Epidemiology and Prevention of Hepatitis A in Korea

Associate Professor
Department of Pediatrics, College of Medicine,
The Catholic University of Korea

Director
Division of Enteric and Hepatitis Viruses, NIH,
Korea Centers for Disease Control and Prevention

Jong-Hyun Kim, M.D.
Contents

- Etiology of Acute Viral Hepatitis
- Change of Hepatitis A Epidemiology
  - Seroprevalence of anti-HAV
  - Age distribution of acute hepatitis A patients
- Status of current hepatitis A vaccine
About South Korea

Population: about 48 million, Capital: Seoul
Gross domestic products (GDP): $791 billion (12th)
Gross national income (GNI): $765 billion (11st)
Personal GNI: $18,372 (41-49th)
Etiology of Acute Viral Hepatitis

- HBsAg+ rate
  - 1970s: 7-8%
  - 2005: 3.5%
  - school age: <1%

- Anti-HCV rate: <1%

- HEV, 1.6%
- HCV 4%
- HBV 45%
- HAV 49%

- Asan Medical Center, University of Ulsan, Seoul
- Study periods: 2002-2004
- Fulminant hepatitis: 10 cases (all: hepatitis B)

Change of Hepatitis A Epidemiology

- Due to the absence of reporting system in the past, it was impossible to determine the exact disease burden of hepatitis A.
- In the 70s, the prevalence of hepatitis A was so high that, hepatitis A accounted for approximately 2-5% of all hospitalized children in South Korea. This situation remained the same until the mid-80s.
- Thereafter, the cases had significantly decreased until an outbreak had occurred in a city in 1996. Since then, the number of hepatitis A cases gradually increased and in 2006, 1,923 cases were officially reported.
## Proportion of In-patient with Hepatitis A in 1970s

St. Mary's Hospital, The Catholic University of Korea

<table>
<thead>
<tr>
<th>Year</th>
<th>No of HepA</th>
<th>Total No of In-Pt</th>
<th>%</th>
<th>Year</th>
<th>No of HepA</th>
<th>Total No of In-Pt</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1968</td>
<td>31</td>
<td>931</td>
<td>3.3</td>
<td>1973</td>
<td>26</td>
<td>1,010</td>
<td>2.6</td>
</tr>
<tr>
<td>1969</td>
<td>15</td>
<td>1,084</td>
<td>1.4</td>
<td>1974</td>
<td>24</td>
<td>844</td>
<td>2.9</td>
</tr>
<tr>
<td>1970</td>
<td>16</td>
<td>937</td>
<td>1.7</td>
<td>1975</td>
<td>35</td>
<td>895</td>
<td>3.9</td>
</tr>
<tr>
<td>1971</td>
<td>18</td>
<td>922</td>
<td>2.0</td>
<td>1976</td>
<td>20</td>
<td>847</td>
<td>2.4</td>
</tr>
<tr>
<td>1972</td>
<td>29</td>
<td>963</td>
<td>3.0</td>
<td>1977</td>
<td>27</td>
<td>1,036</td>
<td>2.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>241</strong></td>
<td></td>
<td><strong>Total</strong></td>
<td></td>
<td><strong>9,469</strong></td>
<td></td>
</tr>
</tbody>
</table>

* HepA, hepatitis A; Pt, patient


**Other reports from 1970s: 1.3 - 6.4%**

Park et al. J Kor Pediatr Soc 1975;19:180
Lee et al. J Kor Pediatr Soc 1978;21:376
First Outbreak of Hep A at Daejeon City in 1990s

- **Periods:** July to Dec, 1996
- **Institution:** St. Mary’s Hospital, The Catholic University of Korea
- **Total number of patients:** 60 cases (31 children, 30 adults)
- **Age distributions:** age 4 – 26 years
  - Children: 3 cases in 4-5 year of age, 13 cases in 6-10 year of age, 15 cases in 11-15 year of age
  - Adults: 29 cases in 16-26 year of age

Choi et al. J Kor Pediatr Infect Dis 1997;4:90-6
Prevalence of Hepatitis A on 1988-98

Four hospitals attached to The Catholic University of Korea

M : F = 1.2 : 1.0

Kim et al. J Kor Pediatr Infect Dis 1998;5:230-8
Age Distribution of Hepatitis A on 1988-98

Four hospitals attached to The Catholic University of Korea

Kim et al. J Kor Pediatr Infect Dis 1998;5:230-8
### Reported Cases of Hepatitis A in National Sentinel Surveillance System (Korea CDC)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>5-9</td>
<td>20</td>
<td>13</td>
<td>8</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>10-14</td>
<td>63</td>
<td>33</td>
<td>15</td>
<td>12</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>15-19</td>
<td>105</td>
<td>58</td>
<td>28</td>
<td>35</td>
<td>47</td>
<td>6</td>
</tr>
<tr>
<td>20-29</td>
<td>914</td>
<td>370</td>
<td>182</td>
<td>166</td>
<td>147</td>
<td>48</td>
</tr>
<tr>
<td>30-39</td>
<td>659</td>
<td>241</td>
<td>100</td>
<td>80</td>
<td>77</td>
<td>24</td>
</tr>
<tr>
<td>40-49</td>
<td>116</td>
<td>60</td>
<td>15</td>
<td>8</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>50-59</td>
<td>16</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>26</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1923</strong></td>
<td><strong>796</strong></td>
<td><strong>359</strong></td>
<td><strong>312</strong></td>
<td><strong>317</strong></td>
<td><strong>105</strong></td>
</tr>
</tbody>
</table>
Hepatitis A Cases on 2006

Seoul: 793 cases
Incheon: 121 cases
Kyonggi: 768 cases
Pusan: <10 cases
Daegu: 10 cases

Total cases: 1,923

Seoul to Pusan (400km)
by car: 5 hrs
by high speed train: 3 hrs

1st city: Seoul
2nd city: Pusan
3rd city: Daegu

Why so different?
Outbreak of Hepatitis A in Kongju City (June, 2004)

- Confirmed acute hepatitis A patients = 54 cases
  - < 9 yrs, 2; 10-19 yrs, 12; 20-29 yrs, 31; 30-39 yrs, 6; > 40 yrs, 3

- Epidemiological survey was performed.

- Thirty-nine out of 54 patients: visiting history of a restaurant with family or friends from late April to mid-May.

- That restaurant used the underground water kept in water-tank to clean tableware.
Most recent sero-prevalance Study I

- Study period: 2006'
- Enrolled institutes: 5 university hospital
- Regions: Seoul (2), Incheon (1), Suwon (1), Daegu (1)

Seoul, Suwon, Incheon regions are relatively endemic area in Korea.
Most recent sero-prevalacne Study II

- **Sample Sizes:** total 1,000 (equally divided by each institute)
  - 1-4 year: 100 cases (every age interval)
  - 5-9 year: 125 cases (every age interval)
  - 10s: 250 cases (every age interval)
  - 20s, 30s: 150 cases each (2 year interval)
  - 40s: 100 cases (2 year interval)
  - 50s, > 60s: 50 cases each

- **Test:** Elecsys Anti-HAV reagent kit (Roche)
  
  Electrochemiluminescence Immunoassay (ECLIA)

  Positive: Immunity by past infection or vaccination
Result: Age-specific Sero-prevalence of Hepatitis A Antibody in Korea
Result: Sero-prevalence of Hepatitis A Antibody by Age Groups

<table>
<thead>
<tr>
<th>Anti-HAV+ (%)</th>
<th>1-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>61-69</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>56</td>
<td>57</td>
<td>13.6</td>
<td>8</td>
<td>15.8</td>
<td>73.2</td>
<td>96</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>5-9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61-69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(yr)
Result: Sero-prevalence of Hepatitis A Antibody by Regions

Seoul, Suwon, Incheon regions are relatively endemic area in Korea.
Changes of anti-HAV IgG in Korea

J Kor Pediatr Soc 1997 Symposium Abs Book p96
First launch of a hepatitis A vaccine in the late 1997

Now, KFDA has licenced four different HepA vaccines
- Havrix (GSK)
- Vaqta (MSD)
- Epaxal (Berna Biotech)
- Avaxim (Sanofi-Pastuer)

Recommend vaccination at above 12 months of age with interval over 6 months (not universal)
Incidence of Hepatitis A among Korean Soldiers

Total No. of Korean Soldiers ≈ 500,000
Range of Ages: 19 - 27

No. of reported cases 37 8 22 49 31
No. of Outbreak 2 1 1 5 2
No. of epidemic cases 23 3 3 31 4

Age-specific Seroprevalence of Anti-HAV Antibody in Korean Patients with Chronic Liver Diseases (2005)

Age distribution: >40, 79%; 31-39, 15%
Cause of CLD: HBV 65%, alcohol 17.7%, HCV 12.9%

Ewha University Hospital
Coverage Rate of Hepatitis A Vaccines

<table>
<thead>
<tr>
<th>Year</th>
<th>Birth No</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>675,227</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>640,126</td>
<td>103,455</td>
</tr>
<tr>
<td>1999</td>
<td>616,322</td>
<td>182,463</td>
</tr>
<tr>
<td>2000</td>
<td>636,780</td>
<td>296,508</td>
</tr>
<tr>
<td>2001</td>
<td>557,228</td>
<td>365,602</td>
</tr>
<tr>
<td>2002</td>
<td>494,625</td>
<td>498,882</td>
</tr>
<tr>
<td>2003</td>
<td>493,471</td>
<td>562,186</td>
</tr>
<tr>
<td>2004</td>
<td>476,052</td>
<td>591,505</td>
</tr>
<tr>
<td>2005</td>
<td>438,062</td>
<td>744,995</td>
</tr>
<tr>
<td>2006</td>
<td>942,061</td>
<td></td>
</tr>
</tbody>
</table>

- sum of total doses 4,184,202 / sum of total birth No. 5,027,893 during 1998-2006 = 41.6% (estimation)
- Actual coverage rate of Hepatitis A vaccine in 1-2 year old on 2006: 40% (Kim KH et al. unpublished data)
For those aged less than 10 years old, anti-HAV prevalence was above 50%, mainly contributed to the result of vaccination.

However, the prevalence of antibody in the 10s and 20s were 10-30%, a number significantly lower than other age groups.

Almost all people above 40 years old have antibody to HAV.
According to Regions, there is a difference of prevalence of acute hepatitis A in small country. → why?

10s having lowest anti-HAV among 10s, 20s and 30s → lowest reported cases?