Hepatitis A

Medical Summary

Note: This article also contains information on the combination hepatitis A-hepatitis B (HepA-HepB) vaccine.

What's New

Hepatitis A (HepA) vaccination is now recommended by ACIP for:

- All susceptible persons aged ≥ 6 months traveling to or living in developing countries and areas of intermediate or high risk for hepatitis A virus (HAV) transmission. Infants aged 6-11 months should be given 1 dose (noncountable) prior to travel. Following this dose, routine vaccination with HepA vaccine (2 additional age-appropriate doses) should occur.
- Postexposure prophylaxis for all persons aged ≥ 12 months. Additionally, immune globulin (if available) may be administered to persons aged > 40 years depending on the provider's risk assessment (e.g., patient's age, immune status and underlying conditions, and risk of exposure).
- Persons experiencing homelessness and all persons with HIV aged ≥ 1 year.
- Catch-up vaccination of all unvaccinated children aged 2-18 years.
- Pregnant women at risk for HAV infection during pregnancy or a severe outcome from HAV infection.
- All unvaccinated persons aged ≥ 1 year at risk for HAV infection during a HAV outbreak.

Clotting-factor disorders are no longer considered an indication for vaccination.

Additional HepA doses (i.e., booster or revaccination) beyond the primary series are not recommended because protective antibodies are estimated to persist for at least 40 years in more than 90% of immunocompetent adult vaccines. Data regarding booster doses or revaccination with a complete series are not available for immunocompromised persons.

In community outbreak settings propagated by person-to-person transmission, preexposure HepA vaccination may be offered to high-risk persons in the vicinity of the outbreak due to increased risk of HAV infection among persons in congregate settings (correctional facilities, homeless shelters, and syringe service programs).

Postvaccination serologic testing is recommended for persons whose subsequent clinical management depends on knowledge of their immune status.

See Recommended Child and Adolescent Immunization and Catch-up Schedules and Recommended Adult Immunization Schedule for the 2020 US recommended schedules. No significant changes have occurred since the 2019 schedules.

Introduction

Hepatitis A (HepA) infection occurs worldwide and is caused by hepatitis A virus (HAV) which is primarily transmitted via the fecal-oral route and then replicates in the liver. Although virus is present in the serum, its concentration is much less than in feces. The resulting immune response causes liver inflammation and hepatic dysfunction. Infection with any of the genotypes (4 of 7 affect humans) results in lifelong immunity against all strains of HAV.

Epidemiology

HAV infection is highly endemic in developing countries (particularly in Africa, Asia, Central and South America, the Middle East, and the Western Pacific) with inadequate sanitation, limited access to clean water, and poor hygienic conditions. Endemicity rates are intermediate in developing countries with transitional economies and in some regions of industrialized countries where sanitary conditions are variable. Although endemicity rates are low in developed countries with good hygienic practices, foci of high transmission may occur in certain risk populations or may be due to consumption of imported HAV-contaminated food from global sources.

Mode of Transmission

Humans are the only natural hosts of the virus; no insect or animal vectors exist. Transmission occurs most often through consumption of contaminated foods (e.g., undercooked shellfish, raw or inadequately cooked or frozen foods [including fruits and vegetables]), water, or ice). The virus is also spread through person-to-person contact via the direct fecal-oral route (e.g., contaminated surfaces or oral-anal sexual acts) or via food contaminated by acutely infected food handlers. Blood-borne transmission, although uncommon, is possible via contaminated blood products.

Persons can shed the virus in stool beginning several weeks before the onset of symptoms and for about 1 to 3 weeks afterward. Viral concentration in stool is highest in the prodromal stage, and children may excrete virus much longer (up to 6 months after infection) than adults. Risk of transmission decreases after the onset of jaundice.

HAV is relatively resistant to heat and freezing; thus, it survives well in the environment outside the human host. The virus can persist on hands for several hours and in room-temperature food for considerably longer.

Risk Factors

Current risk in travelers is estimated to be high (6-30/100,000 travelers per month of travel to developing countries) and increases with duration of travel. For individuals going to countries with intermediate or high rates of transmission, risk is highest for long-stay travelers; for persons who live in or visit rural areas; trek in remote, undeveloped backcountry areas; eat or drink frequently in high-risk situations; have close physical contact with local persons (especially young children) in settings with poor sanitary conditions; and for persons who travel outside prearranged, fixed itineraries (including common tourist packages). However, cases can also occur in settings with good sanitary conditions because of an infected food handler or consumption of contaminated food.

Risk of significant clinical illness or jaundice is practically nonexistent for infants aged < 12 months, even if acutely infected. Individuals residing in settings with good hygiene (e.g., infants who are breastfed or bottle-fed using safe water for formula reconstitution or who eat commercial baby food with no exposure to locally prepared foods) have low risk of infection. Because children generally have asymptomatic or unrecognized illness, they may serve as a source of infection for unvaccinated household or other close contacts upon return home.

In countries with very low HAV infection rates, disease may occur among travelers ingesting undercooked shellfish.

Homelessness and use of injection and noninjection drugs have emerged as risk factors for outbreaks of HAV infection in the US

Clinical Presentation

Infection can be asymptomatic or range in severity from a mild illness lasting 1 to 2 weeks to a severely disabling disease lasting several months. In young children (aged < 6 years), HAV usually causes either asymptomatic infection or very mild illness without jaundice. Older children and adults are more likely to have symptomatic infection, with jaundice occurring in more than 70% of patients.

Following an asymptomatic incubation period of 15 to 50 days (average: 28 days), an abrupt onset of fever, anorexia, nausea, vomiting, abdominal pain, diarrhea, and malaise may occur, followed within days by jaundice. Dark urine usually occurs before onset of jaundice, and hepatic tenderness may also be present. Severe hepatic and extrahepatic complications (including fulminant hepatitis and liver failure) are rare, but they commonly occur in older adults and people with underlying liver disease.

Among older children and adults, the illness usually lasts less than 2 months, although approximately 10% to 15% of infected people have prolonged or relapsing symptoms (relapsing hepatitis) lasting from 6 months to a year. Chronic hepatitis and carrier states do not occur.

A fatal course is rare in previously healthy individuals. The overall case-fatality ratio is 0.3% but can reach 1.8% among adults aged > 50 years. Older age and chronic liver disease increase risk of death due to HAV infection.

Immune globulin G (IgG) antibodies to HAV (which appear early in the course of infection) provide lifelong protection against the disease.

Need for Medical Assistance

Persons with symptoms of HAV infection, those who have been exposed to an individual with acute HAV infection, or those possibly exposed during an outbreak situation should seek medical attention.

Prevention

Nonvaccine

Travelers should observe food and beverage precautions and hand hygiene (frequent, thorough handwashing), regardless of vaccination status; see *Food and Beverage Precautions*. Travelers should also observe safer-sex practices.

Vaccine

HepA vaccines are highly immunogenic; a single dose of a single-antigen HepA vaccine given any time before travel will provide nearly complete protection for healthy persons. Following 2 doses, nearly 100% of vaccinees (children and adults) will seroconvert within 4 weeks, with protective antibodies estimated to persist for at least 40 years in more than 90% of adult vaccinees. (See *Literature Watch Review:* Long-Term Protection against Hepatitis A: Serological and Cellular Studies). Due to the robust anamnestic response to the second HepA vaccine dose, it has been suggested that vaccine recipients who seroconverted will be protected, even if their antibody levels have fallen below protective levels. Revaccination (i.e., booster dose, challenge dose, or revaccination with a complete series) is not generally recommended for previously vaccinated persons with a normal immune status.

Since 2008, HepA vaccine has been given routinely to children in the US at age 1 year; older children may or may not have had catch-up doses.

The protective efficacy of HepA vaccine given for postexposure prophylaxis within 2 weeks after exposure to children and adults aged < 40 years is 86% compared to the 90% efficacy of immune globulin (IG) in this age group. Limited data suggest protection at 2 weeks after vaccination for adults aged 40-49 years and protection at 4 weeks after vaccination for adults aged 50-59 years. IG performs well in all populations.

A combined HepA-HepB vaccine is also available, and immunogenicity is equivalent to that of the monovalent HepA and HepB vaccines after completion of the recommended schedule.

Indications for Vaccination

Note: Shoreland's vaccine recommendations, which focus primarily on the risk to the individual traveler, reflect a synthesis and reconciliation of available advice from CDC, ACIP, AAP, and WHO, as well as ongoing global surveillance and the published literature. These recommendations may differ from those of individual countries' public health authorities.

Routine

HepA vaccine is routinely recommended for:

- All children in the US at age 1 year (i.e., 12-23 months)
  - Children aged 2-18 years who have not been vaccinated at the recommended time should be vaccinated at any age.
- Men who have sex with men
- Persons who use illegal drugs, injectable or noninjectable
- Persons working with HAV-infected primates or with HAV in a research laboratory setting
- Persons with chronic liver disease (including but not limited to persons with hepatitis B virus or hepatitis C virus infections, 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)
- Unvaccinated persons who anticipate close personal contact (household or regular babysitting) with an international adoptee from a country with high or intermediate endemicity during the first 60 days after arrival of adoptee. The first dose should be administered as soon as adoption is planned, ideally more than 2 weeks before arrival of the adoptee. The second dose should be given at least 6 months later to provide long-term immunity.
- Any person seeking protection from HAV infection
- Persons aged ≥ 1 year experiencing homelessness
- Persons with HIV aged ≥ 1 year (regardless of CD4 count)

Pregnant women who meet any of the above high-risk criteria for HAV infection should be vaccinated during pregnancy.

HepA vaccination may be offered to individuals in congregate settings in which a high proportion of persons have risk factors for HAV infection.

Travel

HepA vaccination is recommended for:

- All susceptible persons aged ≥ 6 months, including pregnant women, traveling to or living in developing countries and areas of intermediate or high risk for HAV transmission, especially persons who plan frequent trips or have prolonged stays
  - In infants aged 6-11 months, vaccination is noncountable toward the routine schedule and should be followed by routine vaccination with HepA vaccine (2 additional age-appropriate doses).
  - Some experts recommend that travelers consider HepA vaccination regardless of destination.
- Susceptible travelers going to some developing countries who engage in risk behaviors (see Risk)
- Risk-averse travelers desiring maximum pretravel protection

IG given intramuscularly (IM) is recommended for:

- At-risk travelers who choose not to receive the vaccine or who cannot receive the vaccine due to allergy or if HepA vaccine is unavailable

IG given IM may be considered (in addition to the initial dose of HepA vaccine) for:

- Persons aged > 40 years (planning to depart in < 2 weeks), immunocompromised persons, those with chronic liver disease, and pregnant women traveling to intermediate or high risk areas

Combination HepA-HepB vaccine is recommended for:

- Persons aged ≥ 18 years who are at risk for both forms of hepatitis.

Outbreak Situations

Preexposure vaccination is recommended for all unvaccinated persons aged ≥ 1 year at risk for HAV infection during a HAV outbreak. In community outbreak settings propagated by person-to-person transmission, vaccination may be offered to high-risk persons in the vicinity of the outbreak due to increased risk of HAV infection among persons in congregate settings (correctional facilities, homeless shelters, and syringe service programs).

HepA vaccine or IG should be used as indicated below:

- HepA vaccine (1 dose) should be administered for preexposure prophylaxis in all persons aged ≥ 12 months (aged ≥ 6 months in Canada) at risk for HAV infection during an outbreak.
- IG may be administered in addition to HepA vaccine for:
  - Persons aged > 40 years (aged ≥ 60 years in Canada) who are high-risk persons in a congregate setting
  - Persons of any age based on the following considerations: altered immune status, underlying conditions (especially chronic liver disease or infection), provider's risk assessment, and availability of IG
- IG should be used as a single agent for children aged < 12 months, for those for whom the vaccine is otherwise contraindicated, and if HepA vaccine is indicated but unavailable.

Postexposure Prophylaxis

Postexposure prophylaxis is recommended as soon as possible (within 2 weeks) after exposure to a clinical case of HAV infection in these settings:

- Household and sexual contacts
- Persons who have shared illegal drugs
- Daycare center staff, attendees, and household members of attendees
- Common-source exposure such as a known infected food handler or an exposure in a known outbreak setting where the specific source is unknown
- Schools, hospitals, and work settings, if close contact exists with the index patient
- Some experts recommend IG for newborn infants of acutely HAV-infected mothers, if the mother's symptoms began between 2 weeks before and up to 1 week after delivery.

HepA vaccine or IG should be used as indicated below:

- HepA vaccine (1 dose) should be administered for postexposure prophylaxis in all persons aged ≥ 12 months (aged ≥ 6 months in Canada) at risk for HAV infection during an outbreak.
- IG may be administered in addition to HepA vaccine for:
  - Persons aged > 40 years (aged ≥ 60 years in Canada) who are household contacts, sexual contacts, or caretakers of the index case
  - Persons of any age based on the following considerations: altered immune status, underlying conditions (especially chronic liver disease or infection), provider's risk assessment, and availability of IG
- IG should be used as a single agent for children aged < 12 months, for those for whom the vaccine is otherwise contraindicated, and if HepA vaccine is indicated but unavailable.

Note: Because HAV has a relatively long incubation period, the vaccine may not prevent the disease in individuals who have an unrecognized HAV infection at the time of vaccination.

Vaccines and Immune Globulins

See Administration for Hepatitis A Vaccine

Vaccines: US

Hepatitis A Virus Vaccines, Inactivated

Havrix (HepA; GSK)

- Approved for use in persons aged ≥ 12 months
- Available in 0.5 mL and 1 mL single-dose vials and prefilled syringes.
- Formulations include:
  - Pediatric - each 0.5 mL dose contains 720 ELISA units of HAV antigen.
  - Adult - each 1 mL dose contains 1,440 ELISA units of HAV antigen.
- Contains aluminum, formalin, polysorbate 20, and neomycin sulfate
- Thimerosal- and preservative-free
- The tip caps of the prefilled syringes may contain natural rubber latex (NRL).

Vaqta (HepA; Merck)

- Approved for use in persons aged ≥ 12 months
- Available in 0.5 mL and 1 mL single-dose vials and prefilled syringes
- Formulations include:
  - Pediatric/adolescent - 0.5 mL dose contains 25 units of HAV antigen
  - Adult - 1 mL dose contains 50 units of HAV antigen
- Contains aluminum, trace amounts of formaldehyde, bovine serum albumin, and neomycin
- Thimerosal- and preservative-free
- The vial stoppers, syringe plunger stoppers, and tip caps contain dry NRL.

Hepatitis A and Hepatitis B (Recombinant) Vaccine, Inactivated

Twinrix (HepA-HepB; GSK) is a combination of Havrix and Engerix-B.

- Approved for use in persons aged ≥ 18 years
- Available in 1 mL single-dose vials and prefilled syringes; each 1 mL dose contains 720 ELISA units of HAV antigen and 20 µg of HBV antigen.
- Contains aluminum and trace amounts of neomycin, residual formalin, polysorbate 20, and yeast protein
- Thimerosal- and preservative-free
- The tip caps of the prefilled syringes may contain NRL.

In contrast to IG, HepA vaccine (an inactivated, viral antigen vaccine) is not derived from blood products.

See *Immune Globulin* for information on IG used for prevention of HAV infection.

Immune Globulins: US

Immune Globulin Intramuscular (IGIM)

GamaSTAN S/D (Grifols Therapeutics Inc.)

- Approved for prophylaxis of HepA and measles and for the modification of rubella (in exposed women who will not consider a therapeutic abortion) and varicella.
- Available in 2 mL and 10 mL single-dose vials for IM administration
- Contains human plasma and glycine
- Preservative- and thimerosal-free
- Latex-free

Vaccines: Available Outside the US

Hepatitis A Virus Vaccines, Inactivated

Avaxim (Sanofi Pasteur): Australia, Canada, Europe (except Switzerland), and UK

- In Canada, Avaxim is available in both adult and pediatric (Avaxim Pediatric) formulations approved for use in persons aged ≥ 12 years and 1-15 years, respectively; either vaccine can be used for persons aged 12-15 years. A booster is given after 6 to 36 months.
- In Europe and the UK, Avaxim is approved for use in persons aged ≥ 16 years.

- In Australia, Avaxim is approved for use persons aged ≥ 2 years.
- In other countries, approved age ranges and booster schedules may vary; check the package insert for the country of use.
- Available in 0.5 mL prefilled syringes; each 0.5 mL dose contains 80 antigen units (pediatric) or 160 antigen units (adult) of HAV antigen.
- Contains 2-phenoxyethanol, formaldehyde, aluminum hydroxide, polysorbate 80, ethanol anhydrous, phenylalanine, trace amounts of neomycin, and may contain bovine serum albumin
- Thimerosal-free

Havrix (GSK): Australia, Canada, and UK

- In Canada, Havrix is available in both adult (Havrix 1440) and pediatric (Havrix 720 Junior) formulations approved for use in persons aged ≥ 19 years and 1-18 years, respectively.
- In Australia, Havrix is available in both adult (Havrix 1440) and pediatric (Havrix Junior) formulations approved for use in persons aged ≥ 16 years and 2-15 years, respectively.
- In the UK, Havrix is available in both adult (Havrix Monodose) and pediatric (Havrix Junior Monodose) formulations approved for use in persons aged ≥ 16 years and 1-15 years, respectively.
- Available in 0.5 mL and 1 mL single-dose vials and prefilled syringes; 1 mL of Havrix adult dose contains 1,440 ELISA units of HAV antigen; 0.5 mL of Havrix pediatric dose contains 720 ELISA units of HAV antigen.
- Contains aluminum hydroxide, trace amounts of neomycin, polysorbate 20, and formaldehyde (not in UK formulation)
- Thimerosal-free

Note: Different strengths and/or concentrations of Havrix may be available or may be used for different patient populations in some countries. Contact the manufacturer directly for any questions that may arise concerning these other formulations.

Vaqta (CSL/Merck): Australia, Canada, and UK

- Same as US vaccine

Healive (Sinovac Biotech Co. Ltd): China

- Approved for use in children aged 1-15 years (pediatric formulation) and in persons aged ≥ 16 years (adult formulation)
- Available as single-dose prefilled-syringes or single-dose vials; 0.5 mL of Healive pediatric dose contains 250 antigen units; 1 mL of Healive adult dose contains 500 antigen units
- Preservative-free

Hepatitis A Virus Vaccines, Live Attenuated

ZhePu (Zhejiang Pukang Biotechnology Co): China; branded as Biovac-A (Wockhardt) in India

- Vaccines (freeze-dried) are based on H2 or LA-1 strains.
- H2 vaccine is also available in Bangladesh, Guatemala, Philippines, and Thailand.
- Approved for use in China in persons aged ≥ 1 year as 1 dose
- Meta-analysis showed protective efficacy of 95% for both vaccines, which was equivalent to international inactivated vaccines.

Hepatitis A and Hepatitis B (Recombinant) Vaccine, Inactivated

Twinrix (HepA-HepB; GSK): Australia and Canada; a pediatric formulation, Twinrix Junior (3-dose pediatric formulation) is also available in these countries. Branded as Twinrix Adult and Twinrix Pediatric in Europe and UK.

- Twinrix adult formulation is approved for persons aged ≥ 1 year in Australia and Canada, and for persons aged ≥ 16 years in Europe and UK
- Twinrix Junior/Pediatric approved for persons aged 1-15 years in Australia, Europe, and UK, and for persons aged 1-18 years in Canada
- Available in 1 mL and 0.5 mL single-dose, prefilled syringes and vials
- Each 1 mL dose (Twinrix adult formulation) contains 720 ELISA units HAV and 20 µg HBsAg.
- Each 0.5 mL dose (Twinrix Junior/Pediatric) contains 360 ELISA units HAV and 10 µg HBsAg.
- Contains aluminum and trace amounts of formalin, neomycin, polysorbate 20, and yeast protein

Ambirix (HepA-HepB; GSK): Europe, UK; 2-dose pediatric formulation

- Approved for use in persons aged 1-15 years
- Available in single-dose, prefilled syringes
- Each 1 mL dose contains 720 ELISA units HAV and 20 µg HBsAg.

- Contains aluminum, yeast, and a trace amount of thimerosal

Combination Hepatitis A-Vi Polysaccharide Typhoid Vaccines, Inactivated

Several combined inactivated HepA and Vi polysaccharide typhoid vaccines are available outside the US. Check package inserts carefully for full prescribing information.

Vivaxim (Sanofi Pasteur): Australia, Canada, Europe (except Switzerland), New Zealand, and elsewhere; branded as Viatim in the UK.

- Approved for use in persons aged ≥ 16 years
- One dose (1 mL) of the combination vaccine (administered IM) is followed by a booster dose of HepA vaccine 6 to 36 months later.
- Protection against typhoid lasts about 3 years.
- Available in single-dose, prefilled, dual-chambered syringe containing 0.5 mL purified Vi polysaccharide typhoid vaccine and 0.5 mL inactivated HepA vaccine, which are mixed immediately prior to administration to produce a 1 mL dose
- Contains aluminum, 2-phenoxyethanol, formaldehyde, traces of polysorbate 80, neomycin, and bovine serum albumin.
- Thimerosal-free
- Latex-free

Immune Globulins: Available Outside the US

Immune Globulin Intramuscular (IGIM)

GamaSTAN S/D (Grifols Therapeutics): Canada

- Same as the US product

Normal Human Immunoglobulin-VF (CSL Ltd): Australia, New Zealand

- Approved for prophylaxis of HepA and measles for use in persons aged ≥ 12 months via IM administration
- Available in 2 mL and 5 mL vials
- Contains human plasma and glycine
- Preservative-free
- Latex-free

Side Effects

Side effects of HepA vaccination tend to be mild and transient. The most frequently reported side effects are injection-site reactions (pain, redness, warmth, swelling, and tenderness). Headache in some adults, feeding problems in children, and secondary respiratory tract infections have also been reported. No serious adverse events have been observed.

Side effects of Twinrix (Havrix + Engerix-B) are similar to those of the individual vaccines given concurrently.

Side effects of IGIM include injection-site reactions as well as thromboembolic events, which may occur in the absence of usual risk factors and despite administration route; underlying risk factors may further increase the risk.

Suspected allergic or adverse effects or medical care required after any vaccination should be reported through the Vaccine Adverse Event Reporting System (VAERS). See also Table: Reportable Events following Vaccination and the VAERS form.

Precautions and Contraindications

Precautions

Consider postponing vaccination in persons with moderate or severe illness (with or without a fever) until recovery, to minimize potential adverse effects.

Contraindications

Anaphylactic reaction to a previous dose or a vaccine constituent contraindicates further vaccination with that vaccine or any vaccine containing that constituent.

Persons who are allergic to a vaccine component or who choose not to receive the vaccine should receive IG (0.1-0.2 mL/kg), which provides effective protection for up to 2 months depending on the dose. See *Immune Globulin Intramuscular (IGIM)* for more information.

Conditions commonly misperceived as contraindications or precautions

Conditions incorrectly perceived as contraindications or precautions to vaccination (i.e., vaccines may be given under these conditions)

- Mild acute illness, with or without fever
- Mild to moderate local reaction (e.g., swelling, redness, soreness); low-grade or moderate fever after previous dose
- Lack of previous physical examination in well-appearing person
- Current antimicrobial therapy
- Convalescent phase of illness
- Preterm birth
- Recent exposure to an infectious disease
- History of penicillin allergy, other nonvaccine allergies, relatives with allergies, or receiving allergen extract immunotherapy
- History of Guillain-Barré syndrome

Bleeding Disorders

All HepA and HepA-containing vaccines are intramuscular injections and may pose a risk for persons with bleeding disorders or those receiving anticoagulation drugs. Consider scheduling vaccination just prior to the next dose of anticoagulant drugs. Morning anticoagulant doses can be deferred until after an early morning vaccine dose, or the vaccine dose can be given late in the afternoon in the case of evening anticoagulant doses. Use a fine-gauge needle (23-gauge or smaller) and apply firm, direct pressure to the site for at least 2 minutes following the injection. Do not rub or massage the injection site. A bruising rate of less than 4% results using this approach. See *Bleeding Disorders and Vaccination*.

Alternatively, single antigen HepA vaccines may be administered subcutaneously.

Compromised Immunity and HIV

Data indicate that immunocompromised persons being treated with immunosuppressive drugs may have inadequate seroprotection after a single dose of HepA vaccine. Such travelers should make efforts to receive 2 doses of the HepA vaccine over a 6-month period prior to their trip. However, instead of giving concomitant IG with the initial dose of HepA vaccine per CDC recommendation, many experienced clinicians recommend giving a second dose at least 4 weeks after the first dose for time-constrained travelers. However, if this second dose is administered less than 6 months after the first dose, it is invalid for completion of the routine series. See Administration Errors.

Limited data exist to determine the need for booster doses or revaccination with a complete series for immunocompromised persons (e.g., persons with HIV, hematopoietic stem cell transplant recipients, persons receiving chemotherapy). No special precautions need to be taken when vaccinating such persons. If this vaccine is administered to persons with malignancies, immune disorders, or those on immunosuppressive therapy, the expected immune response may not be obtained.

Among adults with HIV infection, 50% to 95% were seroprotected after vaccination with the complete series, and final antibody concentrations were much lower than in HIV-negative persons. Data indicate that high viremia at the time of vaccination is associated with decreased seroprotection in persons with HIV; however, HepA vaccination should not be delayed until the CD4 count exceeds a particular threshold. Additionally, HepA vaccination may not provide long-term protection and IG may be needed after a high risk HAV exposure (e.g., sexual or household contact).

When indicated for the prevention of hepatitis A in immunocompromised persons, IG should be administered using the same dose and schedule as that used for immunocompetent persons. Household and other close contacts of immunocompromised persons should receive all age- and exposure-appropriate vaccines, with the exception of smallpox vaccine.

For administration and dosage schedules for those with compromised immunity, see Accelerated, Altered, or Lapsed Schedules.

See also *Immunocompromised Travelers* and *Travelers with HIV*.

Pregnancy and Breastfeeding

Pregnancy

Non-immune pregnant women at risk for HAV (including travelers) should be vaccinated during pregnancy. Unvaccinated pregnant women or women who choose not to be vaccinated during pregnancy should be counseled about HAV infection prevention methods. IG is a safe and effective alternative for preventing HAV infection in pregnancy, but vaccination with HepA vaccine gives a more complete and prolonged protection.

See *Pregnant Travelers*.

Breastfeeding

Whether HepA is excreted in human breast milk is unknown. Receipt of HepA-containing vaccines is not a contraindication to breastfeeding and poses no risk to the mother or infant.

Compatibility

HepA-containing vaccines can be administered simultaneously with (or at any time before or after) other vaccines.

All vaccine doses in a series should come from the same manufacturer; however, if this is not possible or if the manufacturer of the previously given doses is unknown, providers should not defer vaccination but instead administer the vaccine that they have available. See Administration of Hepatitis A Vaccine.

The efficacy and safety of combination vaccines are comparable to previously licensed monovalent or combination products with similar component antigens from the same manufacturer and may be used interchangeably with these products to continue the vaccination series.

HepA and HepA-containing vaccines can be administered simultaneously with (or at any time before or after) any antibody-containing preparation (e.g., immune globulin, hyperimmune globlin, and intravenous immune globulin) but should be given at a different injection site if administered simultaneously.

Separate vaccines should not be combined into the same syringe to be administered together unless indicated for the patient's age and explicitly specified on the FDA-approved product label inserts. The safety, immunogenicity, and effectiveness of unlicensed combinations are unknown.

IG and measles, mumps, rubella (MMR) vaccine should not be administered simultaneously. MMR and varicella vaccines should not be administered < 3 months after IG administration.

Special Considerations

Prevaccination Serological Testing

Prevaccination serologic testing is rarely done in clinical practice but may be considered in specific settings to reduce costs by not vaccinating persons who are likely already immune such as:

- Persons who were born in or lived in areas with high or intermediate prevalence of HAV infection
- Older adolescents and adults in certain population groups (i.e., Native Americans, Alaskan Natives, and Hispanics)
- Adults in groups that have a high prevalence of infection (e.g., men who have sex with men and injection-drug users)

The inability to perform prevaccination serologic testing should not be a barrier to vaccination of susceptible persons, especially in populations difficult to access. Testing is not generally indicated in children because of low incidence of HAV infection.

Commercially available tests for total anti-HAV or IgG anti-HAV should be used.

- Elevated anti-HAV IgM indicates acute HAV infection, and antibodies decline over several months. This test is inappropriate for determining long-term immunity.
- Elevated anti-HAV IgG or total anti-HAV indicates previous HAV infection, and protective antibodies persist for life.

Vaccination history should be obtained where practical, prior to testing or vaccination of populations expected to have high rates of previous HAV vaccination. Vaccination should not be deferred if vaccination history cannot be obtained, records are unavailable, or prevaccination testing is not feasible. Vaccination of an immune person is not contraindicated and does not incur increased risk for adverse effects.

Postvaccination Serological Testing

Postvaccination serologic testing is not generally indicated because of the high rate of vaccine response among adults and children; however, persons whose subsequent clinical management depends on knowledge of their immune status (e.g., persons with HIV and other immunocompromised persons) should be tested. If indicated, testing should be performed with total anti-HAV or IgG anti-HAV assays ≥ 1 month after completing the vaccine series.

Anti-HAV persistence studies do not indicate a need for additional HepA doses (i.e., booster or revaccination) beyond the 2-dose primary HepA series (or 3-dose HepA-HepB series) because protective antibodies are estimated to persist for at least 40 years in more than 90% of immunocompetent adult vaccinees.

Persons who do not respond to vaccination should be considered susceptible to HAV infection and counseled about HAV exposure precautions and the need to obtain IG postexposure prophylaxis for known or likely exposures to HAV.

Travax content represents decision-relevant, expert synthesis of real-time data reconciled with new and existing available advice from authoritative national and international bodies. National body recommendations such as ACIP/CDC may differ from the manufacturers' recommendations as found in vaccine package inserts. Travax recommendations may differ from those of individual countries' public health authorities.

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