Hepatitis A vaccine response 22 years after vaccination

Emily Mosites, MPH PhD
Epidemic Intelligence Service Officer
CDC Arctic Investigations Program
HEPATITIS A FACTS

1. Is a viral infection of the liver spread when faecal matter enters the mouth.

2. May last several weeks and can be debilitating but most people recover completely.

3. Preventable with carefulhand washing, keeping toilets and bathrooms clean, avoiding infected water sources.

SYMPTOMS INCLUDE:
- Nausea
- Vomiting

SPREAD BY:
- Direct contact
- Food & beverages
- Cups & spoons
- And any other objects handled by the infected person

Poster from: NYC Health Department
In the past, large outbreaks of Hepatitis A occurred in Alaska.

![Graph showing the rate of Hepatitis A cases per 100,000 people from 1972 to 2011 for Alaska Native and Non-Native populations. The graph indicates a significant decrease in cases after the Hep A vaccine was rolled out in 1996.]
How long will the vaccine protection last?

Are booster shots necessary?
Hepatitis A vaccine cohort in Alaska

Who:
- 143 children from Anchorage
  - Age 3-6 years
  - No existing anti-Hepatitis A virus antibodies

When:
- Recruited in 1992-1993
- Yearly follow-up until 1997, then follow-up every 2-3 years
The vaccine: Havrix (Glaxosmithkline)

- Inactivated hepatitis A virus
- 3 dose series
  - Same vaccine as 2 dose but 25% less antigen
  - No differences in antibody levels at 15 years (Vaccine 2013;31)
Three hepatitis A vaccine dosing schedules

Group A: 0, 1, 2 months

Group B: 0, 1, 6 months

Group C: 0, 1, 12 months
Methods- 22 year follow-up time point

- Antibody level testing (ELISA)
- >20 mIU/mL considered “protective” against Hepatitis A virus
- Compared log levels between groups and between years

- Imputed missing values
  - Statistical method to fill in values for participants who didn’t come back
Anti-hepatitis A virus antibody 22 years after vaccination

22-year time point
- 46 participants
- 28 (60%) female
- Average age 28 years
- 90 mIU/mL (min 9, max 3886)

Not statistically different
## Significant difference in antibody titers between groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Geometric Mean Concentration (GMC)</th>
<th>Ratio</th>
<th>N(%) below 20mIU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>46 mIU/mL</td>
<td>Reference</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Group B</td>
<td>122 mIU/mL</td>
<td>2.7 (p=0.010)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Group C</td>
<td>138 mIU/mL</td>
<td>3.0 (p=0.005)</td>
<td>1 (7%)</td>
</tr>
</tbody>
</table>
Three hepatitis A vaccine dosing schedules

- **Group A**: 0, 1, 2 months
- **Group B**: 0, 1, 6 months
- **Group C**: 0, 1, 12 months
Did loss-to-follow-up over time affect results?

After imputing missing data points:
- No change in estimated antibody levels
- No change in differences between dose groups (slightly more significant)
Conclusions

- Booster dose not necessary at 22 years after initial vaccination
- Delayed third dose groups showed better responses than doses separated by one month
- Minimal impact of loss-to-follow-up
Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
HAVRIX vaccine details

2 dose vs 3 dose
- Same vaccine
- Two dose schedule is 720 EU of vaccine 6 to 12 months apart.

Adverse reactions
- soreness where the shot was given (*about 1 out of 2 adults, and up to 1 out of 6 children*)
- headache (*about 1 out of 6 adults and 1 out of 25 children*)
- loss of appetite (*about 1 out of 12 children*)
- tiredness (*about 1 out of 14 adults*)
- serious allergic reaction, within a few minutes to a few hours after the shot (*very rare*).
**TWINRIX**

- Combined hepatitis A and hepatitis B vaccine
  - 720 EL.U. of hepatitis A antigen (half of the HAVRIX adult dose)
  - 20 mcg of recombinant hepatitis B surface antigen protein (the same as the ENGERIX-B adult dose).

- Primary immunization consists of 3 doses, administered on a 0-, 1-, and 6-month schedule, the same schedule as that commonly used for single-antigen hepatitis B vaccine.
Predicted Antibody GMC Over Time, by Vaccination Schedule at 14 Year Follow-Up

Predicted anti-HAV GMC (mIU/mL)

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Years Since Third Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (0, 1, 2)</td>
<td>24 years</td>
</tr>
<tr>
<td>B (0, 1, 6)</td>
<td>28 years</td>
</tr>
<tr>
<td>C (0, 1, 12)</td>
<td>30 years</td>
</tr>
</tbody>
</table>

Sero-protective level

Slide from: G. Racznia k