Universal Vaccination Against Hepatitis A

Lessons From the Experience in Immunization of Toddlers in Israel

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Hepatitis A epidemiology shifts with improving hygiene

Increase in susceptibility

Improvement in hygiene
Reported Acute Viral Hepatitis Through Passive Surveillance

Incidence - Israel, 1960-1998
Demographics

Israel's population: 6.3 million in 2000

- Jewish population - 78%
- Non-Jewish population - 22%, of whom
  - 82% Moslems
  - 9% Christians
  - 8.8% others
Incidence of Viral Hepatitis A per 100,000 in Israel During 1963-1996 by Population

- **Non-Jewish population**
- **Jewish population**
Age-Specific Incidence of Reported HAV in Israel during 1993-8

Overall incidence Per 100,000
Jews  non-Jews
46.8  65.1
Highlights of HAV Epidemiology in Israel

Background information:

➢ Heterogeneous population (contact between high and low socioeconomic risk groups)

➢ Highest attack rate in children 5-9 years old

➢ Maternal anti-HAV IgG is usually cleared in babies by the age of 18 months

➢ Hepatitis A is rarely observed < age of 18m

➢ Toddlers seem to be the main vehicle for HAV transmission (pilot study results)
Hepatitis A Surveillance Systems in Israel

Passive surveillance:

*National*
Through notifications to the Ministry of Health
(HAV committee: coordinator - Ron Dagan)

Active Surveillance:

*Only in Jerusalem*
(coordinator - Daniel Shouval)
Annual Incidence of Acute HAV per District

Overall incidence: 42.4/100,000
\[(N=5,066,200)\]

**Passive surveillance**

*1999 data, active surveillance*
There are two major ethnic populations residing in Jerusalem:

- The Jewish population comprises of various ethnic and socioeconomic subgroups (secular, religious and orthodox). N=732,163*

- The non-Jewish population is mostly of Arab origin (Moslems and Christians). N=205,000*

Sub-populations differ in:

- Socioeconomic status
- Different birthrate
- Living conditions
- Hygienic infra-structure

*2002
Active Surveillance in the Jerusalem District
1999-2004

- Contact with all HMO labs and hospitals in the Jerusalem district twice a week
- Established contact with family physician or pediatrician
- Obtained informed consent
- Recruit index cases (or their custodians) and their household contacts for serologic survey
- Anti-HAV IgM+ samples re-tested and checked for HAV-RNA by PCR followed by sequencing
Universal Vaccination Against Hepatitis A

Pros:
- Area of intermediate endemicity in transition
- Contact between populations with high and low risk
- True incidence >5x of reported cases/year through passive surveillance
- Increased incidence of fulminant hepatitis A
- Favorable cost/benefit analysis*
- High acceptance rate by population

The Israeli Project: Toddler-only 2-dose vaccination

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JAMA 2005;294:202
Universal vaccination started July 1, 1999 in babies immunized at age 18 and 24 months.

- Vaccine: HAVRIX<sup>R</sup>- Pediatric dose of 720EU x2
- The vaccine is provided free of charge, as a part of the regular immunization program
- ~ 90% received 1 dose; > 80% received 2 doses
- No catch-up program beyond toddlers was introduced

*It is estimated that <10% of children <18y and <4% of adults >18y received at least one dose of HAVRIX or Vaqta through non-governmental initiatives*
<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Doses</th>
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<tbody>
<tr>
<td>1999</td>
<td>19,000</td>
</tr>
<tr>
<td>2000</td>
<td>36,520</td>
</tr>
<tr>
<td>2001</td>
<td>59,130</td>
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<td>2002</td>
<td>43,986</td>
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</table>

Total: 158,636

Number of HAV Vaccine Doses Delivered to the Jerusalem District
<table>
<thead>
<tr>
<th>Year</th>
<th>Passive Surveillance*</th>
<th>Active Surveillance**</th>
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<tr>
<td>1999</td>
<td>1246</td>
<td>671</td>
</tr>
<tr>
<td>2000</td>
<td>501</td>
<td>654</td>
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<tr>
<td>2001</td>
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<td>105</td>
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<tr>
<td>2005</td>
<td>137</td>
<td>57</td>
</tr>
<tr>
<td>Total</td>
<td>2575</td>
<td>2020</td>
</tr>
</tbody>
</table>

* N = ~6,300,000  ** N = ~900,000
Dendogram of HAV Isolates in Jerusalem

*709 isolates
Reporting of HAV Cases in Israel: 1993 Through 2004

Incidence/100,000 inhabitants

Year

93 94 95 96 97 98 99 00 01 02 03 04

Reporting of HAV Cases in Israel:
1993 Through 2004
Reporting of HAV Cases in Israel: Passive Surveillance 1993 - 2004

Year

Incidences/100,000 inhabitants

93 94 95 96 97 98 99 00 01 02 03 04
Reporting of HAV Cases in Israel by Ethnic Groups: 1993 Through 2004

Incidence/100,000 inhabitants

Jewish pop.
Non-Jewish pop.
Reporting of HAV Cases in Israel: 1993 Through 2004 by Age-Group and Ethnic Population

- **1 - 4 yrs**
- **5 - 9 yrs**
- **10 - 14 yrs**
- **15 - 44 yrs**

Graphs showing the incidence of HAV cases per 100,000 inhabitants by age-group and ethnic population from 1993 through 2004.
Reporting of HAV Cases, Extremes of Life in Israel: 1993 Through 2004

[Graph showing incidence of HAV cases per 100,000 inhabitants by age group and year.]
Cases of HAV Reported Since 1999: Jerusalem County vs the Rest of Israel

Jerusalem (active surveillance)

Rest of country (passive surveillance)
Summary of National Age-Specific Reduction in Reported HAV Disease 1993-8 vs 2002-4

1-4 yrs - 99%
Summary of Age-Specific Reduction in Reported HAV Disease 1993-8 vs 2002-4

- 1-4 yrs: 99%
- 5-9 yrs: 97%
- 10-14 yrs: 97%
- 15-44 yrs: 93%
- <1 yr: 94%
- 45-64 yrs: 89%
- ≥65 yrs: 75%

TOTAL: 95.6%
Exposure opportunity

Disease rate

Time

High endemicity

Intermediate endemicity

Low endemicity
Sero-prevalence

Disease rate

Time

High endemicity

Intermediate endemicity

Low endemicity
Conclusions

- The universal toddler-only immunization program in Israel is leading to:
  - a dramatic reduction of HAV circulation and disease in all ages
  - a marked herd protection
- regional HAV universal vaccination programs in other countries demonstrate a marked decline in incidence of HAV infection

The experience gained in Israel raises two important issues:

- The need to plan for catch-up programs is questioned, if the toddlers-only approach is adopted
- Cost-benefit studies must take in account that vaccination programs aimed at only a small fraction of the population (in the present case < 3%) can reduce profoundly disease in the entire population
Universal vaccination against hepatitis A in toddlers is leading to disappearance of HAV infection in the entire population in Israel.
Hepatitis A Virus Infection in Israel

An End to an Era?
Participating Investigators

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