In response to enquiries from public health units related to the public health management of hepatitis A, we have developed this document to address the following questions:

1. **What should be used for hepatitis A post-exposure prophylaxis, by age and underlying medical conditions?**

2. **Has the dose changed for serum immune globulin for hepatitis A post-exposure prophylaxis?**

3. **Should infants aged 6 to 12 months receive hepatitis A vaccine when hepatitis A protection is required?**

4. **Should Twinrix® be used for hepatitis A post-exposure prophylaxis?**

5. **Is genetic sequencing performed on all anti-hepatitis A virus IgM reactive specimens?**

6. **A) When should it be suspected that a reactive anti-hepatitis A IgM test result may not be due to acute hepatitis A infection?**

   **B) What actions should be taken if you suspect a reactive anti-hepatitis A IgM test result may not be due to acute hepatitis A infection?**

**Q1. What should be used for hepatitis A post-exposure prophylaxis by age and underlying medical conditions?**

Susceptible contacts of a hepatitis A case should receive post-exposure prophylaxis (PEP) as soon as possible after exposure and up to 14 days from the last exposure to the hepatitis A case while they were infectious. Similarly, susceptible individuals exposed to a contaminated common source (e.g., food product) should receive PEP as soon as possible after exposure and up to 14 days from the last exposure. PEP using hepatitis A vaccine may be considered beyond 14 days after exposure, but benefits are unknown.¹
The following is advised for hepatitis A PEP in susceptible individuals:

<table>
<thead>
<tr>
<th>Age group OR underlying condition</th>
<th>Post-exposure prophylaxis (PEP)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 6 months of age</td>
<td>Serum immune globulin&lt;sup&gt;1, 2&lt;/sup&gt; +</td>
<td>Other options may be considered; please contact PHO for consultation as needed.</td>
</tr>
<tr>
<td>6 months to less than 12 months of age (who are not immunocompromised and do not have chronic liver disease)</td>
<td>Hepatitis A vaccine&lt;sup&gt;1, 3&lt;/sup&gt; #</td>
<td>For this age group, use of the hepatitis A vaccine is considered off-label and is not publicly-funded in Ontario.</td>
</tr>
<tr>
<td>12 months to 49 years of age (who are not immunocompromised and do not have chronic liver disease)</td>
<td>Hepatitis A vaccine&lt;sup&gt;1, 2&lt;/sup&gt;</td>
<td>If immunocompromised or have chronic liver disease, see appropriate row below.</td>
</tr>
<tr>
<td>50 years of age and over</td>
<td>Serum immune globulin&lt;sup&gt;*&lt;/sup&gt; + and hepatitis A vaccine&lt;sup&gt;2&lt;/sup&gt;</td>
<td>For large scale responses, using only hepatitis A vaccine may be indicated.</td>
</tr>
<tr>
<td>Immunocompromised (by medical condition or medication)</td>
<td>Serum immune globulin&lt;sup&gt;*&lt;/sup&gt; + and hepatitis A vaccine&lt;sup&gt;1, 2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>Serum immune globulin&lt;sup&gt;*&lt;/sup&gt; + and hepatitis A vaccine&lt;sup&gt;1, 2, 3&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

Table symbol footnotes:

<sup>+</sup> When serum immune globulin is indicated, the dose in the product monograph (0.1 mL/kg for GamaSTAN® S/D IG) should be followed.<sup>4</sup> (see Question 2 below).

<sup>#</sup> For 6 to 12 months of age, the National Advisory Committee on Immunization now recommends hepatitis A vaccine in preference to serum immune globulin.<sup>3</sup> (see Question 3 below).

<sup>*</sup> Hepatitis A immune globulin PEP advice from the Provincial Infectious Diseases Advisory Committee on Immunization (PIDAC-I) (immune globulin plus hepatitis A vaccine for individuals 50 years of age and over)<sup>3</sup> differs from that of the National Advisory Committee on Immunization (immune globulin may be provided in addition to hepatitis A vaccine for those 60 years of age and over).<sup>3</sup>

- Concurrent administration of vaccine plus serum immune globulin is delivered via separate needles/syringes and separate anatomical sites. Only one dose of hepatitis A vaccine is indicated for PEP. A second dose is indicated for long term protection.<sup>1</sup> The second dose would not be publicly funded.
Q2. Has the dose of serum immune globulin for hepatitis A post-exposure prophylaxis changed?

- Yes, the dose of serum immune globulin for hepatitis A post-exposure prophylaxis (PEP) using GamaSTAN® S/D has increased from the previously recommended dose of 0.02 mL/kg. For hepatitis A PEP using GamaSTAN® S/D, follow the current (2018) product monograph, which recommends a dose of 0.1 mL/kg. This differs from the serum immune globulin dosing recommended in the Canadian Immunization Guide, which remains at 0.02 mL/kg.

- The United States Centers for Disease Control and Prevention has indicated that the increased dose for hepatitis A PEP reflects concerns about decreased potency of anti-hepatitis A IgG in the immune globulin product, likely due to decreased hepatitis A infection prevalence among plasma donors.

Q3. Should infants aged 6 to 12 months receive hepatitis A vaccine when hepatitis A protection is required?

- Yes, the National Advisory Committee on Immunization (NACI) now recommends hepatitis A vaccine in preference to serum immune globulin for healthy infants 6 to 12 months of age when indicated, including for post-exposure prophylaxis (PEP) (see Question 1 above).

- NACI’s evidence review found that vaccination of infants 6 to 12 months of age with inactivated hepatitis A vaccines is immunogenic and safe. Please see the full NACI statement for details.

- Please note that use of hepatitis A vaccine in infants 6 to less than 12 months of age is considered off-label use.

Q4. Should Twinrix® be used for hepatitis A post-exposure prophylaxis?

- No, Twinrix®, the combined hepatitis A and hepatitis B vaccine, is not indicated for hepatitis A post-exposure prophylaxis (PEP). Only monovalent hepatitis A vaccines should be used for PEP.

- A dose of Twinrix® contains half the hepatitis A antigen content as the monovalent vaccine (i.e., Twinrix® contains 720 ELISA units of hepatitis A antigen, which is half of the 1,440 ELISA units of hepatitis A antigen in a dose of monovalent Havrix® and Twinrix Junior® contains 360 ELISA units, which is half the 720 ELISA units in monovalent Havrix Junior®).

- The product monograph for Twinrix® states that it is not known whether Twinrix® will prevent hepatitis A in individuals in the incubation period (i.e., those who are already exposed). Similarly, the United States’ Centers for Disease Control and Prevention has emphasized the lack of data to support use of Twinrix® for hepatitis A PEP.

Q5. Is genetic sequencing performed on all anti-hepatitis A virus IgM reactive specimens?

- Yes, genetic sequencing is performed for any specimen tested at or sent to the PHO laboratory if sufficient sample is available.
- Genetic sequencing is very important to identify clusters or outbreaks of hepatitis A.\(^9\)

- For any reactive anti-hepatitis A (anti-HAV) IgM specimen not initially tested at the PHO laboratory (e.g., tested at a private or hospital laboratory), please follow up with the testing laboratory to ensure the specimen is forwarded to the PHO laboratory.

- The PHO laboratory forwards all reactive anti-HAV IgM specimens with sufficient volume to the National Microbiology Laboratory (NML) for genotyping and genetic sequencing; this includes specimens tested at PHO and those that we receive from private or hospital laboratories.

Q6A. When should it be suspected that a reactive anti-hepatitis A IgM test result may not be due to acute hepatitis A infection?

- Ensure the anti-hepatitis A (anti-HAV) IgM result is not combined with the total (IgM and IgG) results. If you have received a total IgM and IgG combined, a separate IgM should be requested.

- False-positive anti-HAV IgM test results can occur. In the absence of clinically compatible illness, the following factors increase the probability that a reactive anti-HAV IgM test result is not due to acute hepatitis A infection:
  - Recent hepatitis A vaccination.
  - Normal liver enzymes (e.g., alanine transaminase (ALT) and aspartate transaminase (AST)) and bilirubin; liver enzymes (e.g., ALT, AST) are usually markedly elevated in acute hepatitis A infection (i.e., 500 to 5,000 U per L).\(^{10}\)
  - No known epidemiologic risks for acquiring hepatitis A during the possible incubation period (e.g., not a known contact of a laboratory-confirmed case, no history of travel to an endemic area, not in a community/setting at risk of an outbreak or hepatitis A virus transmission, has not consumed food implicated in an outbreak).

Background contextual information to assist with the interpretation of hepatitis A IgM:

- Hepatitis A infection is estimated to be asymptomatic in 70% of children under 6 years of age and most of these children do not develop jaundice; however, most older children and adults with hepatitis A infection have symptoms and approximately 70% have jaundice.\(^{11}\)

- Anti-HAV IgM generally appears in serum approximately five to 10 days before symptom onset and falls to non-detectable levels within six months after infection, although it has remained detectable more than one year after infection.\(^{11}\)

- Anti-HAV IgM can be positive due to recent hepatitis A vaccination.

- False-positive anti-HAV IgM test results may be due to factors such as non-specific cross-reacting antibodies (e.g., rheumatoid factor).\(^{12}\) A review of anti-HAV IgM positive tests in older persons without typical symptoms of hepatitis A found the results are more likely to be due to false-positive test results or hepatitis A infection that occurred months to years previously, rather than more recent hepatitis A infection.\(^{13}\)
Q6B. What action should be taken if you suspect that a reactive anti-hepatitis A IgM test result is not due to acute hepatitis A infection?

- If you suspect that an anti-hepatitis A (anti-HAV) IgM result may not be due to acute infection, in consultation with the patient’s health care provider, the following information can inform decision-making about case and contact management:
  1. Reason for testing and any additional clinical information;
  2. If the case had recent or remote vaccination against hepatitis A, noting that:
     - Pre-exposure hepatitis A vaccination is 90 to 97% effective.¹
     - Post-exposure hepatitis A vaccination is approximately 80% effective if given within one week of exposure.¹
     - Anti-HAV IgM appears in serum in up to 20% of vaccine recipients when measured two weeks after hepatitis A vaccination.¹¹
  3. Past anti-HAV IgM or IgG positive test results, noting that past infection should confer immunity;
  4. Results of liver enzyme tests (e.g., ALT, AST) and bilirubin; if not available, consider obtaining serum for liver enzyme and bilirubin testing along with a repeat IgM and IgG to hepatitis A;
  5. Contact PHO laboratory to:
     - Enquire about past anti-HAV IgM or IgG positive test results; and
     - Discuss the anti-HAV IgM results with a microbiologist (contact Customer Service at 416-235-6556 or toll free at 1-877-604-4567).

- For additional information on positive anti-HAV IgM, see: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5418a1.htm.¹³

For any additional questions on hepatitis A, please contact Public Health Ontario at ezybd@oahpp.ca.
References


Citation


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