Hepatitis A Virus Infections in Urban Children—Are Preventive Opportunities Being Missed?

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To determine the prevalence of hepatitis A virus (HAV) infections in children in a large urban center, a point prevalence survey was conducted using a novel, ultrasensitive assay for HAV-specific IgG in saliva. A structured sample of 224 grade-six students (5.8% of grade registrants) was obtained from 23 schools throughout Vancouver. All students provided saliva samples adequate for testing. The anti-HAV prevalence rate was 7.1% (95% confidence interval, 4.1%–11.3%). Among 167 Canadian-born students, only 5 (3%) were positive, whereas among 57 students born elsewhere, 11 (19.3%) were positive ($P < .001$), with circumstances in the latter group supporting infection prior to emigration. No clustering of positive persons was evident. The cumulative risk of HAV infection in Canadian-born children was low through age 11–12 years even in less affluent parts of the city, speaking against a need for routine use of HAV vaccine in this setting.

Although the first written description of hepatitis A virus (HAV) infection is believed to be in the writings of Hippocrates, modern medicine can offer infected persons little more than Hippocrates could. No specific antiviral therapy is available, so control of disease relies mainly on preventive measures, such as improvements in sanitation, passive immunization of case contacts, and active immunization with newly available inactivated vaccines of persons at increased risk of exposure [1–3]. Inactivated hepatitis A vaccine has been licensed in Canada for >2 years; however, a lack of epidemiologic data regarding children at risk for HAV infection has precluded national recommendations for routine immunization [4], except in isolated communities experiencing high rates of infection or in persons with predictable exposure risk.

As a busy port of entry from the Pacific Rim, Vancouver, with its 1.86 million people, is likely to be at increased risk of HAV importation and secondary spread. High immigration rates, high population densities, ethnic and socioeconomic diversity, and extensive and rapidly expanding day care services for children all could contribute to HAV transmission in this and similar urban environments.

Although >200 cases of confirmed hepatitis A infection have been reported annually in Vancouver in recent years, mainly in gay men, such figures [5] are incomplete. Typically missing from such estimates are cases occurring in young children in whom infection is often mild and unrecognized. Measurement of the prevalence of anti-HAV immunity in populations offers more reliable data regarding cumulative disease incidence and risk distribution. Data on the seroprevalence of anti-HAV in British Columbians are nonexistent, and data concerning other Canadian populations are limited to a few studies [6–9] conducted more than a decade ago.

While serosurveys are the ideal means of determining cumulative infection rates in populations, current attitudes about their ethical propriety severely limit their use in children. Assessment of HAV immunity based on analysis of noninvasively obtained specimens (e.g., saliva) offers an acceptable approach that has been successfully used in epidemiologic investigations of HAV outbreaks in the United Kingdom [10, 11].

This study was designed to determine whether opportunities for preventing HAV infection in children in an urban setting were being missed, as determined by the prevalence of anti-HAV measured noninvasively in a structured cohort.

**Methods**

**Study population.** We studied grade-six students attending public schools under the jurisdiction of the Vancouver School Board between December 1995 and June 1996. Our objective was to obtain samples from 10% of the students (total, 400) by enlisting half the schools and randomly selecting for testing 20% of eligible students therein. By assuming an anti-HAV prevalence of ~10%, we determined that this sample size would have a 95% probability of estimating the actual value within ±3% ($\alpha = 0.05$). School selection was stratified between the east and west halves of the city because they differ in socioeconomic level, with the East Side being less affluent, more densely populated, and more often the...
receiving area for new immigrants. No exclusion criteria applied to volunteers apart from the capacity to provide informed consent.

**Enrollment procedures.** Principals of all 57 Vancouver public schools with grade-six programs were invited by the School Board to participate in the study. The acceptance rate was lower than anticipated, so all willing participants were accepted. Notices describing the study and parental consent forms were sent home with the grade-six students. Translations of study notices were available for families with English as a second language. From among students who obtained parental consent, the study nurse randomly selected a number of students equivalent to 20% of the grade-six enrollment of the participating school and invited them to take part in the study.

Students were shown how to provide a salivary specimen. The study nurse also completed a structured interview with each student, encompassing their birth and residency history, family size, language spoken at home, and day care attendance. Information about subjects was recorded on a specific case report form. Personal identifiers were limited to postal code and school number.

**Measurement of HAV-specific IgG in saliva.** Saliva was collected using Salivette pads (Sarstedt, Numbrecht, Germany) with a neutral insert, which subjects chewed until thoroughly wet. Saliva was subsequently recovered by centrifugation. All specimens were refrigerated immediately and frozen at −70°C in small aliquots on the day of collection.

Prior to being tested for HAV-specific IgG, all saliva specimens were screened for the presence of a satisfactory amount of IgG class antibodies, using an in-house capture-type EIA. Only specimens containing >100 ng/mL of total IgG were considered suitable for specific antibody analysis.

Salivary specimens of adequate volume and total IgG content were tested for HAV-specific IgG content, using a novel ultrasensitive EIA [12]. This assay is 99% specific and 99% sensitive in detecting anti-HAV–seropositive samples.

**Data analysis.** Case report forms were checked for completeness and then entered along with test results into an electronic database. Dual data entry, done by different technicians, and programmed consistency checks were used to minimize transcription errors.

Proportional data were compared by use of χ² and Fisher’s exact tests, two sided. Relationships between household size or number of siblings and anti-HAV positivity were evaluated using analysis of variance. Differences with values of \( P \leq 0.05 \) were considered significant.

**Results**

Principals of 23 (40%) of Vancouver’s 57 public schools with grade-six programs agreed to participate. Study enrollment totaled 224 children representing 20.3% of grade-six students at participating schools and 5.8% of all registered grade-six students. Participants originated in 16 schools (of 31 total) located in Vancouver’s East Side (166 students [74% of study enrollment]) and in 7 schools (of 26) located in Vancouver’s West Side (58 children [26% of sample]). All 224 saliva samples were adequate for anti-HAV testing. Demographic characteristics of participants are presented in table 1. Children’s ages ranged from 10 to 12 years, with 168 participants (75%) being 11 years old, and only 2 (0.9%) being 10 years old at the time of enrollment. Although 75% of the students were born in Canada, only 51% (113) spoke primarily English at home (82% on the West Side and 32% on the East Side). Previous day care attendance was reported by 144 students (94% from West Side and 61% from East Side).

Evidence of past HAV infection was detected in 16 of 224 tested students, which is an overall prevalence rate of 7.1% (95% confidence interval: 4.1, 11.3). Of the 16 who tested positive, 13 were girls (81.3%), whereas among 208 negative students, only 51.4% were girls (\( P < .05 \)). The mean age of anti-HAV–positive (11.38 ± 0.5 years) and–negative (11.22 ± 0.4 years) students did not differ significantly. Among children positive for HAV-specific IgG, the average number of people in the household (5.5) and the average number of siblings (2.5) were significantly higher than in children who tested negative (4.5 and 1.5, respectively; \( P < .01 \)). All 16 anti-HAV–positive students in our sample attended East Side schools. No further geographic clustering of positive students was observed because they were distributed among 10 schools, and each had a different postal code. The proportion of children who reported past day care attendance was similar among anti-HAV–positive (60%) and negative (65.5%) students. Use of a language other than English as the primary language spoken at home and the number of bedrooms in a household were not associated with an increased positivity rate for anti-HAV. Medical histories were not available to determine if students positive for anti-HAV had had recognized hepatitis A infection.

Although students born outside of Canada constituted only 25% of our sample, they accounted for 69% (11/16) of the positive cases. The prevalence rate for anti-HAV among the 57 foreign-born children was 19.3% (95% confidence limit: 10.0, 31.9). Girls constituted two-thirds (66.7%) of foreign-

**Table 1.** Selected demographic characteristics of anti-HAV–positive and –negative students.

<table>
<thead>
<tr>
<th></th>
<th>Anti-HAV positive</th>
<th>Anti-HAV negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Total</td>
<td>16 (7.1)</td>
<td>208 (92.9)</td>
<td>224</td>
</tr>
<tr>
<td>Male</td>
<td>3(^*) (2.9)</td>
<td>101(^*) (97.1)</td>
<td>104</td>
</tr>
<tr>
<td>Female</td>
<td>13(^*) (10.8)</td>
<td>107(^*) (89.2)</td>
<td>120</td>
</tr>
<tr>
<td>Canadian born</td>
<td>5(^*) (3.0)</td>
<td>162(^*) (97.0)</td>
<td>167</td>
</tr>
<tr>
<td>Born outside Canada</td>
<td>11(^*) (19.3)</td>
<td>46(^*) (80.7)</td>
<td>57</td>
</tr>
<tr>
<td>Attended day care in past</td>
<td>9 (6.3)</td>
<td>135 (93.7)</td>
<td>144</td>
</tr>
<tr>
<td>No day care in past</td>
<td>6 (7.8)</td>
<td>71 (92.2)</td>
<td>77</td>
</tr>
<tr>
<td>Average no. of people in household</td>
<td>5.5(^*)</td>
<td>4.5(^*)</td>
<td>4.55</td>
</tr>
<tr>
<td>Average no. of bedrooms in household</td>
<td>3.38</td>
<td>3.09</td>
<td>3.11</td>
</tr>
<tr>
<td>Average number of siblings</td>
<td>2.5(^*)</td>
<td>1.47(^*)</td>
<td>1.54</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) or no. \( P < .05, ^* .001, ^{1} .01 \).
born children and accounted for 10 (91%) of 11 positive tests. Nearly 90% of foreign-born students originated from countries considered to be at increased risk for HAV transmission, with Asian countries predominating (74%). The average age at which these children left their country of birth was 5.4 years, and this did not differ between HAV-positive and -negative students. Past day care attendance was reported by 5 students, a proportion identical to that for the noninfected students ($P = 1.0$). Foreign-born children positive for anti-HAV were more likely to have a larger number of siblings and larger families than were children negative for anti-HAV ($P < .001$ and $P < .05$, respectively).

Among 167 Canadian-born children, only five tested positive for anti-HAV, a prevalence rate of 3.0% (95% confidence interval: 1.0, 6.9). The difference in positivity rates between students born in Canada or elsewhere was statistically significant ($P < .001$). All positive, Canadian-born students attended schools on the East Side, but none attended the same school. Among the 119 Canadian-born students attending East Side schools the HAV positivity rate was 4.2% (95% confidence limit: 1.4, 9.5). Four Canadian-born positive students (80%) reported past day care attendance, but this experience was common (70%) among Canadian-born students.

**Discussion**

By taking advantage of a newly developed, ultrasensitive salivary assay [12] for antibody to HAV, we were able to gauge the cumulative infection rate during the first 11–12 years of life among children in an urban center. Contemporary risk estimates have not previously been available. Our data indicate a low rate of infection among Canadian-born children living in Vancouver.

We chose to survey grade-six students (11–12 years old) because they are old enough to reflect considerable exposure risk accumulation but not so old as to reflect risk rates that no longer apply because of social changes. They are also the oldest cohort still attending neighborhood-centered primary schools, a fact that might permit a structured survey to detect pockets of increased infection risk. We intended to randomly sample half the available schools and 10% of grade-six registrants. We achieved the intended school participation on the East Side of the city but fell short of our target on the West Side by six schools. The final sample included 40% of schools. Their selection proved to be arbitrary (determined by the school principals) rather than random, but good geographic distribution was achieved nevertheless. The largest schools more often declined to participate.

Our final enrollment represented 5.8% of all registered students. We chose not to compensate for the shortfall in schools by exceeding the planned 20% sampling of students at the last participating schools, as they would have been overrepresented in consequence. We omitted private and religious schools from the survey because they draw students from wide areas, including the suburbs. Such schools house ~15% of grade-six students in Vancouver. The final composition of the sample was weighted in favor of the less affluent half of the city with its greater population density and larger share of recent immigrants, circumstances that might be expected to favor the spread of HAV infections. Thus, the observed overall prevalence of 7.1% is more likely to be an over- than an underestimation.

The overall prevalence of HAV infection markers in our sample (7.1%) is lower than the 11% and 10% seroprevalence reported in the NHANES (National Health and Nutrition Examination Survey) II [13] and III [14] surveys of American children of comparable age completed in 1980 and 1991, respectively. Most (69%) anti-HAV–positive students in our sample were born outside the country, mostly in countries where HAV infection is endemic. The mean age of these children at emigration was 5 years; therefore, it is likely that they were infected before their arrival in Canada. However, the possibility of infection having occurred after arrival cannot be excluded.

The low anti-HAV positivity rate among adolescents in Vancouver is reassuring, given the city’s crowded, cosmopolitan, urban environment. Its role as a major portal for visitors and immigrants from Pacific Rim countries might predispose Vancouver to frequent virus importation and extended circulation, but this was not evident among children surveyed, even in the least affluent areas of the city. While the observed rates of anti-HAV positivity in Canadian-born students ranged from 0% on the West Side to 4.2% on the East Side, the latter area was surveyed more intensively (74% of enrollment), and the 95% confidence intervals of the estimates overlap considerably. Similarly, low rates of infection were recently reported among children in Montreal [9], another large cosmopolitan Canadian city, suggesting that Canadian urban centers in general are not experiencing a significant spread of HAV infection.

Despite reports of HAV outbreaks involving child day care centers in the United States [reviewed in 15] and Europe [16], such outbreaks have rarely occurred in Canada. Prior attendance at day care facilities did not emerge as a risk factor for HAV infection in our survey. However, our treatment of this variable was categorical. We did not attempt to gather details pertaining to day care (e.g., age at entry, size of the facility, hours of attendance per week) that have been shown to be relevant in outbreaks elsewhere [15].

Our data support previous reports that HAV infection is more frequent in larger families with numerous children [17]. Gender has little influence on HAV infection rates, so we ascribe the predominance of girls among children with anti-HAV in our survey to chance.

In summary, our survey showed a low rate of prior HAV infection among 11- to 12-year-old students in an urban Canadian area, particularly in those born in Canada. There appears to be little justification to consider routine universal immunization to protect children against HAV. Existing preventive measures appear to be adequate for this age group. However, our survey also indicated that this population is highly susceptible...
to HAV should control measures fail (as in natural disasters) or circumstances change. Active immunization is advisable for persons at increased risk of exposure, such as those traveling to areas endemic for HAV.

Acknowledgments

We thank the Vaccine Evaluation Center, in particular Giselle Lightle and Lisa Chen, whose skillful assistance and dedication made completion of this study possible. We also thank the staff of the Vancouver School Board for their support and assistance in school recruitment.

References