

Chapter 3: Hepatitis A

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I. Disease Description

Hepatitis A is caused by infection with hepatitis A virus (HAV), a non-enveloped RNA virus that is classified as a picornavirus. HAV was first identified by immune electron microscopy in 1973 and initially replicated in mammalian cell culture in 1979.^{1,2} Humans are the only natural host, although several nonhuman primate species have been infected in laboratory settings.^{3–6} Depending on conditions, HAV can be stable in the environment for months.⁷ The virus is relatively stable at low pH levels and freezing to moderate temperatures, but can be inactivated by high temperature (185°F [85°C] or higher for one minute) or through disinfection of surfaces with a 1:100 dilution of sodium hypochlorite in water.^{8,9}

Transmission and symptomology

Hepatitis A is typically acquired through fecal-oral transmission, either from direct person-to-person contact or consumption of contaminated food or water. HAV replicates in the liver, is excreted in bile, and is shed in the stool of infected people in high concentrations 2–3 weeks before and 1 week after onset of illness.¹⁰ Peak infectivity occurs during the 2 weeks prior to onset of clinical signs and symptoms (jaundice or elevated liver enzymes). Most persons cease to be infectious 1 week after jaundice appears.¹¹ Although virus is present in serum of an infected person, its concentration is several orders of magnitude less than in feces. Infected children and infants may excrete virus longer than adults.^{12,13}

The mean incubation period of hepatitis A is approximately 28 days (range 15–50 days). Symptomatic hepatitis A infection is clinically indistinguishable from other types of acute viral hepatitis, but is usually mild and self-limited. Fulminant hepatic failure occurs in less than 1% of cases.¹⁴ The likelihood of symptomatic illness from HAV infection is directly related to age. In children younger than 6 years of age, most (70%) infections are asymptomatic.¹⁵ In older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients.^{15,16} Clinical manifestations vary, but may include the abrupt onset of fever, malaise, anorexia, nausea, and abdominal discomfort, followed within a few days to a week by dark urine, pale stools, and jaundice.¹⁵ Clinical illness usually resolves within 2–3 months (85% of cases), and complete recovery is seen within 6 months for nearly all cases.¹⁷ However, up to 10% of persons with hepatitis A experience a biochemical and/or clinical relapse during the 6 months after acute illness.¹⁸ Virus may be excreted in stool during a relapse.¹⁹ Consequently, persons experiencing relapsing hepatitis A should be considered infectious. There is no specific treatment for hepatitis A. Disease is usually self-limiting and treatment and management of HAV infection are supportive. HAV infection does not result in chronic infection or chronic liver disease. However, HAV infection can complicate chronic liver disease.

II. Background

Prevalence

Population-based seroprevalence surveys play a critical role in the development of vaccination policies by supplementing data systems that monitor disease incidence, vaccination coverage, and vaccine adverse events. In the United States, seroprevalence is monitored by the National Health and Nutrition Examination Survey (NHANES). NHANES is conducted by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics and obtains nationally representative data on the health and nutritional status of the non-institutionalized, civilian U.S. population. Before the availability of vaccine in 1995, seroprevalence of antibody to hepatitis A virus (anti-HAV) in the population solely reflected prior infection. Currently, seroprevalence can reflect immunity due to either previous infection or to vaccination. In US-born persons ≥ 2 years of age, the overall anti-HAV prevalence was 27.5% (95%



confidence interval (CI) 25.8–29.2%) in 1999–2006 and increased to 31.2% (95% CI 29.5–33.0%) in 2007–2012.²⁰ However, in US-born persons ≥ 20 years of age, there was a significant decrease among adults in the overall age-adjusted prevalence of anti-HAV from 1999–2006 (29.5%) to 2007–2012 (24.2%).²⁰ These anti-HAV prevalence estimates suggest that a substantial proportion of the U.S. adult population remains susceptible to hepatitis A at ages when risk of morbidity and mortality from HAV infection is highest. Among US-born adults ≥ 20 years of age, older age, race/ethnicity other than non-Hispanic white, lower income, less education, and any health insurance coverage were significantly associated with anti-HAV positivity during 2007–2012.²⁰ Lower prevalence of immunity among adults increases the possibility of susceptible population clusters of adults at risk leading to outbreaks; examples of these occurrences are well documented in the European Union.²¹ Additionally, a 2013 hepatitis A outbreak in the United States associated with frozen pomegranate arils imported from Turkey involved 165 identified case-patients; of these, 154 (93%) were adults 18 years of age or older.²² Prevention of secondary transmission of HAV in the United States comes at an enormous public health cost, in large part due to the number of persons offered prophylaxis.²³

Risk factors

The distribution of risk behaviors and exposures among hepatitis A cases has changed dramatically in the United States since implementation of hepatitis A vaccination. During 1983–1995, data from the Sentinel Counties Study identified international travel as a minor source (4%) of infection among hepatitis A cases.²⁴ In sites conducting enhanced hepatitis surveillance during 2005–2007, however, the most frequent (46%) potential source of infection among reported hepatitis A cases was travel outside the United States and Canada. These cases mostly reflected persons who traveled, but also included some persons who were exposed to a traveler without having traveled themselves.²⁵ Although data are limited, current risk factors are similar today. In 2014, only 7% of hepatitis A cases reported in the United States had an identified risk factor; the remaining 93% of cases either had no identified risk factors or were missing data on risk factors entirely.²⁶ Based on the cases with an identified risk factor, international travel continues to be the most frequently identified risk factor.²⁶ Other potential sources of infection identified among hepatitis A cases in 2014 included contact with a hepatitis A patient, being an employee or child in a daycare center, injection drug use, being a man who has sex with men, or exposure during a common-source (food- or water-borne) outbreak. Food-borne hepatitis A outbreaks are of increasing concern globally.²⁷

III. Importance of Rapid Identification

Rapid identification and prompt reporting of cases of hepatitis A are important because post-exposure prophylaxis, administered within 2 weeks after exposure, is highly efficacious and can prevent development of symptomatic illness in exposed persons and prevent further transmission to other persons. Contacts of infected persons are eligible to receive post-exposure prophylaxis within 2 weeks of exposure; the efficacy of hepatitis A post-exposure prophylaxis has not been established beyond this timeframe.

IV. Importance of Surveillance

The main goals of hepatitis A surveillance are to:

1. detect and provide data to control outbreaks;
2. identify contacts of case-patients who require post-exposure prophylaxis;
3. characterize changes in the epidemiology of infected populations and risk factors; and
4. guide vaccination policies and other prevention efforts.

Surveillance depends heavily on laboratory-initiated reporting of positive markers of hepatitis A. Persons with positive test results are investigated using traditional, notifiable diseases methods in most health departments in the United States. Hepatitis A case investigations can be labor intensive. As a result, providers should be discouraged from using immunoglobulin M (IgM) anti-HAV as a screening tool or as part of testing panels in workups of non-acute liver function abnormalities, since IgM screening of non-acute, abnormal liver function tests may result in a high percentage of false-positive IgM results.²⁸ Adherence to this practice will limit the need for health departments to conduct investigations of persons who are unlikely to have acute HAV infection.

Routine surveillance can supplement case notifications using seroprevalence surveys and administrative data. Additionally, electronic medical records, with coded clinical and laboratory criteria, hold promise as a means to improve completeness and timeliness of symptomatic hepatitis A infection identification.

V. Disease Reduction Goals

Healthy People 2020 disease reduction goals have been established for achieving the prevention of HAV transmission in the United States.²⁹

IID–23: Reduce hepatitis A.

Baseline: 1.0 cases of hepatitis A virus per 100,000 population were reported in 2007.

Target: Reduce the rate of incident hepatitis A to 0.3 cases per 100,000 population.

In 2014, 21 states (42%) had met the *Healthy People 2020* hepatitis A reduction goal.²⁹

VI. Case Definition

The following surveillance case definition for hepatitis A was adopted by the Council of State and Territorial Epidemiologists (CSTE) in 2018. Current and previous hepatitis A case definitions are available at: <https://www.cdc.gov/nndss/conditions/hepatitis-a-acute/>

Clinical description

An 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

- a) jaundice, or elevated total bilirubin levels ≥ 3.0 mg/dl, OR
- b) elevated serum alanine aminotransferase (ALT) levels >200 IU/L,

AND

- c) the absence of a more likely diagnosis

Laboratory criterion for diagnosis:

Confirmatory laboratory evidence

- Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive,
- OR**
- Nucleic acid amplification test (NAAT: such as polymerase chain reaction [PCR] or genotyping) for hepatitis A virus RNA positive

Epidemiologic linkage

Contact (e.g., household or sexual) with a laboratory-confirmed hepatitis A case 15–50 days prior to onset of symptoms.

Case classification

Confirmed:

- A case that meets the clinical criteria and is IgM anti-HAV positive[‡], OR
 - A case that has hepatitis A virus RNA detected by NAAT (such as PCR or genotyping),
- OR**
- A case that meets the clinical criteria and occurs in a person who had contact (e.g., household or sexual) with a laboratory-confirmed hepatitis A case 15–50 days prior to onset of symptoms.

[‡] And not otherwise ruled out by IgM anti-HAV or NAAT for hepatitis A virus testing performed in a public health laboratory.

VII. Laboratory Testing

Specimen collection

Specimen collection and shipping are important steps in obtaining laboratory diagnosis or disease confirmation. Guidelines have been published for specimen collection and handling of microbiologic agents. Information is also available on using CDC laboratories as support for reference and disease surveillance; this includes:

- a central website (<https://www.cdc.gov/laboratory/specimen-submission/index.html>) for requesting lab testing;
- the form required for submitting specimens (<https://www.cdc.gov/laboratory/specimen-submission/form.html>) to CDC (See Appendix 23, Form # CDC 50.34);
- information on general requirements for shipment of etiologic agents (Appendix 24 <https://www.cdc.gov/vaccines/pubs/surv-manual/appx/appendix24-etiological-agent.pdf>); and
- the CDC Infectious Diseases Laboratories Test Directory (<https://www.cdc.gov/laboratory/specimen-submission/list.html>), which provides an online test directory that contains not only a list of orderable tests for that institution, but also detailed information on appropriate specimen types, collection methods, specimen volume, and points of contact.

Serologic testing and CDC laboratory special studies

Diagnostic tests used to confirm hepatitis A virus infection include serologic testing, and occasionally, PCR-based assays to amplify and sequence viral genomes. Refer to Chapter 22, “Laboratory Support for Surveillance of Vaccine-Preventable Diseases” (<https://www.cdc.gov/vaccines/pubs/surv-manual/chpt22-lab-support.html>) for detailed information on laboratory testing for hepatitis A and for specific information on specimen collection and shipment.

VIII. Reporting and Case Notification

Case reporting within a jurisdiction

Each state and territory has regulations and laws governing the reporting of diseases and conditions of public health importance.³⁰ These regulations and laws list the diseases that are to be reported, and describe those persons or institutions responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, daycare and childcare facilities, and other institutions. Detailed information on reportable conditions in each state is available through CSTE.³¹ The Viral Hepatitis Case Report is included as Appendix 6 to serve as a guide for data collection during investigation of reported cases.

Case notification to CDC

Hepatitis A became nationally notifiable as a distinct entity in 1966. State health departments transmit hepatitis A case reports weekly to the National Notifiable Diseases Surveillance System (NNDSS) at CDC. This surveillance system monitors basic demographic information (excluding personal identifiers)—age, race/ethnicity, sex, date of onset, date of report, and county of residence of individual cases in addition to disease-specific information. At CDC, the Division of Viral Hepatitis uses the hepatitis A case reports submitted to NNDSS to develop and disseminate an annual report available at <https://www.cdc.gov/hepatitis/statistics/index.htm>

Incidence rates of hepatitis A disease were high in the 1960s and 1970s (>12 cases per 100,000 population). The last substantial peak in reported hepatitis A rates was in 1995. Since the introduction of effective vaccines in the United States in 1995, and due in large part to progressively expansive recommendations from the Advisory Committee on Immunization Practices (ACIP) issued between 1996 and 2006 (culminating in routine childhood vaccination nationwide), hepatitis A rates in the United States have declined by >96% from 1995 to 2014.^{26,32} In 2014, the overall incidence rate was 0.4 cases per 100,000 population (1,239 cases).²⁶ In 2014, the hepatitis A incidence rate was highest for persons 20–29 years of age (0.55 cases per 100,000 population); the lowest age group incidence rate was among children 0–9 years of age (0.10 cases per 100,000 population).²⁶

The CDC/CSTE hepatitis A surveillance case definition entails a combination of clinical and laboratory criteria. To estimate all new infections, case reports are adjusted for the proportion of asymptomatic cases and surveillance underreporting. In 2014 there were an estimated 2,500 new hepatitis A infections. Notifications for confirmed cases of acute hepatitis A should be sent to CDC using event code 10110 in the NNDSS.³³ Case notification should not be delayed because of incomplete information or lack of confirmation. The state in which the patient resides at the time of diagnosis should submit the case notification to CDC.

IX. Vaccination

For specific information about hepatitis A vaccination, refer to The Pink Book [<https://www.cdc.gov/vaccines/pubs/pinkbook/index.html>], which provides general recommendations, including vaccine use and scheduling, immunization strategies for providers, vaccine content, adverse events and reactions, vaccine storage and handling, and contraindications and precautions.

X. Enhancing Surveillance

Provider education and case investigation

Providers should be educated about the importance of reporting all cases of hepatitis A to their respective health department. A common risk factor identified in persons with acute hepatitis A infection is contact with a previously identified case-patient. Aggressive case investigations of persons with acute disease provide the best opportunity for post-exposure prophylaxis of contacts and for reducing further transmission.

Surveillance and epidemiology staff should routinely investigate suspected cases of viral hepatitis. Basic information that should be routinely collected in the course of a hepatitis A case investigation is described below. Each jurisdiction may have their own protocols for conducting these investigations, and CDC is available to provide support as needed. (<https://www.cdc.gov/hepatitis/contactus.htm>)

Information to collect

Additional information may also be collected at the discretion of the local or state health department.

Basic information should include:

- Demographic information
- Clinical details, including
 - Date of onset of illness
 - Symptoms (i.e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, dark urine, acholic stool, jaundice)
- Laboratory results
- Vaccination status
- Risk factors and occupation
- Contacts for investigation and prophylaxis

Streamlining reporting using electronic methods

Although many surveillance systems still rely on paper and pencil for data collection, use of data from sources such as electronic medical records, electronic case reporting,^{34–40} and clinical laboratory information systems (LIMS) can significantly improve reporting speed, enhance data quality, and reduce workload.

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