Herd Immunity/Protection: Case Studies

Hepatitis A Vaccines

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The Hepatitis A Epidemiological Paradox

- Improved hygienic conditions

- Proportion of susceptibles among older children & adults

- Proportion of symptomatic with increasing age

- Risk for symptomatic disease
Disease rate

Exposure opportunity

Time

High endemicity

Intermediate endemicity

Low endemicity
Estimated prevalence of hepatitis A virus 2005

Symptomatic HAV Infection by Age

Symptomatic cases (%) vs. Age (years)

- Age (years): 1, 2, 3, 4, 5+
- Symptomatic cases (%): 0, 10, 20, 30, 40, 50, 60, 70, 80, 90
In countries of intermediate endemicity, a relatively large proportion of the adult population is susceptible while virus is circulating, and where hepatitis A represents a significant public health burden, often with large outbreaks – universal mass childhood vaccination may be a priority.
Global Experience with HAV Vaccines and Herd Immunity
Impact of a Mass HAV Vaccination Programme of Preadolescents 7 Years After Introduction – Catalonia, Spain

• At the end of 1998, universal vaccination with a combined hepatitis A + B vaccine was started in 12-year-old preadolescents

• 3 doses were administered subcutaneously at 0, 1 and 6 months

<table>
<thead>
<tr>
<th>Age group</th>
<th>Before vaccination 1992–1998</th>
<th>After vaccination 1999–2005</th>
<th>% Rate decline (95% CI)</th>
<th>P</th>
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<tbody>
<tr>
<td></td>
<td>Rates&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Cases</td>
<td>%</td>
<td>Rates&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>32</td>
<td>1.36</td>
<td>0.34</td>
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<td>Total</td>
<td>5.51</td>
<td>2,356</td>
<td>100</td>
<td>2.98</td>
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</table>

<sup>a</sup> Per 100,000 person-years.

* Per 100,000 population.
USA Hepatitis A Incidence by Age and by Region

States Where Childhood Vaccination Is Recommended or Considered (17 Vaccinating States)

States With No Statewide Childhood Vaccination Recommendation (33 States and DC)

Wasley et al. JAMA 294:194-201, 2005
HAV Vaccination Coverage in the USA

Hepatitis A vaccination coverage among children aged 24-35 months - United States, 2003

Mean HAV Vaccination Coverage among Children 12-23 Months (Immunization Information Systems (IIS) Sentinel Sites, 2006-2009)

CDC, MMWR; 54:141-4, 2005

CDC, MMWR; 59:776-9, 2010
Impact of HAV Vaccination of Indigenous children on HAV Notifications in north Queensland

- North Queensland population was 596,500 people, including about 6900 Indigenous children <5 yrs

- HAV vaccine was provided to Indigenous children in north Queensland from February 1999
  - 2 doses (18, 24 m) + catch-up vaccination <6 years

* The vaccination program was implemented from February 1999

Control of Hepatitis A by Universal Vaccination of Toddlers and Adolescents, Puglia, Italy

- In 1998, after a large epidemic of HAV, a vaccination program for toddlers and adolescents was initiated in Puglia in southeastern Italy (population >4 million)
- Free to all children 15–18 months and adolescents 12 years
- No catch-up vaccination campaign has been planned

**Puglia and Tourism**

- Vaccination could also be effective because by reducing circulation among individuals it also reduces circulation in seafood.

- Data from Puglia, 1999-2000 reported that HAV-RNA was detected in 20.0% of non-depurated mussels and in 11.1% of depurated samples.

- In contexts where bad eating habits still persist and not all urban centers have effective sewage treatment plants, universal routine vaccination, aimed at the control of direct transmission, remains the milestone in the strategy for the containment of the disease, supplemented by health education and improvements in sanitation.

Israel, Pre-Vaccination Data

- Until 1999, Israel was considered a country with intermediate HAV endemicity
- Average annual incidence rate during the period from 1993-1998 was **50.4/100,000**
- Israel's population: 6.3 million in 2000
  - Jewish population: 78%
  - non-Jewish population: 22%
    - 82% Muslims
- In general, the non-Jewish population lives in lower socioeconomic conditions than the Jewish population
  - more crowded living conditions
  - greater proportion of children aged <15 years
  - lower proportion of elderly
  - more rapid population growth

![Graph showing seroprevalence by age and population group](#)
HAV Nationwide Vaccination in Israel

- Starting July 1999 all toddlers in Israel receive 2 doses of HAV vaccine at age 18 and 24m
- The vaccine is provided free of charge, as a part of the regular immunization program
- ~ 90% receive 1 dose; > 80% receive 2 doses
- No Catch-up program beyond toddlers was introduced
HAV Nationwide Vaccination in Israel

Dagan et al. JAMA 294:202-10, 2005 + additional data from Israel MoH
Seropositivity Rate in Non-immunized Bedouin Toddlers Aged 16-20 m from the Town of Rahat 1991 through 2008

Year of specimen collection

Seropositivity Rate in Non-immunized Bedouin Toddlers Aged 16-20 m from the Town of Rahat 1991 through 2008

Born before introduction of the universal immunization program

Born after introduction of the universal immunization program

Year of specimen collection

HAV outbreaks in DCC and School Settings - Israel Southern Region 1993-2005

• Of the 983 cases reported nationwide, the vaccination status could be ascertained in 846 (86%)

• Of these
  – 830 (98.1%) received no vaccine
  – 16 (1.9%) received 1 dose
  – 0 received 2 doses
• National Infant HAV Immunization Program started in mid 2005
  – Age 1 year
  – No catch-up

• Estimated coverage in 2006, 2007, 2008, 2009 83%, 92%, 99.9% and 98% respectively
**Hepatitis A—Argentina, 1994-2008**

- **Graph:** The graph shows the number of hepatitis A cases in Argentina from 1994 to 2008, with a marked increase in 2004 followed by a significant decrease by 2006.
- **Vaccination:** An 88.0% vaccination rate is indicated, with 1 dose administered.

**Fuente:** notificaciones al SINAVE-Dirección de Epidemiología-Ministerio de Salud de Nación
Fulminant Hepatic Failures, Argentina
1993-2008

Hepatitis A vaccination

Cervio et al. 49th ICAAC, September 12-15, San Francisco, 2009
Conclusions

- HAV biology sets the conditions that make vaccines against this virus a perfect fit for expecting significant herd immunity
- All immunization programs with HAV vaccines showed impressive herd immunity
- A significant herd immunity can be observed even when HAV vaccine uptake is partial
- Immunization of toddlers is most promising, but data show that adolescents may be also a good target group
- HAV vaccines are licensed as 2-dose vaccines, but data from Argentina suggest (although did not yet prove unequivocally) that one dose may be similarly effective in the prevention of HAV transmission