

August 2017

Re: Hepatitis A Post-exposure Prophylaxis

The National Advisory Committee on Immunization (NACI) has updated their recommendations on hepatitis A post-exposure prophylaxis. To be consistent with the new National Advisory Committee on Immunization (NACI) recommendations, the recommended recipients of hepatitis A virus (HAV) vaccine and human immune globulin for post-exposure prophylaxis are as follows:

- One dose of HAV vaccine given intramuscularly should be given to susceptible contacts (individuals with no documented history of infection or vaccination with hepatitis A vaccine) \geq six months of age as soon as possible and preferably within 14 days of last exposure.
- Human immune globulin (Ig)* given as soon as possible and preferably within 14 days of last exposure is recommended for the following:
 - Infants < six months of age;
 - Individuals for whom vaccine is contraindicated;
 - Individuals who are immunocompromised or who have chronic liver disease (all of these individuals should also receive one dose of HAV vaccine);
 - All susceptible individuals when HAV vaccine is unavailable.

* Ig may also be considered for individuals who are \geq 60 years of age and are susceptible, in addition to provision of HAV vaccine.

Please refer to section 8.2.1 of the Hepatitis A protocol
<http://www.gov.mb.ca/health/publichealth/cdc/protocol/hepa.pdf> for additional information.

Please share this communication with all relevant colleagues in your facility or clinic.

As the prevention, management and control of communicable diseases requires the active participation and cooperation of all health care professionals and practitioners, your attention to this information is most appreciated.

Sincerely,

“Original Signed By”

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Hepatitis A

1. Case Definition

1.1 Confirmed Case

Laboratory confirmation of infection with or without acute clinical illness^a:

- Detection of immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) in the absence of recent vaccination
OR
- Positive HAV RNA on serum or stool specimen.

1.2 Probable Case

Acute clinical illness^a in a person without laboratory confirmation of infection who is epidemiologically linked to a confirmed case (1).

2. Reporting and Other Requirements

Laboratory:

- All positive test results are reportable by laboratory to the Public Health Surveillance Unit (204-948-3044 secure fax).
- Operators of Manitoba clinical laboratories are required to submit the residual serum or plasma specimens from individuals who tested positive for hepatitis A virus to Cadham Provincial Laboratory within seven days of report for surveillance purposes.

Health Care Professional:

- Probable cases are reportable to the Public Health Surveillance Unit (form available at: www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf) ONLY if a positive lab result is not anticipated (e.g., poor or no specimen taken, person has recovered). Confirmed cases do not require reporting by health care professional as they will be reported to Manitoba Health by the laboratory.
- Adverse events following immunization should be reported by health care professional by completing and returning the form available at: www.gov.mb.ca/health/publichealth/cdc/docs/aefi_form.pdf.

Public Health:

- The Hepatitis A investigation form available at: http://www.gov.mb.ca/health/publichealth/surveillance/hepatitis_a_questionnaire_2012.pdf should be completed for all individuals testing positive for hepatitis A with assistance from the ordering practitioner (as needed), and returned to the Public Health Surveillance Unit, Manitoba Health.
- The Enteric Outbreak Summary Report form should be completed for all outbreaks and returned to Manitoba Health, Public Health Surveillance Unit. CNPHI (Canadian Network for Public Health Intelligence) users should login to CNPHI and enter data into the Enteric Outbreak Summary. Non-CNPHI users may request the form by email: outbreak@gov.mb.ca.

3. Clinical Presentation/Natural History

Onset is usually abrupt with fever, malaise, anorexia, nausea and abdominal discomfort (2). Jaundice and dark urine are typical but symptomatic hepatitis A without jaundice also occurs (3). The disease varies in clinical severity from a mild illness lasting one to two weeks, to a severely disabling disease lasting several months (rare) (2). The clinical manifestations of acute hepatitis A are indistinguishable from hepatitis caused by other viruses (4). Convalescence is often prolonged (2). No chronic infection is known to occur (2, 5). Most infections in children younger than five years of age are asymptomatic and the proportion of symptomatic infections increases with age (6). Hepatitis A virus (HAV) infection in patients with chronic liver disease is more severe and more likely to result in fulminant hepatitis A (6). Hepatitis A infection is occasionally complicated by cholestasis (3).

^a Characterized by discrete onset of symptoms, including fever, malaise, anorexia, nausea and abdominal pain followed by jaundice or elevated aminotransferase levels within a few days (1).

4. Etiology

Hepatitis A virus is a 27nm picornavirus (i.e., a positive strand RNA virus) (2). It has been classified as a Hepatovirus, a member of the family, Picornaviridae (2). At least four genotypes are known to occur; however, no correlation has been observed between infecting genotype, clinical characteristics or clinical outcomes (3).

5. Epidemiology

5.1 Reservoir and Source

Humans are considered to be the only important reservoir of HAV (6). A chronic HAV carrier state has not been reported in humans (7). It is unclear whether some primates serve as reservoirs of infection or as transient hosts after exposure to HAV from human sources (6).

5.2 Transmission

Person-to-person transmission by the fecal-oral route is the primary means of hepatitis A virus transmission (6). Young children are often the source of infection for others because infections in this age group are often asymptomatic and standards of hygiene are generally lower among children compared with adults (6). Transmission by saliva has not been demonstrated (6, 8). Casual contact among people does not spread the virus (9).

Waterborne outbreaks of hepatitis A are uncommon in developed countries (6). However, hepatitis A virus can remain infectious in the environment for long periods of time, allowing for common source outbreaks and sporadic cases to occur from exposure to fecally contaminated food or water (6). In addition, the hepatitis A virus is resistant to several preservative methods used in the food industry (e.g., acidification, freezing) (10) and is more resistant to heat than other picornaviruses (5). Foodborne hepatitis A outbreaks are most commonly associated with contamination of food during preparation by a food handler with HAV infection (6, 11). Food contaminated before retail distribution, such as lettuce or fruits contaminated during cultivation, harvesting, processing, or distribution has been increasingly recognized as the source of hepatitis A outbreaks (6, 12).

The risk of transmission from pregnant women who develop hepatitis A during the third trimester of pregnancy to newborns seems to be low (6). The risk of hepatitis A from a blood transfusion or from plasma derivatives is extremely low, but both have been reported (6). Groups at increased risk for hepatitis A or its complications include international travelers, men who have sex with men, and users of illegal drugs (7). Outbreaks have been reported among men who have sex with men (MSM) (13) and illicit drug users (6). Transmission among injection drug users is believed to occur through both the percutaneous and fecal-oral routes (6).

Health care associated transmission of hepatitis A is rare (7) because if hospitalization is required, most patients are hospitalized after the onset of jaundice, when infectivity is low (3).

Nearly 50% of patients with hepatitis A do not have a recognized source of infection, but may be contacts of individuals with asymptomatic infection (3).

5.3 Occurrence

5.3.1 General

Globally, it was estimated that 119 million people were infected with hepatitis A virus in 2005 with 31 million symptomatic illnesses and 34,000 deaths (14). It is estimated that 1,400,000 new hepatitis A virus infections occur globally each year (14). As water and sanitation systems improve in developing countries, infections occur later in life when the risk for severe disease from hepatitis A is greatest (14). Areas of high endemicity include parts of Africa, Asia, Central and South America where poor hygienic and sanitary conditions facilitate the spread of hepatitis A virus (6). In these areas, infection is nearly universal in early childhood, when asymptomatic infection predominates (6). Hepatitis A virus infects more than 80% of the population by late adolescence in many developing countries (3). Outbreaks in child care facilities are more common in larger facilities but rarely occur in centres that do not have children in diapers (3, 8). Outbreaks have been regularly reported among illicit drug users in North America, Australia and

Europe (6). Hepatitis A outbreaks among MSM have been reported frequently in urban areas of the United States, Canada, Europe and Australia (6). In areas of moderate endemicity, the overall incidence and average age of reported cases are often higher than in highly endemic areas because high levels of virus circulate in a population that includes many susceptible older children, adolescents, and young adults, who are more likely to develop symptoms with hepatitis A infection than young children(3).

5.3.2 *Canada*

The incidence of hepatitis A has declined since the introduction of HAV vaccine in Canada (15). Incidence has decreased from 10.6 per 100,000 population in 1991 to 0.9 per 100,000 population in 2008 (15). Age-specific incidence (2.1 per 100,000) is highest among those five to nine years of age (15). Given the under-diagnosis and under-reporting of HAV and the occurrence of sub-clinical infections, the actual number of HAV cases is estimated to be seven times higher than reported (15).

5.3.3 *Manitoba*

There were 175 cases of hepatitis A reported to Manitoba Health between the period of January 1, 2000 and October 21, 2013. The number of cases varied between a low of 4 (2001 and 2012) and a high of 34 (2003). The average number of cases in a year was 13 (excluding 2013 as it is an incomplete year) and the median number of cases was 11. The age group 40-59 years accounted for 31% of the total cases. The annual incidence rate of hepatitis A peaked in 2003 at 3 cases/100,000 population and has since declined to a low of 0.31 cases/100,000 population in 2012.

5.4 Incubation Period

Ranges from 15 to 50 days with an average of 28 days (5).

5.5 Host Susceptibility and Resistance

Susceptibility is general (2). HAV infection produces lifelong immunity to hepatitis A (7). Both inactivated and live attenuated hepatitis A vaccines are capable of providing protection in those

immunized for up to 15 years as defined by currently accepted, conservative correlates of protection (16).

5.6 Communicability

Data from epidemiologic studies suggest that peak infectivity occurs during the two weeks prior to symptom onset (6). Shedding of HAV in stool may continue for longer periods in infected infants and children than adults (6). For practical purposes, both children and adults with hepatitis A can be assumed to be non-infectious one week after jaundice appears (6). Chronic shedding of HAV does not occur; however, the virus has been detected in stool during relapsing illness (6).

6. Laboratory Diagnosis

Diagnosis is established by the demonstration of IgM antibodies against hepatitis A virus (anti-HAV IgM) in the serum of acutely or recently ill persons. Anti-HAV IgM may remain detectable for four to six months after onset. IgG antibodies against HAV (anti-HAV IgG) become detectable shortly after the appearance of IgM. Persons who are total anti-HAV positive (anti-HAV IgM and anti-HAV IgG positive) and IgM anti-HAV negative have serologic markers indicating immunity consistent with either past infection or vaccination (7).

An alternative is to perform nucleic acid testing (RT-PCR) on serum or stool specimens, preferably early during the clinical course; however, a negative result should not exclude the diagnosis of hepatitis A. The molecular method is normally done as reflex testing on IgM positive serum specimens for genotyping/RNA finger printing purposes, which are important for public health and epidemiological investigations.

7. Key Investigations for Public Health

History:

- International travel, especially to an endemic area;
- Attending day care;
- Contact with a known case (e.g. day care, household);

- Similar illness in household or other close contact;
- Food and water consumption;
- Sexual risk factors (e.g., oral-anal contact);
- Immunization history.

8. Control

8.1 Management of Cases

- Supportive.

Infection Control Measures:

Contact Precautions are indicated in children who are incontinent or unable to comply with hygiene and should be considered for incontinent adults if stool cannot be contained or for adults with poor hygiene who contaminate their environment.

Otherwise, Routine Practices are adequate. Refer to page 88 of the Manitoba Health document *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at: <http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf>.

Public Health Measures:

Stress the importance of hand washing on the part of the case.

Exclusion of Cases:

- Food handlers with acute HAV infection should be excluded for one week after jaundice appears (or after onset of symptoms if jaundice is absent) (5).
- Children and adults with hepatitis A should be excluded from child care facilities for one week after onset of jaundice (or after onset of symptoms if jaundice is absent) (5). A Medical Officer of Health may modify the exclusion period following the completion of the post-exposure program in the centre.

8.2 Management of Contacts

Unless it is contraindicated, post-exposure prophylaxis should be offered to the following:

- **Household and close contacts of confirmed or probable cases of HAV** (15). This would

include children of different households who play together frequently, regular babysitters, sexual contacts and illicit drug sharing contacts (17). Without post-exposure prophylaxis, secondary attack rates of 15-30% have been reported in households, with higher rates of transmission occurring from infected young children than from infected adolescents and adults (17).

- **When HAV occurs in kindergartens and group child care centres (as described below under *Child Care Facilities*)** (15).
- **Co-workers of infected food handlers** (15). As common source transmission to patrons is unlikely, post-exposure prophylaxis with HAV vaccine or human immune globulin (Ig) is usually not indicated (5).
- **Considered for patrons of a food establishment (if they can be located)** if the food handler directly handled food during the time when the food handler was likely infectious and had diarrhea and poor hygiene practices and if prophylaxis can be provided within 14 days of exposure (15).

Post-exposure prophylaxis is usually not necessary for other contacts, such as school, workplace or health care workers caring for HAV cases unless an outbreak is suspected (15) (refer to Section 8.3). If a case occurs in a primary school (in either a student or staff member) and no source of infection can be identified outside the school (e.g., history of travel to endemic area), assume the case may have acquired the infection through contact with an asymptomatic person within the school (18). In these circumstances, offering hepatitis A vaccine to all susceptible (no prior documented infection or vaccination with hepatitis A vaccine) children and adults working within the same class as the index case, and other close friends within the school, may prevent continuing transmission (18).

8.2.1 Post-exposure Prophylaxis

Serologic testing of contacts is not recommended because testing may delay administration of post-exposure prophylaxis (5).

- One dose of HAV vaccine given intramuscularly should be given to susceptible^b contacts \geq one year of age as soon as possible and preferably within 14 days of last exposure (15). HAV vaccine should still be considered if more than 14 days have elapsed since last exposure, as there are no data on the outer limit of efficacy (15). The safety of hepatitis A containing vaccine during pregnancy has not been studied in clinical trials (15). HAV vaccine should be considered for pregnant women in high risk situations when benefits outweigh the known risks (15). Hepatitis A vaccine is available in different formulations. Refer to product monograph and product insert for dose and administration of vaccine.
- Human immune globulin (Ig) is recommended for the following:
 - Infants < one year of age;
 - Those for whom vaccine is contraindicated;
 - Those who are immunocompromised (in addition to vaccine as described above) (15);
 - Ig may also be used when HAV is unavailable (15).

The recommended dose of Ig for post-exposure prophylaxis is 0.02 mL/kg, given as soon as possible after the exposure, preferably within 14 days (5, 15). The efficacy of Ig is unknown if given later than 14 days after exposure (15). A separate needle and syringe should be used for Ig and vaccine. Pregnancy or lactation is not a contraindication to immune globulin administration (3).

Child Care Facilities:

Precise data concerning the onset of protection after post-exposure prophylaxis are not available. Allowing prophylaxis recipients to return to the child care setting immediately after receipt of prophylaxis seems reasonable (5).

Child Care Facilities Accepting Diapered Children:

HAV vaccine or Ig as recommended above should be administered to all previously unimmunized staff

members and attendees of child care facilities or homes if:

- One or more cases of hepatitis A are recognized in children or staff members; or
- Cases are recognized in two or more households of facility attendees (5).

Child Care Facilities Without Diapered Children:

In facilities that provide care only to children not wearing diapers, it is recommended that HAV vaccine and/or Ig (when indicated) be given only to classroom contacts of the index case (5).

Newborn Infants of HAV-infected Mothers:

Perinatal transmission of HAV is rare. Some experts advise giving Ig (0.02mL/kg) to an infant if the mother's symptoms began between two weeks before and one week after delivery (5). Efficacy in this circumstance has not been established (5). Severe disease in healthy infants is rare (5).

Ordering Hepatitis A Vaccine and Human Immune Globulin:

During regular business hours, contact the Provincial Vaccine Warehouse at 204-948-1333 or 1-855-683-3306. A current Biologics/Vaccine Order Form is available by calling the warehouse. After regular office hours the on-call warehouse staff may be contacted at 204-805-4096.

8.2.2 Post-exposure Prophylaxis Follow-up

- Post-vaccination testing is not indicated because of the high rate of vaccine response among adults and children (7).
- Contacts at continued risk of infection (i.e., those individuals recommended for pre-exposure immunization) should receive a second dose of hepatitis A vaccine. Refer to the current *Canadian Immunization Guide* for individuals at higher risk of hepatitis A infection and the vaccine product monograph for schedule.

b Susceptible contacts are individuals with no documented history of infection or vaccination with hepatitis A vaccine.

8.3 Management of Outbreaks

Determine mode of transmission by epidemiologic investigation, whether person-to-person or by common vehicle, and identify the population exposed to increased risk of infection. Search for missed cases and maintain surveillance of persons exposed to the same risk in a potential common source outbreak. Eliminate any common sources of infection.

8.3.1 Child Care Facility Outbreaks

- When an outbreak occurs (i.e., hepatitis A cases in three or more families of child care facility attendees), HAV vaccine and/or Ig (when indicated) should be considered for members of households that have children (facility attendees) in diapers (5, 17).
- Because infections in children are usually mild or asymptomatic, outbreaks are often identified only when adult contacts (e.g., parents) become ill (5). Serologic testing to confirm HAV infection in suspected cases is indicated (5).
- There is no evidence characterizing the onset of protection following post-exposure prophylaxis (5). Allowing prophylaxis recipients to return to the child care facility immediately after receipt of the vaccine or Ig seems reasonable (5).

8.3.2 Institutional Outbreaks

- Focal outbreaks in institutions (e.g., for developmentally challenged, inmates/staff of correctional facilities) may warrant mass prophylaxis with vaccine (2).

8.3.3 Common Exposure Outbreaks

- Common source foodborne or waterborne outbreaks require prompt investigation and intervention. Refer to the *Enteric Illness Protocol* available at: www.gov.mb.ca/health/publichealth/cdc/protocol/enteric.pdf for suspected foodborne and waterborne outbreaks.
- Public notification should occur. The level of notification will usually be at the discretion of regional Public Health and/or the provincial Public Health Division for local outbreaks but may be at the discretion of the Federal

Government for nationally linked foodborne outbreaks as per *Canada's Foodborne Illness Outbreak Response Protocol (FIORP) 2010: To guide a multijurisdictional response* available at: www.phac-aspc.gc.ca/zoono/fiorp-pritioa/index-eng.php.

- Post-exposure prophylaxis is usually not recommended because these outbreaks are often not recognized until it is too late for prophylaxis to be effective (5). Data from epidemiologic studies suggest that peak infectivity occurs during the two weeks before the onset of symptoms (3).
- HAV vaccine and Ig may be considered if it can be administered to exposed people within two weeks of an exposure to the HAV-contaminated water or food (5).
- Make special efforts to improve sanitary and hygienic practices to eliminate fecal contamination of foods and water (2).

8.3.4 Community Outbreaks

- Community-wide outbreaks may warrant consideration of mass hepatitis A immunization. Crowded living conditions, lack of running water, lack of sewage systems, history of previous outbreaks, two or more cases within 50 days of each other and incidence of cases $\geq 30/100,000$, are Manitoba empirically derived criteria supporting immunization. Decisions to implement an immunization program should be made in consultation with regional and/or First Nations and Inuit Health Medical Officers of Health.

8.4 Preventive Measures

- Travelers to developing countries should be advised to eat only properly cooked food and be careful of uncooked vegetables and shellfish (6). They should be encouraged to receive the hepatitis A vaccine prior to travel.
- Oysters, clams and other shellfish from contaminated areas should be heated to a temperature of 85°-90°C (185°-194°F) for four minutes or steamed for 90 seconds before eating (2).

- There is clear evidence that good hand hygiene and minimization of bare hand contact with ready-to-eat foods are control measures that reduce the risk of foodborne transmission of HAV within a community (11).
- Safe food handler training and practices with proper attention to effective hand washing (11).
- Employers should provide access to hand washing stations and encourage ill food handlers to seek medical attention and to stay out of the workplace (12).
- Management of child care facilities should stress measures to reduce the possibility of fecal-oral transmission including thorough hand washing after every diaper change and before eating (2, 5).
- Immunization as recommended by the current *Canadian Immunization Guide*. Refer to Manitoba Health's *Eligibility Criteria for Publicly-Funded Vaccines* for more information on hepatitis A immunization in Manitoba available at:
<http://www.gov.mb.ca/health/publichealth/cdc/vaccineeligibility.html> .

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