## **SHORT PAPER**

## Hepatitis A antibody prevalence among young adults in Israel – the decline continues

M. GDALEVICH $^{1*}$ , I. GROTTO $^{1}$ , Y. MANDEL $^{1}$ , D. MIMOUNI $^{1}$ , J. SHEMER $^{1,2}$  and I. ASHKENAZI $^{1,2}$ 

(Accepted 5 May 1998)

## **SUMMARY**

This study sought to determine whether the decline in prevalence of hepatitis A virus (HAV) antibodies detected in Israel in 1977, 1984, and 1987 has continued. The anti-HAV antibody prevalence of a systematic sample of 578 male and female recruits inducted into the Israel Defence Force in 1996 was 38.4%. The reduction in antibody prevalence from 1977 (64%) was highly significant (P < 0.001). There was a smaller decrease rate in recruits of European, North American, Australian and South African origin than from elsewhere. A 'strategy' that uses active immunization against hepatitis A (inactivated vaccine, instead of gamma globulin) should be considered, particularly in high risk groups such as field units during military service.

Hepatitis A is endemic in Israel with annual reported rates ranging from 0.5-1.6 cases/1000 population [1, 2]. A decrease in the incidence is apparent during the last 12 years [2]. The annual incidence of clinicallyidentified viral hepatitis in the Israel Defense Forces (IDF) has dropped from an average of 6/1000 troops in the 1960s to 2.5/1000 in the 1970s [3], and to an average of 0.5 cases/1000 troops in the last decade. The decrease in morbidity rates has been attributed mainly to the use of immune serum globulin (ISG) in selected groups during summer and fall as a preexposure prophylaxis, and to all potential contacts of an ill person [3, 4]. This approach could be hampered by worldwide shortage of ISG and a slight risk of transferring pathogens by intramuscular injection of ISG [5].

Concurrently with the decrease in incidence, a significant reduction along the years was observed in hepatitis A virus (HAV) antibody prevalence among military recruits: 64% in 1977, 54% in 1984 and 45.5% in 1987 [6–8]. The lowering of natural

immunity against the illness presents a significant problem for the military.

In previous studies, strong ethnic differences in the prevalence of anti-HAV antibodies have been described, with persons of Asian and African origin having a much higher prevalence of anti-HAV than those of European and North American extraction. Similar results have been observed in the United States and other countries [9, 10].

The aim of our study was to measure the anti-HAV antibody prevalence among military recruits of 1996, who represent a cross section of the young adult population in Israel, and to compare these findings with previous observations from studies of identical design.

A representative sample of male and female recruits was drawn, collecting sera of 578 conscripts who joined the army between 1 August 1995 through 31 July 1996. The sample included 333 male and 245 female recruits, producing a close representation of the usual 3:2 male to female ratio in the IDF. The sample size allowed us to identify 10% absolute change in prevalence from previously reported 1977,

<sup>&</sup>lt;sup>1</sup> Medical Corps, Israel Defense Force

<sup>&</sup>lt;sup>2</sup> Sackler Medical School, Tel Aviv University, Israel

<sup>\*</sup> Author for correspondence: Dr M. Gdalevich, Yahalom 17, Kiriat Ekron, ISRAEL 70500.

1977 1984\* 1987 1996 Positive Positive Positive Positive  $\chi^2$  for P for No. (%)(%)No. (%)No. (%)No. trend trend Origin 83.1  $71 \cdot 1$ 57 50.4 < 0.0001 East 674 218 256 274 117.4 West 35.6 30.8 26.4 430 143 28 201 273 6.63 0.01Israel 42 50 22 54.5 26 50 31 38.7 0.85 0.36Gender Male 751 68.7 383 54 277 49.8 333 41.4 78.5 < 0.0001 Female 396 55.1 206 40.3245 34.3 28.6 < 0.0001 Total 1147 64 383 54 483 45.8 578 38.4 110.9 < 0.0001

Table 1. Trends in anti-HAV antibody prevalence: total and distribution by ethnic origin and gender among young Israeli adults, 1977–96

1984 and 1987 samples with a 2-tailed  $\alpha$  value of 0.05 and a power exceeding 80%.

Induction into military duty is compulsory in Israel both for men and women at the age of 18 years. About 30% of women are exempt from service, mainly due to religious reasons. Among men, about 90% are recruited. Therefore, the study sample is more representative of the total male population with a possible selection bias among the females. Country of origin was defined by the father's birthplace (or where this was Israel, the paternal grandfather's birthplace). Europe (excluding Turkey), the Americas, Australia and South Africa were defined as West. All other birthplaces, except Israel, were classified as East. Sera were stored at -20 °C. The anti-HAV antibody studies were performed at the central IDF laboratories by means of solid phase radioimmunoassay (HAVAB-Abbott Laboratories, N. Chicago, IL).

Statistical analysis included two-tailed Fisher's test for anti-HAV prevalence rate differences between strata and chi-square test for trend between succeeding examinations along the years. Multiple logistic regression was used to control for potential confounding. All tests were performed using the PEPI statistical software [11]. The antibody testing performed among recruits of 1984 included males only. Therefore this result was exempt from the total analysis, and included only when data were stratified by gender.

The anti-HAV antibody prevalence was 38·4% (95% CI, 34·4–42·5%) among the recruits of 1996. This compared to 45·8% (95% CI, 41·2–50·3%) in 1987 and 64% (95%, 61·2–66·7%) in 1977. The overall decrease trend along the years was highly significant (Table 1). The mean age of the recruits in

the sample was 18.7 years (s.d. = 0.96), similar to previous studies in the IDF. The prevalence of anti-HAV was higher among male than female recruits (P = 0.08) and higher in conscripts of Eastern that of Western origin (P < 0.0001). The decrease trend was highly significant when stratified by gender or by ethnicity. When stratified by gender and ethnicity, the decrease trend remained highly significant in both males and females of Eastern origin, but disappeared in Westerners. The prevalence rate was invariably higher among male than among female recruits. A significant difference in anti-HAV prevalence was found between recruits with 12 (high school) or more years of schooling (37.2% positive) compared with less than 12 years (46.2% positive; P = 0.0072). Ethnic origin, educational level and gender were included in the multivariate analysis. The strongest independent correlate of the anti-HAV presence was ethnic origin (P = 0.001). Education level and gender were not significantly associated with anti-HAV prevalence (P = 0.074 and P = 0.33 respectively),when adjusted for ethnicity.

The results of this study point to a relatively low level of natural protection against hepatitis A among young people before they join the army. Over 60% of recruits will start their service lacking immunity against the virus, allowing high morbidity rates and occurrence of outbreaks. The prevalence of anti-HAV is determined by pathogen's endemicity in the region, and personal factors such as exposure to siblings and other possible virus carriers, personal hygiene, family lifestyle and nutritional habits. Many of these factors differ when compared between clusters defined by ethnicity, even though the vast majority of young adults included in the study were Israeli born. We

<sup>\*</sup> Only male recruits were included in the survey of 1984. Not included in total trend analysis.

believe that ethnic origin, and to a lesser extent, educational level, can serve as a proxy for most of these personal influences. A lower prevalence of anti-HAV in soldiers of European than in Asian or North-African origin is possibly a result of Easterners being more heavily exposed during childhood, thus leaving a lower percentage to encounter the virus for the first time whilst in service. Although there are possible genetic influences, they are probably minor and a much larger study group is necessary to evaluate their impact on the seroepidemiology of hepatitis A. The rate of decrease is higher in recruits of Eastern origin, both male and female. In recruits of Western origin the decrease disappears when stratified by gender, possibly as a result of a small sample size. The differences in the decrease rates between strata can be a result of a higher starting point for persons of Eastern origin, since as the next age groups are raised in better hygiene and healthier environment, their exposure diminishes. Another interpretation is possible; that at the current level of endemicity of hepatitis A in Israel, there exists a certain minimal level of exposure, reflected by the small decrease in the Western subgroup who have possibly already reached this minimum.

An important comment, discussed in previous studies [6, 9, 12], is that the decrease results mainly from a cohort effect, since most, if not all the exposure occurs at the 'great equalizer' level of the kindergarten with a low subsequent chance of encountering the pathogen and therefore, no significant changes in anti-HAV prevalence.

We have shown that the prevalence rate of anti-HAV has decreased during the last 20 years and it will probably continue to decline, unless there will be a major national immunization effort against the disease. These findings suggest a reduction in faeco-oral transmission of HAV infection in childhood in Israel, although considerable ethnic differences still exist. The reduced prior exposure to the virus among young adults poses a problem of increasing proportion of susceptibles; a condition common to many developed countries and is particularly threatening in high risk circumstances. Consequently, larger number of

soldiers are at risk for acquisition of HAV infection during their service, especially in high risk conditions such as field units.

In addition to reflecting a change in exposure to a feco-oral infection, seroprevalence data may be useful in planning and assessing hepatitis A prevention and intervention policy in the military as well as the civilian sectors. Combined with the problems of ISG availability and enhanced severity of the disease in adults, the results point in favour of advancing toward active immunization with hepatitis A vaccines as the major prophylactic measure against the disease.

## REFERENCES

- 1. Swartz TA, Levin J, Ben Porat E. Epidemiology of hepatitis A in Israel. Mono Virol 1984; 15: 53–8.
- 2. Israel Ministry of Health. Notifiable infectious diseases in Israel, the Israel Center for Disease Control (ICDC) 1996; Publication No. 201.
- Heering SL, Shohat T, Lerman Y. Thirty years of experience with infectious hepatitis prevention in the Israeli Defense Forces. Milit Med 1992; 157: 530–2.
- Kark JD. Pre-exposure prophylaxis with immune serum globulin for prevention of viral hepatitis in army recruits. J Epidemiol Commun Hlth 1982; 36: 176–82.
- 5. Bresee JS, Mast EE, Coleman PJ, et al. Hepatitis C virus infection associated with administration of intravenous immune globulin. JAMA 1996; **276**: 1563–7.
- 6. Kark JD, Camhy NA, Bar Shany S. Reduction in hepatitis A antibody prevalence among young adults in Israel. Public Hlth Rev 1992/3; **20**: 31–40.
- 7. Kark JD, Bar-Shani S. Hepatitis A antibody in Israel Defense Forces recruits. J Med Virol 1980; **6**: 341–5.
- 8. Green MS, Cohen D, Slepon R, et al. Sociodemographic correlates of neutralizing poliovirus and hepatitis A virus antibodies as markers of different modes of acquiring immunity. Am J Publ Hlth 1990; **80**: 1270–1.
- 9. Koff RS. Seroepidemiology of hepatitis A in the United States. J Infect Dis 1995; **171** (Suppl): S19–23.
- 10. Forbes A, Williams R. Changing epidemiology and clinical aspects of hepatitis A. Brit Med Bull 1990; **46**: 308–18.
- 11. Gahlinger PM, Abramson JH. Computer programs for epidemiologic analysis: PEPI, Version 2. Stone Mountain, Georgia: USD Inc, 1995.
- Gust ID, Lehmann NI, Lucas CR. Relation between prevalence of antibody to hepatitis antigen and age: a cohort effect. J Infect Dis 1978; 138: 425–6.