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Hepatitis vaccination update

Immunization rates for hepatitis B are still suboptimal; a new 2-dose vaccine may help turn that around. HepA vaccine is now preferred as post-exposure prophylaxis for adults >40 years.

One of the most important commitments family physicians can undertake in protecting the health of their patients and communities is to ensure that their patients are fully vaccinated. This task is increasingly complicated as new vaccines are approved every year and recommendations change regarding new and established vaccines. To assist primary care providers, the Centers for Disease Control and Prevention (CDC) annually updates 2 immunization schedules—one for children and adolescents, and one for adults. These schedules are available on the CDC Web site (https://www.cdc.gov/vaccines/schedules/index.html).

These updates originate from the Advisory Committee on Immunization Practices (ACIP), which meets 3 times a year to consider and adopt changes to the schedules. During 2018, relatively few new recommendations were adopted. The September 2018 Practice Alert[1] in this journal covered the updated recommendations for influenza immunization, which included reinstating live attenuated influenza vaccine (LAIV) to the active list of influenza vaccines.

This current Practice Alert reviews 3 additional updates: 1) a new hepatitis B (HepB) vaccine; 2) updated recommendations for the use of hepatitis A (HepA) vaccine for post-exposure prevention and before travel; and 3) inclusion of the homeless among those who should be routinely vaccinated with HepA vaccine.

Hepatitis B: New 2-dose product

As of 2015, the annual incidence of new hepatitis B cases had declined by 88.5% since the first HepB vaccine was licensed in 1981 and recommendations for its routine use were issued in 1982.[2] The HepB vaccine products available in the United States are 2 single-antigen products, Engerix-B (GlaxoSmithKline) and Recombivax HB (Merck & Co.). Both can be used in all age groups, starting at birth, in a 3-dose series. HepB vaccine is also available in 2 combination products: Pediarix, containing HepB, diphtheria and tetanus toxoids, acellular pertussis, and inactivated poliovirus (GlaxoSmithKline), approved for use in children 6 weeks to 6 years old; and Twinrix (GlaxoSmithKline), which contains both HepB and HepA and is approved for use in adults 18 years and older.

The HepB vaccine is recommended for all children and unvaccinated adolescents as part of the routine vaccination schedule. It is also recommended for unvaccinated adults with specific risks (**TABLE 1**[2]). However, the rate of HepB vaccination in adults for whom it is recommended is suboptimal (**FIGURE**),[3] and just a little more than half of adults who start a 3-dose series of HepB complete it.[4]

A new vaccine against hepatitis B, HEPLISAV-B (Dynavax Technologies), was licensed by the US Food and Drug Administration in late 2017. ACIP now recommends it as an option along with other available HepB products. HEPLISAV-B is given in 2 doses separated by 1 month. It is hoped that this shortened 2-dose series will increase the

TABLE 1

Adults who should receive hepatitis B vaccination (if previously unvaccinated)[2]

Individuals at risk for infection by sexual exposure
• Sex partners of people who test positive for hepatitis B surface antigen (HBsAg)
• Sexually active people who are not in a long-term, mutually monogamous relationship (eg, those with more than 1 sex partner in the previous 6 months)
• People seeking evaluation or treatment for a sexually transmitted infection
• Men who have sex with men
Individuals at risk for infection by percutaneous or mucosal exposure to blood
• Current or recent injection drug users
• Household contacts of HBsAg-positive people
• Residents and staff of facilities for developmentally disabled people
• Health care and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
• Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
• People with diabetes ages 19 to 59 years; people with diabetes, ages ≥60 years (at the discretion of the treating clinician)
Others
• International travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence of ≥2%)
• People with hepatitis C virus infection
• People with chronic liver disease (including, but not limited to, those with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal)
• People with human immunodeficiency virus infection
• People who are incarcerated
• All other people seeking protection from HBV infection

If a HepB series must be completed with different products, just be sure 3 doses are given—even if HEPLISAV-B is one of the agents.

number of adults who achieve full vaccination. In addition, it appears that HEPLISAV-B provides higher levels of protection in some high-risk groups—those with type 2 diabetes or chronic kidney disease.[3] However, initial safety studies have shown a small absolute increase in cardiac events after vaccination with HEPLISAV-B. Post-marketing surveillance will be needed to show whether this is causal or coincidental.[3]

As with other HepB products, use of HEPLISAV-B should follow the latest CDC directives on who to test serologically for prior immunity, and on post-vaccination testing to ensure protective antibody levels were achieved.[2] It is best to complete a HepB series with the same product, but, if necessary, a combination of products at different doses can be used to complete the HepB series. Any such combination should include 3 doses, even if one of the doses is HEPLISAV-B.

Hepatitis A: Vaccination assumes greater importance for more people

A Practice Alert in early 2018 described a series of outbreaks of hepatitis A around the country and the high rates of associated hospitalizations.[5] These outbreaks have occurred primarily among the homeless and their contacts and those who use illicit drugs. This nationwide outbreak has now spread, resulting in more than 7500 cases since July 1, 2016.[6] The progress of this epidemic can be viewed on the CDC Web site (https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm).[7] At its October 2018 meeting, ACIP added homelessness to the list of those (previously

TABLE 2

Individuals who should receive hepatitis A vaccine if not previously vaccinated[6]

• Travelers to countries with high rates of hepatitis A virus infections
• Men who have sex with men
• Users of injection and non-injection drugs
• People with clotting-factor disorders
• People who work with nonhuman primates
• People who anticipate close personal contact with an international adoptee
• People with chronic liver disease
• People who are homeless

unvaccinated) who should receive the HepA vaccine (**TABLE 2**).[6]

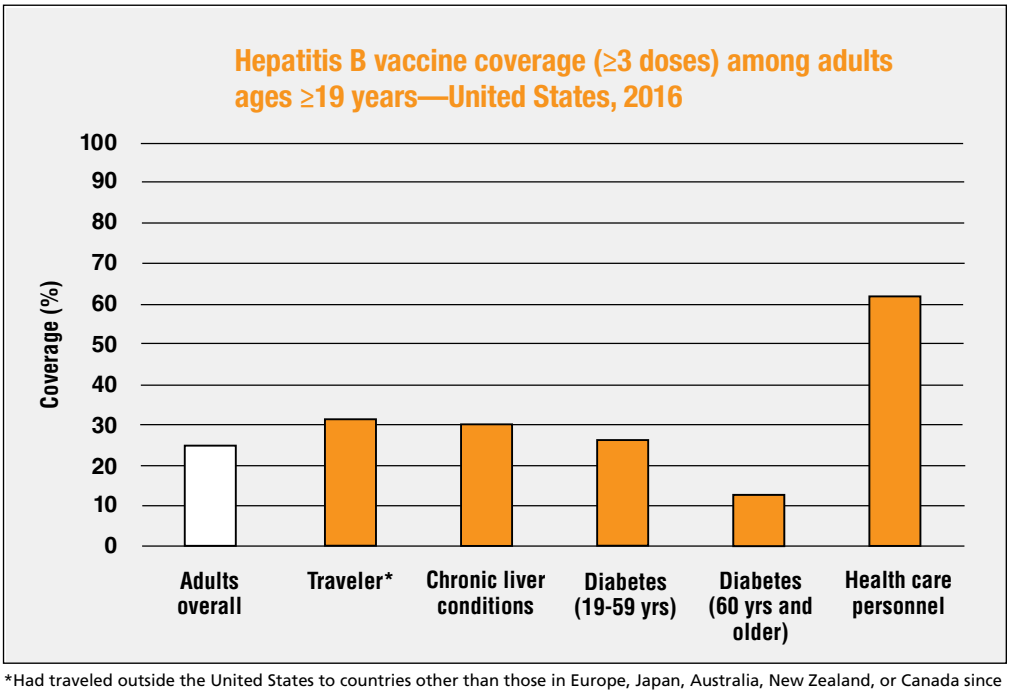
Remember that the current recommendation is to vaccinate all children 12 to 23 months old with HepA, in 2 separate doses. Two single-antigen HepA products are available: Havrix (GSK) and Vaqta (Merck). For the 2-dose sequence, Havrix is given at 0 and 6 to 12 months; Vaqta at 0 and 6 to 18 months. Even a single dose will provide protection for up to 11 years. In addition to these vaccines, there is the combination HepA and HepB vaccine (Twinrix) mentioned earlier.

Previous recommendations for preventing hepatitis A after exposure, made in 2007, stated that HepA vaccine was preferred for healthy individuals ages 12 months through 40 years, while immune globulin (IG) was preferred for adults older than 40, infants before their first birthday, immunocompromised individuals, those with chronic liver disease, and those for whom HepA vaccine is contraindicated.[8] The 2007 recommendations also advised vaccinating individuals traveling to countries with intermediate to high hepatitis A endemicity.

A single dose of HepA vaccine was recommended for all those 12 months or older, although older adults, immunocompromised individuals, and those with chronic liver disease or other chronic medical conditions planning to visit an endemic area in ≤ 2 weeks were

FIGURE

Rates of immunization against hepatitis B in the United States are inadequate[3]



*Had traveled outside the United States to countries other than those in Europe, Japan, Australia, New Zealand, or Canada since 1995.

supposed to receive the initial dose of vaccine and could also receive IG (0.02 mL/kg) if their provider advised it. Travelers who declined vaccination, those younger than 12 months, or those allergic to a vaccine component could receive a single dose of IG (0.02 mL/kg), which provides protection up to 3 months.

Several factors influenced ACIP to reconsider both the pre- and post-exposure recommendations. Regarding IG, evidence of its decreased potency over time led the committee to increase the recommended dose (see below). IG also must be re-administered every 2 months, the supply of the product is questionable, and many health care facilities do not stock it. By comparison, HepA vaccine offers the advantages of easier administration, inducing active immunity, and providing longer protection. Another issue involved infants ages 6 to 11 months traveling to an area with endemic measles transmission and who must therefore receive the measles, mumps, and rubella (MMR) vaccine. MMR and IG should not be co-administered, and, for infants, the health risk from measles outweighs that from hepatitis A.

Updated recommendations. After considering all this information, ACIP made the following changes to its hepatitis A virus (HAV) prevention recommendations (in addition to adding homeless people to the list of HepA vaccine recipients)[9]:

- Administer HepA vaccine as post-exposure prophylaxis to all individuals 12 months and older.
- IG may be administered, in addition to HepA vaccine, to those older than 40 years, depending on the provider's risk assessment (degree of exposure and medical conditions that might lead to severe complications from HAV infection). The recommended IG dose is now 0.1 mL/kg for post-exposure prevention; it is 0.1 to 0.2 mL/kg for pre-exposure prophylaxis for travelers, depending on the length of planned travel.
- Administer HepA vaccine alone to infants ages 6 to 11 months traveling outside the United States when protection against hepatitis A is recommended.

These recommendations have been published in the *Morbidity and Mortality Weekly Report*.[9] JFP

The recommended dose of immune globulin for post-exposure prevention of hepatitis A infection is now 0.1 mL/kg.

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