CLINICAL GUIDELINES PROGRAM
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

Prevention and Management of Hepatitis A Virus Infection in Adults With HIV

Updates, Authorship, and Related Guidelines

Date of current publication	May 21, 2021
Highlights of changes, additions, and updates in the May 21, 2021 edition	• Updated recommendation in Transmission and Prevention section: Clinicians should obtain an HAV IgG antibody measurement for all individuals with HIV and should administer the HAV vaccine to those who are HAV antibody-negative, regardless of CD4 count. • Updated citations and references throughout the guideline. • New epidemiologic data to Burden of HAV section: A study using nationally representative data found that from 2007 to 2016, HAV susceptibility among nonvaccinated U.S.-born adults aged 20 years or older was approximately 74.1% [Yin, et al. 2020].
Intended users	New York State clinicians in ambulatory settings who provide primary and HIV specialty care for adults who have or are at risk of acquiring hepatitis A virus infection
Lead author	Hector I. Ojeda-Martinez, MD
Writing group	Joseph P. McGowan, MD, FACP, FIDSA; Steven M. Fine, MD, PhD; Rona Vail, MD; Samuel T. Merrick, MD; Asa Radix, MD, MPH, PhD; Christopher J. Hoffmann, MD, MPH; Charles J. Gonzalez, MD
Author and writing group conflict of interest disclosures	None
Date of original publication	August 24, 2018
Committee	Medical Care Criteria Committee
Developer and funder	New York State Department of Health AIDS Institute (NYSDOH AI)
Development process	See Supplement: Guideline Development and Recommendation Ratings
Related NYSDOH AI guideline	Immunizations for Adults With HIV

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Purpose of This Guideline

This guideline on hepatitis A virus (HAV) and HIV coinfection was developed by the New York State Department of Health AIDS Institute (NYSDOH AI). The purpose of this guideline is to inform New York State clinicians about HAV/HIV coinfection, including screening, vaccination, and post-exposure prophylaxis, to accomplish the following:

- Increase the number of individuals in New York State with HIV who are screened and vaccinated against HAV.
- Provide evidence-based recommendations for post-exposure prophylaxis in adults with HIV who experience an HAV exposure.
- Integrate current evidence-based clinical recommendations into the healthcare-related implementation strategies of the Ending the Epidemic initiative, which seeks to end the AIDS epidemic in New York State.

The NYSDOH AI guideline Immunizations for Adults With HIV includes recommendations for HAV vaccination.

Note on "experienced" and "expert" HIV care providers: Throughout this guideline, when reference is made to "experienced HIV care provider" or "expert HIV care provider," those terms are referring to the following 2017 NYSDOH AI definitions:

- Experienced HIV care provider: Practitioners who have been accorded HIV Experienced Provider status by the American Academy of HIV Medicine or have met the HIV Medicine Association's definition of an experienced provider are eligible for designation as an HIV Experienced Provider in New York State. Nurse practitioners and licensed midwives who provide clinical care to individuals with HIV in collaboration with a physician may be considered HIV Experienced Providers as long as all other practice agreements are met (8 NYCRR 79-5:1; 10 NYCRR 85.36; 8 NYCRR 139-6900). Physician assistants who provide clinical care to individuals with HIV under the supervision of an HIV Specialist physician may also be considered HIV Experienced Providers (10 NYCRR 94.2)
- Expert HIV care provider: A provider with extensive experience in the management of complex patients with HIV.

Burden of HAV

The total annual reported cases of HAV in the United States decreased consistently between 2000 (13,397 cases) and 2014 (1,239 cases), with the decline attributed to the inclusion of HAV vaccination in the recommended pediatric immunization panels for children aged 2 to 18 years [CDC 2018]. Since 2014, however, the number of cases reported in the United States has increased, reaching 12,474 in 2018 [CDC 2022]. In 2017 and 2018, outbreaks among people who use drugs, homeless people, and men who have sex with men (MSM) contributed to substantial increases in the reported cases of HAV. A study using nationally representative data found that from 2007 to 2016, HAV susceptibility among nonvaccinated U.S.-born adults aged 20 years or older was approximately 74.1% [Yin, et al. 2020].

In 2019, the NYSDOH issued an advisory on increases in HAV infection and noted the following:

- In New York State (excluding New York City) the annual number of reported HAV cases (2,019) represented a 235% increase between 2016 and 2018 [NYSDOH 2019].
- People at high risk for HAV infection are those who use injection or noninjection drugs, have unstable housing or are homeless, are or were recently incarcerated, and who are MSM [NYSDOH 2019].
- In New York City, the number of reported HAV cases increased 64% from 2018 to 2019, with the increase largely due to outbreaks among MSM [NYCDOHMH 2020].

Transmission and Prevention

☑ RECOMMENDATIONS

Pre-Exposure Vaccination

- Clinicians should obtain an HAV IgG antibody measurement for all individuals with HIV [a] and should administer the HAV vaccine to those who are HAV antibody-negative, regardless of CD4 count.
- Clinicians should administer the 2-dose anti-HAV vaccine series, with the initial dose followed 6 to 12 months later to ensure maximal antibody response [b]. (A1)
- Clinicians should obtain a post-vaccination HAV IgG antibody measurement at least 1 month after final dose in patients who are at increased risk for HAV-related morbidity and mortality. (B3)

Post-Exposure Immune Globulin

- Clinicians should administer a single dose of immune serum globulin (as a 0.1 mL/kg intramuscular injection) as HAV post-exposure prophylaxis to susceptible patients with HIV within 2 weeks of an exposure to close personal contacts with serologically confirmed HAV infection (i.e., through a blood test), including:
  - Household and sexual contacts (A2)
  - Individuals who have shared illicit drugs with someone with HAV (A2)
- Patients for whom HAV vaccination is also indicated should receive the HAV vaccine concurrently with immune serum globulin to protect against future infection.
- Clinicians must report all suspected or confirmed HAV infections to the local health department of the area where the patient resides according to New York State requirements (also see NYSDOH Communicable Disease Reporting Requirements).
  - Infections that occur among food handlers or in other settings that pose a high risk of transmission are immediately reportable by telephone to the local health department.

Abbreviations: CDC, Centers for Disease Control and Prevention; HAV, hepatitis A virus; IgG, immunoglobulin G.

Notes:

a. Citing the missed opportunity to vaccinate a patient when available and the possible prolonged risk of exposure to HAV, the CDC no longer recommends deferring HAV vaccination in patients with a CD4 count <200 cells/mm^3 [CDC 2022].
b. The HAV vaccine at the age-appropriate dose is preferred over immune globulin; however, for optimal protection, adults aged >40 years, immunocompromised people, and people with chronic liver disease or other chronic medical conditions planning to depart to an area with a high HAV transmission rate in <2 weeks should receive the initial dose of vaccine along with immune globulin (0.1 mL/kg) at a separate injection site. For additional information regarding HAV vaccination for travelers, see CDC Health Information for International Travel > Travel-Related Infectious Diseases: Hepatitis A.

Transmission

The modes of HAV transmission are well established: ingestion of contaminated water and food, such as raw clams or oysters; oral-anal contact; person-to-person spread via fomites, such as shared utensils or bath towels; or, very rarely, blood or blood product transfusion. In the last few years, HAV outbreaks have largely been attributed to foodborne transmission and close person-to-person contact with an individual with HAV [CDC 2022].

Men who have sex with men (MSM) and individuals who use drugs are at increased risk for HAV infection, and data from the National Health and Nutrition Examination Survey 2007 to 2016 indicate that, among adults born in the United States aged ≥20 years, the prevalences of HAV susceptibility and nonvaccination, respectively, were 67.5% and 65.2% among MSM and 72.9% and 73.1% among individuals who reported injection drug use [Yin, et al. 2020].

Pre-Exposure Vaccination

All adults with HIV should receive an HAV IgG test, and those who are antibody-negative should be vaccinated against HAV [Nelson, et al. 2020].

Infection with HAV can be prevented by active immunization before exposure with either of the 2 currently licensed vaccines, which are considered equivalent in efficacy. HAV vaccines are highly immunogenic in immunocompetent adults, with >95% seroconversion. However, the seroconversion rates and the geometric mean serum antibodies in individuals with HIV are lower than in those without HIV, with response rates from 50% to 95% [Mena, et al. 2013; Shire, et al. 2006; Weissman, et al. 2006; Rimland and Guest 2005; Wallace, et al. 2004; Kemper, et al. 2003]. HAV vaccine appears to have no effect on the course of HIV infection or on plasma HIV viral load. A combined HAV and hepatitis B virus vaccine is also available and can be used in people susceptible to both hepatitis A and B. It is given in three total doses at 0, 1, and 6 months.

Administration of HAV vaccine is recommended for all adults with HIV regardless of CD4 count. An effective antibody response may not occur in up to 15% of immunocompromised patients [Mena, et al. 2013; Wallace, et al. 2004]. This committee recommends follow-up HAV antibody testing for patients who are at increased risk for HAV-related morbidity and mortality (see above) to verify vaccine efficacy and to identify those who should be counseled to avoid infection because of continued susceptibility.

Post-Exposure Immune Globulin

Immune serum globulin is the recommended HAV post-exposure prophylaxis for patients with HIV and should be given to individuals who are susceptible to HAV infection within 2 weeks after an exposure to an HAV-infected household contact, sexual partner, or needle-sharing partner [CDC 2022; ACIP 2007]. Consideration should also be given to patients with HIV who are providing other types of ongoing, close personal contact with someone with HAV (e.g., a regular babysitter or caretaker) [CDC 2022; ACIP 2007]. A single dose of 0.1 mL/kg intramuscularly is effective in preventing infection or attenuating HAV infection that might result from such an exposure [Nelson 2017]. Concurrent administration of HAV vaccine with immune serum globulin is indicated for individuals at risk for future infection (see above).

Management of HAV/HIV Coinfection

☑ RECOMMENDATION

Management of HAV/HIV Coinfection

- Whenever possible, ART should not be interrupted in patients with HIV/HAV coinfection; when interruption of ART is indicated for management of severe or fulminant liver disease, clinicians should consult with a care provider experienced in the treatment of hepatitis and HIV. (A3)

Abbreviations: ART, antiretroviral therapy; HAV, hepatitis A virus.

Morbidity and mortality: The incubation period of HAV infection averages 28 days (range, 15 to 50 days). Although HAV does not cause chronic hepatitis, it is not a benign disease; the morbidity in adults is substantial. Young children tend to have asymptomatic or minimally symptomatic disease, whereas older children and adults have more severe illness, with jaundice

occurring in approximately 70% of cases [Cuthbert 2001]. Approximately 40.8% of patients with reported cases of acute HAV required hospitalization in 2013 [CDC 2015]. Overall case fatality is low, ranging from 0.3% to 0.6% for all ages and up to 1.8% among adults aged >50 years [CDC 2015].

→ KEY POINT

- Currently, no specific treatment is available for HAV, although infection can be prevented by both pre-exposure vaccination and post-exposure serum immune globulin administration.

Coinfection: HAV does not cause more severe clinical illness in people with HIV than in people without. Patients with HIV may have significantly higher HAV viral load levels and significantly prolonged durations of HAV viremia than people who do not have HIV [Gallego, et al. 2011], which may result in a prolonged duration of risk of HAV transmission to others.

Maintain ART: Patients with HIV and acute HAV infection rarely require even temporary interruption of ART. Cessation of ART should be avoided whenever possible because of the potential long-term consequences, such as reduced viral suppression when ART is reinstituted [El-Sadr, et al. 2008; Lutwick 1999]. In the rare instances when interruption of ART is indicated for management of fulminant liver disease, clinicians should consult with a care provider experienced in the treatment of hepatitis and HIV.

All Recommendations

☑ ALL RECOMMENDATIONS: PREVENTION AND MANAGEMENT OF HEPATITIS A VIRUS INFECTION IN ADULTS WITH HIV

Pre-Exposure Vaccination

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References

ACIP. 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(41):1080-84. [PMID: 17947967] https://pubmed.ncbi.nlm.nih.gov/17947967

CDC. Surveillance for viral hepatitis – United States, 2013. 2015 May 31. https://www.cdc.gov/hepatitis/statistics/2013surveillance/index.htm [accessed 2021 Mar 19]

CDC. Surveillance for viral hepatitis – United States, 2016. 2018 Apr 16. https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm [accessed 2021 Mar 19]

CDC. Hepatitis A outbreaks in the United States. 2022 Jan 19. https://www.cdc.gov/hepatitis/outbreaks/hepatitisaoutbreaks.htm [accessed 2021 Mar 19]

Cuthbert JA. Hepatitis A: old and new. *Clin Microbiol Rev* 2001;14(1):38-58. [PMID: 11148002] https://pubmed.ncbi.nlm.nih.gov/11148002

El-Sadr WM, Grund B, Neuhaus J, et al. Risk for opportunistic disease and death after reinitiating continuous antiretroviral therapy in patients with HIV previously receiving episodic therapy: a randomized trial. *Ann Intern Med* 2008;149(5):289-99. [PMID: 18765698] https://pubmed.ncbi.nlm.nih.gov/18765698

Gallego M, Robles M, Palacios R, et al. Impact of acute hepatitis A virus (HAV) infection on HIV viral load in HIV-infected patients and influence of HIV infection on acute HAV infection. *J Int Assoc Physicians AIDS Care (Chic)* 2011;10(1):40-42. [PMID: 21368013] https://pubmed.ncbi.nlm.nih.gov/21368013

Kemper CA, Haubrich R, Frank I, et al. Safety and immunogenicity of hepatitis A vaccine in human immunodeficiency virus-infected patients: a double-blind, randomized, placebo-controlled trial. *J Infect Dis* 2003;187(8):1327-31. [PMID: 12696015] https://pubmed.ncbi.nlm.nih.gov/12696015

Lutwick LI. Clinical interactions between human immunodeficiency virus and the human hepatitis viruses. *Infect Dis Clin Pract* 1999;8(1):9-20. https://journals.lww.com/infectdis/Fulltext/1999/01000/CLINICAL_INTERACTIONS_BETWEEN_HUMAN.3.aspx

Mena G, García-Basteiro AL, Llupià A, et al. Factors associated with the immune response to hepatitis A vaccination in HIV-infected patients in the era of highly active antiretroviral therapy. *Vaccine* 2013;31(36):3668-74. [PMID: 23777950] https://pubmed.ncbi.nlm.nih.gov/23777950

Nelson NP. Updated dosing instructions for immune globulin (human) GamaSTAN S/D for hepatitis A virus prophylaxis. *MMWR Morb Mortal Wkly Rep* 2017;66(36):959-60. [PMID: 28910270] https://pubmed.ncbi.nlm.nih.gov/28910270

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(5):1-38. [PMID: 32614811] https://pubmed.ncbi.nlm.nih.gov/32614811

NYCDOHMH. Hepatitis A, B, and C in New York City: 2019 annual report. 2020 Dec. https://hepfree.nyc/wp-content/uploads/2020/12/Viral-Hep-2019-Annual-Report_Final_Web.pdf [accessed 2021 Mar 24]

NYSDOH. Health advisory: outbreak of hepatitis A virus. 2019 Dec 12. https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_a/docs/2019-12-12_health_advisory.pdf [accessed 2021 Mar 19]

Rimland D, Guest JL. Response to hepatitis A vaccine in HIV patients in the HAART era. *AIDS* 2005;19(15):1702-4. [PMID: 16184045] https://pubmed.ncbi.nlm.nih.gov/16184045

Shire NJ, Welge JA, Sherman KE. Efficacy of inactivated hepatitis A vaccine in HIV-infected patients: a hierarchical bayesian meta-analysis. *Vaccine* 2006;24(3):272-79. [PMID: 16139398] https://pubmed.ncbi.nlm.nih.gov/16139398

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(8):1207-13. [PMID: 15486846] https://pubmed.ncbi.nlm.nih.gov/15486846

Weissman S, Feucht C, Moore BA. Response to hepatitis A vaccine in HIV-positive patients. *J Viral Hepat* 2006;13(2):81-86. [PMID: 16436125] https://pubmed.ncbi.nlm.nih.gov/16436125

Yin S, Barker L, Ly KN, et al. Susceptibility to hepatitis A virus infection in the United States, 2007-2016. *Clin Infect Dis* 2020;71(10):e571-79. [PMID: 32193542] https://pubmed.ncbi.nlm.nih.gov/32193542

Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B. Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.