

## Perspective

# Vaccination and Immunoprotection in People with HIV

*Vaccines play an important role in HIV primary care and are available for several sexually transmitted infections, including those caused by hepatitis A virus (HAV), hepatitis B virus (HBV), and human papillomavirus (HPV). HAV vaccination is increasingly important, given recent hepatitis A outbreaks and lack of immunity in many adults. A novel formulation of the hepatitis B vaccine shows promise in increasing rates of seroprotection. The Advisory Committee on Immunization Practices recommends the meningococcal conjugate vaccine for all individuals with HIV and has expanded the age range for administration of the HPV vaccine, recommending shared decision making about its administration in adults aged 27 to 45 years. This article summarizes a presentation by Steven C. Johnson, MD, at the International Antiviral Society–USA (IAS-USA) annual continuing education program held in New York, New York, in September 2019.*

**Keywords:** HIV, STI, sexually transmitted infection, vaccine, hepatitis, immunoprotection, HBV, HPV, HAV

Currently, vaccines for 28 infectious diseases are available in the United States.<sup>1</sup> For individuals with HIV, the Centers for Disease Control and Prevention (CDC) provide guidance on which vaccines are appropriate, based on CD4+ cell count, and how often they should be administered (see Table).<sup>2</sup>

Hepatitis A virus (HAV), hepatitis B virus (HBV), and human papillomavirus (HPV) can all be transmitted sexually. Transmission of meningococcal disease is linked to close intimate or non-intimate contact, such as coughing or kissing. Therefore, discussions of these vaccines should be included in sexual health discussions between practitioners and patients.

## Hepatitis A Virus

Historically, hepatitis A was common in the United States because of conditions such as crowding, poor sanitation, and lack of food safety, and it was a common infection in childhood. As society developed, housing became more separate and food safety measures increased, and rates of HAV infection

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began to decline. From 1995 to 2011, the incidence of HAV infection decreased by more than 95%.<sup>3</sup> In 2016,

## Currently, the most effective way to prevent HAV infection is through vaccination.

outbreaks of HAV infection began to occur in the United States, likely spread via person-to-person contact,<sup>4</sup> and from 2011 to 2017, the incidence of HAV infection increased by 140%.<sup>3</sup> This increasing incidence of HAV infection in the United States is illustrated in Figure 1.<sup>3</sup>

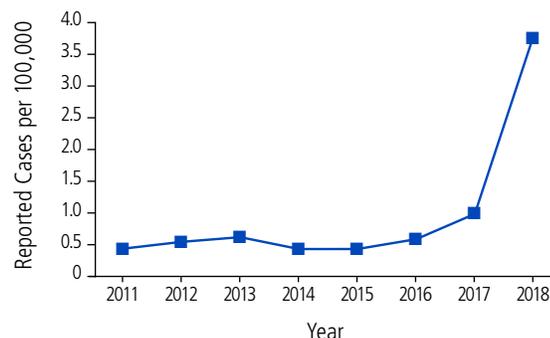
Currently, the most effective way to prevent HAV infection is through vaccination. The CDC recommends the HAV vaccine for all susceptible men who have sex with men (MSM) and for individuals who use drugs (injection or noninjection); have clotting factor disorders; are homeless or unstably housed; have been incarcerated; are researchers who work with HAV; will travel to countries with high or intermediate endemic HAV; or have close contact with an international adoptee.<sup>5</sup> The CDC also notes that HAV vaccination can be considered for all non-immune individuals.<sup>5</sup>

## Hepatitis A Virus Postexposure Prophylaxis

In some cases, the HAV vaccine or immunoglobulin may be given as HAV postexposure prophylaxis (PEP). Individuals recently exposed to HAV who have not previously received the hepatitis A vaccine may be given a single dose of the monovalent HAV vaccine or immunoglobulin (0.02 mL/kg) as soon as possible after exposure, ideally within 2 weeks because the efficacy of vaccine or immunoglobulin when administered more than 2 weeks after exposure has not been established.<sup>6</sup> If hepatitis A immunoglobulin is administered to individuals for whom the vaccine is recommended, a dose of vaccine should be provided simultaneously with immunoglobulin, and the second vaccine dose should be administered according to the licensed schedule to complete the series.<sup>6</sup> The combined HAV/HBV vaccine should be considered for individuals for whom both vaccines are recommended.<sup>6</sup>

## Hepatitis B Virus

HBV and HIV are transmitted via the same routes, and individuals with HIV often have HBV. There has been a gradual decline in the number of cases of HBV infection in the United States (see Figure 2),<sup>7</sup> at least partly due to the rollout of vaccines, including in adolescents.



**Figure 1.** Incidence of hepatitis A virus infections in the United States from 2011 to 2018. Adapted from Centers for Disease Control and Prevention.<sup>3</sup>

**Table.** Immunization Schedule for Adults with HIV by Vaccine and Age Group<sup>a</sup>

Vaccine	Age			
	19-26 years	27-59 years	60-64 years	≥65 years
Influenza	1 dose annually			High dose <sup>c</sup>
Td/Tdap	Substitute Tdap for Td once, then Td booster every 10 years			
Varicella <sup>b</sup>	2 doses 3 months apart (if CD4+ cell count ≥200/μL and no immunity to varicella)			
HPV	3 doses at 0, 2, and 6 months	27-45 years		
Herpes zoster virus recombinant <sup>d</sup> or				2 doses at 0 and 2-6 months if ≥50 years
Zoster virus live <sup>b,d</sup>				1 dose if >60 years (if CD4+ cell count ≥200/μL)
MMR <sup>b,c</sup>	1 or 2 doses (if CD4+ cell count ≥200/μL and no immunity)			
PCV-13	1 dose, preferably before PPSV-23 vaccine			
PPSV-23	2 doses 5 years apart, at least 8 weeks after PCV-13 vaccine			1 dose
Hepatitis A virus	2 or 3 doses, depending on the vaccine, at 0 months and at 6-18 months. Check hepatitis A virus antibody after vaccination.			
Hepatitis B virus	2 or 3 doses depending on the vaccine. Check anti-HBs after vaccination.			
Meningococcal conjugate	If no prior vaccine, 2 doses of either available MenACWY vaccine given 8-12 weeks apart. Boost every 5 years.			

Abbreviations: anti-HBs, hepatitis B surface antibody; MenACWY, meningococcal serogroups A, C, W, Y; MMR, measles, mumps, and rubella; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; Td, tetanus and diphtheria toxoids; Tdap, tetanus and diphtheria toxoids and acellular pertussis.

<sup>a</sup>After assessing age, presence of immunity, and CD4+ cell count. Note that oral typhoid and live influenza vaccines are contraindicated in individuals with HIV.

<sup>b</sup>Live vaccines (MMR, varicella, zoster virus live, and yellow fever) should not be given to individuals with CD4+ cell counts below 200/μL.

<sup>c</sup>High-dose influenza vaccine is recommended by the author, but has not been specified by the Centers for Disease Control and Prevention.

<sup>d</sup>Recombinant herpes zoster vaccine is preferred to the live herpes zoster vaccine for individuals with HIV.

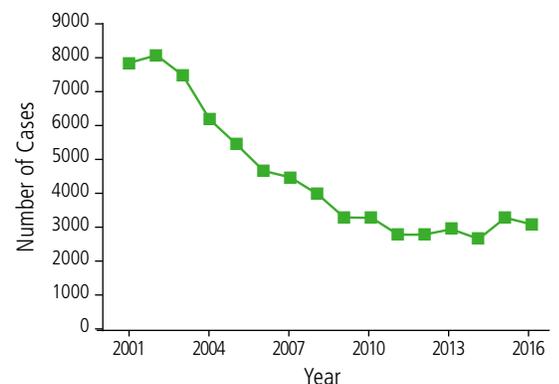
Adapted from Centers for Disease Control and Prevention.<sup>2</sup>

Hepatitis B vaccines include the standard recombinant vaccine, a newer novel adjuvant vaccine, and the combination HAV/HBV vaccine. The US Department of Health and Human Services (DHHS) Opportunistic Infection Guidelines recommend that HBV vaccination not be deferred based on CD4+ cell count, because some individuals with HIV and low CD4+ cell counts (<200/μL) respond to vaccination.<sup>8</sup> Of individuals with HIV who did not respond to a 3-dose recombinant HBV vaccine, 25% to 50% responded to an additional vaccine dose, and 44% to 100% responded to revaccination with a 3-dose series.<sup>8</sup> Therefore, the DHHS Opportunistic Infection Guidelines recommend that persons who do not respond to a complete hepatitis B vaccination series with one of the recombinant vaccines should receive a 3-dose revaccination series. However, some experts suggest delaying revaccination until antiretroviral therapy results

in a sustained increase in CD4+ cell count.<sup>8</sup> In 2 randomized trials, 4 doses of a double-dose recombinant HBV vaccine produced higher titers of hepatitis B surface antibody (anti-HBs) than 3 doses of the standard-dose vaccine.<sup>8</sup>

The newest HBV vaccine contains a novel adjuvant toll-like receptor 9 agonist, and was approved by the US Food and Drug Administration (FDA) in November 2017.<sup>9</sup> It is administered as 2 doses separated by 1 month. In clinical trials, seroprotection (anti-HBs ≥10 mIU) was achieved in 90% to 95% of participants who received the 2-dose HBV vaccine and in 65% to 81% of those who received a 3-dose standard recombinant HBV vaccine.<sup>8</sup> However, the safety and efficacy of the novel adjuvant HBV vaccine in individuals with HIV have not been studied.

Similar to HAV, there is a potential role of passive immunization in HBV. Passive-active PEP (the simultaneous administration of Hepatitis B Immune Globulin (HBIG) and vaccine at separate sites) and active PEP (the administration of HBV vaccine alone) are highly



**Figure 2.** Reported number of acute hepatitis B virus infections in the United States from 2001 to 2016. Adapted from Centers for Disease Control and Prevention.<sup>7</sup>

effective in preventing transmission after exposure to HBV.<sup>10</sup> HBIG has also been demonstrated to be effective in preventing HBV transmission, but with the availability of the HBV vaccine, HBIG is typically used as an adjunct to vaccination, especially in newborns of mothers with chronic infections.

In a retrospective cohort study of 2,942 individuals with HIV, 381 MSM were identified who had negative HBV serology results and a second serology available for evaluation.<sup>11</sup> Among these 381 men, the incidence rate of HBV

### **Sixty-two cases of meningococcal disease were reported in HIV-seropositive individuals from 1995 to 2014.**

infection was 1.1 per 1000 person-years overall, 2.85 per 100-person-years in those not taking active HBV treatment, 1.36 per 100-person-years in those taking lamivudine as the only HBV active drug, and 0.014 per 100-person-years in those taking tenofovir. These data suggest that tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) used to treat HBV can also act as a form of preexposure prophylaxis for HBV. Given the prevalence of tenofovir-based regimens, this may account for the lack of acute HBV infection in many individuals with HIV who are taking antiretroviral therapy.

### **Human Papillomavirus**

The estimated prevalence of HPV infection (all serotypes) in the United States is 79 million, with an estimated incidence of 14 million new cases each year. There were more than 40,000 cases of HPV-associated cancer in 2015, including cervical, vulvar, vaginal, penile, anal, and oropharyngeal cancers.

The 4-valent HPV vaccine was FDA approved in 2006, followed by a 2-valent vaccine in 2009, and then a 9-valent vaccine in 2014, which became the only available HPV vaccine in the United States in 2017. In 2018, the FDA expanded the use of the 9-valent vaccine to include individuals aged 27

to 45 years.<sup>12</sup> Subsequently, in 2019, the Advisory Committee on Immunization Practices (ACIP) adopted this age range in their recommendations.<sup>13</sup>

According to the ACIP recommendations, clinicians can consider HPV vaccination for adults aged 27 to 45 years who have not been adequately vaccinated and may benefit.<sup>13</sup> They note that having a new sex partner carries risk for acquiring a new HPV infection, regardless of age, and that most sexually active individuals have been exposed to some type of HPV. Additionally, adolescents aged 11 or 12 years remain the best target group for the HPV vaccine.

Current HPV vaccines do not prevent progression of HPV disease and are therefore preventative rather than therapeutic. Researchers are examining the possibility of a therapeutic HPV vaccine to perhaps change the natural history of established dysplasia.

### **Meningococcal Disease**

In a surveillance system in the United States that included approximately 43 million people, 62 cases of meningococcal disease were reported in individuals with HIV from 1995 to 2014.<sup>14</sup> The estimated incidence of meningococcal disease for individuals with HIV ranges from 3.4 to 6.6 cases per 100,000, with a relative risk approximately 5- to 13-fold higher among individuals with HIV than the general population.<sup>14</sup> In 2016, the ACIP recommended the meningococcal conjugate vaccine for all individuals with HIV.<sup>14</sup> The meningococcal conjugate vaccine is generally administered as 2 doses given 8 to 12 weeks apart, followed by a boosting dose at 5 years.<sup>14</sup>

### **Vaccines and Travel**

In addition to vaccines for sexual health, a number of other vaccines are recommended for people with HIV (see Table).

Vaccines are also important for travel, as individuals with HIV may acquire new sexually transmitted infections (STIs) while traveling. Certain vaccines may be indicated based on the travel destination (see Box).

#### **Box. Indicated Vaccinations Based on Travel Destination for Individuals With HIV**

- **Cholera:** Selected destinations with outbreaks and anticipated contact.
- **Hepatitis A virus:** Many parts of Central and South America, Mexico, Africa, and Asia.
- **Hepatitis B virus:** If not immune, most destinations where sexual activity is planned.
- **Influenza:** All destinations.
- **Japanese encephalitis:** Parts of Asia.
- **Meningitis:** Parts of Africa.
- **Polio:** Rarely given, although polio is still present in Nigeria, Afghanistan, and Pakistan.
- **Rabies:** Many destinations where the trip is prolonged or animal exposure is likely.
- **Typhoid:** Many parts of Central and South America, Mexico, Africa, and Asia.
- **Yellow Fever:** Parts of Africa and South America.

### **Summary**

Vaccines play an important role in HIV primary care and are available for several STIs, including HAV, HBV, and HPV infections. HAV vaccination is increasingly important, given recent HAV outbreaks and a large group of nonimmune adults. A novel formulation of the HBV vaccine shows promise in providing higher rates of seroprotection but has not yet been studied in the context of HIV. The ACIP recommends the meningococcal conjugate vaccine for all individuals with HIV and has expanded the age range for administration of the HPV vaccine, recommending shared decision making about its administration in adults aged 27 to 45 years. 

*Presented by Dr Johnson in September 2019 and updated in October 2020. First draft prepared from transcripts by Rachel Lastra. Reviewed and updated by Dr. Johnson in November 2020.*

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