



Hepatitis A Guidelines: Homelessness, Post-exposure Prophylaxis and International Travel

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Current issues in Immunization Webinar

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Homelessness

Background

- In the U.S., approximately 3 million persons, 1% of the population, are homeless in a given year.
- Rates of homelessness have been increasing for the last decade. Men, women and children of all ages and ethnicities are affected.
- In 2017, in a single night more than 553,742 people experienced homelessness in the United States (HUD, 2017).
- Individuals experiencing homelessness have an increased risk of mortality ranging from 1.5 to 11.5 times the risk in the general population (Gambatese et al, 2013).

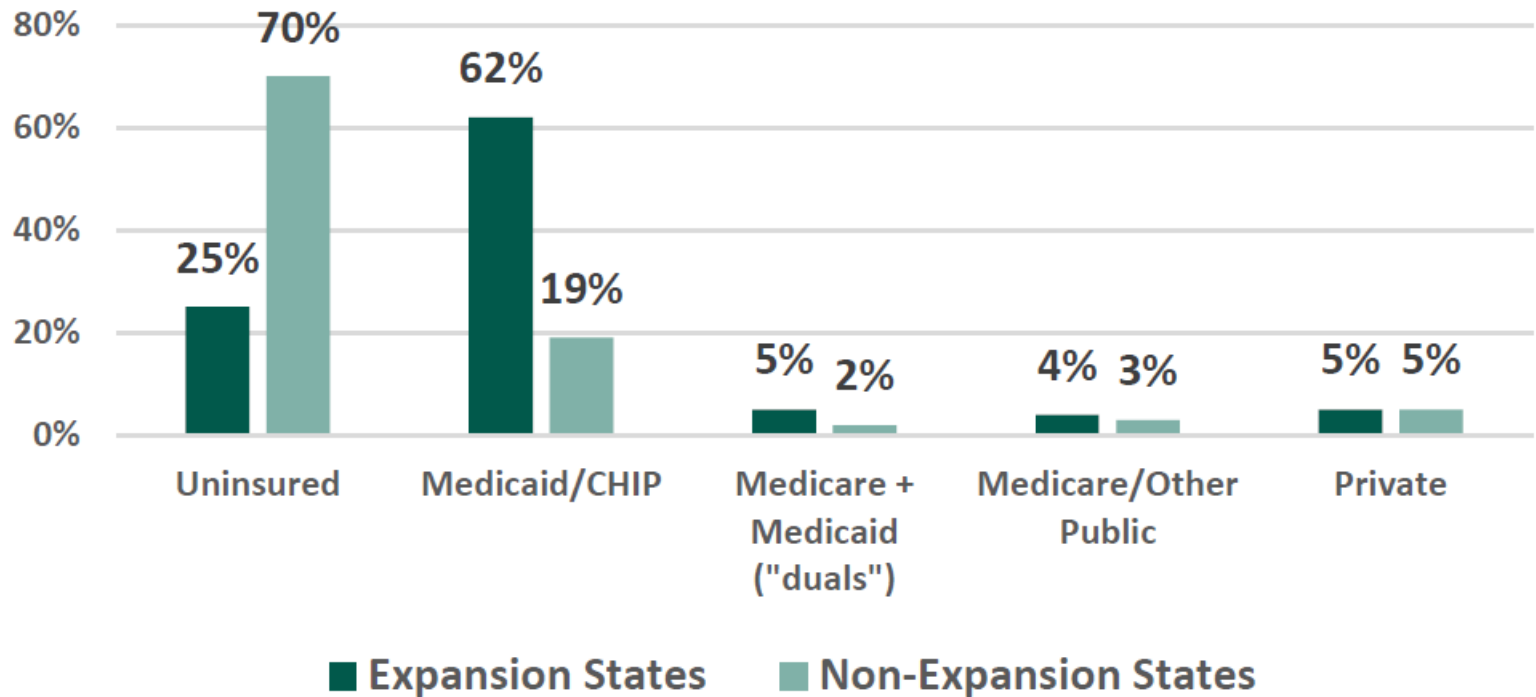
Gambatese M, Marder D, Begier E, et al. Programmatic impact of 5 years of mortality surveillance of New York City homeless populations. *Am J Public Health*. 2013;103:S193–S198.

Background

- Community health centers provide preventive and primary health services to meet the specific needs of persons experiencing homelessness.
- Congregate living conditions increase the risk of disease transmission, which can result in outbreaks (Tjon et al, 2005).
- Thirty four states expanded Medicaid, leading to an increase in coverage and access to care among homeless (National Healthcare for the Homeless Council, 2018).

Tjon, G. M., et al. (2005). "An outbreak of hepatitis A among homeless drug users in Rotterdam, The Netherlands." *Journal of Medical Virology* 77(3): 360-366.

Figure 2. Health Insurance Sources at HCH Programs, 2016



Background

Vaccinations are critical to the prevention of disease in such individuals

- Due to limited access to healthcare, and low rates of insurance coverage, majority of homeless adults have no protection from vaccine preventable diseases.
- Vaccine induced antibodies persist for 20 years in adults¹ and detectable antibodies were estimated to persist for 40 years or longer based on mathematical modeling and anti-HAV kinetic studies.^{2,3}
- Appropriate street/shelter based interventions for targeted populations are the most efficient methods for mass vaccination of the homeless.
- Vaccines are a cornerstone in preventing spread of infectious diseases and in the prevention of future disease in the homeless population.⁴

¹Plumb ID, Bulkow LR, Bruce MG, et al. Persistence of antibody to Hepatitis A virus 20 years after receipt of Hepatitis A vaccine. *J Virol* 2007;81:1111-1115.

²Theeten H, Van Herck K, Van De Meeren O, Crasta P, Van Damme P, Hens N. 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.

³Hens N, Habteab Ghebretinsae A, Hardt K, Van Damme P, Van Herck K. Model based estimates of long-term persistence of inactivated hepatitis A vaccine induced antibodies in adults. *Vaccine* 2014;32:1507-1513.

⁴Smith, Rubeena "Interventions to Increase Vaccination Rates in Homeless Adults Aged 50 Years and Older in a Shelter Clinic" (2016). *Door of Nursing Practice*. 2.

Case Counts-Hepatitis A Virus Outbreak among Persons Who Report Drug Use and/or Homelessness—Multiple States, 10/19/2018 - publically available

State	Cases	Hospitalizations	Deaths
Arkansas	169	81 (48%)	1
Indiana (10/19/2018)	559	251 (45%)	1
Kentucky (10/15/18)	2,050	1,126 (55%)	14
Michigan (10/17/2018)	899	723 (80%)	28
Missouri (10/15/2018)	206	81 (39%)	0
Ohio (10/15/2018)	666	419 (63%)	0
Tennessee (10/12/2018)	332	195 (59%)	1
Utah (10/15/2018)	279	151 (54%)	2
West Virginia (10/12/2018)	1,527	791 (52%)	5
California (4/11/18) ^a	704	461 (65%)	21
North Carolina (10/22/2018)	31	24 (77%)	0
Massachusetts (10/18/2018)	98	83 (85%)	1
Total	7,520	4,386 (58%)	74

*Outbreak case definition and criteria for reporting of case totals differs by state

<https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm>

a. California case counts included but case reporting ceased April 2018

Current Recommendations

- ACIP Hepatitis A Vaccine Recommendations
 - Groups at increased risk of HAV or severe HAV disease
 - Travelers
 - Men who have sex with men
 - Users of injection and non-injection drugs
 - Persons with clotting-factor disorders
 - Persons who work with nonhuman primates
 - Persons who anticipate close personal contact with an international adoptee
 - Persons with chronic liver disease
 - **Homelessness**

Policy question: Should routine inactivated two dose hepatitis A vaccination be recommended for protection against hepatitis A among persons experiencing homelessness?

Population	Homeless (all ages)
Intervention	Inactivated Hepatitis A (HepA) vaccine administered as a two dose series
Control	Unvaccinated homeless individuals
Outcomes	Benefits: <ul style="list-style-type: none">• Reduction in disease burden (Hepatitis A virus [HAV]-related disease and fulminant hepatitis A)• Protection against HAV related disease (efficacy, immunogenicity) Harms: <ul style="list-style-type: none">• Local reactions: injection site pain/tenderness, erythema, fever, malaise, headache, loss of appetite drowsiness, irritability• Systemic adverse events: anaphylaxis, transient purpura, interference with other vaccines

Evidence Type for Benefits and Harms

Outcome	Design (# studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Evidence type	Overall quality of evidence
Reduction in disease burden	1 clinical trial	Serious	Serious	Serious	Serious	*	4**	***
Adverse events	1 clinical trial 3 observational studies	Serious	Serious	Serious	Serious	*	4**	⊕⊖⊖⊖ VERY LOW

*Limitations in determining the estimates of the effect as no study had a comparison group available.

**Evidence from clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations

***Unable to determine the overall quality of evidence as only one study was available for GRADE.

Limitations/gaps

- Clinical trial study had limitations in detailed design and execution and no comparison/control groups were present.
- Observational studies had severe limitations, and some studies did not report any quantitative data.
- Only one study on immunogenicity of the vaccine in the homeless population, but it included a non-U.S. population.
- Studies did not look at homelessness as a risk factor in isolation.

Balance of Consequences

- Undesirable consequences clearly outweigh desirable consequences in most settings
- Undesirable consequences probably outweigh desirable consequences in most settings
- The balance between desirable and undesirable consequences is closely balanced or uncertain
- Desirable consequences probably outweigh undesirable consequences in most settings
- Desirable consequences clearly outweigh undesirable consequences in most settings
- There is insufficient evidence to determine the balance of consequences

Should Routine Inactivated Two dose Hepatitis A Vaccination be Recommended for Protection Against Hepatitis A Among Persons Experiencing Homelessness?

Type of recommendation

- We recommend against the intervention
- We recommend that the intervention not be routinely recommended for all persons but be available for individual clinical decision-making
- We recommend the intervention
- We do not recommend the intervention at this time

Work Group Considerations:

Homelessness as an indication for vaccination vs. No indication for homelessness

- Pros:
 - Protection of a vulnerable population
 - Providers are more likely to administer vaccine to homeless persons if homelessness is an ACIP recommended indication for vaccination
 - Vaccination of homeless persons would reduce an at risk population and therefore reduce the risk of large-scale outbreak, and increase the herd immunity among the homeless population over time
 - Vaccinating homeless in an outbreak setting and controlling an outbreak among homeless is challenging compared to integrating services into a familiar setting
 - Routine vaccination is likely less costly than vaccination as part of an outbreak response
- Cons:
 - Vaccine administration record-keeping
 - Limited published data exist on hepatitis A or vaccination that specifically focuses on persons who are homeless
 - Routine vaccination of homeless who do not utilize health services might not be feasible

- All persons aged 1 year and older experiencing homelessness should be routinely immunized against hepatitis A.

Post-exposure Prophylaxis

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

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Nelson NP, Link-Gelles R, Hofmeister MG, Romero JR, Moore KL, Ward JW, Schillie SF. 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 Nov 2;67(43):1216-1220.

Hepatitis A Vaccine for Post-Exposure Prophylaxis

- **Recommendations for post-exposure prophylaxis (PEP) for hepatitis A**
 - Hepatitis A (HepA) vaccines should be administered for post-exposure prophylaxis for all persons age ≥ 12 months
 - In addition to hepatitis A vaccine, IG may be administered to persons age >40 years depending on the providers' risk assessment
 - Factors to consider in the decision to use IG in addition to vaccine
 - Age
 - Immune status and underlying conditions
 - Exposure type (risk of transmission)
 - Availability of IG

Hepatitis A Vaccine for Post-Exposure Prophylaxis, cont.

Infants aged <12 months and persons for whom vaccine is contraindicated

- Infants aged <12 months and persons for whom vaccine is contraindicated (persons who have had a life-threatening allergic reaction after a dose of hepatitis A vaccine, or have a severe allergy to any part of this vaccine) should receive IG (0.1 mL/kg) instead of vaccine as soon as possible and within 2 weeks after exposure
- Note: The recommended interval for administration of MMR vaccine is no earlier than 3 months after IG administration for hepatitis A prophylaxis

Hepatitis A Vaccine for Post-Exposure Prophylaxis, cont.

Persons aged ≥ 12 months

- Persons aged ≥ 12 months who have been exposed to hepatitis A virus (HAV) within the prior 14 days and have not previously completed the 2-dose HepA vaccine series should receive a single dose of HepA vaccine as soon as possible
- In addition to HepA vaccine, IG (0.1 mL/kg) may be administered to persons aged >40 years depending on the providers' risk assessment
- For long-term immunity, the HepA vaccine series should be completed with a second dose at least 6 months after the first dose; the second dose is not necessary for PEP

Hepatitis A Vaccine for Post-Exposure Prophylaxis, cont.

Persons aged ≥ 12 months who are immunocompromised or have chronic liver disease

- Immunocompromised persons and persons with chronic liver disease who have been exposed to HAV within the prior 14 days and have not previously completed the 2-dose HepA vaccine series should receive both IG (0.1 mL/kg) and HepA vaccine simultaneously in a different anatomical site as soon as possible after exposure
- For long-term immunity, the HepA vaccine series should be completed with a second dose at least 6 months after the first dose; the second dose is not necessary for PEP

Supplement 1: Post-exposure Prophylaxis

- Decision Making for Hepatitis A Post-Exposure Prophylaxis
 - 2-dose and 1-dose HepA vaccination coverage
 - Assessment of Risk

- Risk for HAV Transmission in Various Settings and For Various Groups

Close Personal Contact

- PEP should be administered to all previously unvaccinated persons who have been exposed or who are at risk of exposure due to close personal contact with a person who has serologically confirmed hepatitis A infection (e.g., household and sexual contacts; persons using injection or non-injection drugs with the case; caretakers not using appropriate personal protective equipment).

Child Care Centers

- PEP should be administered to all previously unvaccinated staff members and attendees of child care centers or institutions if:
 - 1) one or more cases of hepatitis A infection are recognized in children or
 - 2) cases are recognized in two or more households of center attendees.
- If one or more cases of hepatitis A infection occurs among employees, PEP should be considered based on the duties, hygienic practices and presence of symptoms at work.
- In centers that do not provide care to children who wear diapers, PEP may be administered only to care center contacts of the index patient.
- When an outbreak occurs (i.e., hepatitis A cases in two or more families), PEP also should be considered for members of households that have children (center attendees) in diapers.

Common-source Food Exposure and Food Handlers

- Food handlers are not at increased risk for hepatitis A because of their occupation.
- Most food handlers with HAV infection do not transmit HAV to exposed consumers or restaurant patrons.
- Because common-source transmission to patrons is unlikely, administering PEP to patrons typically is not indicated.
 - If, during the time when the food handler was likely to be infectious, the food handler both directly handled uncooked or cooked foods without gloves and had diarrhea or poor hygienic practices, the risk for individual patrons remains low, but PEP may be considered.
 - PEP in this scenario should generally consist of vaccination for persons aged ≥ 12 months, though IG may be considered in addition to vaccine for exposed persons (patrons during the time the food handler was symptomatic and worked) who are immunocompromised or have chronic liver disease.

Fiore AE. Hepatitis A transmitted by food. *Clin Infect Dis* 2004;38:705–15.

Sharapov UM, et al. *Public Health Rep* 2016;131:26–9.

Morey RJ, et al. *Public Health Rep* 2017;132.

Ridpath A, et al. *J Public Health Manag Pract* 2017;23:571–6.

Settings Providing Services to Children and Adults

- PEP is not routinely indicated when a single case occurs in an elementary or secondary school or an office or other work setting, and the source of infection is outside of the setting.
- Similarly, when a person who has HAV infection is admitted to a hospital, staff members should not routinely be administered PEP; instead, appropriate infection control practices should be emphasized
- PEP should be administered to persons who have close contact with index patients if an epidemiologic investigation indicates HAV transmission has occurred among students in a school or among patients or between patients and staff members in a hospital
- PEP should be considered for all previously unvaccinated residents and employees when a confirmed hepatitis A case occurs in a setting where close personal contact occurs regularly and hygiene standards are difficult to maintain (e.g., correctional facility, homeless shelter, psychiatric facility, group home or residential facility for the disabled).
- In a setting containing multiple enclosed units or sections (e.g., prison ward), PEP administration should be limited only to persons in the area where there is exposure risk.

Immunocompromised Persons

- Although most persons who have completed the recommended 2-dose HepA vaccine series at any time do not need additional vaccine, vaccination or revaccination doses of HepA vaccine are recommended after hematopoietic cell transplant¹; therefore, recipients who have not been revaccinated after transplant should receive HepA vaccine and IG.
- Other severely immunocompromised persons who have been vaccinated in the past may also benefit from PEP and should be assessed on an individual basis.
- Persons who receive routine IG administration for an immunocompromising condition should also be assessed on an individual basis.

Kroger AT, Duchin J, Vázquez M. General Best Practice Guidelines for Immunization. (www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf).

Supplementary Text 1, <https://staging-stacks.cdc.gov/view/cdc/59777>

Pregnancy

- Data show vaccine is safe during pregnancy¹
- Review published data in November 2015 on hepatitis A during pregnancy²
 - Generally, infants born to mothers with HAV infection are healthy, but there are rare exceptions
 - Hepatitis A infection during pregnancy is associated with gestational complications (e.g. preterm labor, placental abruption, premature rupture of membranes)³
 - No increased risk of maternal or infant mortality after HepA vaccination in pregnancy
- Vaccination of pregnant women who have a specific risk or who lack a risk but want protection is included in the CDC Adult Immunization Schedule by “Medical and Other Indications”

¹ Moro PL, Museru OI, Niu M, Lewis P, Broder K. Reports to the Vaccine Adverse Event Reporting System after hepatitis A and hepatitis AB vaccines in pregnant women. *Am J Obstet Gynecol* 2014;210:561 e561-566.

² Chaudhry SA, Koren G. Hepatitis A infection during pregnancy. *Can Fam Physician* 2015;61:963-964.

³ Elinav E, Ben-Dov IZ, Shapira Y, Daudi N, Adler R, Shouval D, Ackerman Z. Acute hepatitis A infection in pregnancy is associated with high rates of gestational complications and preterm labor. *Gastroenterology*. 2006 Apr;130(4):1129-34. PubMed PMID: 16618407.

Pregnancy

- Pregnant women who have a specific risk (e.g., HAV exposure) are recommended to receive the HepA vaccine.
- IG can be administered in addition to HepA vaccine with consideration of the likelihood of HAV exposure during pregnancy.

Recommended Immunization Schedule for Adults Aged 19 Years or Older by Medical Conditions and Other Indications, United States, 2018. <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html#f8>.
Supplementary Text 1, <https://staging-stacks.cdc.gov/view/cdc/59777>

Health Care Institutions

- Healthcare personnel do not have increased prevalence of HAV infection and health care-associated outbreaks of HAV are rare.
 - Therefore, HepA vaccination is not routinely recommended for health care personnel in the United States.
- Outbreaks have been observed in neonatal intensive care units because of infants acquiring infection from transfused blood and subsequently transmitting HAV to other infants and staff. ^{1,2}
- Outbreaks of hepatitis A caused by transmission from patients to health care personnel are typically associated with fecal incontinence and inadequate hand hygiene³, although the majority of hospitalized patients who have hepatitis A infection are admitted after onset of jaundice, when they are beyond the point of peak infectivity.^{4,5}

1. Rosenblum LS, et al. J Infect Dis 1991;164:476-82.

3. Foster MA, et al. Emerg Infect Dis 2017;23:5906.

5. Goodman RA. Ann Intern Med 1985;103:452.

2. Noble RC, et al. JAMA 1984;252:2743.

4. Klebs, et al. JAMA 1984;252:2743.

Health Care Institutions, cont.

- In hospitals, sharing food or beverages between patients, families and healthcare personnel has been associated with HAV transmission.^{1,2}
- If a healthcare provider receives a diagnosis of hepatitis A infection, PEP should be administered to other healthcare personnel at the same facility.
- In a setting containing multiple enclosed units or sections (e.g., hospital, psychiatric facility), PEP administration can be limited only to health care personnel in the area where there is exposure risk (e.g., cardiology ward, intensive care unit).
- PEP administration to patients can be considered if during the time of patient care the infected healthcare provider was likely to be infectious, did not use gloves when appropriate and had diarrhea or poor hygienic practices.

1. Drusin LM, et.al. Arch Dis Child 1987;62:690–5.

2. Hanna JN, et.al. Anaesth Intensive Care 1996;24:440–4.

Workers Exposed to Sewage

- Studies on the incidence of clinical hepatitis A infection do not show an increased risk in workers exposed to sewage.
- No work-related instances of HAV transmission have been reported among wastewater workers in the United States.
- Persons who work with sewage (e.g., plumbers) are not a risk group for HAV infection.

Glas C, Hotz P, Steffen R. Hepatitis A in workers exposed to sewage: a systematic review. *Occup Environ Med* 2001;58:762–8. Supplementary Text 1, <https://staging-stacks.cdc.gov/view/cdc/59777>

Natural Disaster Settings with Flooding

- Waterborne HAV outbreaks are infrequent in developed countries with properly maintained sanitation and water supplies.
- In the United States, floods are unlikely to cause outbreaks of communicable diseases, and outbreaks of HAV caused by flooding have not been documented.

International Travel

Hepatitis A Vaccines for International Travelers

Infants aged 6-11 months

- Recommendations for pre-exposure protection against hepatitis A for travelers
 - Hepatitis A vaccine should be administered to infants age 6-11 months traveling outside the United States when protection against hepatitis A is recommended
 - The travel-related dose for infants age 6-11 months does not count towards the routine 2-dose series
 - Therefore, the 2-dose hepatitis A vaccine series should be initiated at age 12 months according to the routine, age-appropriate vaccine schedule

Hepatitis A Vaccines for International Travelers, cont.

Rationale

- IG cannot be administered simultaneously with MMR vaccine, which is recommended for all infants aged ≥ 6 –11 months traveling internationally from the U.S., because antibody-containing products such as IG can inhibit the immune response to measles and rubella vaccines for ≥ 3 months
- Due to the greater severity of measles in infancy compared to HAV infection in infancy, MMR vaccine should be administered preferentially to IG for HAV infection pre-exposure prophylaxis
- Administration of HepA vaccine (indication for off-label use) and MMR vaccine to infants aged 6–11 months provides protection against both HAV and measles and allows for simultaneous prophylactic administration

Hepatitis A Vaccines for International Travelers, Cont.

Infants aged <6 months, and travelers who elect not to receive vaccine or for whom vaccine is contraindicated

- Infants aged <6 months, and travelers who elect not to receive vaccine or for whom vaccine is contraindicated should receive a single dose of IG (0.1 mL/kg for travel up to 1 month; 0.2 mL/kg for travel up to 2 months) prior to travel when protection against hepatitis A is recommended
- If travel is 2 months or longer, a repeat dose of 0.2 mL/kg every 2 months should be administered

Hepatitis A Vaccines for International Travelers, Cont.

Healthy persons aged ≥ 12 months–40 years

- Healthy persons aged ≥ 12 months–40 years who are planning travel to an area with high or intermediate hepatitis A endemicity and have not received HepA vaccine should receive a single dose of HepA vaccine as soon as travel is considered and complete the 2-dose series according to the routine schedule

Hepatitis A Vaccines for International Travelers, Cont.

Older adults, immunocompromised persons, persons with chronic liver disease

- Persons with chronic liver disease as well as older adults (aged >40 years), immunocompromised persons, and persons with other chronic medical conditions planning to depart to a risk area in <2 weeks should receive the initial dose of vaccine, and also simultaneously can be administered IG at a separate anatomic injection site (0.1 mL/kg for travel up to 1 month at a separate anatomic injection site; 0.2 mL/kg for travel up to 2 months; repeat dose of 0.2 mL/kg every two months)

Supplement 2: International Travel

- Specifics of hepatitis A vaccine (single-antigen), IG and HepA/HepB (Twinrix) dosing
- Assessment of Risk
- Pregnancy

Pregnancy

- Pregnant women who have a specific risk (e.g., international travel) are recommended to receive the HepA vaccine.
- In addition to HepA vaccine, IG can be administered with consideration of the likelihood of HAV exposure during pregnancy.

Recommended Immunization Schedule for Adults Aged 19 Years or Older by Medical Conditions and Other Indications, United States, 2018. <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html#f8>.

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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