In 1991, the US adopted a public health strategy aimed at eliminating transmission of HBV. Nearly 30 years later, the goal remains the same and vaccination is still a critical component—including universal hepatitis B vaccination of children and vaccination of at-risk adults in the US.

Experts stress importance of vaccinating adults against hepatitis B

The recommendations in this Call to Action are based on discussions at a June 2018 multidisciplinary Roundtable convened by the National Foundation for Infectious Diseases (NFID).

Roundtable participants included subject matter experts, healthcare professionals, and representatives from medical, healthcare, public health, and patient advocacy organizations.

Discussions focused on the burden of hepatitis B virus (HBV) infection in the US and key strategies to promote vaccination as a highly effective tool in preventing HBV infection.

Call to Action
Preventing Hepatitis B in US Adults through Increased Vaccination Rates

Overview: Protecting US Adults Against Hepatitis B Virus Infection

Despite the availability of highly effective hepatitis B vaccines, only one-quarter (24.8 percent) of US adults at high risk for hepatitis B virus (HBV) infection get vaccinated as recommended by the Centers for Disease Control and Prevention (CDC) (Figure 1). Those who are not immunized remain at risk for acute HBV infection, which can progress to chronic infection, leading to liver cirrhosis, liver cancer, or premature death. They can also pass the infection on to others—for example, mothers can pass the infection on to their babies, who are then at high risk of progressing to chronic infection.

Figure 1. Hepatitis B vaccine coverage (≥3 doses) among US adults age ≥19 years, 2015

In 1991, the US adopted a public health strategy aimed at eliminating transmission of HBV. Nearly 30 years later, the goal remains the same and vaccination is still a critical component—including universal hepatitis B vaccination of children and vaccination of at-risk adults in the US. In a pattern typical of vaccines recommended for both children and adults, hepatitis B vaccination coverage rates...
are far higher among children (>90 percent) than adults.\textsuperscript{7} The rate of reported cases of acute HBV infection in the US declined nearly 90 percent following widespread uptake of hepatitis B vaccination in infants and children, but that decline has leveled off in recent years.\textsuperscript{8}

In 2017, a National Academy of Medicine report concluded that hepatitis B could be eliminated as a public health problem in the US and that immunization, which can prevent 95 percent of infections, is the first key step.\textsuperscript{9} The report noted that “eliminating the public health problem of hepatitis B will take more time and require public will, resources, and attention to vaccination barriers.”\textsuperscript{9}

Burden of HBV Infection

The burden of acute HBV infection in the US is mainly in adults, with most new infections occurring in those age 30 to 59 years.\textsuperscript{5} Lower incidence in adults age 20 to 29 years reflects the success of higher hepatitis B vaccination rates in this age group, as they were born after infant and childhood hepatitis B vaccination recommendations were widely adopted in the US.

In 2016, there were 3,218 acute HBV infections reported in the US, but because many acute infections are asymptomatic and unreported, CDC estimates that 21,000 US infections actually occur each year.\textsuperscript{10} The national incidence of acute HBV infection has been stable in recent years (Figure 2).\textsuperscript{8} However, one study conducted in Kentucky, Tennessee, and West Virginia\textsuperscript{11} found a 114 percent increase in new HBV cases between 2009 and 2014. The increase is attributed to high rates of injection drug use due to the growing opioid crisis and low hepatitis B vaccination coverage in US adults.

Acute HBV infection will progress to chronic infection in about 1 in 20 adults overall,\textsuperscript{12} and is more likely in individuals with immunosuppression (e.g., HIV or on hemodialysis) or diabetes.\textsuperscript{13,14} The virus replicates primarily in the liver, and can do so asymptotically for decades among those with chronic infection. Most people are not aware they are infected until the virus has caused serious liver damage.\textsuperscript{15}

There are as many as 2.2 million individuals living with chronic hepatitis B in the US\textsuperscript{16} and two-thirds (67 percent) are not aware that they are infected,\textsuperscript{9,17} contributing to ongoing transmission. Up to 40 percent of those with chronic hepatitis B will progress to cirrhosis, liver cancer, or liver failure; and 25 percent will die prematurely from these complications.\textsuperscript{3-5} Many studies have shown a sharply increased risk of liver cancer among people with chronic hepatitis B\textsuperscript{4} and several indicate a possible association with an increased risk of pancreatic cancer.\textsuperscript{18-20} Chronic hepatitis B cannot be cured, but antiviral therapy may reduce the risk of progression to cirrhosis, liver cancer, or premature death.\textsuperscript{21}

More than one-half of US adults with acute HBV infection (52 percent) reported no risk behaviors for infection during the previous 6 weeks to 6 months.\textsuperscript{1} Among those who do report risk factors, injection drug use and multiple sex partners are the most commonly reported sources of HBV acquisition.\textsuperscript{8} Patients may either not recognize or acknowledge these high-risk behaviors.

\textsuperscript{7}Healthcare professionals, men who have sex with men, injection-drug users, hemodialysis patients, household and sexual partners of persons with chronic hepatitis B, persons in certain institutional settings (e.g., inmates of long-term correctional facilities).

\textsuperscript{8}HBsAg=hepatitis B virus surface antigen; HBV=hepatitis B virus.

\begin{figure}  
\centering
\includegraphics[width=\textwidth]{incidence_of_hbv_infection_in_the_united_states_1980-2016.png}
\caption{Incidence of HBV infection in the United States, 1980-2016\textsuperscript{8}}
\end{figure}
HBV Transmission and Clinical Presentation in Adults

HBV is transmitted through contact with the blood or other bodily fluids of an infected person and is 50 to 100 times more infectious than HIV. The virus remains infectious outside the body for at least 7 days and can be transmitted in the absence of visible blood.

Symptoms in adults may include nausea, vomiting, abdominal pain, fever, dark urine, changes in stool color, and jaundice. At least one-half of adults with an acute HBV infection will be asymptomatic.

In addition to immunization, screening and linkage to care are essential tools in the strategy to eliminate HBV in the US. As many individuals with chronic hepatitis B do not know they are infected, only about 15 percent of those eligible are undergoing treatment. Identifying individuals with chronic infection allows them to take steps to reduce virus transmission to others and allows for identification and vaccination of their close contacts.

CDC Recommendations for Hepatitis B Vaccination in US Adults

As shown in figure 1, hepatitis B vaccination series coverage averages only 25 percent for adults age ≥19 years, with minor variations among specific risk groups (from a high of 31.1 percent in travelers to a low of 26.2 percent in adults age <60 years with diabetes). Coverage in healthcare professionals (HCPs) is higher (61 percent), but still not optimal. Better adoption of hepatitis B immunization recommendations is essential to achieve the goal of eliminating transmission of HBV in the US.

Hepatitis B vaccination is recommended for any adult seeking protection from HBV infection. HCPs should provide vaccination even in the absence of patient acknowledgement of having a specific risk factor or engaging in a specific risk behavior.

Hepatitis B vaccination recommendations in adults are categorized in several groups: individuals at risk from sexual exposure; those at risk from exposure to contaminated blood (including people who inject drugs); and individuals based on their existing health condition, living situation, or travel plans. The complete list of adults recommended to receive hepatitis B vaccination is included in Table 1.

<table>
<thead>
<tr>
<th>Table 1. US Adults Recommended for HBV Vaccination by Risk Group¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk: Sexual Exposure</strong></td>
</tr>
<tr>
<td>• Sexual contact with HBV-infected individual (many do not know they are infected)</td>
</tr>
<tr>
<td>• More than one sex partner during previous 6 months</td>
</tr>
<tr>
<td>• Individuals seeking evaluation or treatment for a sexually-transmitted infection (STI)</td>
</tr>
<tr>
<td>• Men who have sex with men</td>
</tr>
<tr>
<td><strong>Risk: Exposure to Infected Blood</strong></td>
</tr>
<tr>
<td>• People who inject drugs</td>
</tr>
<tr>
<td>• Household contact of HBV-infected individual</td>
</tr>
<tr>
<td>• Healthcare and public safety personnel who are exposed to blood or blood-contaminated body fluids</td>
</tr>
<tr>
<td>• Hemodialysis patients</td>
</tr>
<tr>
<td>• Unvaccinated persons with diabetes &lt;60 years of age (60+ at discretion of treating clinician)</td>
</tr>
<tr>
<td><strong>Risk: Certain Health, Living or Travel Situations</strong></td>
</tr>
<tr>
<td>• People with HIV, hepatitis C, or chronic liver disease</td>
</tr>
<tr>
<td>• Residents and staff of facilities for developmentally disabled individuals</td>
</tr>
<tr>
<td>• Inmates of correctional facilities (prisons)</td>
</tr>
<tr>
<td>• International travelers to countries with high or intermediate levels of endemic HBV infection</td>
</tr>
<tr>
<td>• Pregnant women at risk for HBV infection during pregnancy</td>
</tr>
</tbody>
</table>

All persons seeking protection from HBV infection without acknowledgement of a specific risk factor should be vaccinated.

Hepatitis B Vaccines

Three single-antigen hepatitis B vaccines are licensed in the US for use in adults—two long-standing vaccines, Engerix-B® (GlaxoSmithKline) and Recombivax HB® (Merck & Co., Inc.), and one newer vaccine licensed in November 2017, Heplisav-B® (Dynavax Technologies Corporation). One combination hepatitis A and hepatitis B vaccine, Twinrix® (GlaxoSmithKline), is licensed for use in US adults.

Heplisav-B® is administered as a 2-dose series. Standard dosing for all other hepatitis B vaccines is a 3-dose series, with each having alternate dosing schedules and/or special formulations for specific patient types and for accelerated dosing (Table 2).
Vaccination with any of the 3-dose vaccines is seroprotective in >90 percent of adults younger than age 40 years and in 75 percent of adults age ≥60 years. Vaccination with the newer 2-dose vaccine is seroprotective in >90 percent of adults aged 18 to 70 years, remaining high even in the oldest group (91.6 percent in adults age 60 to 70 years).

Three-dose vaccines are less effective in adults with diabetes, hemodialysis/chronic kidney disease (CKD) patients, and immunocompromised adults. Vaccination with the newer 2-dose series is similarly seroprotective in adults with CKD with and without diabetes (89.5 and 90.5 percent, respectively) and seroprotection remains >90 percent among populations where hyporesponsiveness to 3-dose vaccines has been noted (people with diabetes, smokers, obese persons, and men). Seroprotection rates with the 2-dose series were lower for patients on dialysis compared to the overall population (86.4 percent) but were significantly higher than seroprotection rates for the 3-dose comparator vaccine (74.1 percent).

### Barriers to Hepatitis B Vaccination in US Adults

General and vaccine-specific (e.g., influenza, human papillomavirus [HPV]) barriers to adult vaccination as well as recommendations to overcome them have been well-documented. These barriers to adult vaccination are also relevant to hepatitis B vaccination—limited access to care; low consumer awareness of vaccines and the risk of the diseases they prevent, as well as incorrect beliefs about vaccine safety and efficacy; complexity of recommendations and ability of HCPs to implement complex vaccine recommendations; competing priorities during healthcare visits; lack of systems to remind HCPs to vaccinate; lack of strong HCP recommendations; and logistical challenges with ordering and stocking vaccines.

#### In addition to common barriers to adult vaccination, barriers of special concern for hepatitis B vaccines include:

- **Hepatitis B vaccine recommendations include more than a dozen target populations,** complicating identification of patients who may need vaccination.

- **The need for multiple doses over time** may be a barrier to completing the vaccine series.

- **Patients may not readily admit to the two leading risk factors for HBV acquisition—sexual exposure and injection drug use.**

- **HCPs may also face logistical and financial challenges** in stocking hepatitis B vaccines, especially since many have difficulty predicting how quickly doses will be used, which may be easier to do for influenza vaccine and other vaccines with age-based recommendations.

- **Health insurance coverage for hepatitis B vaccines is complicated,** despite the CDC recommendation that vaccination be given to anyone who requests it even if no risk factor is obvious to the HCP.
Summary and Call to Action

Achieving high hepatitis B vaccination coverage in US adults is a complex undertaking that requires active participation and coordination by a range of immunization stakeholders. All HCPs, professional societies, patient and health advocacy groups, state and local public health departments, policy makers, and payers should evaluate current programs and implement best practices to improve vaccine delivery and uptake.

Due to the complexity of hepatitis B vaccine recommendations in US adults, an important first step is to provide ongoing education and awareness among all frontline HCPs regarding which adults should receive hepatitis B vaccination, why they are at risk, and the burden of chronic hepatitis B.

Vaccination should be provided to all adults requesting protection from HBV infection. In addition to targeted education and awareness building, strategies to improve hepatitis B vaccination coverage in adults may include the following:

- **Avoid missed vaccination opportunities.**
  While HCPs working with high-prevalence populations (e.g., immigrants from Southeast Asia and Sub-Saharan Africa) may choose to screen patients to help identify those in need of treatment, screening is not required before administering hepatitis B vaccination. Likewise, pregnancy is not a contraindication to hepatitis B vaccination. Pregnant women at risk of HBV infection should be vaccinated during pregnancy.

- **Implement standing orders,** which are among the most effective strategies to improve vaccination rates in adults.44-47 Sample standing orders are readily available at no cost from many reliable sources.

- **Track vaccine administration and ensure patients return for follow-up doses.** Tactics may include using immunization registries, scheduling follow-up appointments, setting up transportation when needed, and having the patient self-address a reminder that can be mailed prior to the follow-up appointment.

- **Ensure hepatitis B vaccinations are in best practice guidelines** for relevant adults (e.g., patients with diabetes) to be sure vaccination becomes a part of their routine care.

- **Integrate hepatitis B vaccination into nontraditional settings,** such as:
  - Community events at local community centers and/or churches;
  - Syringe service and substance abuse treatment programs that work with and treat people who inject drugs;
  - Primary care practices with HCPs who are approved to prescribe buprenorphine treatment for patients with opioid use disorder; and
  - Sexually transmitted infection clinics and screening events.

- **Consider alternative locations for follow-up hepatitis B vaccination doses.** Some patients may find it more convenient to receive additional doses at their local pharmacy or other nontraditional settings.
Capitalize on and enhance existing disease surveillance information from state and local public health departments that:

- Identifies pregnant women and women of childbearing age who may have chronic HBV infection (in an effort to reduce perinatal HBV transmission) to also identify household and other close contacts who may require vaccination
- Tracks and identifies local outbreak activities that can be used to target groups and geographic areas for increased hepatitis B vaccination efforts and can assess impact
- Allows HCPs and public health groups to utilize regional outbreaks as an opportunity to educate the community about the burden of hepatitis B and the benefits of vaccination
- Partner with facilities and professionals that see and serve individuals with opioid addiction to integrate hepatitis B vaccination into their care. End stigmatization against individuals living with or at risk of addiction and viral hepatitis. Educate HCPs about engaging patients in comfortable and frank conversations about risk behaviors.
- Engage with the correctional system to identify opportunities to vaccinate incarcerated individuals because of their high risk of HBV infection and ability to spread infection once reintegrated into society.

Educate the next generation of HCPs about the importance of adult vaccines. Experts agree that most education about adult immunization occurs in the clinic, not the classroom, which can lead to inconsistent knowledge levels among trainees.

Lead by example and make a strong recommendation. In addition to ensuring that they are up-to-date on their own hepatitis B vaccination, HCPs should make a strong recommendation to all at-risk patients for optimal protection.

All relevant stakeholder groups can and should implement strategies and evidence-based best practices to increase hepatitis B vaccination among at-risk populations. Raising awareness about the burden of HBV infection in US adults and the link to cirrhosis, liver failure, and liver cancer is an important first step to eliminating hepatitis B as a public health problem in the US.
Participating Organizations

The following organizations support the goals of this Call to Action:

- American Academy of Family Physicians
- American Academy of Physician Assistants
- American Association of Diabetes Educators
- American College of Physicians
- American Liver Foundation
- American Nurses Association
- American Pharmacists Association
- American Sexual Health Association
- Asian and Pacific Islander American Health Forum
- Association of Immunization Managers
- Association of State and Territorial Health Officials
- Centers for Disease Control and Prevention
- Council of State and Territorial Epidemiologists
- Hepatitis B Foundation
- Hepatitis B Initiative of Washington, DC
- Hep B United Coalition
- Immunization Action Coalition
- Infectious Diseases Society of America
- National Association of County and City Health Officials
- National Task Force on Hepatitis B: Focus on Asian and Pacific Islander Americans
- National Foundation for Infectious Diseases
- US Department of Health and Human Services, Office of HIV/AIDS and Infectious Disease Policy

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HEPATITIS B: ARE YOU AT RISK?

HEPATITIS B IS A SERIOUS & DEADLY DISEASE

Hepatitis B virus infects people of all ages & as many as 2.2M people in the US are chronically infected.

Up to 40% of chronic infections lead to cirrhosis, liver failure, and liver cancer, which may lead to death.

HEPATITIS B IS EASILY SPREAD

Hepatitis B is 50 to 100X more infectious than HIV and can live outside the body for 7+ days and still cause infection.

2/3 of those living with chronic hepatitis B do not know they are infected but can still spread the virus to others.

MANY ADULTS ARE AT RISK

Brenda Diabetes
Phil Chronic Liver Disease
Mai Immigrant from SE Asia
Ken Infected with HIV
Thomas Multiple Sexual Partners
Lola IV Drug User (Shares Needles)

SAFE & EFFECTIVE VACCINES ARE AVAILABLE

Only 25% of US adults get vaccinated against hepatitis B as recommended by the Centers for Disease Control & Prevention (CDC).

TALK TO A HEALTHCARE PROFESSIONAL ABOUT VACCINATION TO HELP PROTECT YOURSELF AGAINST HEPATITIS B