The prevalence of hepatitis A antibodies among Israeli travellers and the economic feasibility of screening before vaccination

Eli Schwartz\(^a\) and David Raveh\(^b\)

**Background**  Hepatitis A (HA) is the most common vaccine-preventable disease among travellers. The probability of contracting the disease depends on the endemicity in both the destination and country of origin of the traveller. The introduction of the new highly effective but expensive inactivated HA vaccine necessitates a re-evaluation of HA prevention policy. In highly developed countries all travellers require vaccination. In highly endemic areas the entire population is immune. In Israel, HA seroprevalence declined from 94% in the early 1970s to <60% in the mid 1980s. Living in a country in which the HA endemicity is changing, we studied the current situation of HA seroprevalence among travellers and the cost-benefit of screening for HA IgG before vaccination.

**Methods**  Israeli travellers of all ages, (range 22–74 years) expecting to spend a considerable time abroad presented to the travel clinic for pre travel advice and vaccination. A brief medical history was taken, including history of jaundice. Blood for HA IgG testing was drawn.

**Results**  In the present study, 389 Israeli travellers were screened for HA IgG. Overall, 46% were seropositive: 26% in the 21–30 group (n = 102); 37% in the 31–40 group (n = 145); 62% in the 41–50 group (n = 62); and 79% in the >50 group (n = 80).

**Conclusions**  In countries where hepatitis A endemicity is changing, an evaluation of seroprevalence and then a cost benefit calculation should be made. In Israel, assuming a current cost of $130 for vaccination and $30 for the IgG test, it is economically valid to screen Israeli travellers >30 years old for HAV IgG before vaccination. A formula is presented for calculating the cost benefit ratio in any country, based on local endemicity according to age group.

**Keywords**  Hepatitis A vaccine, hepatitis A antibodies, travellers, Israel

**Accepted**  29 May 1997
This fact, coupled with the reported reduction in seroprevalence, led us to investigate the economic efficacy of screening before vaccination, and to study the current antibody status among Israelis embarking on long term travel to endemic areas in relation to age group.

Patients and methods

The study population consisted of 389 Israelis about to embark on an extended stay abroad for more than 6 months, who were referred to the Travel Medicine Center at Moshav Lachish Hospital during 1993 to 1995. Age, sex, and past history of jaundice were recorded. All were screened for HAV-IgG status using a commercial ELISA kit (BIO KIT S.A. Barcelona, Spain). The sensitivity of the test is 99.9% and the specificity is 99.6%.

Results

Of the 389 people who were screened, 54% were males, and 46% were females (age range 22–74 years, average 39.5 years). Of these 46% were seropositive for HA. The distribution of seropositivity among the age groups ranged from 26% in the 21-30 group, to 82% in the >61 group (Figure 1). History of jaundice was obtained for 188 patients, of whom 28 recalled having had jaundice and 160 did not. Of the 28 who had had jaundice, 27 tested positive for HA antibodies, therefore the positive predictive value for HAV-IgG with a history of jaundice is 96.4%. Of the 160 patients who did not recall having had jaundice, 61 were found to be HAV-IgG positive. Altogether 88 people were found to be HAV seropositive, 61 of whom did not recall having jaundice, therefore 69.3% had evidence of a subclinical infection. Table 1 shows a breakdown of the prevalence of subclinical HA episodes according to age: a significant drop is apparent under 30 years of age (P = 0.027).

To be economically worthwhile, the cost of vaccinating the entire population must be equal to or less than the cost of testing the entire population plus the cost of vaccinating the non-immune:

\[ A = B + A(1 - x) \]

where A is the total cost of the vaccine including the cost of manpower, B the total cost of the test including all visits to the clinic, and x the HAV-IgG positive fraction of the population. It must be noted that a series of vaccinations at our clinic requires 2–3 visits. On the first visit HA-IgG is tested, and if negative, on a subsequent visit the patient can be vaccinated at no extra cost for the actual visit. Based on a cost of $130 for the vaccine and $30 for the initial testing, the calculation shows that screening is valid for a population with a prevalence of HA-IgG of >23%. In Israel this translates to travellers above 30 years old.
Table 2 Published hepatitis A virus seroprevalence in Israel

<table>
<thead>
<tr>
<th>Year</th>
<th>Reference</th>
<th>Age</th>
<th>% HAV-IgG+</th>
<th>Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>Bar Shany et al. 1977</td>
<td>18-60</td>
<td>94%</td>
<td>90-100%</td>
</tr>
<tr>
<td>1987</td>
<td>Green MS et al. 1989</td>
<td>25-42</td>
<td>80%</td>
<td>70-92%</td>
</tr>
<tr>
<td>1989</td>
<td>Green MS et al. 1992</td>
<td>21-30</td>
<td>55%</td>
<td>47-84%</td>
</tr>
<tr>
<td>1995</td>
<td>Present study</td>
<td>21-70</td>
<td>46%</td>
<td>26-82%</td>
</tr>
</tbody>
</table>

* The lower percentage is in the younger age group.

In the >50 age group screening before vaccination could save 57% of the total vaccine expenditure; in the 31-50 group screening could save 22% of the expenditure.

Discussion
The development of the inactivated HA vaccine which gives an ultimate solution to the non-immune population, coupled with the decline of HA endemicity in developed countries warrants a new look at vaccination policies for travellers. The economic efficacy of prior testing for HAV antibodies becomes a valid issue for organizations that cover the costs of sending representatives abroad. Travellers from highly developed countries or from highly endemic areas pose no dilemma: in the first case the risk is high and all must be vaccinated unless they have had jaundice, and in the second the risk is very low since all are immune from early childhood. However, in countries of origin in which HAV endemicity is on the decline, the situation is not clear-cut, and a decision has to be based on the distribution of seropositivity in relation to age.

In Israel, HAV endemicity has been decreasing since the 1970s, as shown in several studies (Table 2). The first published in 1977, was a screening of blood donors over 18 years of age. Overall, HA-IgG prevalence was found to be 93.7%, with seropositivity being 100% in the >40 age group. During the 1980s, several other surveys were conducted among the adult population in Israel, mainly among soldiers of the Israel Defense Forces (IDF). In 1987, seroprevalence was 82% among permanent army personnel aged 25-44, decreasing to 55% in 1989, even though military service in itself is known to be a high risk factor. A comparative study of military recruits aged 18-19, showed a decline from 69% to 54% between 1977 and 1984.

Since in Israel military service is compulsory, these results reflect the situation in the Israeli population as a whole. In the present study, all the people screened were highschool graduates, some with university education, and the majority were IDF veterans. This cohort may not reflect the situation in the entire population but it does represent Israeli travellers. Despite this bias, the changing pattern of HA endemicity is apparent, with a much lower rate of HA-IgG among the younger age groups compared to the >40 group.

Based on subjective histories, subclinical events of HA in the young age group also display an obvious decline, and this observation may be another marker for the declining HA endemicity in Israel. Recording the history of clinical jaundice as a predictor for HA status is important. In Israel, a positive history of jaundice is a reliable marker for previous HA, since the incidence of hepatitis B is very low. It must however be kept in mind that a negative history does not exclude seropositivity, due to the high incidence (69%) of subclinical HA in the past.

The general policy of the health authorities in Israel is not to recommend HA vaccine for those over 40 years because previous studies have shown almost 100% immunity in this group. The present study clearly shows this not to be true, and even among the >60 group, a significant fraction, around 20%, were not immune. Since the morbidity and mortality of HA increase with age, and the case fatality rate is up to 2.5% for >40 years old, this group must be screened for the HA antibody status in order to vaccinate if necessary.

Israel, with its rapid development and improved hygiene can serve as a model for similar countries with changing HA endemicity. The present study shows that although HA prevalence is lower than that found in previous studies significant fractions of people who are non-immune appear in all age groups. Given the present endemicity pattern in Israel, and assuming a cost of $30 for the IgG status test and $130 for the vaccine, it is economically valid to pre-test travellers over 30 years of age.

References