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QUESTIONS AND ANSWERS

Public Health Management of Hepatitis A

March 26, 2019

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:

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

Table symbol footnotes:

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

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

[*] 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)[3] 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).[3]

- 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.[1] 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.[4] This differs from the serum immune globulin dosing recommended in the Canadian Immunization Guide, which remains at 0.02 mL/kg.[1]

- 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.[5]

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).[3]

- 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.[3]

- 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).[6] 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[6], which is half of the 1,440 ELISA units of hepatitis A antigen in a dose of monovalent Havrix®[7] and Twinrix Junior® contains 360 ELISA units[6], which is half the 720 ELISA units in monovalent Havrix Junior®[7]).

- 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).[6] 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.[8]

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 ezvbd@oahpp.ca.

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