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## Hepatitis A virus infection: progress made, more work to be done

Maureen M. Jonas\*

Hepatitis A virus (HAV) has a global distribution, being the most common cause of viral hepatitis worldwide. Approximately 1.4 million new infections are diagnosed each year, but the true incidence is considered to be much higher due to under reporting. South America is considered an endemic area, with a high prevalence of seropositivity, especially in young individuals. Lower socioeconomic status, overcrowding, poor sanitation, and inadequate water treatment are commonly associated with higher incidence and asymptomatic childhood infection in developing countries.

Reported disease rates in these areas are therefore low, and outbreaks of disease are rare, since most adults are immune. In countries with transitional economies and in some regions of industrialized countries where sanitary conditions vary, children may escape infection in early childhood. These improved conditions may lead to more clinically evident hepatitis, as infections occur in older, more symptom-prone age groups, and reported rates will be higher. A large

population of susceptible adolescents and adults increases the likelihood of outbreaks. This shift in the epidemiology of HAV infection has been noted in various countries around the world.<sup>1-3</sup> In addition, adoption of hepatitis A vaccination has been variable, so that interpretation of endemicity using seroprevalence of antibody to HAV (anti-HAV) is problematic.

It is with this background, investigating a potential shift in epidemiologic pattern, that Krebs et al.<sup>4</sup> undertook an epidemiologic study of anti-HAV seroprevalence in children and adolescents in Porto Alegre, Brazil.

This was a follow-up of a similar study done in the same region a decade earlier.<sup>5</sup> The aim of this work was to compare anti-HAV seroprevalence in the pediatric populations of two clinical laboratories, after demonstrating that the laboratory and payment structure were surrogates for subject socioeconomic stratum. In addition, seroprevalence rates across age groups were compared for the two study periods.

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Over a period of 10 months beginning in April 2007, serum samples were obtained from 222 children and adolescents who had had blood tests at a public government-supported laboratory and 243 who had had blood tests at a private laboratory for whom payment had been made by either personal funds or third-party private insurance companies. Appropriate measures were instituted to detect duplicate samples from the same subject, and to exclude those who did not live in the region of interest. Results were compared to those from similar numbers of subjects in two analogous cohorts that had been described in 1996.

Interestingly, the overall seroprevalence of anti-HAV did not differ between populations at the two laboratories, i.e., by socioeconomic stratum. However, when broken down by age group, there were striking differences. In the population felt to represent the low socioeconomic group, prevalence of anti-HAV clearly increased with increasing age, probably representing continued exposure and infection over time. However, in the population from the private laboratory, representing the high socioeconomic group, high rates of antibody were found in the young age group, with a drop-off in the adolescents. In the Discussion, the authors allude to the confounding factor of HAV vaccination, which apparently is not government subsidized, but available to those who can afford it. They mention that the majority of 1-4 year old children in a private immunization clinic had received HAV vaccine; of course this would significantly impact the anti-HAV seroprevalence. Although the study is still valid from the point of view of quantifying non-immune children "at risk" for HAV infection, the actual exposure/infection rates cannot be inferred from these data.

Additional, and perhaps even more valuable, insight is gained when comparing the pediatric seroprevalence rates from this study with those documented 11 to 12 years earlier. There is a discrete change in all but the youngest age group between the earlier and current public laboratory (low socioeconomic group) cohorts, with the overall anti-HAV seroprevalence going from 54.4 to 37.6%. If it is assumed that vaccination is not generally accessible to this group for financial reasons, then this difference can be attributed to changes in sanitation, food safety, and perhaps the socioeconomic condition of the population as a whole. This, in itself, makes a cogent argument for support of continued public health efforts in these areas. However, comparing the private laboratory (high socioeconomic) groups from the two time points demonstrates a dramatic difference, which at first might seem paradoxical. It appears that children in the 1990's in the higher socioeconomic stratum had somewhat low risk of HAV infection over time, indicating the importance of the public health factors that have previously been implicated. But now, in the high socioeconomic group,

seroprevalence of HAV antibody is high. However, this is unlikely to represent a large increase in natural infection in this group, since many were positive by age 4; most likely, this is due to the availability and accessibility of effective HAV vaccination to this population. Unfortunately, this study was not designed to explore this possibility.

Regardless of the limitations and difficulties with interpretation of some of these data, some findings are clear: 1) improvements in living conditions that accompany socioeconomic advancement are associated with lower rates of HAV infection in children and probably in the population as a whole, 2) a large proportion of the population is not immune at adulthood, when HAV infection has considerable morbidity, in both direct effects of illness and outbreaks, as well as indirect effects on productivity and lost work days, 3) HAV vaccination decreases the population at risk for infection and should be expected to eventually substantially decrease morbidity and mortality due to this infection in both children and adults, 4) countries and geographic regions with endemic HAV infection should strongly support both public health measures designed to improve water and food safety and overall hygiene, as well as universal childhood HAV vaccination, regardless of the individuals' ability to pay. In the long run, the costs, in both financial and health terms, will be lower and the benefits to society undeniable.

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