Hepatitis A virus infection: Treatment and prevention

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INTRODUCTION

Hepatitis A virus (HAV) infection is prevalent in many resource-limited countries and is among the most common preventable infections acquired by travelers (figure 1). Tools for prevention of HAV infection include vaccination, immune globulin, and attention to hygienic practices.

Humans are the only known reservoir for HAV; therefore, the virus could be eradicated with successful employment of widespread prevention strategies. Since hepatitis A vaccine became available in the United States in 1995, the rate of HAV infection has declined by 95 percent (figure 2).

Issues related to prevention of HAV are reviewed here. The epidemiology, clinical manifestations, diagnosis, and management of HAV infection are discussed separately. (See "Hepatitis A virus infection in adults: Epidemiology, clinical manifestations, and diagnosis".)

TREATMENT

HAV infection is usually self-limited, and treatment consists of supportive care. Medications that might cause liver damage or are metabolized by the liver should be used with caution. Full clinical and biochemical recovery is observed within three months in 85 percent of patients, and complete recovery is observed by six months in nearly all patients [1].

Patients with fulminant hepatic failure require aggressive supportive therapy and should be transferred to a center capable of performing liver transplantation. (See "Acute liver failure in adults: Management and prognosis".)

PROTECTION PRIOR TO EXPOSURE

Tools for prevention of HAV infection include vaccination, immune globulin, and attention to hygienic practices. Indications for pre-exposure protection and clinical approach are discussed in the following sections.

Indications — We are in agreement with recommendations issued by the Advisory Committee on Immunization Practices (ACIP) of the United States Centers for Disease Control and Prevention, which recommends protection (ideally vaccination) prior to potential hepatitis A exposure for the following individuals (table 1) [2-9]:

- **Children:**
  - All children aged 12 to 23 months.
  - All children and adolescents aged 2 to 18 years who have not previously received hepatitis A vaccine (ie, children and adolescents are recommended for catch-up vaccination).
  - For infants age 6 to 11 months who are traveling internationally, vaccination should be administered; the travel-related dose should not be counted toward the routine two-dose series [3].
- **Individuals at increased risk for HAV infection**:
  - Individuals traveling to or working in countries with high or intermediate rates of HAV; some experts advise that travelers outside the United States consider hepatitis A vaccination regardless of their destination [10].
  - Men who have sex with men.
  - Individuals who use injection or noninjection illegal drugs.
  - Individuals with occupational risk for exposure, including individuals working with HAV-infected primates or with HAV in a research laboratory.
  - Individuals who anticipate close personal contact with an international adoptee.

- Individuals experiencing homelessness.
- Unvaccinated individuals in outbreak settings who are at risk for HAV infection or at risk for severe disease from HAV.
- Individuals in settings that provide services to adults in which a high proportion of individuals are at increased risk for HAV infection (eg, settings with a focus on those who use injection or noninjection illegal drugs, group homes, and nonresidential day care facilities for developmentally disabled persons).

- **Individuals at increased risk for severe disease from HAV infection:**
  - Individuals with chronic liver disease, including but not limited to individuals with hepatitis B virus infection, hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, or an alanine aminotransferase or aspartate aminotransferase level persistently greater than twice the upper limit of normal.
  - Individuals ≥1 year with HIV infection.
- **Other individuals recommended for vaccination**
  - Pregnant women at risk for HAV infection or severe disease from HAV infection based on risk categories summarized above.
  - Any person who requests vaccination.

The World Health Organization (WHO) has stated that whether or not to include the vaccine in routine childhood immunizations depends on the local context [11]. The proportion of susceptible people in the population and the level of exposure to the virus should be considered. Generally speaking, countries with intermediate endemicity will benefit the most from universal immunization of children. Countries with low endemicity may consider vaccinating high-risk adults. In countries with high endemicity, the use of vaccine is limited as most adults are naturally immune.

Individuals who do not need routine vaccination against hepatitis A include:

- Children under 12 months of age
- Childcare center personnel (in the absence of an outbreak)
- Health care workers (in the absence of an outbreak)
- Food service workers (in the absence of an outbreak)
- Individuals who receive blood products for clotting disorders (eg, hemophilia)

- Sewage workers
- Residents of institutions for developmentally disabled individuals

Food service workers have a critical role in common-source foodborne outbreaks, but they are not at increased risk for hepatitis A because of their occupation. Consideration may be given to HAV vaccination of food service workers in areas where community-wide outbreaks are occurring and regional health authorities or private employers determine that vaccination is cost-effective [12]. (See 'Protection following exposure' below.)

Routine HAV vaccination is not necessary for childcare center personnel or health care workers; vaccination of these individuals may be warranted in an outbreak setting. (See 'Protection following exposure' below.)

HAV vaccination of individuals who receive blood products for clotting disorders (eg, hemophilia) was previously recommended but is no longer recommended by the ACIP as of 2020 [2]. In the past, blood product sterilization procedures consisted of treatment with solvents and detergents, which inactivated lipid-enveloped viruses but not nonenveloped viruses such as HAV; additional sterilization procedures are now common. In addition, most individuals with clotting disorders in the United States receive sterilized recombinant clotting factor concentrates, eliminating risk for HAV contamination.

Clinical approach — The primary tool for protection against hepatitis A prior to exposure is vaccination, which is superior to immune globulin with respect to achievable antibody concentrations and durability of immune response [13,14]. For individuals at risk for hepatitis A exposure who are allergic to the hepatitis A vaccine or are <12 months of age, passive immunization via immune globulin may be given.

Role of prevaccine serology — There is no indication for serologic testing of children prior to vaccination. The decision to pursue prevaccination serologic testing of adults should be based on the expected prevalence of immunity, whether testing will interfere with initiation of vaccination, and the cost of vaccination compared with the cost of testing [15,16].

Individuals for whom prevaccination serologic testing is most cost effective include adults from areas with high or intermediate HAV endemicity (figure 2), older adolescents, adults in certain population groups (ie, Native Americans including Alaska natives, and Hispanic individuals), and adults in groups with high prevalence of infection (such as injection drug users). Prevaccination serologic testing of adults >40 may be cost effective [16]; according to a large population-based survey conducted from 1988 to 1994, more than one-third of adults >40 in the United States had anti-HAV antibodies [17].

Serologic testing following vaccination is not required in immunocompetent hosts given the high rate of vaccine response among adults and children [15]. In general, completion of the vaccination may be presumed to confer lifelong protection.

Vaccination

Available vaccines — Two single-antigen inactivated hepatitis A vaccines are licensed in the United States: HAVRIX and VAQTA [18,19]. A combination inactivated vaccine, TWINRIX, is also licensed in the United States; it contains both hepatitis A (HAVRIX) and hepatitis B (Engerix-B).

Combined hepatitis A virus and typhoid vaccine formulations (Viatim and Vivaxim) are available in some areas outside the United States.

Live attenuated hepatitis A vaccine is not available in the United States but is available in India (BioVac-A) and other countries (MEDVAC-A) including Guatemala, the Philippines, Bangladesh, Nepal, Uzbekistan, and Chile. Live attenuated hepatitis A vaccine is well-tolerated and highly immunogenic [20-24]. Live attenuated virus has been observed in the stools of individuals who received the vaccine (75 percent), although HAV transmission from vaccinees to unvaccinated seronegative individuals has not been observed.

Efficacy — Vaccination is superior to immune globulin with respect to achievable antibody concentrations and durability of immune response [13,14]. The seroconversion rate (defined as an antibody concentration of >20 milli-international units/mL measured by enzyme-linked immunosorbent assay) following primary vaccination series approximates 100 percent in healthy adults and children [25-30]. Since hepatitis A vaccine became available in the United States in 1995, the rate of HAV infection has declined by 95 percent (figure 2) [31,32].

The single-antigen inactivated hepatitis A vaccines, HAVRIX and VAQTA, have comparable immunogenicity; fewer side effects (most commonly local reactions) were observed with VAQTA [33]. The combination inactivated hepatitis A-hepatitis B vaccine, TWINRIX, is also well tolerated and highly immunogenic [34,35].

In healthy individuals, the persistence of antibody in adults is >95 percent more than 20 years after vaccination [36-38] and in children is >85 percent more than 15 to 20 years after vaccination [39,40].

In infants as young as age 2 months, hepatitis vaccine has been demonstrated to be safe and efficacious; however, vaccination of infants <12 months may be associated with potential interference with passively acquired maternal antibody [30,41,42]. For these reasons,

administration of a travel-related dose to infants age 6 to 11 months should not be counted toward the routine two-dose series [3].

In individuals with advanced liver disease, the serologic response to HAV vaccination may be diminished; if feasible, patients with liver disease should undergo vaccination before development of advanced disease. In one study comparing vaccination response among patients with decompensated disease to patients with compensated disease, seroconversion rates and serum antibody concentrations were lower among those with decompensated disease [43]; Child-Pugh class B or C was predictive of a lower response rate. (See "Immunizations for adults with chronic liver disease".)

In immunocompromised individuals, the serologic response to HAV vaccination may be diminished. In HIV-infected individuals, seroconversion rates range from 52 percent to 94 percent [44]. Individuals with lower CD4 cell counts (<300 cells/mm^3) have lower seroconversion rates than those with CD4 cell counts ≥300 cells/mm^3 (87 percent versus 100 percent) [45]. Among patients with rheumatoid arthritis on tumor necrosis factor inhibitors and/or methotrexate, a good response to the two-dose vaccination series was observed in one study (86 percent seroconversion), but one dose of vaccine was insufficient protection (33 percent seroconversion rate six months later) [46].

Dosing and administration

Clinical approach — Immunization with single-antigen inactivated hepatitis A vaccine (HAVRIX or VAQTA) consists of two doses for children and adults; dosing is summarized in the table (table 2). Immunization with the combination inactivated hepatitis A-hepatitis B vaccine, TWINRIX, consists of three doses for adults; it is not indicated for children. (See "Hepatitis B virus immunization in adults".)

For healthy individuals ≤40 years, the first dose of single-antigen hepatitis A vaccine should be given as soon as travel to areas with an intermediate or high rate of hepatitis A infection is considered and can be given at any time prior to departure.

For individuals >40 years, immunocompromised individuals, and persons with chronic liver disease or other chronic medical conditions with insufficient time to receive the full two-dose vaccination series before traveling, the first dose of vaccine should be administered together with a dose of immune globulin at a separate injection site. (See 'Passive immunization' below.)

There is no need for HAV booster vaccination after completion of the primary two-dose vaccination series.

If the immunization schedule is interrupted, the second dose can be given without restarting the series. It is good practice to use the same brand of vaccine to complete a course. If this is not possible, products for the second dose are interchangeable (eg, VAQTA can be used for the second dose following primary dose of HAVRIX and vice versa).

The most common adverse events are fever, injection-site reaction, rash, and headache. Serious adverse events (including Guillain-Barré syndrome, elevated liver biochemical tests, and immune thrombocytopenia) have been reported [22,47,48], although their relationship to vaccination is uncertain.

The inactivated HAV vaccine can be given concurrently with the vaccines for diphtheria, tetanus, pneumococcus, typhoid, cholera, Japanese encephalitis, rabies, or yellow fever without adversely affecting immunogenicity or safety [15,49,50]. Injections should be given at different sites. Studies in children ≤18 suggest that the HAV vaccine does not affect immunogenicity or reactogenicity to diphtheria-tetanus-acellular pertussis, *Haemophilus influenzae* type b, hepatitis B, measles-mumps-rubella, pneumococcus, oral poliovirus, or inactivated poliovirus vaccines [15,50-53].

Data on the safety of hepatitis A vaccination during pregnancy are limited; because the vaccine is produced from inactivated HAV, the theoretical risk to the developing fetus is low. The risk associated with vaccination should be weighed against the risk for hepatitis A exposure [12]. Hepatitis A vaccination is warranted for pregnant women who have a specific risk (such as international travel) (figure 3).

Limited role for single-dose strategy — In October 2022, the World Health Organization issued guidance indicating that, for children ≥12 months, inactivated hepatitis A vaccine may be administered as either a single-dose (off-label) or two-dose schedule [54]. This approach may be useful during hepatitis A outbreaks, emphasizing early intervention focused on a self-contained or well-defined population. This guidance is based in part on a 2012 systematic review including 13 studies and more than 800 children in which protective anti-HAV antibody levels persisted for up to 14 years following administration of single vaccine dose [55].

The WHO guidance continues to favor a two-dose schedule for adults ≥40 years, due to a lack of evidence for a single-dose strategy (with respect to immunogenicity or long-term protection) in this group.

Passive immunization — Immune globulin can decrease the incidence of HAV infection by more than 90 percent [56-59]. Pre-exposure protection against HAV via passive immunization with immune globulin is warranted for nonimmune individuals at risk for hepatitis A exposure in the following categories (table 1) [3,60]:

Groups warranting immune globulin in **addition** to HAV vaccination (administered at a separate anatomic site) include:

- Adult travelers >40 years, based on the provider's risk assessment.

  Travelers >40 years who may warrant immune globulin in addition to HAV vaccination include individuals at risk for relatively severe manifestations of hepatitis A infection, individuals with diminished ability to mount an adequate immune response to HAV vaccine, and individuals with increased risk for HAV transmission following exposure (eg, high endemicity of HAV in the area of travel).

- Individuals with chronic liver disease.

- Immunocompromised individuals incapable of mounting an adequate immune response to HAV vaccine.

Groups warranting immune globulin (in the absence of HAV vaccination) include:

- Infant travelers <6 months of age.

- Travelers for whom vaccine is contraindicated (eg, who are allergic to the hepatitis A vaccine).

The immune globulin product available in the United States is GamaSTAN. Dosing consists of 0.1 mL/kg intramuscularly (for anticipated risk of exposure up to one month) or 0.2 mL/kg intramuscularly (for anticipated risk of exposure up to two months); for anticipated risk of exposure greater than two months, a repeat dose of 0.2 mL/kg should be administered every two months for the duration of exposure risk [61,62].

This dosing regimen was increased from the prior dosing regimen in July 2017 due to concerns about decreased HAV immunoglobulin G antibody (anti-HAV IgG) potency, likely resulting from decreasing prevalence of previous HAV infection among plasma donors, leading to declining anti-HAV antibody levels in donor plasma [63].

Widespread use of immune globulin for hepatitis A prophylaxis is precluded by expense, injection site discomfort, need for repeat administration, and risk of bloodborne pathogen transmission (since the preparation is derived from pooled blood products). (See "Immunizations for travel".)

PROTECTION FOLLOWING EXPOSURE

Indications — Individuals who warrant postexposure protection (ie, hepatitis A vaccine and/or immune globulin) after exposure to HAV include (table 1) [12]:

- Close personal contacts of an individual with laboratory-confirmed HAV infection:
  - Household and sexual contacts
  - Individuals who have shared illicit drugs
- Childcare center contacts, in the setting of ≥1 case of hepatitis A among children or staff or ≥2 household cases of center attendees:
  - For centers providing care to children in diapers – Postexposure protection is warranted for all previously unvaccinated staff and attendees. In the setting of an outbreak (cases in ≥3 families), postexposure protection is also appropriate for household members of diaper-wearing children.
  - For centers providing care to children who no longer wear diapers – Postexposure protection is warranted for classroom contacts of the index patient (but not for children or staff in other classrooms).
- Food handlers:
  - In establishments with a food handler diagnosed with hepatitis A, postexposure protection is warranted for other food handlers at the same establishment. Administration of postexposure protection to patrons is typically not indicated; it is appropriate if the food handler had diarrhea or poor hygienic practices and directly handled uncooked foods or foods following cooking, and patrons can be identified and prophylaxed within two weeks of exposure.
  - Postexposure prophylaxis is reasonable in settings in which repeated exposures to hepatitis A might have occurred, such as institutional cafeterias.

Postexposure prophylaxis is not warranted in association with a single case of hepatitis A in a school, office, or hospital if the source of infection is outside the school or work setting. Rather, careful hygienic practices should be emphasized (see 'Hygienic practices' below). However, if it is determined that hepatitis A has spread among students in a school or among patients and health care workers in a hospital, postexposure protection is warranted for unvaccinated individuals who have had close contact with an infected person.

Clinical approach — The approach to HAV postexposure prophylaxis is as follows:

- For individuals with recent HAV exposure who have not previously received HAV vaccine, postexposure prophylaxis should be administered with either a single dose of single-antigen HAV vaccine or immune globulin as soon as possible, within two weeks of exposure (table 1) [3,5]:

  - For healthy individuals aged ≥12 months, HAV vaccine should be administered. Vaccination is preferred over immune globulin since it induces active immunity and greater durability of protection, is easier to administer, and is more readily available than immune globulin.

  - For individuals >40 years, HAV vaccine should be administered; in addition, immune globulin may be administered (depending on individual risk assessment), because of limited data regarding vaccine performance in this age group and because of the more severe manifestations of hepatitis A in older adults [64].

  - For individuals ≥12 months who are immunocompromised or have chronic liver disease, both HAV vaccine and immune globulin should be administered in different anatomic sites.

  - For children <12 months and for individuals for whom HAV vaccine is contraindicated (eg, who are allergic to the vaccine), immune globulin should be administered.

- For individuals with HIV infection and recent high-risk HAV exposure, administration of postexposure prophylaxis may be warranted regardless of prior vaccination history or immune status [65].

The immune globulin product available in the United States is GamaSTAN. Dosing for postexposure prophylaxis consists of 0.1 mL/kg intramuscularly. This dosing regimen was increased from the prior dosing in September 2017 due to decreasing prevalence of previous HAV infection among plasma donors in the United States [61,63].

For long-term immunity, the HAV vaccination should be completed with a second dose at least six months after the first dose; however, the second dose is not necessary for postexposure prophylaxis.

The above approach is based on a study including 1090 healthy individuals (ages 2 to 40) who were contacts of HAV cases and susceptible to HAV infection [66]. Subjects were randomly assigned to HAV vaccine or immune globulin within 14 days after exposure. The primary outcome (laboratory-confirmed symptomatic HAV) occurred in a similar proportion of patients

in the vaccine and immune globulin groups (4.4 versus 3.3 percent), suggesting that the interventions provide comparable protection.

The combination hepatitis A-hepatitis B vaccine, TWINRIX, should not be used for postexposure prophylaxis.

HYGIENIC PRACTICES

Hygienic practices for prevention of HAV infection include [67,68]:

- Handwashing (including after using the bathroom, changing diapers, and before preparing or eating foods).
- Avoiding tap water and raw foods in areas with poor sanitation.
- Heating foods appropriately (the virus can be inactivated by heating to >185°F [>85°C] for one minute). Cooked foods can transmit HAV if the temperature during food preparation is inadequate to kill the virus or if food is contaminated after cooking.
- Chlorine, iodine, and disinfecting solutions (household bleach 1:100 dilution) are effective for inactivation of HAV.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Immunizations in children and adolescents" and "Society guideline links: Travel medicine".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Hepatitis A (The Basics)")
- Beyond the Basics topic (see "Patient education: Hepatitis A (Beyond the Basics)")

SUMMARY

- **Treatment** – Hepatitis A (HAV) infection is usually self-limited, and treatment consists of supportive care. Medications that might cause liver damage or are metabolized by the liver should be used with caution. Full clinical and biochemical recovery are observed within two to three months in most patients, and complete recovery is observed by six months in nearly all patients. HAV infection confers lifelong immunity. (See 'Treatment' above.)
- **Protection prior to exposure** – Prior to hepatitis A exposure, the primary tool for protection is vaccination, which is superior to immune globulin with respect to achievable antibody concentrations and durability of immune response. Individuals who warrant protection prior to potential hepatitis A exposure include (table 1) (see 'Indications' above):
  - **Children:**
    - All children aged 12 to 23 months.
    - All children and adolescents aged 2 to 18 years who have not previously received hepatitis A vaccine (ie, children and adolescents are recommended for catch-up vaccination).
    - For infants age 6 to 11 months who are traveling internationally, vaccination should be administered; the travel-related dose should not be counted toward the routine two-dose series [3].
  - **Individuals at increased risk for HAV infection:**
    - Individuals traveling to or working in countries with high or intermediate rates of HAV; some experts advise that travelers outside the United States consider hepatitis A vaccination regardless of their destination [10].
    - Men who have sex with men.

- Individuals who use injection or noninjection illegal drugs.
- Individuals with occupational risk for exposure, including individuals working with HAV-infected primates or with HAV in a research laboratory.
- Individuals who anticipate close personal contact with an international adoptee.
- Individuals experiencing homelessness.
- Unvaccinated individuals in outbreak settings who are at risk for HAV infection or at risk for severe disease from HAV.
- Individuals in settings that provide services in which a high proportion of adults are at increased risk for HAV infection (eg, settings with a focus on those who use injection or noninjection illegal drugs, group homes, and nonresidential day care facilities for developmentally disabled persons).

- **Individuals at increased risk for severe disease from HAV infection:**
  - Individuals with chronic liver disease, including but not limited to individuals with hepatitis B virus infection, hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, or an alanine aminotransferase or aspartate aminotransferase level persistently greater than twice the upper limit of normal.
  - Individuals ≥1 year with HIV infection.
- **Other individuals recommended for vaccination:**
  - Pregnant women at risk for HAV infection or severe disease from HAV infection based on risk categories summarized above.
  - Any person who requests vaccination.

- **Vaccine dosing and administration**
  - Immunization with single-antigen inactivated hepatitis A vaccine (HAVRIX or VAQTA) consists of two doses for children and adults; dosing is summarized in the table (table 2). Immunization with the combination inactivated hepatitis A-hepatitis B vaccine, TWINRIX, consists of three doses for adults; it is not indicated for children. (See 'Dosing and administration' above and "Hepatitis B virus immunization in adults".)

- For healthy individuals ≤40 years, the first dose of single-antigen hepatitis A vaccine should be given as soon as travel to areas with risk of hepatitis A infection is considered and can be given at any time prior to departure. (See 'Dosing and administration' above.)

- For individuals >40 years, immunocompromised individuals, and persons with chronic liver disease or other chronic medical conditions with insufficient time to receive the full two-dose vaccination series before traveling, the first dose of vaccine should be administered together with a dose of immune globulin at a separate injection site. (See 'Dosing and administration' above.)

- Other groups who warrant pre-exposure protection against HAV via passive immunization with immune globulin include individuals who are allergic to the hepatitis A vaccine and children <12 months of age. (See 'Passive immunization' above.)

- **Protection following exposure**

  - **Indications** – Individuals who may warrant postexposure protection after exposure to HAV include (see 'Indications' above):

    - Close personal contacts of an individual with laboratory-confirmed HAV infection

    - Child care center contacts, in the setting of ≥1 case of hepatitis A among children or staff or ≥2 household cases of center attendees

    - Food handlers

    Postexposure prophylaxis is not warranted in association with a single case of hepatitis A in a school, office, or hospital. Rather, careful hygienic practices should be emphasized.

  - **Clinical approach** – Tools for protection against HAV following exposure include vaccination and immune globulin; the approach depends on individual patient circumstances. (See 'Clinical approach' above.)

- **Hygienic practices** – Hygienic practices for prevention of HAV infection include handwashing, avoiding tap water and raw foods in areas with poor sanitation, and heating foods appropriately (the virus can be inactivated by heating to >185°F [>85°C] for one minute). Cooked foods can transmit HAV if the temperature during food preparation is inadequate to kill the virus or if food is contaminated after cooking. (See 'Hygienic practices' above.)

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REFERENCES

1. Koff RS. Clinical manifestations and diagnosis of hepatitis A virus infection. Vaccine 1992; 10 Suppl 1:S15.
2. Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR Recomm Rep 2020; 69:1.
3. Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Postexposure Prophylaxis and for Preexposure Prophylaxis for International Travel. MMWR Morb Mortal Wkly Rep 2018; 67:1216.
4. Foster M, Ramachandran S, Myatt K, et al. Hepatitis A Virus Outbreaks Associated with Drug Use and Homelessness - California, Kentucky, Michigan, and Utah, 2017. MMWR Morb Mortal Wkly Rep 2018; 67:1208.
5. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Update: Prevention of hepatitis A after exposure to hepatitis A virus and in international travelers. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2007; 56:1080.
6. Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices. Updated recommendations from the Advisory Committee on Immunization Practices (ACIP) for use of hepatitis A vaccine in close contacts of newly arriving international adoptees. MMWR Morb Mortal Wkly Rep 2009; 58:1006.
7. American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for administering hepatitis A vaccine to contacts of international adoptees. Pediatrics 2011; 128:803.
8. Doshani M, Weng M, Moore KL, et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Persons Experiencing Homelessness. MMWR Morb Mortal Wkly Rep 2019; 68:153.

9. Freedman M, Kroger A, Hunter P, et al. Recommended Adult Immunization Schedule, United States, 2020. Ann Intern Med 2020; 172:337.
10. Centers for Disease Control and Prevention. Health Information for International Travel 2020: The Yellow Book. https://wwwnc.cdc.gov/travel/page/yellowbook-home (Accessed on October 29, 2020).
11. World Health Organization. Hepatitis A. http://www.who.int/mediacentre/factsheets/fs328/en/ (Accessed on February 17, 2017).
12. Centers for Disease Control and Prevention. Hepatitis A Questions and Answers for Health Professionals. http://www.cdc.gov/hepatitis/hav/havfaq.htm#vaccine (Accessed on October 05, 2016).
13. Leentvaar-Kuijpers A, Coutinho RA, Brulein V, Safary A. Simultaneous passive and active immunization against hepatitis A. Vaccine 1992; 10 Suppl 1:S138.
14. Shouval D, Ashur Y, Adler R, et al. Safety, tolerability, and immunogenicity of an inactivated hepatitis A vaccine: effects of single and booster injections, and comparison to administration of immune globulin. J Hepatol 1993; 18 Suppl 2:S32.
15. Advisory Committee on Immunization Practices (ACIP), Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2006; 55:1.
16. Bryan JP, Nelson M. Testing for antibody to hepatitis A to decrease the cost of hepatitis A prophylaxis with immune globulin or hepatitis A vaccines. Arch Intern Med 1994; 154:663.
17. Bell BP, Kruszon-Moran D, Shapiro CN, et al. Hepatitis A virus infection in the United States: serologic results from the Third National Health and Nutrition Examination Survey. Vaccine 2005; 23:5798.
18. Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1999; 48:1.
19. Armstrong ME, Giesa PA, Davide JP, et al. Development of the formalin-inactivated hepatitis A vaccine, VAQTA from the live attenuated virus strain CR326F. J Hepatol 1993; 18 Suppl 2:S20.
20. Mao JS, Xie RY, Huang HY, et al. Studies in monkeys of attenuated hepatitis A variants. Sci Sin B 1988; 31:338.
21. Mao JS, Dong DX, Zhang HY, et al. Primary study of attenuated live hepatitis A vaccine (H2 strain) in humans. J Infect Dis 1989; 159:621.
22. Midthun K, Ellerbeck E, Gershman K, et al. Safety and immunogenicity of a live attenuated hepatitis A virus vaccine in seronegative volunteers. J Infect Dis 1991; 163:735.

23. Mao JS. Development of live, attenuated hepatitis A vaccine (H2-strain). Vaccine 1990; 8:523.
24. Wang XY, Xu ZY, Ma JC, et al. Long-term immunogenicity after single and booster dose of a live attenuated hepatitis A vaccine: results from 8-year follow-up. Vaccine 2007; 25:446.
25. Provost PJ, Hilleman MR. An inactivated hepatitis A virus vaccine prepared from infected marmoset liver. Proc Soc Exp Biol Med 1978; 159:201.
26. André FE, D'Hondt E, Delem A, Safary A. Clinical assessment of the safety and efficacy of an inactivated hepatitis A vaccine: rationale and summary of findings. Vaccine 1992; 10 Suppl 1:S160.
27. Just M, Berger R. Reactogenicity and immunogenicity of inactivated hepatitis A vaccines. Vaccine 1992; 10 Suppl 1:S110.
28. McMahon BJ, Williams J, Bulkow L, et al. Immunogenicity of an inactivated hepatitis A vaccine in Alaska Native children and Native and non-Native adults. J Infect Dis 1995; 171:676.
29. Balcarek KB, Bagley MR, Pass RF, et al. Safety and immunogenicity of an inactivated hepatitis A vaccine in preschool children. J Infect Dis 1995; 171 Suppl 1:S70.
30. Bell BP, Negus S, Fiore AE, et al. Immunogenicity of an inactivated hepatitis A vaccine in infants and young children. Pediatr Infect Dis J 2007; 26:116.
31. Ly KN, Klevens RM. Trends in disease and complications of hepatitis A virus infection in the United States, 1999-2011: a new concern for adults. J Infect Dis 2015; 212:176.
32. Wasley A, Samandari T, Bell BP. Incidence of hepatitis A in the United States in the era of vaccination. JAMA 2005; 294:194.
33. Braconier JH, Wennerholm S, Norrby SR. Comparative immunogenicity and tolerance of Vaqta and Havrix. Vaccine 1999; 17:2181.
34. Ambrosch F, Wiedermann G, André FE, et al. Clinical and immunological investigation of a new combined hepatitis A and hepatitis B vaccine. J Med Virol 1994; 44:452.
35. Van Damme P, Thoelen S, Cramm M, et al. Reactogenicity and immunogenicity of a combin ed hepatitis A and hepatitis B vaccine in healthy adults. In: Viral Hepatitis and Liver Disease, Nishioka K, Suzuki H, Mishiro S, Oda T (Eds), Springer, Tokyo, Japan 1994. p.514.
36. Bovier PA, Bock J, Ebengo TF, et al. Predicted 30-year protection after vaccination with an aluminum-free virosomal hepatitis A vaccine. J Med Virol 2010; 82:1629.
37. Hens N, Habteab Ghebretinsae A, Hardt K, et al. Model based estimates of long-term persistence of inactivated hepatitis A vaccine-induced antibodies in adults. Vaccine 2014; 32:1507.

38. Theeten H, Van Herck K, Van Der Meeren O, et al. Long-term antibody persistence after vaccination with a 2-dose Havrix (inactivated hepatitis A vaccine): 20 years of observed data, and long-term model-based predictions. Vaccine 2015; 33:5723.

39. López EL, Contrini MM, Mistchenko A, et al. Modeling the long-term persistence of hepatitis A antibody after a two-dose vaccination schedule in Argentinean children. Pediatr Infect Dis J 2015; 34:417.

40. Raczniak GA, Bulkow LR, Bruce MG, et al. Long-term immunogenicity of hepatitis A virus vaccine in Alaska 17 years after initial childhood series. J Infect Dis 2013; 207:493.

41. Dagan R, Amir J, Mijalovsky A, et al. Immunization against hepatitis A in the first year of life: priming despite the presence of maternal antibody. Pediatr Infect Dis J 2000; 19:1045.

42. Letson GW, Shapiro CN, Kuehn D, et al. Effect of maternal antibody on immunogenicity of hepatitis A vaccine in infants. J Pediatr 2004; 144:327.

43. Arguedas MR, Johnson A, Eloubeidi MA, Fallon MB. Immunogenicity of hepatitis A vaccination in decompensated cirrhotic patients. Hepatology 2001; 34:28.

44. Overton ET, Nurutdinova D, Sungkanuparph S, et al. Predictors of immunity after hepatitis A vaccination in HIV-infected persons. J Viral Hepat 2007; 14:189.

45. Wallace MR, Brandt CJ, Earhart KC, et al. Safety and immunogenicity of an inactivated hepatitis A vaccine among HIV-infected subjects. Clin Infect Dis 2004; 39:1207.

46. Askling HH, Rombo L, van Vollenhoven R, et al. Hepatitis A vaccine for immunosuppressed patients with rheumatoid arthritis: a prospective, open-label, multi-centre study. Travel Med Infect Dis 2014; 12:134.

47. Werzberger A, Mensch B, Kuter B, et al. A controlled trial of a formalin-inactivated hepatitis A vaccine in healthy children. N Engl J Med 1992; 327:453.

48. HAVRIX IM injection, hepatitis A vaccine IM injection. GlaxoSmithKline, Research Triangle Pa rk, NC 2011.

49. Kruppenbacher J, Biensie U, Bock HL, Clemens R. Coadministration of an inactivated hepatit is A vaccine with other travelers vaccines: Interference with the immune response. Proc 34t h Intersci Conf on Antimicrobial Agents and Chemotherapy, American Society of Microbiolo gists, Washington, 1994; 256.

50. Trofa AF, Levin M, Marchant CD, et al. Immunogenicity and safety of an inactivated hepatitis a vaccine administered concomitantly with a pneumococcal conjugate vaccine in healthy children 15 months of age. Pediatr Infect Dis J 2008; 27:658.

51. Nolan T, Bernstein H, Blatter MM, et al. Immunogenicity and safety of an inactivated hepatitis A vaccine administered concomitantly with diphtheria-tetanus-acellular pertussis

and haemophilus influenzae type B vaccines to children less than 2 years of age. Pediatrics 2006; 118:e602.

52. Guerra FA, Gress J, Werzberger A, et al. Safety, tolerability and immunogenicity of VAQTA given concomitantly versus nonconcomitantly with other pediatric vaccines in healthy 12-month-old children. Pediatr Infect Dis J 2006; 25:912.
53. Dagan R, Amir J, Livni G, et al. Concomitant administration of a virosome-adjuvanted hepatitis a vaccine with routine childhood vaccines at age twelve to fifteen months: a randomized controlled trial. Pediatr Infect Dis J 2007; 26:787.
54. World Health Organization. Weekly Epidemiological Record, 2022, vol. 97 (40), 493 - 512. https://apps.who.int/iris/handle/10665/363396 (Accessed on November 29, 2022).
55. Ott JJ, Irving G, Wiersma ST. Long-term protective effects of hepatitis A vaccines. A systematic review. Vaccine 2012; 31:3.
56. Stokes J, Neefe JR. The prevention and attenuation of infectious hepatitis by gamma globulin: Preliminary note. JAMA 1945; 127:144.
57. Winokur PL, Stapleton JT. Immunoglobulin prophylaxis for hepatitis A. Clin Infect Dis 1992; 14:580.
58. Conrad ME, Lemon SM. Prevention of endemic icteric viral hepatitis by administration of immune serum gamma globulin. J Infect Dis 1987; 156:56.
59. Stapleton JT. Passive immunization against hepatitis A. Vaccine 1992; 10 Suppl 1:S45.
60. Centers for Disease Control and Prevention. Hepatitis A Questions and Answers for Health Professionals. https://www.cdc.gov/hepatitis/hav/havfaq.htm#D1 (Accessed on September 08, 2017).
61. US Food and Drug Administration. New Recommendations to Increase the Dose of GamaSTAN S/D (Immune Globulin [Human]) When Used for Prophylaxis for Hepatitis A. https://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm574795.htm (Accessed on September 07, 2017).
62. Nelson NP. Updated Dosing Instructions for Immune Globulin (Human) GamaSTAN S/D for Hepatitis A Virus Prophylaxis. MMWR Morb Mortal Wkly Rep 2017; 66:959.
63. Tejada-Strop A, Costafreda MI, Dimitrova Z, et al. Evaluation of Potencies of Immune Globulin Products Against Hepatitis A. JAMA Intern Med 2017; 177:430.
64. Link-Gelles R, Hofmeister MG, Nelson NP. Use of hepatitis A vaccine for post-exposure prophylaxis in individuals over 40 years of age: A systematic review of published studies and recommendations for vaccine use. Vaccine 2018; 36:2745.

65. Brennan J, Moore K, Sizemore L, et al. Notes from the Field: Acute Hepatitis A Virus Infection Among Previously Vaccinated Persons with HIV Infection - Tennessee, 2018. MMWR Morb Mortal Wkly Rep 2019; 68:328.

66. Victor JC, Monto AS, Surdina TY, et al. Hepatitis A vaccine versus immune globulin for postexposure prophylaxis. N Engl J Med 2007; 357:1685.

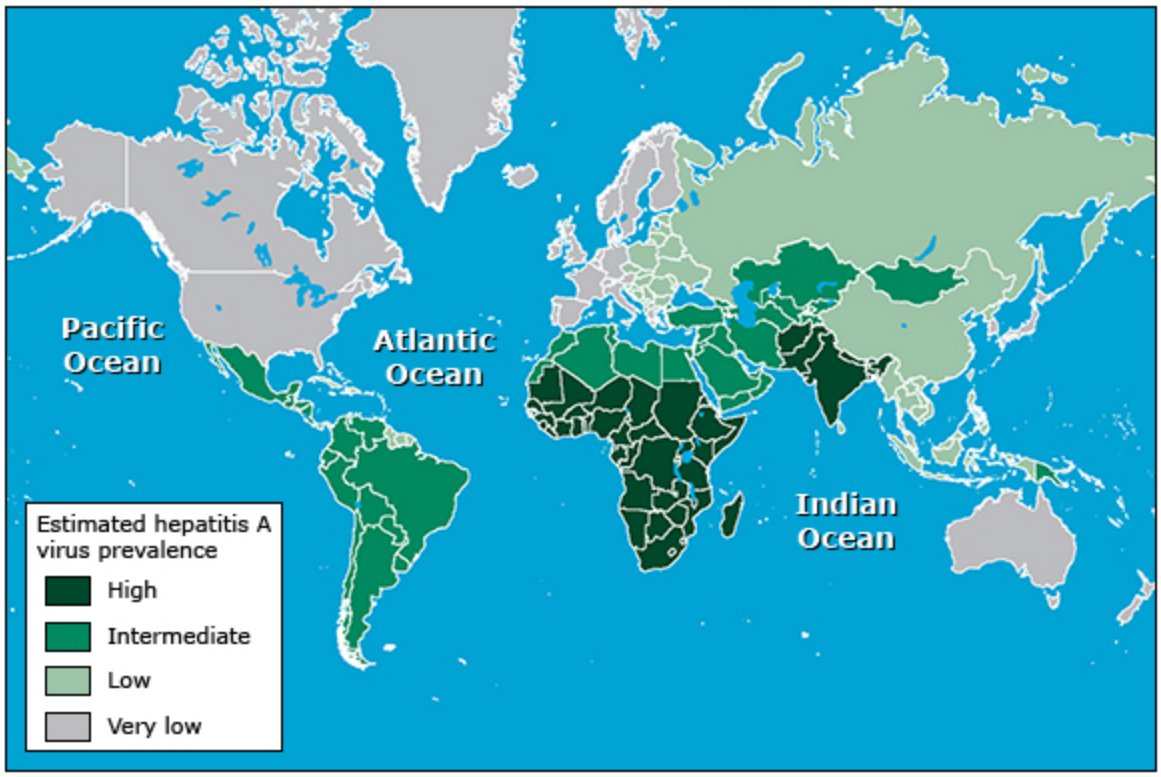
67. Centers for Disease Control and Prevention. Hepatitis A Questions and Answers for Health Professionals. http://www.cdc.gov/hepatitis/hav/havfaq.htm#general (Accessed on July 13, 2016).

68. Mbithi JN, Springthorpe VS, Boulet JR, Sattar SA. Survival of hepatitis A virus on human hands and its transfer on contact with animate and inanimate surfaces. J Clin Microbiol 1992; 30:757.

Topic 3900 Version 42.0

GRAPHICS

Prevalence of antibodies against hepatitis A



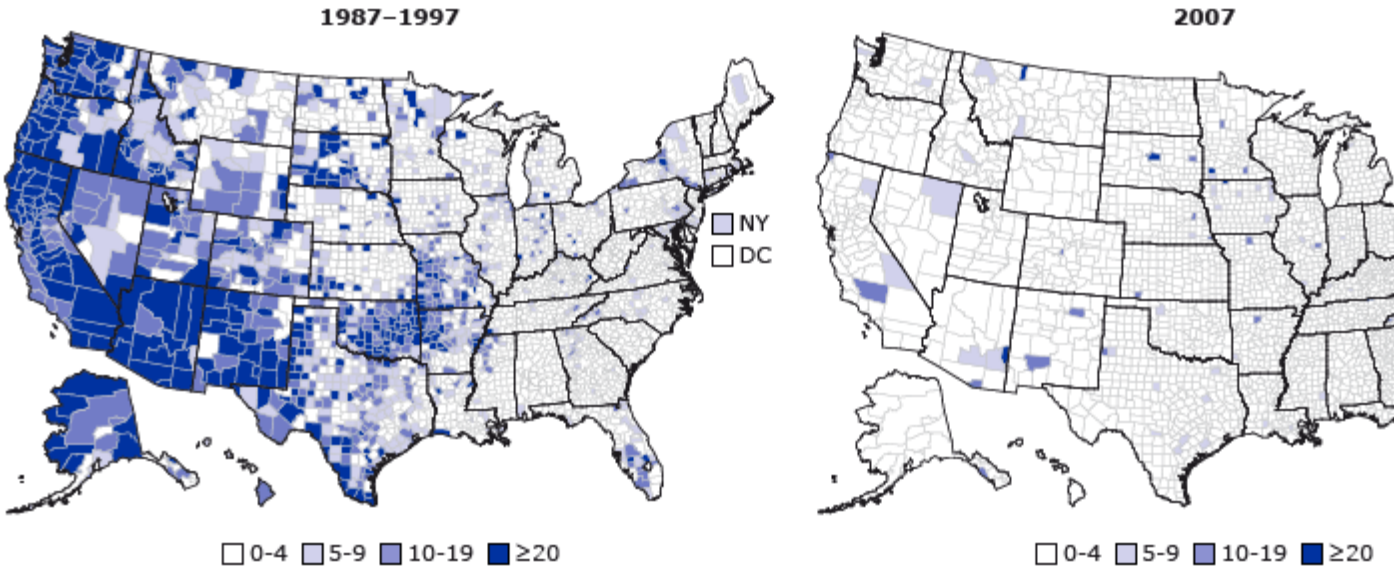
Estimates of prevalence of antibody to hepatitis A virus (anti-HAV IgG), a marker of previous HAV infection, are based on a systematic literature review conducted for the period of 1990 to 2005. In addition, anti-HAV prevalence might vary within countries by subpopulation and locality. As used on this map, the terms "high," "medium," "low," and "very low" endemicity reflect available evidence of how widespread HAV infection is within each country, rather than precise quantitative assessments.

HAV: hepatitis A virus; IgG: immunoglobulin G.

Original figure from: Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. Vaccine 2010; 28:6653. Reproduced with the permission of Elsevier Inc. All rights reserved. Original figure modified and reproduced from: Centers for Disease Control and Prevention. Yellow Book 2012.

Graphic 69392 Version 6.0

Incidence* of reported acute hepatitis A cases, by county — National Notifiable Surveillance System, United States, 1987 to 1997¶ (prevaccine) and 2007



* Rate per 100,000 population.

¶ Annual average incidence.

Reproduced from: Murphy TV, Denniston MM, Hill HA, et al. Progress Toward Eliminating Hepatitis A Disease in the United States. MMW 65:29.

Graphic 60763 Version 8.0

Recommendations for hepatitis A postexposure prophylaxis and pre-exposure protection, by age group and risk category

Indication and age group	Risk category and health status	HepA vaccine	IG*
Postexposure prophylaxis			
<12 months	Healthy	No	0.1 mL/kg
12 months to 40 years	Healthy	1 dose¶	None
>40 years	Healthy	1 dose¶	0.1 mL/kgΔ
≥12 months	Immunocompromised or chronic liver disease	1 dose¶	0.1 mL/kg◇
≥12 months	Vaccine contraindicated§	No	0.1 mL/kg
Preexposure protection (eg, travel)¥			
<6 months	Healthy	No	0.1 to 0.2 mL/kg‡
6 to 11 months	Healthy	1 dose†	None
12 months to 40 years	Healthy	1 dose**	None
>40 years	Healthy	1 dose**	0.1 to 0.2 mL/kg‡, ¶¶
>6 months	Immunocompromised or chronic liver disease	1 dose**	0.1 to 0.2 mL/kg‡, ¶¶
>6 months	Persons who elect not to receive vaccine or for whom vaccine is contraindicated§	No	0.1 to 0.2 mL/kg‡

HepA: hepatitis A; IG: immune globulin; HAV: hepatitis A virus.

* Measles, mumps, and rubella vaccine should not be administered for at least 2 weeks before and 6 months after administration of IG.

¶ A second dose of HepA vaccine is not required for postexposure prophylaxis; however, for long-term immunity, the vaccination series should be completed with a second dose at least 6 months after the first dose.

Δ The provider's risk assessment should determine the need for IG administration. If the provider's risk assessment determines that both vaccine and IG are warranted, HepA vaccine and IG should be administered simultaneously in a different anatomic site (eg, separate limbs).

◇ Vaccine and IG should be administered simultaneously in a different anatomic site (eg, separate limbs).

§ Life-threatening allergic reaction to a previous dose of HepA vaccine or allergy to any vaccine component.

¥ IG should be considered before travel for persons with special risk factors for either HAV infection or severe disease from HAV infection.

‡ 0.1 mL/kg for travel up to 1 month; 0.2 mL/kg for travel up to 2 months, 0.2mL/kg every 2 months for travel of ≥2 months' duration.

† This dose should not be counted toward the routine 2-dose series, which should be initiated at age 12 months.

** For persons not previously vaccinated with HepA vaccine, administer dose as soon as travel is considered, and complete series according to routine schedule if the next dose is needed before travel.

¶¶ May be administered based on provider's risk assessment.

Reproduced from: Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR Recomm Rep 2020; 69:1.

Graphic 119479 Version 4.0

Hepatitis A vaccination: Dosing and schedule

Vaccine	Trade name	Age group (years)	Dosage	Route	Schedule	Booster
Hepatitis A vaccine, inactivated	Havrix	1 to 18	0.5 mL (720 ELU)	IM	0, 6 to 12 months	None
		≥19	1 mL (1440 ELU)	IM	0, 6 to 12 months	None
Hepatitis A vaccine, inactivated	Vaqta	1 to 18	0.5 mL (25 U)	IM	0, 6 to 18 months	None
		≥19	1 mL (50 U)	IM	0, 6 to 18 months	None
Combined hepatitis A and B vaccine*	Twinrix	≥18 (primary)	1 mL (720 ELU HAV + 20 mcg HBsAg)	IM	0, 1, 6 months	None
		≥18 (accelerated)	1 mL (720 ELU HAV + 20 mcg HBsAg)	IM	0, 7, 21 to 30 days	12 months

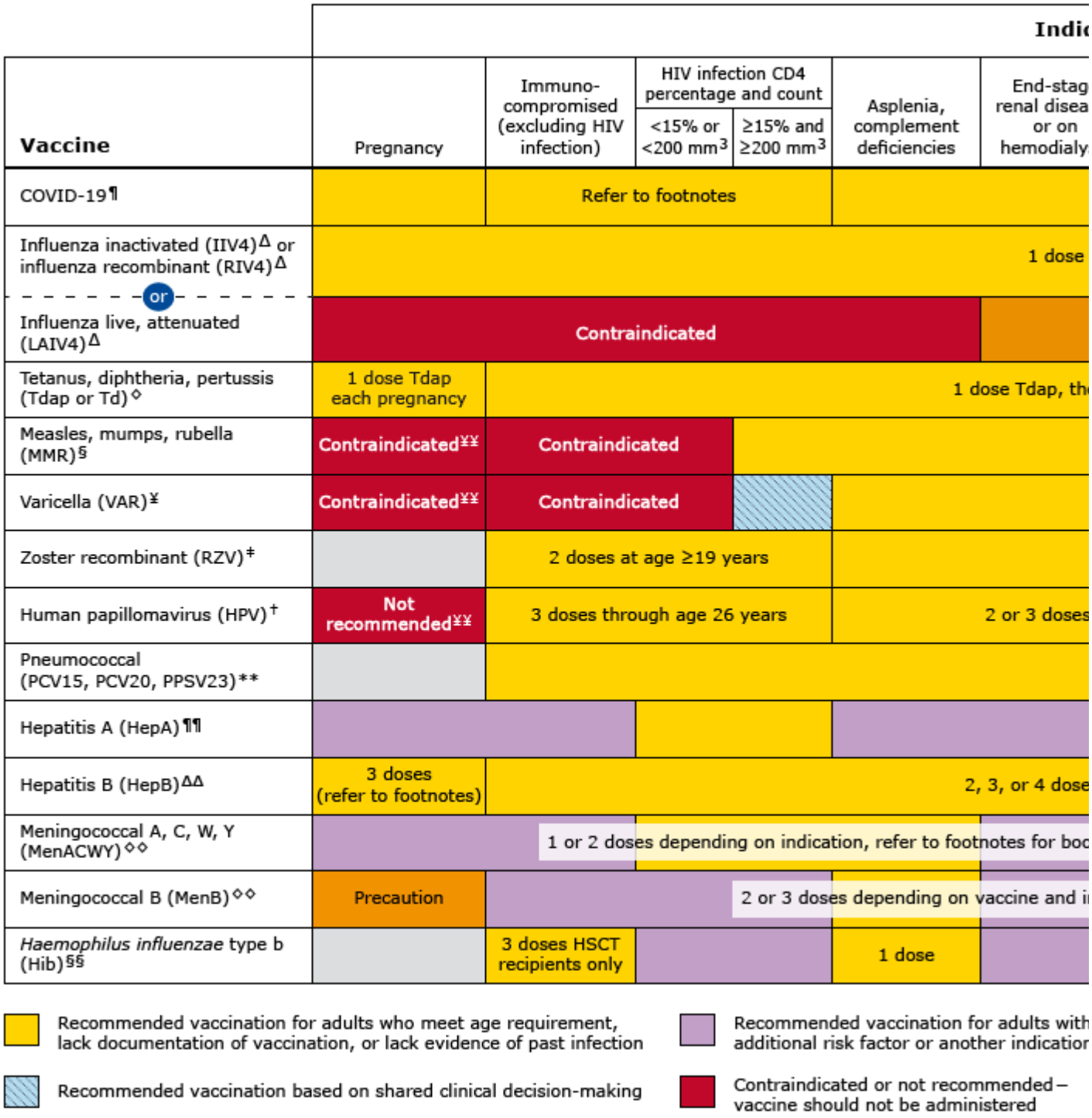
HAV: hepatitis A virus; ELU: enzyme-linked immunosorbent assay units of inactivated HAV; IM: intramuscular; U: units of HAV antigen; HBsAg: hepatitis B surface antigen.

* Combined hepatitis A and B vaccine (Twinrix) should not be used for postexposure prophylaxis.

Reproduced from: Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for use of hepatitis A vaccine for postexposure prophylaxis and for preexposure prophylaxis for international travel. MMWR Morb Mortal Wkly Rep 2018; 67:1216.

Graphic 110077 Version 6.0

Recommended adult immunization schedule by medical condition and other in



Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add dc use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.

Polio vaccination

- **Routine vaccination:**
  - Routine poliovirus vaccination of adults residing in the United States is not necessary.
- **Special situations:**

- **Adults at increased risk of exposure to poliovirus with:**
  - **No evidence of a complete polio vaccination series (ie, at least 3 doses):** Administer remain
  - **Evidence of completed polio vaccination series (ie, at least 3 doses):** May administer one life
- For detailed information, refer to www.cdc.gov/vaccines/vpd/polio/hcp/recommendations.html.

HSCT: hematopoietic stem cell transplant.

* Precaution for LAIV4 does not apply to alcoholism.

¶ COVID-19 vaccination

- **Routine vaccination:**
  - **Primary series:** 2-dose series at 0, 4 to 8 weeks (Moderna) or 2-dose series at 0, 3 to 8 weeks (Nov
  - **Booster dose:** Refer to www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerati
- **Special situations:**
  - **Persons who are moderately or severely immunocompromised**.
    - **Primary series:**
      - 3-dose series at 0, 4, 8 weeks (Moderna) or 3-dose series at 0, 3, 7 weeks (Pfizer-BioNTech).
      - 2-dose series at 0, 3 weeks (Novavax).
    - **Booster dose:** Refer to www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-conside
    - **Pre-exposure prophylaxis (eg, monoclonal antibodies)** may be considered to complement C considerations/interim-considerations-us.html#immunocompromised.
  - **For Janssen COVID-19 Vaccine recipients** refer to COVID-19 schedule at www.cdc.gov/vaccines/c
  - **NOTE:** Current COVID-19 schedule available at www.cdc.gov/vaccines/covid-19/downloads/COVID- information on Emergency Use Authorization (EUA) indications for COVID-19 vaccines, please visit disease-2019-covid-19/covid-19-vaccines.
- **Contraindications and precautions:**
  - Refer to contraindications and precautions to COVID-19 vaccination.

Δ Influenza vaccination

- **Routine vaccination:**
  - **Age 19 years or older:** 1 dose any influenza vaccine appropriate for age and health status annual
  - **Age 65 years or older:** Any one of quadrivalent high-dose inactivated influenza vaccine (HD-IIV4), adjuvanted inactivated influenza vaccine (aIIV4) is preferred. If none of these three vaccines is ava
  - For the 2022–2023 season, refer to www.cdc.gov/mmwr/volumes/71/rr/rr7101a1.htm.
  - For the 2023–2024 season, refer to the 2023–2024 ACIP influenza vaccine recommendations.
- **Special situations:**
  - **Egg allergy, hives only:** Any influenza vaccine appropriate for age and health status annually.
  - **Egg allergy–any symptom other than hives** (eg, angioedema, respiratory distress, or required e vaccine appropriate for age and health status may be administered. If using egg-based IIV4 or LA provider who can recognize and manage severe allergic reactions.
  - **Close contacts (eg, caregivers, health care workers) of severely immunosuppressed persons** receive LAIV4. If LAIV4 is given, they should avoid contact with/caring for such immunosuppressed
  - **Severe allergic reaction (eg, anaphylaxis) to a vaccine component or a previous dose of any i** precautions.
  - **History of Guillain-Barré syndrome within 6 weeks after previous dose of influenza vaccine:** risks for those at higher risk for severe complications from influenza.
- **Contraindications and precautions:**
  - For contraindications and precautions to influenza vaccination, refer to IIV4 Appendix, LAIV4 Appe

◇ **Tetanus, diphtheria, and pertussis (Tdap) vaccination**

- **Routine vaccination:**
  - **Previously did not receive Tdap at or after age 11 years:** 1 dose Tdap, then Td or Tdap every 10
- **Special situations:**
  - **Previously did not receive primary vaccination series for tetanus, diphtheria, or pertussis:** 1 dose of Td or Tdap 6 to 12 months later (Tdap can be substituted for any Td dose, but preferred as
  - **Pregnancy:** 1 dose Tdap during each pregnancy, preferably in early part of gestational weeks 27 t
  - **Wound management:** Persons with 3 or more doses of tetanus-toxoid-containing vaccine: For cle last dose of tetanus-toxoid-containing vaccine; for all other wounds, administer Tdap or Td if more preferred for persons who have not previously received Tdap or whose Tdap history is unknown. I use Tdap. For detailed information, refer to www.cdc.gov/mmwr/volumes/69/wr/mm6903a5.htm.
- **Contraindications and precautions:**
  - For contraindications and precautions to tetanus, diphtheria, and acellular pertussis (Tdap), refer t

§ **Measles, mumps, and rubella vaccination**

- **Routine vaccination:**
  - **No evidence of immunity to measles, mumps, or rubella:** 1 dose.
    - **Evidence of immunity:** Born before 1957 (health care personnel, refer below), documentation (diagnosis of disease without laboratory confirmation is not evidence of immunity).
- **Special situations:**
  - **Pregnancy with no evidence of immunity to rubella:** MMR contraindicated during pregnancy; a
  - **Nonpregnant women of childbearing age with no evidence of immunity to rubella:** 1 dose.
  - **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm^3 for at least 6 mon** dose series at least 4 weeks apart; MMR contraindicated for HIV infection with CD4 percentage <1
  - **Severe immunocompromising conditions:** MMR contraindicated.
  - **Students in postsecondary educational institutions, international travelers, and household evidence of immunity to measles, mumps, or rubella:** 2-dose series at least 4 weeks apart if pre 1 dose MMR.
  - **In mumps outbreak settings**, for information about additional doses of MMR (including 3rd dose
  - **Health care personnel:**
    - **Born before 1957 with no evidence of immunity to measles, mumps, or rubella:** Consider rubella.
    - **Born in 1957 or later with no evidence of immunity to measles, mumps, or rubella:** 2-dose rubella.
- **Contraindications and precautions:**
  - For contraindications and precautions to measles, mumps, rubella (MMR), refer to MMR Appendix

¥ **Varicella vaccination**

- **Routine vaccination:**
  - **No evidence of immunity to varicella:** 2-dose series 4 to 8 weeks apart if previously did not rece varicella vaccine] for children); if previously received 1 dose varicella-containing vaccine, 1 dose at
    - **Evidence of immunity:** US-born before 1980 (except for pregnant women and health care per vaccine at least 4 weeks apart, diagnosis or verification of history of varicella or herpes zoster
- **Special situations:**
  - **Pregnancy with no evidence of immunity to varicella:** VAR contraindicated during pregnancy; a previously received 1 dose varicella-containing vaccine or dose 1 of 2-dose series (dose 2: 4 to 8 w regardless of whether US-born before 1980.

- **Health care personnel with no evidence of immunity to varicella:** 1 dose if previously received previously did not receive any varicella-containing vaccine, regardless of whether US-born before
- **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm^3 with no evidence** VAR contraindicated for HIV infection with CD4 percentage <15% or CD4 count <200 cells/mm^3.
- **Severe immunocompromising conditions:** VAR contraindicated.

▪ **Contraindications and precautions:**

- For contraindications and precautions to varicella (VAR), refer to VAR Appendix.

‡ **Zoster vaccination**

▪ **Routine vaccination:**

- **Age 50 years or older** (NOTE: Serologic evidence of prior varicella is not necessary for zoster vacc available, providers should follow ACIP guidelines for varicella vaccination first. RZV is not indicate RZV in persons without a history of varicella or varicella vaccination)**:** 2-dose series recombinant zo weeks; repeat dose if administered too soon), regardless of previous herpes zoster or history of zo

▪ **Special situations:**

- **Pregnancy:** There is currently no ACIP recommendation for RZV use in pregnancy. Consider delay
- **Immunocompromising conditions** (including persons with HIV regardless of CD4 count; NOTE: I herpes zoster, providers should refer to the clinical considerations for use of RZV in immunocomp recommendations for further guidance: www.cdc.gov/mmwr/volumes/71/wr/mm7103a2.htm)**:** 2-d (minimum interval: 4 weeks; repeat dose if administered too soon). For detailed information, refer

▪ **Contraindications and precautions:**

- For contraindications and precautions to zoster recombinant vaccine (RZV), refer to RZV Appendix.

† **Human papillomavirus vaccination**

▪ **Routine vaccination:**

- **HPV vaccination recommended for all persons through age 26 years:** 2- or 3-dose series depe
  - **Age 15 years or older at initial vaccination:** 3-dose series at 0, 1 to 2 months, 6 months (min dose 1 to dose 3: 5 months; repeat dose if administered too soon).
  - **Age 9 to 14 years at initial vaccination and received 1 dose or 2 doses less than 5 months**
  - **Age 9 to 14 years at initial vaccination and received 2 doses at least 5 months apart:** HPV
- **Interrupted schedules:** If vaccination schedule is interrupted, the series does not need to be rest
- **No additional dose recommended when any HPV vaccine series has been completed using th**

▪ **Shared clinical decision-making:**

- **Some adults age 27 to 45 years:** Based on shared clinical decision-making, 2- or 3-dose series as

▪ **Special situations:**

- **Age ranges recommended above for routine and catch-up vaccination or shared clinical deci**
  - **Immunocompromising conditions, including HIV infection:** 3-dose series, even for those w
  - **Pregnancy:** Pregnancy testing is not needed before vaccination; HPV vaccination is not recom vaccinated while pregnant.

▪ **Contraindications and precautions:**

- For contraindications and precautions to human papillomavirus (HPV) vaccination, refer to HPV Ap

** **Pneumococcal vaccination**

▪ **Routine vaccination:**

- **Age 65 years or older who have:**
  - **Not previously received a dose of PCV13, PCV15, or PCV20 or whose previous vaccination** this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A min for adults with an immunocompromising condition (NOTE: Immunocompromising conditions

iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Ho transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable gr

- **Previously received only PCV7:** Follow the recommendation above.
- **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR comp www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.
- **Previously received only PPSV23:** 1 dose PCV15 OR 1 dose PCV20 at least 1 year after the PP PPSV23.
- **Previously received both PCV13 and PPSV23 but NO PPSV23 was received at age 65 years** vaccine dose OR complete the recommended PPSV23 series as described here: www.cdc.gov/
- **Previously received both PCV13 and PPSV23, AND PPSV23 was received at age 65 years o** least 5 years after the last pneumococcal vaccine dose.
- For guidance on determining which pneumococcal vaccines a patient needs and when, pleas www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html.

- **Special situations:**
  - **Age 19 to 64 years with certain underlying medical conditions or other risk factors who hav** alcoholism, chronic heart/liver/lung disease, chronic renal failure, cigarette smoking, cochlear im generalized malignancy, HIV, Hodgkin disease, immunodeficiency, iatrogenic immunosuppressio organ transplants, or sickle cell disease, or other hemoglobinopathies)**:**
    - **Not previously received a PCV13, PCV15, or PCV20 or whose previous vaccination history** should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimu adults with an immunocompromising condition(NOTE: Immunocompromising conditions incl iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Ho transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies
    - **Previously received only PCV7:** Follow the recommendation above.
    - **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR comp www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.
    - **Previously received only PPSV23:** 1 dose PCV15 OR 1 dose PCV20 at least 1 year after the PP PPSV23.
    - **Previously received both PCV13 and PPSV23 but have not completed the recommended** dose OR complete the recommended PPSV23 series as described here: www.cdc.gov/vaccines
  - For guidance on determining which pneumococcal vaccines a patient needs and when, please re www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html.
- **Contraindications and precautions:**
  - For contraindications and precautions to Pneumococcal conjugate (PCV15 and PCV20), refer to P PPSV23 Appendix.

¶¶ Hepatitis A vaccination

- **Routine vaccination:**
  - **Not at risk but want protection from hepatitis A (identification of risk factor not required):** apart [minimum interval: 6 months]) or 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [mini
- **Special situations:**
  - **At risk for hepatitis A virus infection:** 2-dose series HepA or 3-dose series HepA-HepB as above
    - **Chronic liver disease** (eg, persons with hepatitis B, hepatitis C, cirrhosis, fatty liver disease, a [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal).
    - **HIV infection**.
    - **Men who have sex with men**.

- **Injection or noninjection drug use**.
- **Persons experiencing homelessness**.
- **Work with hepatitis A virus** in research laboratory or with nonhuman primates with hepatit
- **Travel in countries with high or intermediate endemic hepatitis A** (HepA-HepB [Twinrix] r to 30 days, followed by a booster dose at 12 months).
- **Close, personal contact with international adoptee** (eg, household or regular babysitting) endemic hepatitis A (administer dose 1 as soon as adoption is planned, at least 2 weeks befor
- **Pregnancy** if at risk for infection or severe outcome from infection during pregnancy.
- **Settings for exposure**, including health care settings targeting services to injection or noninj for developmentally disabled persons (individual risk factor screening not required).

- **Contraindications and precautions:**
  - For contraindications and precautions to hepatitis A (HepA) vaccination, refer to HepA Appendix.

ΔΔ **Hepatitis B vaccination**

- **Routine vaccination:**
  - **Age 19 through 59 years:** Complete a 2- or 3-, or 4-dose series.
    - 2-dose series only applies when 2 doses of Heplisav-B (NOTE: Heplisav-B and PreHevbrio are persons) are used at least 4 weeks apart.
    - 3-dose series Engerix-B, PreHevbrio (NOTE: Heplisav-B and PreHevbrio are not recommended Recombivax HB at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 weeks / dose 2 to d
    - 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 w
    - 4-dose series HepA-HepB (Twinrix) accelerated schedule of 3 doses at 0, 7, and 21 to 30 days,
  - **Age 60 years or older with** known risk factors for hepatitis B virus infection **should** complete a H
  - **Age 60 years or older without** known risk factors for hepatitis B virus infection **may** complete a
    - **Risk factors for hepatitis B virus infection include:**
      - **Chronic liver disease** (eg, persons with hepatitis C, cirrhosis, fatty liver disease, alcoholic aspartate aminotransferase [AST] level greater than twice upper limit of normal).
      - **HIV infection**.
      - **Sexual exposure risk** (eg, sex partners of hepatitis B surface antigen [HBsAg]-positive pe persons seeking evaluation or treatment for a sexually transmitted infection; men who ha
      - **Current or recent injection drug use**.
      - **Percutaneous or mucosal risk for exposure to blood** (eg, household contacts of HBsAg disabled persons; health care and public safety personnel with reasonably anticipated risk maintenance dialysis, including in-center or home hemodialysis and peritoneal dialysis, a
      - **Incarceration**.
      - **Travel in countries with high or intermediate endemic hepatitis B**.
- **Special situations:**
  - **Patients on dialysis:** complete a 3- or 4-dose series.
    - 3-dose series Recombivax HB at 0, 1, 6 months (NOTE: use Dialysis Formulation 1 mL = 40 mc
    - 4-dose series Engerix-B at 0, 1, 2, and 6 months (NOTE: use 2 mL dose instead of the normal a
- **Contraindications and precautions:**
  - For contraindications and precautions to hepatitis B (HepB) vaccination, refer to HepB Appendix.

◇◇ **Meningococcal vaccination**

- **Special situations for MenACWY:**
  - **Anatomical or functional asplenia (including sickle cell disease), HIV infection, persistent c eculizumab, ravulizumab) use:** 2-dose series MenACWY-D (Menactra, Menveo, or MenQuadfi) a

- **Travel in countries with hyperendemic or epidemic meningococcal disease, or microbiologi** (Menactra, Menveo, or MenQuadfi) and revaccinate every 5 years if risk remains.
- **First-year college students who live in residential housing (if not previously vaccinated at a** Menveo, or MenQuadfi).
- For MenACWY **booster dose recommendations** for groups listed under "Special situations" and among men who have sex with men) and additional meningococcal vaccination information, refe

▪ **Shared clinical decision-making for MenB:**
- **Adolescents and young adults age 16 to 23 years (age 16 to 18 years preferred) not at increa** making, 2-dose series MenB-4C (Bexsero) at least 1 month apart or 2-dose series MenB-FHbp (Tru after dose 1, administer dose 3 at least 4 months after dose 2); MenB-4C and MenB-FHbp are not

▪ **Special situations for MenB:**
- **Anatomical or functional asplenia (including sickle cell disease), persistent complement co ravulizumab) use, or microbiologists routinely exposed to *Neisseria meningitidis*** (NOTE: Men if indicated, but at a different anatomic site, if feasible)**:** 2-dose primary series MenB-4C (Bexsero) at 0, 1 to 2, 6 months (if dose 2 was administered at least 6 months after dose 1, dose 3 not need dose should be administered at least 4 months after dose 3); MenB-4C and MenB-FHbp are not ir booster 1 year after primary series and revaccinate every 2 to 3 years if risk remains.
- **Pregnancy:** Delay MenB until after pregnancy unless at increased risk and vaccination benefits o
- For MenB **booster dose recommendations** for groups listed under "Special situations" and in ar among men who have sex with men) and additional meningococcal vaccination information, refe

▪ **Contraindications and precautions:**
- For contraindications and precautions to meningococcal ACWY (MenACWY) [MenACWY-CRM (Mer MenACWY Appendix.
- For contraindications and precautions to meningococcal B (MenB) [MenB-4C (Bexsero); MenB-FH

§§ ***Haemophilus influenzae*** **type b vaccination**

▪ **Special situations:**
- **Anatomical or functional asplenia (including sickle cell disease):** 1 dose if previously did not r before splenectomy.
- **Hematopoietic stem cell transplant (HSCT):** 3-dose series 4 weeks apart starting 6 to 12 month

▪ **Contraindications and precautions:**
- For contraindications and precautions to *Haemophilus influenzae* type b (Hib) vaccination, refer to

¥¥ Vaccinate after pregnancy.

Reproduced from: Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule for ages 19 years or https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html (Accessed on February 15, 2023).

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