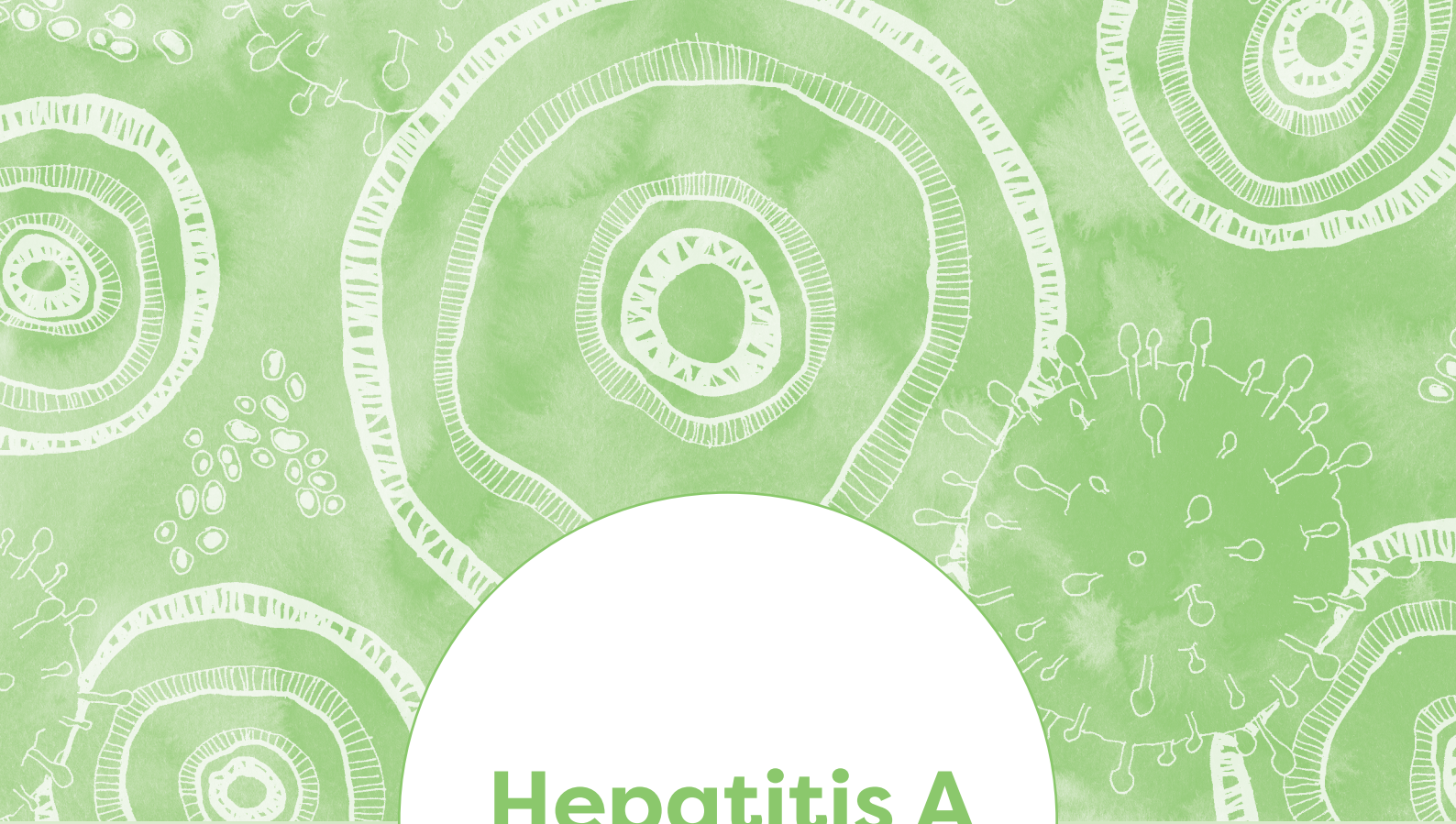




Hepatitis A

Last updated: September 5, 2018

This is a summary of WHO's *Technical considerations and case definitions to improve surveillance for viral hepatitis*, available at http://apps.who.int/iris/bitstream/handle/10665/204501/9789241549547_eng.pdf?sequence=1.



DISEASE AND VACCINE CHARACTERISTICS

The hepatitis A virus (HAV) is transmitted primarily via the faecal/oral route either through ingestion of contaminated food and water or through direct contact with an infectious person. The incubation period is usually 14–28 days, but can be up to 50 days (1). Young children usually have asymptomatic infection, but older children and adults commonly experience symptomatic disease. The clinical manifestations of acute HAV infection are malaise, fatigue, anorexia, vomiting, abdominal discomfort, diarrhea and jaundice, and are indistinguishable from acute hepatitis caused by other viruses. HAV resolves completely in the vast majority of cases but relapses can occur. Rarely, acute liver failure occurs. The estimated case fatality ratio varies with age from 0.1% among children < 15 years of age, to 0.3% among persons 15–39 years of age, to 2.1% among adults aged ≥ 40 years of age. In contrast to hepatitis B and C, HAV does not cause chronic liver disease.

Endemicity of HAV influences how countries implement hepatitis surveillance. High endemic areas are those in which ≥ 90% of children have been infected by 10 years of age, and include much of sub-Saharan Africa and parts of south Asia. High endemic areas tend not to have outbreaks because of the high levels of population immunity conferred by near universal childhood infection. Countries with improving levels of hygiene and sanitation (middle income countries) have transitional endemicity. In these settings, some children will not be infected, leaving some adolescents and adults susceptible to HAV. As the endemicity decreases from

high to transitional endemicity, localized outbreaks become more common. Outbreaks can persist for extended time periods, often occurring within higher-risk communities; these are referred to in this document as community-wide outbreaks. In low or very low endemicity settings, HAV circulation is low and most children are not infected. Infections and symptomatic disease usually occur either in localized foodborne outbreaks or among high-risk groups such as non-immune travelers to endemic countries, men who have sex with men, persons who inject drugs, persons with clotting factor disorders and persons with occupational risk of infection.

HAV vaccines are licensed for use in persons ≥ 12 months of age. Efficacy of two doses is > 94%. WHO recommends that vaccination against hepatitis A be integrated into the national immunization schedule for children aged ≥ 1 year if indicated based on incidence of hepatitis A, change in the endemicity from high to intermediate, and cost-effectiveness. Hepatitis A vaccination is not undertaken in high endemicity countries due to near universal immunity from asymptomatic childhood infections. In transitional endemicity countries, nationwide vaccination might be considered. In low endemicity countries, vaccination is considered for high-risk groups. Surveillance and vaccination against hepatitis A should be part of a comprehensive plan for the prevention and control of viral hepatitis.



RATIONALE AND OBJECTIVES OF SURVEILLANCE

The objectives of hepatitis A surveillance are to:

- detect outbreaks of viral hepatitis (local)
- monitor trends in incidence and identify risk factors for new incident infections (local, national)
- provide data to inform vaccine introduction (national).



TYPES OF SURVEILLANCE RECOMMENDED

MINIMAL SURVEILLANCE

Syndromic surveillance for unspecified acute hepatitis based on clinical signs and symptoms will allow for detection and investigation of outbreaks of viral hepatitis. Syndromic acute hepatitis surveillance is usually national, passive, aggregate and facility-based. Increases in the number of acute hepatitis cases should lead to laboratory testing, preferably for all hepatitis viruses, to confirm the etiology of the outbreak. The epidemiology of outbreaks of hepatitis A should dictate vaccination strategies.

ENHANCED SURVEILLANCE

Routine syndromic surveillance can be supplemented by case-based surveillance that includes laboratory confirmation and collection of more data elements on all presumptive cases. This is referred to “enhanced case reporting” in the WHO guidance document (2). This is usually done in sentinel sites, unless the health system allows implementation at the national level.



CASE DEFINITIONS AND FINAL CLASSIFICATION

PRESUMPTIVE CASE OF ACUTE HEPATITIS

For viral hepatitis, the preferred term for suspected cases is *presumptive* because of possible stigma related to use of the word *suspected*.

A presumptive case of acute hepatitis A is a person with either or both of the following:

- discrete onset of an acute illness with symptoms of acute infectious illness (fever, malaise, fatigue) AND signs of liver damage (anorexia, nausea, jaundice, dark urine, right upper quadrant tenderness)

OR

- raised alanine aminotransferase (ALT) levels more than ten times the upper limit of normal (400 IU/L), the threshold used by the U.S. Council of State and Territorial Epidemiologists (CSTE) (2). Countries may also select lower thresholds that could be more sensitive or higher thresholds that could be more specific.

FINAL CASE CLASSIFICATION WITH ENHANCED REPORTING

Confirmed cases include:

- **Laboratory-confirmed case:** Someone who meets the presumptive case definition and is positive for IgM anti-HAV.
- **Epidemiologically linked case:** Someone who meets the presumptive case definition and is epidemiologically linked to a laboratory-confirmed case (contact with a person with hepatitis A

BOX 1 Syndromic surveillance for acute hepatitis

This chapter discusses only hepatitis A because of the unique aspects of its epidemiology and vaccination strategy. Two options are available for surveillance. Syndromic surveillance for acute hepatitis only detects outbreaks that then need to be investigated. This mostly detects hepatitis A and hepatitis E outbreaks. Enhanced case detection with biomarker testing and risk factor information collection allows surveillance for type-specific hepatitis. WHO recommends that enhanced case reporting include testing for all viral hepatitis that cause acute infection (hepatitis A, B and E).

confirmed by biomarker testing, two to six weeks before onset, or occurrence in the context of an outbreak confirmed by biomarker testing). Contact can be among household members, sexual contact or drug-sharing contact.



CASE INVESTIGATION

With syndromic surveillance for acute hepatitis, individual cases are not investigated. All clusters should be investigated immediately and confirmed serologically. An outbreak investigation can then investigate the causes of the outbreak.

In the setting of enhanced case reporting, individual cases of acute hepatitis should have case report forms filled out and appropriate specimens should be collected for biomarker testing.



SPECIMEN COLLECTION

If biomarker testing is available, a venipuncture blood specimen should be collected and sent to the laboratory for testing by ELISA. Blood should be drawn from acutely ill patients; IgM can persist up to six months after onset. Blood collection tubes can be those for serum or plasma. Serum and plasma samples may be

stored for up to five days at 2–8°C or four weeks at –20°C.

At this time, dried blood spot specimens have not been validated for acute HAV IgM.



LABORATORY TESTING

ELISA testing for immunoglobulin M antibodies to HAV virus (anti-HAV IgM) is the confirmatory test for diagnosis of acute HAV infection. IgM generally becomes detectable 5–10 days before the onset of symptoms and can persist for up to 6 months. IgG is not used to diagnose acute HAV virus infections because anti-HAV IgG appears in the convalescent phase of infection, remains present in serum for the lifetime of the person, and confers enduring protection against disease. In addition, IgG is also positive after vaccination.

In most settings with enhanced case reporting, patients meeting the presumptive case definition at sentinel sites should undergo testing with a standard panel

of hepatitis serologic assays for all the main hepatitis viruses: anti-HAV IgM, anti-HBc IgM, anti-HCV IgM and anti-HEV IgM. In limited-resource settings, a serial approach to testing might be considered, in which initial testing is performed for the most common type of hepatitis. If this first test is negative, a test is done of the next common type, and so on.

ALT level might also be tested for to determine if a patient should be considered a presumptive case, though this cannot be used to confirm the case.



DATA COLLECTION, REPORTING AND USE

RECOMMENDED DATA ELEMENTS

- For aggregated data collection
 - » Number of total acute hepatitis cases by age group, month and geographical area
- For case-based data collection
 - » Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
 - » Unique identifier
 - » Date of birth (or age if date of birth not available)
 - » Sex
 - » Place of residence (city, district and province)
 - » Date of onset
 - » Signs and symptoms: Fever, malaise, fatigue, anorexia, nausea, jaundice, dark urine, right upper quadrant tenderness
 - » Acute liver failure?
 - » Contact with a laboratory confirmed case of HAV?
 - » Number of hepatitis A vaccine doses received
 - » Dates of all hepatitis A vaccine doses (if card available)
 - » Laboratory Methods and Results
 - Specimen collected?
 - Date of specimen collection
 - Date specimen sent to laboratory
 - Date specimen received in laboratory
 - Results of HAV IgM serology (positive, negative, indeterminate, no specimen, unknown)
 - Results of testing for other viral hepatitis
 - ALT result
 - » Date of notification to public health
 - » Date of investigation
 - » Final case classification (laboratory-confirmed, epidemiologically linked)

REPORTING REQUIREMENTS AND RECOMMENDATIONS

- Routine monthly reporting of aggregated data on presumptive cases of acute hepatitis should be done, and if available, the number of confirmed cases of each type of hepatitis should be reported from the peripheral level to the intermediate and central levels.
- Designated reporting sites at all levels should report at a specified frequency (such as weekly or monthly) even if there are zero cases (“zero reporting”).
- If conducting enhanced surveillance, case-based data should be reported routinely from the peripheral level to the intermediate and central levels.
- Hepatitis A is not currently reportable under International Health Regulations (2005) nor as part of the Joint Reporting Form.

RECOMMENDED DATA ANALYSES

- Number of hepatitis A cases and incidence rate by month, year and geographical area
- Age-specific, gender-specific and district-specific hepatitis A incidence rates by month/year

USING DATA FOR DECISION-MAKING

Syndromic surveillance does not provide an accurate estimate of the incidence of type-specific viral hepatitis because of underreporting, the lack of laboratory testing, and the asymptomatic nature of many new infections. As a result, trends in acute hepatitis defined through syndromic surveillance are difficult to interpret. Syndromic surveillance can be used with complementary data (testing results from outbreaks, biomarker data from serosurveys, data from hospitals that test patients with acute hepatitis) to better understand the epidemiology of HAV infection.

When testing is done to distinguish types of hepatitis, the following uses of data are applicable to hepatitis A:

- At the local level, data can be used to identify the etiology of outbreaks and risk factors for infection, describe trends in hepatitis A, and identify issues in the vaccination programme (such as breakthrough infections among vaccinated recipients).

- At the national level, hepatitis A surveillance can be used to guide vaccination policy and monitor its impact. By endemicity level, this can be used as follows:
 - » In high endemic areas, monitor average age of infection to detect a change in the age of infection, which may indicate a possible change towards transitional endemicity.
 - » In areas with transitional endemicity, detect and describe outbreaks. Use data on outbreaks, from routine surveillance of acute hepatitis in sentinel sites, alongside other available data such as population-based serosurveys, to identify where universal immunization might be indicated.
- Occasional population-based serosurveys (or biomarker surveys) that include testing for HAV IgG can supplement acute hepatitis surveillance to define a country with transitional endemicity that might consider universal immunization. Of note, presence of HAV IgG cannot distinguish previous infection from vaccination, so interpretation might be complicated in areas in which the vaccine has been used extensively.
- » In areas with low/very low endemicity, detect and describe outbreaks among populations at higher risk to inform targeted vaccination policy.



SURVEILLANCE PERFORMANCE INDICATORS

There are no formal performance indicators for acute hepatitis surveillance. However, countries might wish to do regular monitoring of surveillance to identify specific areas of the surveillance and reporting system that

need improvement. At the most basic level, syndromic surveillance should be evaluated to determine if it is detecting outbreaks as designed.



CLINICAL CASE MANAGEMENT

No specific treatment for hepatitis A exists. Supportive clinical care for symptomatic infection should be in line with country guidance.



CONTACT TRACING AND MANAGEMENT

In high and transitional endemicity settings, contact investigations are not a priority given the widespread circulation of virus among persons with asymptomatic infections. In low endemicity settings and in the context of an ongoing community-wide outbreak, consider

contact investigations if sufficient resources are available. Post-exposure prophylaxis with hepatitis A vaccine has been shown to be effective in some community-wide outbreaks and can be provided to contacts.



SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

DEFINITION OF AN OUTBREAK

An outbreak is an increase of incidence over the reported baseline.

CHANGES TO SURVEILLANCE DURING AN OUTBREAK

If a country is conducting syndromic surveillance for acute hepatitis, detection of an outbreak should lead to further investigation with laboratory confirmation to confirm the etiology.

PUBLIC HEALTH RESPONSE

Post-exposure prophylaxis with inactivated HAV vaccine can be considered for close contacts in some settings, such as community-wide outbreaks in intermediate

or low endemicity settings. Recommendations for HAV vaccination in outbreak situations depend on the epidemiologic features of hepatitis A in the community and the feasibility of rapidly implementing a widespread vaccination programme. The use of a single dose regimen of HAV vaccine to control community-wide outbreaks has been most successful in small self-contained communities, often among high-risk groups, when vaccination was started early in the course of the outbreak and high coverage of multiple age cohorts can be achieved. Vaccination efforts should be supplemented with health education and improved sanitation.



REFERENCES

REFERENCES CITED

1. World Health Organization. WHO position paper on hepatitis A vaccines – June 2012. *Wkly Epidemiol Rec.* 87(12):261–276; 2012 (http://www.who.int/wer/2012/wer8728_29.pdf?ua=1).
2. World Health Organization. *Technical considerations and case definitions to improve surveillance for viral hepatitis*. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/204501/1/9789241549547_eng.pdf).