October 2023



## **Hepatitis A Basics**

# Infectious agent

Hepatitis A is an acute, self-limiting viral illness caused by infection with hepatitis A virus (HAV). HAV infection is associated with abrupt onset of fever, malaise, jaundice, anorexia, nausea, abdominal discomfort, and dark urine that typically lasts less than 2 months, although 10% to 15% of symptomatic people have prolonged or relapsing disease that lasts as long as 6 months.

Development of clinical symptoms is highly age dependent. Among older children and adults, infection is usually symptomatic, and 70% present with jaundice. In children less than six years of age, 70% of infections are asymptomatic. Older persons and persons with chronic liver disease are more likely to have severe disease and HAV prevention in these groups is particularly important.

#### **Modes of transmission**

HAV is very contagious. It is spread when someone unknowingly ingests fecal material through close personal or sexual contact with an infected person, consuming contaminated food or drink, or by putting contaminated hands or objects in the mouth. HAV is rarely transmitted by blood (e.g., via transfusion) or saliva.

# **Hepatitis A infectious period**

Peak infectious period is 2 weeks prior to onset of jaundice (or elevated ALT) through 1 week after jaundice onset. In the absence of jaundice, onset of symptoms should be used to calculate infectious period. Children and infants may excrete virus longer than adults.

# **Hepatitis A incubation period**

The incubation period is 15-50 days, with a mean of 28 days.

# **Hepatitis A case definition**

Clinical description:

Acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine)

#### **AND**

Jaundice or elevated total bilirubin levels >3.0 mg/dL

# OR

Elevated serum alanine aminotransferase (ALT) levels >200 IU/L

## AND

The absence of a more likely diagnosis.

#### Confirmatory laboratory evidence:

- Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive
  - Nuclaic acid amplification tost

 Nucleic acid amplification test (NAAT, such as polymerase chain reaction [PCR] or genotyping) for HAV RNA positive

# Confirmed case definition:

A case that meets the clinical case criteria and is IgM positive\*

#### OF

· Has hepatitis A virus RNA detected by NAAT (such as PCR or genotyping)

#### OR

• Meets the clinical criteria and occurs in a person who had contact (e.g., household or sexual) with a laboratory-confirmed HAV case 15-50 days prior to onset of symptoms (epidemiologic linkage).

# Criteria to distinguish a new case from an existing case:

Hepatitis A infection is usually self-limiting and does not result in chronic infection. However, 10-15% of persons with hepatitis A may experience a relapse during the 6 months after acute illness. Cases of relapsing hepatitis A should not be counted as new cases.

# **Hepatitis A Laboratory Testing**

Acute HAV infection is confirmed by the presence of IgM anti-HAV in serum. IgM anti-HAV is detectable 5 to 10 days before the onset of symptoms and can persist for up to 6 months. It is also occasionally detectable in adults 2 weeks after receiving HAV vaccine. IgG anti-HAV is detectable shortly after the appearance of IgM and is lifelong (Figure 1). A single total anti-HAV or IgG anti-HAV test does not have diagnostic value for acute infection.

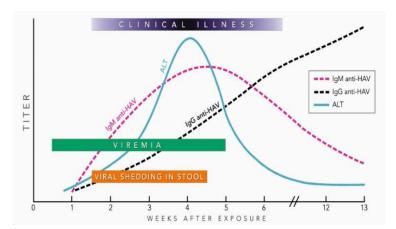


Figure 1: Immunologic and clinical events associated with hepatitis A virus infection and recovery. Source: CDC.

## False positive IgM anti-HAV

A positive IgM anti-HAV test result in a person without typical symptoms of HAV may indicate:

- A false-positive test result (this is common)
- Asymptomatic acute HAV infection
- Previous HAV infection with persistent IgM

Because of the risk of false positive results, IgM anti-HAV testing should be limited to persons with evidence of clinical hepatitis and should not be used as a screening tool or as part of testing panels in the workup of nonacute liver function abnormalities.

Public health actions such as postexposure prophylaxis (PEP) should generally not be undertaken in situations where the clinical criteria of the case definition are not met. In situations of high concern where a positive HAV IgM is received but the clinical criteria are not met, repeat IgM anti-HAV testing and/or HAV PCR testing

<sup>\*</sup> And is not otherwise ruled out by PCR testing for hepatitis A virus performed in a public health laboratory.

at the CDPH Viral and Rickettsial Diseases Laboratory (VRDL) may be helpful for public health decision-making.

# Hepatitis A PCR testing and genotyping

The CDPH VRDL and some local public health laboratories (PHL) can perform HAV PCR testing. CDPH VRDL also offers genotyping. Please inquire with your local PHL where to submit specimens for molecular testing for case-patients who meet the case definition and who use illicit drugs, are experiencing homelessness, are men who have sex with men (MSM) or have no known HAV risk factor. Other risk categories might be of interest and specimens may be submitted in consultation with VPD Epidemiology.

Specimens can be submitted using the <u>VRDL General Purpose Specimen Submittal Form</u>. Please see <u>CDPH HAV</u> <u>testing guidance</u> for additional information.

#### Contacts

#### Close contact definition

Household and sexual contacts, people who share drugs, childcare center staff or attendees, and others with ongoing close contact.

## Risk for HAV transmission in different settings

HAV transmission risk varies by setting. Household secondary attack rates are 15-30%; higher rates of transmission are associated with infected children. In contrast, attack rates are low among restaurant patrons who have been exposed to infected food handlers.

# Food service settings

HAV-infected food handlers should be excluded for 1 week after onset of jaundice (or if no jaundice, onset of symptoms). If asymptomatic, use time of peak ALT. Potentially exposed food handlers in the same setting should be offered PEP.

Because transmission to patrons is unlikely, PEP is not routinely indicated for food service patrons, but may be considered if, while infectious, the food handler:

- directly handled (without gloves) uncooked or cooked foods or beverages
- had diarrhea or poor hygienic practices at work<sup>†</sup>
- patrons can be identified and treated no later than 2 weeks after exposure (see algorithm on page 7).

**Note:** If repeated exposures might have occurred (e.g., in an institutional cafeteria), stronger consideration of PEP for patrons may be warranted.

In a common source outbreak, PEP is not indicated for exposed persons after cases have begun to occur, because the 2-week period during which PEP is known to be effective will have been exceeded. If a common source is suspected in 2 or more cases, please contact the Immunization Branch (IZB) Epidemiology to discuss specimen genotyping.

Healthcare settings

PEP is not routinely indicated for staff who have provided care for an HAV-infected patient. When providing

<sup>&</sup>lt;sup>†</sup> Hygiene assessments are subjective; a visit to the food handling area and interviews with the infected food handler, coworkers, and supervisors are often helpful. Additional factors include availability of hand washing facilities, hygiene training, previous assessments of sanitation practices in the facility, and the presence of medical conditions in the infected food handler that might make hygiene more difficult to maintain.

care for HAV-infected patients, contact precautions are recommended (in addition to standard precautions) for diapered and incontinent patients for at least 1 week after symptom onset. PEP is indicated for persons who have had close contact with HAV cases if an epidemiological investigation indicates that HAV transmission has occurred among patients or between patients and staff.

## Childcare settings

Exclude HAV-infected childcare staff and attendees for 1 week after onset of jaundice (or if no jaundice, onset of symptoms). If asymptomatic, use time of peak ALT. PEP is indicated for previously unvaccinated staff/attendees if a case of HAV is diagnosed in staff/attendees or if HAV cases are diagnosed in 2 or more households of attendees. Because infections in children are usually mild or asymptomatic, clusters in daycares often are identified only when adult contacts (e.g., parents) become ill.

# Schools and other work settings

PEP is not routinely indicated when a single HAV case occurs in elementary or secondary schools or work settings other than those specified above. PEP is indicated for persons who have close contact with cases if an epidemiological investigation indicates that transmission has occurred among students at a school.

# Exposed susceptible pregnant people

Pregnant people who become infected with hepatitis A have an increased risk of gestational complications and preterm labor. Pregnant people should receive PEP for the same indications as nonpregnant people. It may be reasonable to offer IG in addition to vaccine for PEP, particularly if the person is a household contact or sexual contact of a case. There has been no observed increase in maternal or infant adverse events after hepatitis A vaccination or IG administration in pregnancy. Because HAV vaccine is produced from inactivated HAV, the risk to the fetus is expected to be low.

# Incompletely immunized people

Most persons have protective levels of antibody after one dose of HAV vaccine. Persons who have had one prior dose of vaccine may receive their second dose if it has been at least 6 months since their first dose.

## **Hepatitis A Postexposure Prophylaxis (PEP)**

All nonimmune people who are exposed to hepatitis A virus (HAV) and have not been previously infected or vaccinated should receive PEP within 14 days after the date of last exposure. PEP should be given as soon as possible during the appropriate time window.

#### **PEP recommendations**

Persons > 12 months of age, regardless of pre-existing medical conditions, SHOULD receive a dose of single-antigen HAV vaccine. In addition to vaccine, a dose of intramuscular (IM) immune globulin (IG) (0.1 mL/kg¹) MAY also be administered to people > 40 years of age based on the provider's risk assessment.

<sup>&</sup>lt;sup>1</sup> In July 2017, the recommended dose for IMIG (GamaSTAN®) for HAV pre- and post-exposure prophylaxis was increased by the manufacturer due to declining HAV antibody levels in the U.S. blood supply. IMIG (GamaSTAN®) is available in 2 mL and 10 mL single use vials. One source of IG is FFF Enterprises, which can be reached 24/7 at: 1-800-843-7477.

Persons >12 months of age who have chronic liver disease and/or are immunocompromised<sup>2</sup> SHOULD receive a dose of intramuscular immune globulin (IMIG) (0.1 mL/kg<sup>1</sup>) and a dose of HAV vaccine.
 Infants <12 months of age and/or persons who are allergic to a vaccine component SHOULD receive intramuscular immune globulin (IMIG) (0.1 mL/kg<sup>1</sup>) instead of HAV vaccine.

If an LHD has concerns regarding IG administration, contact the CDPH Immunization Branch.

Persons receiving both vaccine and IG for post-exposure prophylaxis may receive them simultaneously, or they may receive whichever product is available first and the second product when it is available, providing it is administered within the 14-day PEP window. Vaccine and IG should be administered at anatomically distant sites (such as different limbs). Vaccine should be given in addition to IG to potentially provide longer-term protection for immunosuppressed persons, but vaccine response may be limited. Clinical guidance should be obtained if patient's immune status is unclear.

The efficacy of combined HAV/HBV vaccine (Twinrix®) for PEP has not been studied and it is not recommended for PEP.

Local health departments and medical providers may wish to evaluate the likelihood and intensity of HAV exposure (e.g., possible commercial food exposure vs. known household or sexual contact) when making decisions and recommendations about PEP regimens.

For more information about the hepatitis A vaccine and hepatitis A post-exposure prophylaxis, please refer to the 2020 ACIP recommendations.

Administration of HAV vaccine with other vaccines

HAV vaccine may be administered simultaneously with other routine and travel vaccines.

Persons exposed to HAV >2 weeks prior to consult

The efficacy of PEP when given >2 weeks of exposure is unknown. IG is not recommended >2 weeks after exposure, but vaccine may be given to susceptible people at any time to protect against future exposures.

## Pediatric vs. adult formulations of HAV vaccine

Single-antigen HAV vaccines are available in a pediatric formulation containing half the dose and volume of the adult formulation. When the adult formulation is unavailable, adults may be given two doses of the same

- with combined primary immunodeficiency disorder (e.g., severe combined immunodeficiency);
- who are receiving cancer chemotherapy;
- on treatment for ALL within and until at least 6 months after completion of immunosuppressive chemotherapy;
- within 2 months after solid organ transplantation;
- who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer in patients who have developed graft-versus-host disease;
- with HIV infection with a CD4 T-lymphocyte count <200 cells/mm3 (age >5 years) and percentage <15 (all ages) (some experts include HIV-infected persons who lack recent confirmation of immunologic status or measles immunity);
- receiving daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or
  equivalent for ≥14 days; or receiving certain biologic immune modulators, such as a tumor necrosis factor-alpha (TNF-α)
  blocker or rituximab</li>

<sup>&</sup>lt;sup>2</sup> Although the CDC HAV guidance does not provide a definition of immunocompromised, IDSA guidance defines patients with high-level immunosuppression as those:

pediatric HAV vaccine (2 pediatric doses = 1 adult dose).

For more information about IMIG

GamaSTAN® is the only U.S. IMIG product. More information can be found on the <u>GamaSTAN® product</u> website.

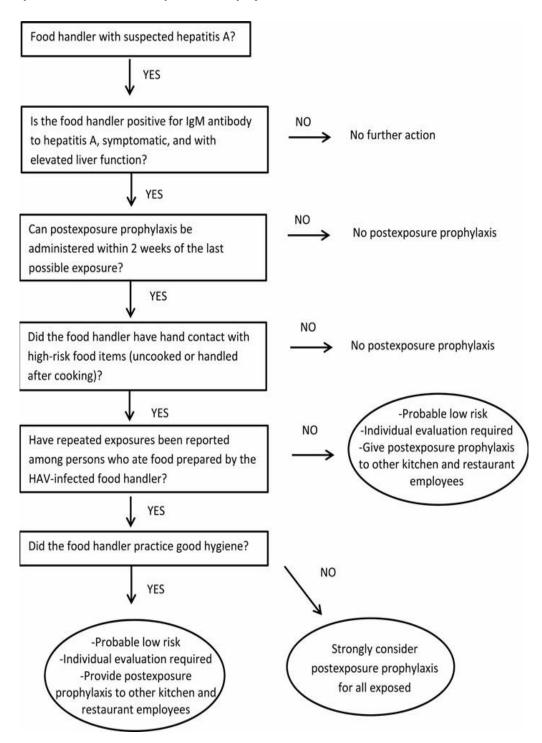
## **Hepatitis A Pre-exposure Prophylaxis**

Susceptible persons traveling to countries with high or intermediate HAV endemicity (See a <u>list of regions</u> where Hepatitis A is endemic) should be vaccinated or receive intramuscular immune globulin (IMIG) (0.1 mL/kg) before travel. A first dose of single-antigen HAV vaccine given up to the date of departure should protect most healthy persons.

In addition to HAV vaccine, IG may be considered before travel for persons with increased risk for complications in the event of HAV infection, such as immunocompromised people and people with liver disease. IG may also be considered in addition to vaccine for people >40 years of age based on the provider's risk assessment.

Infants aged 6-11 months should receive HAV vaccine before travel to high or intermediate HAV endemic countries, but the dose should not be counted towards the routine 2-dose series. Infants <6 months of age, and those for whom vaccine is contraindicated, should receive IG. IG dosing varies by duration of travel. See <a href="CDC hepatitis A prophylaxis guidance">CDC hepatitis A prophylaxis guidance</a> for specifics.

Figure 2: Algorithm Used by New York City Department of Health and Mental Hygiene to Determine the Need for Hepatitis A Virus Postexposure Prophylaxis of Restaurant Patrons<sup>‡</sup>.



<sup>&</sup>lt;sup>‡</sup> From: Ridpath A, et al. Hepatitis A Cases among Food Handlers: A Local Health Department Response—New York City, 2013. J Public Health Manag Pract. 2017;23(6):571-76. Adapted from: Fiore AE. Hepatitis A Transmitted by Food. Clin Infect Dis. 2004;38:705-15 and Carl M, et al. Foodborne Hepatitis A: Recommendations for Control. J Infect Dis. 1983;148:1133-1135.