Note: Tattooing (common in certain refugee groups), when done in noncommercial or unlicensed facilities, may be a risk factor. However, definitive data are lacking.

Screening pregnant women for HBV infection is particularly important. Early identification of maternal infection allows for pre- and postnatal counseling in addition to ensuring appropriate antiviral management during pregnancy (if clinically indicated) as well as post-natal management to prevent transmission to the infant. Pregnant women with high viral loads may be prescribed anti-viral treatment during pregnancy to decrease the risk of in utero infection. If maternal serum HBV DNA is > 200,000, antiviral therapy is recommended in the 3rd trimester [9-12]. Without maternal prophylaxis, the development of chronic HBV infection after exposure is as high as 90% in newborns born to mothers who are HBeAg-positive (typically correlates with higher viral load and active replication); up to 50% of infected children < 5 years of age develop chronic HBV [6, 13-16]. Approximately 25% of people infected with HBV in utero or at birth will die from cirrhosis, liver failure, and/or hepatocellular carcinoma [17].

Screening of Adult Refugees

- Review overseas records (pre-departure testing for infection and vaccination are increasingly common among arriving refugee populations)
    - If hepatitis B infection (HBsAg-positive), additional evaluation and treatment options, or referral to a specialist, is recommended.
    - If HBsAg is negative, and vaccination series has been initiated, the vaccine series should be completed according to the ACIP schedule.
    - If HBsAg is negative, and the patient has a record of complete vaccination before arrival, no further testing or vaccination is necessary.*
    - If HBsAg is negative and no previous doses of vaccine were received, the refugee should be either offered vaccination or tested for immunity by serology.
        - Serologic testing to determine immune status is commonly conducted and generally includes HBsAg (for infection), anti-HBc, and anti-HBs, although other serologic markers may be checked. Figure 2 is an algorithm for interpreting common serology results in refugees. When interpreting HBV serology, if a partial vaccine series is documented (i.e., the refugee has not completed the hepatitis B vaccine series, which is common), isolated anti-HBs positivity does not indicate sustained immunity, and the vaccine series should be completed based on the ACIP-recommended schedule.

Notes:
*In refugees with high risk of future exposure, it is reasonable to check serology for evidence of immunity.

Adults from countries of high endemicity, as well as high-risk adults from countries with low chronic HBV prevalence who are HBsAg negative and have not been vaccinated, should be offered the vaccine according to ACIP guidelines.

Children and Adolescents

All refugee children and adolescents < 18 years of age who were born in or lived in countries where the rate of chronic HBV infection is ≥ 2% (intermediate or high-endemicity countries) should be tested for HBsAg, regardless of vaccination history (Figure 2). All refugee children and adolescents < 18 years of age who were born or lived in countries where the rate of chronic HBV infection is < 2% should be tested as above, if they belong to one of the following high-risk groups:

- Male children or adolescents who have had sex with other males
- Children or adolescents who have had multiple sex partners or have a history of sexual exploitation
- Children or adolescents who have a history of injection drug use
- Children or adolescents with HIV infection
- Children or adolescents with an immediate family or household member who is chronically infected with HBV. If the mother has a history of hepatitis B infection or cleared infection, her children should be tested.
- Subpopulations with known prevalence rates ≥ 2% (e.g., indigenous populations, ethnic minorities)
- Hemodialysis patients
- Children or adolescents who received whole blood products or blood components before migration
- Children or adolescents with elevated liver enzymes of unknown etiology
- Children or adolescents with medical conditions that require immunosuppressive therapy
- Female adolescents who are pregnant

It is important to note that behavioral risk factor based screening among children and adolescents can be challenging, and certain behaviors may be underreported. Language and cultural barriers may make eliciting accurate answers to patient history questions problematic. Therefore, clinicians should use clinical judgement when making decisions regarding screening new refugee arrivals for HBV infection.

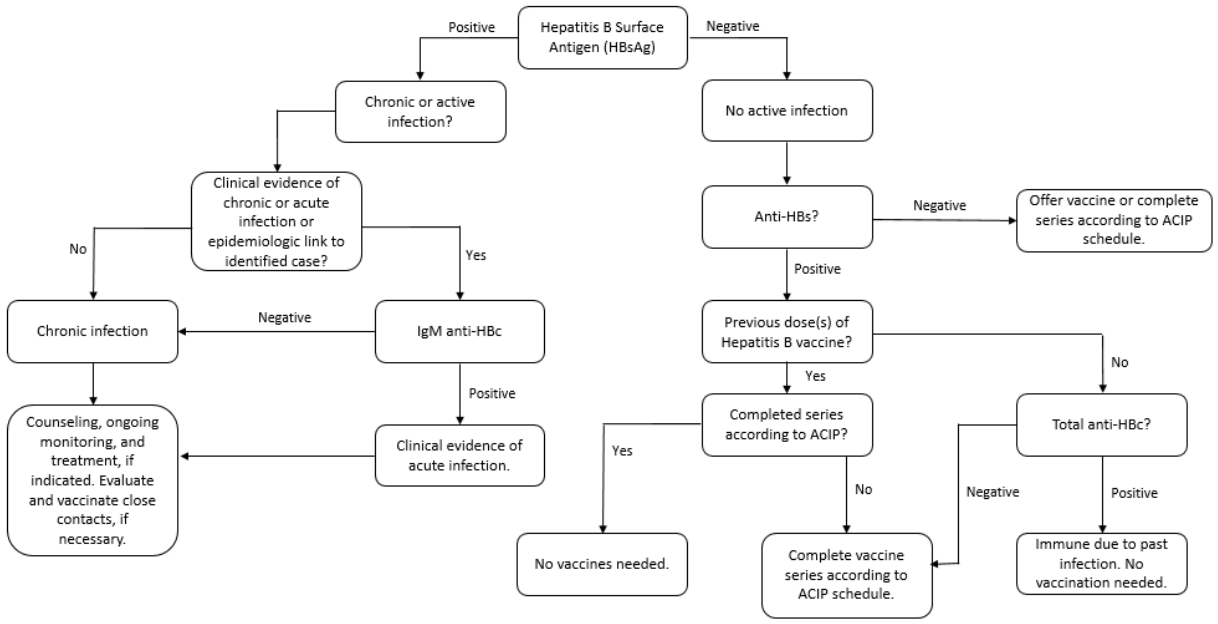
Screening of Children and Adolescent Refugees

- Review overseas records (pre-departure testing for infection and vaccination are increasingly common among arriving refugee populations).
    - If hepatitis B infection is found (HBsAg-positive*), additional evaluation and treatment options, or referral to a specialist, is recommended.
    - If HBsAg is negative, and vaccination series has been initiated, the vaccine series should be completed according to the ACIP schedule.
    - If HBsAg is negative, and the refugee has a record of completing the vaccination series before arrival and at appropriate intervals, no further testing or vaccination is necessary.**
    - If HBsAg is negative and no previous doses of vaccine have been received, the refugee should be either offered vaccination or serologic testing for immunity (Figure 2).

Notes:
*It is reasonable to repeat HBsAg after arrival when there is increased risk based on clinical judgment.
**In children with high risk of future exposure, it is reasonable to check serologies for evidence of immunity.

All children ≤ 18 years old who are HBsAg-negative should receive the complete hepatitis B vaccination series according to ACIP guidelines. The vaccine series can be started while waiting for HBV screening test results.

Figure 2: Hepatitis B Screening and Vaccination Algorithm for Newly Arrived Refugees in the United States



Vaccination Records

An increasing number of countries include hepatitis B in their routine vaccination schedules. Initiation of the hepatitis B vaccine series before departure for US-bound refugees is also increasing worldwide (see Vaccination Program for US-bound Refugees). If HBsAg is negative and a hepatitis B series was initiated overseas and documented on the DS-3025 (Vaccination Documentation Worksheet), the series should be completed according to the ACIP schedule. If the last recorded dose of hepatitis B vaccine was given less than 30 days before the refugee is screened for hepatitis B infection, the HBsAg result might reflect the vaccine antigen, therefore the test should be repeated. Refugees who have not initiated the series should be offered vaccine according to ACIP guidelines, if HBsAg-negative. In accordance with ACIP recommendations, anti-HBs ≥ 10 mIU/mL is only considered a correlate of protection after completion of the HBV

vaccine series. Healthy persons with documented completion of the HBV vaccine series and an anti-HBs < 10, additional vaccination is unnecessary [18]. The immunization section of the domestic refugee medical screening guidelines contains more information on specific issues of vaccination during the new arrival refugee screening examination.

Clinical and Public Health Management of People with HBV Infection

All HBsAg-positive people should have additional testing performed to determine the stage of disease and screen for sequelae of HBV infection, primarily hepatocellular carcinoma. Additional lab testing should include HBV DNA level, HBeAg, anti-HBe, liver enzyme tests for disease staging, and alpha-fetoprotein to screen for hepatocellular carcinoma. If viral load is low or undetectable (and HBeAg is undetectable), primary care providers can typically monitor the refugee's condition until lab tests become abnormal (liver enzymes elevated, HBeAg increases). Persons with abnormal lab test results should be referred to a gastroenterologist and/or hepatologist for additional testing and to ensure patients are managed appropriately.

HBsAg-positive people should be considered infectious. Hepatitis B is a reportable disease in some states, and cases should be reported to the state or local health department, according to state reporting requirements.

HBsAg-positive patients should also receive appropriate counseling about the infection, lifestyle modifications, and mechanisms to reduce transmission to others. Culturally sensitive patient education should be provided, including materials in the refugee's primary language. Additional information on counseling HBsAg-positive patient is available on the CDC Division of Viral Hepatitis website. Patient education materials for hepatitis infection developed by other agencies may be found at:

- HealthReach
- Minnesota Department of Health, Hepatitis B Prevention and Treatment ECHO-TV Program
- The Refugee Patient Education Project of CNY
- Refugee Health Technical Assistance Center

Patients should be counseled regarding the need for lifelong screening for hepatocellular carcinoma (HCC). Hepatic ultrasound and labs are generally recommended every 6 months, consistent with the AASLD guidelines [9]. Patients at higher risk for HCC include those with cirrhosis, hepatic steatosis, heavy alcohol consumption (> 7 drinks/week for women or > 14 drinks/week for men), and those with HCV, HDV, or HIV co-infections.

People living in households or other crowded living conditions with a person with a chronic HBV infection, as well as sexual partners, should be tested for HBV. If susceptible, these individuals should receive the three-dose hepatitis B vaccine series. In addition, any non-immune refugee who has had a potential exposure to HBV within the previous 60 days should have repeat testing 3–6 months after exposure. These individuals should be advised to seek medical care if hepatitis-related symptoms (e.g., jaundice, nausea/vomiting, right upper quadrant pain) occur during this period.

Hepatitis D Virus (HDV)

Background

Hepatitis D virus (HDV) is a defective virus that requires the presence of HBV to be viable in the human host. HDV may be acquired as a co-infection with HBV or as a superinfection after HBV infection. An estimated 5% of chronically HBV-infected people are coinfected with HDV [19]. People chronically infected with HBV who are superinfected with HDV usually also develop chronic HDV infection. Progression to cirrhosis and hepatocellular carcinoma is believed to be more common in individuals coinfected with HBV and HDV than in individuals with only HBV infection.

The epidemiology of chronic HDV infection in refugees is unknown. Additional information on HDV infection can be found here:

- CDC Viral Hepatitis website
- Hepatitis delta: virological and clinical aspects (Botelho-Souza LF, Vasconcelos MPA, Dos Santos AO, Salcedo JMV, Vieira DS. *Virol J*. 2017 Sep 13;14(1):177).

Screening Recommendations for HDV Infection in Refugees

Routine screening is not recommended. HDV has not been reported to infect or cause disease in the absence of HBV infection. The treatment of infection is the same as treatment for hepatitis B.

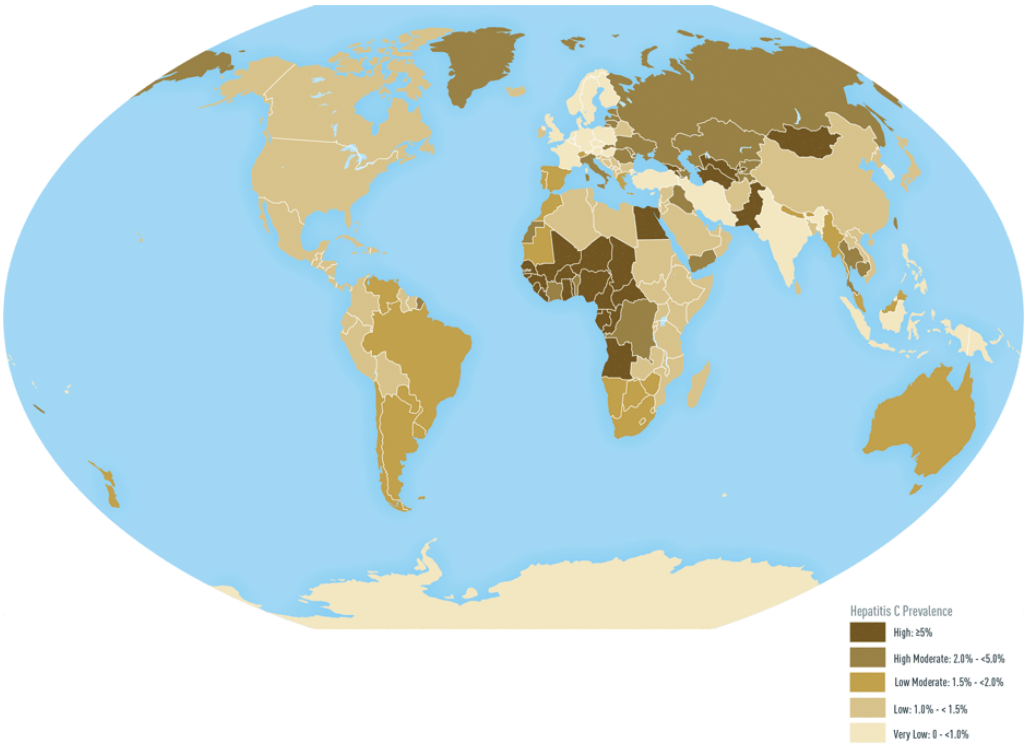
Hepatitis B vaccination is a primary preventive measure that protects against HDV infection.

Hepatitis C Virus (HCV)

Background

Hepatitis C virus (HCV) infection can lead to a chronic, generally asymptomatic viral hepatitis that can eventually result in cirrhosis and hepatocellular carcinoma. The prevalence of HCV varies between regions and countries (Figure 3), and it is estimated that 71 million people worldwide have chronic HCV infection [20]. HCV is transmitted through exposure to infected blood or other body fluids. In developed countries, infection primarily results from injection drug use. However, in developing countries, HCV is predominantly transmitted in medical settings where needles or surgical equipment may be reused or through transfusions of infected blood products. Although transmission can occur through sexual contact, during the perinatal period, and through breastfeeding, these modes of transmission are inefficient and uncommon.

Figure 3: Prevalence of Hepatitis C Virus Infection (2014)



Source: CDC Health Information for International Travel (Yellow Book) 2018

Overall, 75%–85% of HCV-infected people will develop chronic infection [21]. Several factors may accelerate the progression of chronic hepatitis C, particularly moderate to high alcohol intake. Infection at an older age is also associated with faster progression, as is coinfection with HIV.

Epidemiology of HCV Infection in Refugee Populations

Little generalizable data are available on the epidemiology of HCV infection in refugee populations. Published prevalence rates of anti-HCV antibody have ranged from 4.5% (24 of 529) among Asian and African refugees in Italy, to 8.1% (19 of 234) among Cambodian refugees in Australia [22, 23]. Additionally, in a study of Karen refugees < 18 years of age resettled in Australia between July 2006 and October 2009, none of the 214 patients screened tested positive for HCV infection, while 10 of 305 (< 4%) of those ≥ 18 years of age tested positive [24]. Prevalence data on HCV infection in newly arrived refugees in the United States are sparse. Testing of serum specimens obtained from 4,890 Bhutanese, Burmese, Iraqi, and Hmong refugees during 2002-2007 detected HCV RNA in 63 individuals (1.1%). However, infection rates varied by population; HCV prevalence was much higher among Hmong refugees born in Thailand, whose rate was approximately 7% [25]. A study in Minnesota found higher rates of infection with HCV in Somali immigrants than nonimmigrant residents of the same county who were tested. The study also found that HCV infection was the primary viral cause of hepatocellular carcinoma in Somali born individuals [26].

Screening Recommendations for Chronic HCV Infection in Refugees

Screening tests to evaluate for HCV infection are antibody to HCV (anti-HCV), recombinant immunoblot assay (RIBA), and HCV RNA polymerase chain reaction (PCR). Immunocompromised people, such as people living with HIV, those who have end-stage renal disease, and those on immunosuppresive therapy, may have false-negative tests and should screened by PCR for HCV RNA.

Adults

Recommendations for screening for HCV infection in refugees during the new arrival medical examination are the same as the guidelines for the general US population. This recommendation includes routine screening for those born during 1945–1965, and those with risk factors [20]. Identified risk factors that should prompt testing in newly arrived refugees include:

- injection drug use
- HIV infection
- having received whole blood or blood components before migration
- chronic hemodialysis
- persistently abnormal liver enzyme levels
- household contact with known hepatitis C infection

Additional risk factors are noted in the Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965 [20]. These additional risk factors may be indications for HCV screening. Visit CDC's website for updated information on HCV infection.

It is also reasonable to screen all adults who are from or have lived in regions with high moderate (2% to < 5%) or high (≥ 5%) prevalence.

Children and Adolescents

CDC does not recommend HCV screening for refugee children (< 18 years of age) during the new arrival medical examination unless they are members of high-risk groups, which include:

- All children born to HCV-positive mothers
    - Children born to HCV-positive mothers may be tested before 18 months of age. However, a child's HCV antibody testing result may be falsely positive due to passively acquired maternal antibody. In such cases, the child should be tested for HCV RNA [1]. The Council of State and Territorial Epidemiologists (CSTE) has written a position statement on HCV perinatal infection and laboratory criteria for diagnosis.
- Children with the risk factors listed above for adults

In addition, it is reasonable to screen all children who are from or have lived in regions with high moderate (2% to < 5%) or high (≥ 5%) prevalence.

Additional Screening Considerations

Other risk factors in refugee populations may exist, such as traditional tattooing, although data are limited. Limited data exist on the link between FGM/C and hepatitis C infection. In a recent survey of Egyptian men and women aged 15-59 (n=12,780), researchers found that female genital mutilation/cutting (FGM/C) is an independent risk factor for hepatitis C infection [27]. In the study population, HCV prevalence was significantly higher if FGM/C was performed by a non-doctor, and that 79.8% of women infected with HCV had undergone FGM/C [27]. Some experts recommend screening children with a history of FGM/C.

With quickly evolving and improving therapy, the prevalence threshold for when it is cost-effective to screen a population for HCV infection is unknown. Experts recommend threshold population rates range from 0.8% to 3% [28, 29]. Most data indicate that HCV infection rates in refugee populations are below those found in the United States. However, if data become available indicating higher rates in certain populations, further targeted population screening may be recommended.

Testing of low-risk populations is discouraged. Testing increases the likelihood of false-positive anti-HCV screening test results. Further research defining HCV infection rates of refugee subpopulations is needed, and could help target screening efforts.

Clinical and Public Health Management of Chronic HCV Infection

People who have a positive HCV antibody test should be tested for HCV RNA genotype. Those found to be currently infected (HCV RNA positive) should be managed by a healthcare professional experienced in the management of chronic liver disease and hepatitis C. Patients with HCV infection should also be counseled on preventing transmission. Culturally appropriate patient education should be conducted, and materials should be provided in the refugee's primary language, if possible.

Most patients with chronic HCV infection will benefit from treatment with antiviral therapy. Patients with chronic HCV infection should be counseled regarding the need for lifelong screening for hepatocellular carcinoma (HCC). Hepatic ultrasound and labs are generally recommended every 6 months, consistent with the AASLD guidelines [9]. Patients at higher risk for HCC include those with cirrhosis, hepatic steatosis, heavy alcohol consumption (>7 drinks/week for women or >14 drinks/week for men), and with HBV, HDV, or HIV co-infections.

Acute Viral Hepatitis

Hepatitis A Virus (HAV)

Background

Hepatitis A virus (HAV) is endemic in most parts of the world. Most refugees resettling in the United States are from areas that are highly endemic for HAV. HAV is primarily transmitted via

the fecal-oral route, and infection is typically associated with poor sanitation and hygiene. The average incubation period for HAV is 28 days (range: 15–50 days). In highly endemic areas, most people are infected as children. Most refugees resettling in the United States, especially adults, have immunity to HAV infection due to previous exposure; resolved HAV infection results in lifetime immunity and does not lead to chronic infection.

Most adults with HAV infection have symptoms, including fatigue, low appetite, abdominal pain, nausea, and jaundice, that usually resolve within 2 months of infection. Fulminant hepatitis may occur and is more common in people with chronic liver disease. Young children with HAV infection typically are asymptomatic and can spread the virus for up to several months. The risk of spread to the general US population from these children is unknown but appears to be low. Outbreaks have been associated with asymptomatic internationally adopted children placed in nonimmune populations (e.g., host families, daycare). Refugees, unlike international adoptees, tend to live together initially after migration, decreasing the potential for spread outside the refugee community. Additional information on HAV is available on the CDC Viral Hepatitis website.

Screening Recommendations for HAV Infection in Refugees

Routine testing for HAV infection is not recommended. People with signs or symptoms of acute HAV infection should be evaluated for acute HAV infection by testing for anti-HAV IgM. Additionally, people presenting with signs or symptoms of acute HAV infection should also be tested for HBV and HCV infection, as acute HBV and acute HCV often present similarly to HAV.

Screening for asymptomatic infection in children is expensive, and because a high proportion of refugees are immune, CDC does not recommend routine testing for acute HAV infection in asymptomatic refugees.

Ideally, hepatitis A vaccine (at least the initial dose) should be administered to refugee children before migration to the United States. However, refugee populations do not currently receive pre-departure hepatitis A vaccination.

In the United States, the two-dose hepatitis A vaccination series is recommended for all children 12–23 months of age. All refugee children ages 12–23 months should receive the first dose of hepatitis A vaccine, followed by a second dose 6–18 months later. To ensure immunity for any individual over 2 years of age, administer two doses of hepatitis A vaccine separated by 6–18 months. In those older than 2 years, pre-vaccination screening for immunity to hepatitis A virus (total anti-HAV) among refugees may be cost-effective, depending on the prevalence of HAV infection in the population and local costs for screening [30].

For more information on HAV vaccination recommendations, see the immunization guidelines for newly arrived refugees and the ACIP Immunization Schedules for the United States.

Hepatitis E Virus (HEV)

Background

Hepatitis E virus (HEV) causes acute viral hepatitis and is transmitted by the fecal-oral route. The signs and symptoms are similar to those produced by HAV. HEV infection is well described in many resource-limited nations, particularly in South Asia, although its prevalence is likely underestimated, including in developed nations [31]. Although fulminant hepatitis may develop in 0.5%–4% of the overall HEV-infected population, it is particularly virulent in pregnant women, especially those infected during the third trimester. Mortality rates during pregnancy may exceed 25% [32]. The incubation period of HEV ranges from 3 to 8 weeks, with a mean of 40 days. Clinical presentation and epidemiologic characteristics vary by HEV genotype. Of note, infection with HEV genotype 3 has been associated with chronic hepatitis. Only people with signs or symptoms of acute hepatitis should be tested for HEV infection along with HAV, HBV, and HCV infection, since these viruses are clinically indistinguishable. The diagnosis is confirmed by detection of HEV RNA in the blood by reverse transcriptase-PCR. Additional information on HEV is available on the CDC hepatitis webpage.

Screening Recommendations HEV Infection in Refugees

Routine testing for HEV infection is not recommended for refugees of any age.

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