Transmission of Hepatitis B Virus from Adopted Asian Children to Their American Families

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Abstract: In 1985, 6,991 Asian children were adopted by Americans. To estimate the risk that such children may transmit hepatitis B virus to their adoptive families, we conducted a cumulative-incidence follow-up study in the State of Washington. We examined the association between having adopted a hepatitis B surface antigen (HBsAg)-seropositive Asian child and serologic evidence of past or present hepatitis B virus infection in adoptive family members. Seven (9 per cent) of 77 family members exposed to an HBsAg-seropositive child had evidence of past or present infection compared with four (2 per cent) of 232 nonexposed (relative risk = 5.3; 90% confidence limits [CL] = 2.0–13.9). The risk was higher for those with prolonged exposure and was entirely restricted to parents. (*Am J Public Health* 1988; 78:26–29.)

Introduction

In 1985, 6,991 Asian children were adopted into American families.[1] Previous studies indicate that the prevalence of hepatitis B surface antigen (HBsAg) in these children ranges from 4 per cent to 5 per cent.[2,3] The Centers for Disease Control (CDC) Immunization Practices Advisory Committee (ACIP) currently recommends HBsAg screening of children being adopted from countries with high hepatitis B virus (HBV) prevalence, and vaccination of adoptive family members if the screened child is found to be HBsAg-seropositive.[4] These recommendations are based on studies that show that HBV infection is transmitted within families.[5–7]

The results of two studies that specifically addressed the issue of Asian adoptees suggest that these children increase the risk of their adoptive American families for acquiring HBV infection. One study of American families who had adopted an HBsAg-seropositive child from Vietnam found that eight of 59 adoptive family members (14 per cent) had antibody to HBsAg.[6] A second study of Swedish families who had adopted an HBsAg-seropositive child from Korea or India found that 22 of 36 adoptive family members (61 per cent) had clinical or serologic evidence of past or present HBV infection.[3] Neither study included a control group.

To estimate the risk of acquiring HBV infection for members of American families who adopt an HBsAg-seropositive child, and thereby provide additional data on which physicians and public health practitioners might base specific recommendations for vaccination, we carried out a new study.

Methods

Population and Study Design

In 1983, we conducted a cumulative-incidence follow-up study of families residing in the 17 most populous of Washington State's 39 counties. All the study families had adopted a child from Korea or India through the Washington Association of Christian Adoptive Parents, which provided a list of such families. An *adopted child* was eligible if he or she had been adopted between January 1, 1979 (the earliest date that state-specific records were kept) and June 15, 1983 (the beginning of study enrollment), and if he or she had not been previously tested for serologic markers of HBV infection. An adoptive *family member* was eligible if he or she was a parent, a sibling, or a relative, had resided with the family during the entire period of the adopted child's time in the US, had lived with the adopted child for two months or more, and had never received hepatitis B immune serum globulin nor hepatitis B vaccine. All adopted children were asked to participate in the study. A 100 per cent sample of the families who were exposed to an HBsAg child and a 30 per cent random sample of nonexposed families were included in the study.

Data Collection

Laboratory and historical data were collected from all participants. Serum from each adopted child was tested for HBsAg and antibody to core antigen (anti-HBc) by enzyme-linked immunosorbent assay (ELISA)*. Sera that were positive for HBsAg were further tested for hepatitis B e antigen (HBeAg) by radioimmunoassay.* Serum from each family member was tested for HBsAg, anti-HBc, and antibody to surface antigen (anti-HBs) by ELISA.* Each participant was interviewed to obtain information on age, gender, country of birth, current residence, years of education, occupation, and developmental disabilities (children with developmental disabilities may be at increased risk of acquiring and transmitting HBV infection).

Definitions

Disease Status in Adopted Children—An adopted child was defined as *HBsAg-seropositive* if his or her serum tested positive for HBsAg and either anti-HBc or HBeAg, and *HBeAg-seropositive* if his or her serum tested positive for both HBsAg and HBeAg. Thus, the serologic status of an adopted child with a positive HBsAg test was confirmed by a second test. An adopted child was *HBsAg-seronegative* if the serum tested negative for HBsAg.

Disease Status in Family Members—A family member was defined as having evidence of past or present HBV infection if his or her serum tested positive for anti-HBc and either HBsAg or anti-HBs, and as not having evidence of infection if his or her serum tested negative on two of the three tests. This two-test standard was employed because the use of either anti-HBc or anti-HBs alone is associated with a substantial percentage of false positives.[8]

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TABLE 1—Characteristics of Family Members Exposed and Nonexposed to an HBsAg-seropositive Child Adopted from Asia

Characteristics	All Family Members		Parents Only	
	Exposed (N = 77)	Nonexposed (N = 232)	Exposed (N = 50)	Nonexposed (N = 139)
Age, years (mean)	29	26	39	37
Gender (% male)	45	53	48	47
Education, years (mean)	12	10	15	15
Health care occupation (%)	0	3	0	5
Birth in Asia or Africa (%)	3	2	4	4

Exposure Status—A family member was defined as *exposed* if he or she had been living with a seropositive adopted child for two months or more. If there was more than one seropositive adopted child in the family, exposure was defined as starting two months after the first seropositive child came to live with the family. A family member was defined as *nonexposed* if he or she had been living with a seronegative child.

Analysis

The relative risk (RR) of acquiring HBV infection that was associated with living with an HBsAg-seropositive child was defined as the proportion infected among the exposed divided by the proportion infected among the nonexposed. For single tables, confidence limits (CL) were calculated using a chi-square method[9,10]; maximum likelihood methods were used to calculate the RRs for stratified analyses.[11] To test whether increasing duration of exposure to a seropositive child was associated with an increasing risk of infection, we used a chi-square statistic that employs an arc-sine transformation to stabilize variances between small strata.[10]

Results

The HBsAg-serostatus could be determined for 511 (96 per cent) of 531 adopted children; there was sufficient serum for the determination of the HBeAg-serostatus of 25 (71 per cent) of 35 HBsAg-seropositive children. Of 391 otherwise eligible family members, 78 (20 per cent) refused participation and four (1 per cent) provided insufficient serum to complete testing. Hence, 309 family members (79 per cent) were included in the HBsAg analysis. An additional 37 family members (9 per cent) lived with an adopted child who had insufficient serum available for the HBeAg test.

Adopted Children

Overall, 35 (7 per cent) of 511 adopted children were confirmed by two tests to be HBsAg-seropositive; 31 (7 per cent) of 433 Korean children and four (5 per cent) of 78 Indian children were seropositive. Of the adopted children who were HBsAg-seropositive and for whom there was sufficient serum to test for HBeAg, 19 (76 per cent) of 25 were HBeAg-seropositive; 18 (82 per cent) of 22 Korean children, and one (33 per cent) of three Indian children were seropositive.

Family Members

The characteristics of exposed and nonexposed family members were very similar with respect to age, gender, years of education, percentage employed in a health care occupation (physician or nurse), and percentage born in Asia or Africa (Table 1). Adjustment for these small differences did not alter the estimates of reltive risk by more than 5 per cent and the alterations tended to balance each other; furthermore, none of the family members who were both exposed and infected had been born in Asia or Africa. Hence, we present the unadjusted results.

TABLE 2—Prevalence of Serologic Evidence of Past or Present Hepatitis B Virus Infection among Adoptive Family Members by Exposure to an HBsAg-seropositive Child

Group	Number Infected/Total		Relative Risk	90% Confidence Limits
	Exposed	Nonexposed		
All Family Members	7/77	4/232	5.3	(2.0–13.9)
Parents Only	7/50	4/139	4.9	(1.9–12.7)

Overall, 11 (4 per cent) of 309 family members had evidence of past or present HBV infection. Exposed family members were 5.3 times as likely to be infected as nonexposed family members (Table 2). Although 27 (23 per cent) of 118 siblings were exposed, none of the exposed and none of the nonexposed siblings had been infected. Exposed parents were 4.9 times as likely to have been infected as nonexposed parents (Table 2). Exposed mothers and fathers had virtually equal risks of infection: four (15 per cent) of 26 and three (13 per cent) of 24, respectively.

There was an increasing risk of infection associated with prolonged exposure to a seropositive child (Figure 1). This trend persisted when only parents were considered ($p = 0.03$). Because young age at adoption might lead to intensive exposure and HBeAg exposure, but also be associated with duration of exposure, we examined the trend data by these factors. The age at adoption (in days) of the seropositive children who were adopted by the seven infected family members was as follows in the three time periods in Figure 1: 28; 39, 41 (mean = 40); 31, 43, 29, 27 (mean = 33). Furthermore, six of seven were exposed to an HBeAg-seropositive adopted child (and the last may have been, but there was insufficient serum to determine the child's HBeAg serostatus). Hence, the effect of duration of exposure seems to be independent of these other factors. There were 50 HBsAg-exposed family members whose HBeAg exposure status could also be confirmed. Of these, six (15 per cent) of 40 exposed to an HBeAg-seropositive

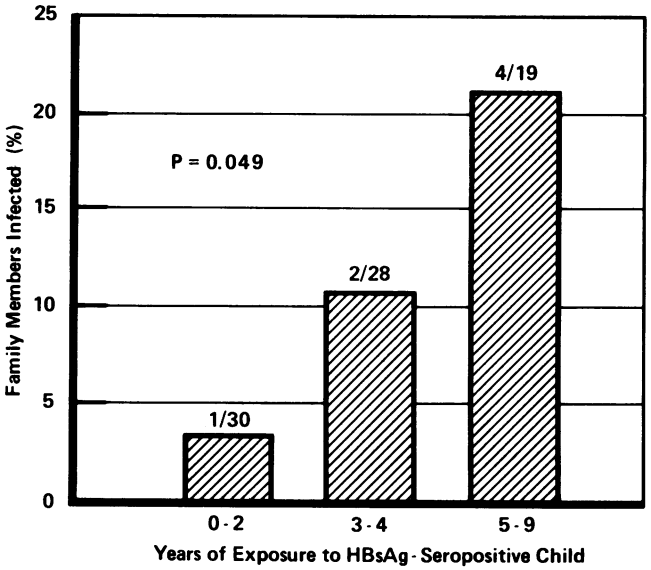

FIGURE 1—Per Cent of Family Members Infected (number infected divided by total) by Duration of Exposure to an HBsAg-seropositive Child.

child were infected, compared with 0 of 10 HBeAg-nonexposed (RR = ∞; 90% CL = 0.7 − ∞).

There was no association between the gender of the adoptive child and the risk of infection. None of the family members exposed to a child born in India was infected. This finding may have been explained by the fact that only two family members were exposed to an HBeAg-seropositive Indian child, compared to 38 family members exposed to such a Korean child. Finally, none of the infected family members was exposed to an adopted child with a developmental disability, suggesting that developmental disabilities did not contribute to the prevalence of HBV infection in this population.

Discussion

We found an increased risk of past or present HBV infection among family members who had adopted an HBsAg-seropositive child. This risk was determined in a controlled study, quantified with the determination of a relative risk and associated confidence intervals, and substantiated by the demonstration of a dose-response relationship (increasing prevalence with increasing duration of exposure). Although the data suggested that exposure to an HBeAg-seropositive child was associated with a higher risk of infection than that associated with exposure to an HBsAg-seropositive child, the data were too sparse to be able to exclude an important role for chance in this association.

For ascertainment bias to explain the observed effect, the ascertainment of infection would have to have been better among exposed family members. Although we had to exclude a few persons in our sample because of insufficient blood, there is no reason to believe that there was any association between difficulty in obtaining blood and either exposure or infection.

For selection bias to explain the observed effect, members of families who had adopted a seropositive child and who had also acquired HBV infection from a source other than an adopted child would have to have been more likely to be selected into the study. This feature is a secondary result of our study design, in that we were unable to ascertain lack of infection at the beginning of this study. Because families with a child who was known to be seropositive might have been more likely to come for testing, families with an adopted child who had been tested previously (whatever the results) were excluded. It is possible that a family member contracted hepatitis as a result of exposure to a seropositive child; such individuals would have been excluded from the study, lowering the estimate of relative risk.

Because approximately one-fifth of eligible family members refused participation, there may have been a bias introduced by self-selection. For this selection to explain the results, family members who were more willing to participate would have to have been both more likely to have adopted a seropositive child and to have been infected from another source than those who refused participation.

Because we performed a retrospective cumulative-incidence study, we had to make one other assumption, namely, that all the infected children were infected before coming to live with their adoptive families, and did not acquire infection in the US from a source that might have transmitted it to the family members.

Confounding bias could have been responsible for these results if family members who adopted a seropositive child were more likely to have acquired infection from another source. However, we found that exposed and nonexposed family members were highly comparable with respect to five factors that are closely correlated with the prevalence of HBV infection: age, gender, years of education, country of birth, and occupation.[12] We did not inquire about three other major risk factors for acquiring HBV infection: multiple blood transfusions, the use of illegal parenteral drugs, and male homosexuality. However, before adoption, the health and backgrounds of the adoptive families were screened; hence the prevalence of these risk factors is likely to have been very low. Moreover, to have explained the observed effect, these risk factors would have to have been both common and more prevalent among family members who adopted a seropositive child than among those who adopted a seronegative child.

To further specify the role of chance in this study, we calculated the corresponding 95 per cent confidence limits for the results presented in Table 2. The 95 per cent CL for the relative risks reported in Table 2 were 1.7–16.4 for all family members, and 1.6–15.0 for parents only.

Why were siblings not at risk? The rate of child-to-child transmission of HBV depends on the type of contact between children. In the developing world, where many children have open skin lesions, skin-to-skin contact is thought to be an important route of transmission.[13] Children who are residents of institutions for the developmentally disabled, and thus have medical and behavioral conditions not present in our population, are thought to transmit HBV to other residents through saliva and blood; in day-only settings, the rate of transmission is lower.[14] By contrast, in our relatively well-educated and healthy population, the rate of transmission would be expected to be low, which is what we found. However, the studies of Vietnamese, Korean, and Indian adoptees cited above, although uncontrolled, may provide some evidence that otherwise healthy young children can transmit HBV to their siblings.

In addition to their health, the opportunity for transmission would be expected to depend on the interactions between the children. Persons susceptible to HBV infection who act as caretakers of seropositive children who are either very young or who are same-age siblings would tend to have the most intimate contact, and thus potentially be at highest risk. In our study, the eight siblings who were exposed to seropositive adoptees under three years of age were themselves from 0 to seven years of age, i.e., too young to act as caretakers. The three exposed siblings who were teenagers, and so might have been expected to act as caretakers, were exposed to children who were adopted at five, seven, and nine years of age. Although eight children were exposed to a seropositive adoptee who was within two years of their own age, only two were exposed to such a child who was adopted at under two years of age. These relative ages and the overall excellent health of this population together might explain the lack of sibling-to-sibling transmission in this study.

In summary, our results add to the findings of Szmuness,[5] Vernon,[6] and Bernier,[7] upon which the current recommendations of the Immunization Practices Advisory Committee are based.

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