# Hepatitis-B Surface Antigen and Antibody: Prevalence and Persistence in Institutionalized and Noninstitutionalized Persons

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THE PREVALENCE OF HEPATITIS-B SURFACE ANTIGEN (HBsAg) has been monitored in many human populations and found to vary widely. This variance is apparently related to environmental conditions, age at onset of the disease, and the relatively long persistence of antigenemia (*1,2*). The highest prevalence of HBsAg occurs in institutions for the mentally retarded, chiefly among children with Down's syndrome (*1,3,4*).

Antibody to hepatitis-B surface antigen (anti-HBs) is also common among institutionalized children. However, anti-HBs is reportedly less common among children with Down's syndrome (DS) than among other mentally retarded children (*3,5*).

In this study, we determined HBsAg and anti-HBs prevalences in a large group of children and young adults with DS in two institutions for the mentally retarded; they were matched by age and sex to non-DS mentally retarded and to normal noninstitutionalized children and young adults.

In addition, we studied paired serums to document the hypothesis that HBsAg persistence in body fluids is long lasting and that antigen clearance may occur after many years of infection. Only a few investigations have been made of HBsAg persistence in children and adults, and the timespan investigated was short (*1*). We found evidence indicating that anti-HBs may not persist and offer lifelong immunity to people with DS.

## Study Subjects and Methods

The total study population consisted of 426 persons, ranging in age from 5 to 24 years. The DS subjects studied comprised 142 who were chosen at random from a large group resident at the Northern Wisconsin Center for the Developmentally Disabled (NWC) and from the Central Wisconsin Center for the Developmentally Disabled (CWC). Both institutions provide residential care and training for the mentally retarded. The NWC consists, in the main, of about 900 ambulatory residents. The CWC has about 800 occupants, many of whom are nonambulatory.

The mean age of the DS subjects studied at CWC (24 males, 17 females) was 11.6 years, and the mean age of those studied at the NWC (61 males, 40 females) was 15.7 years. Each of the 142 DS subjects was matched with respect to age and sex to an institutionalized non-DS mentally retarded subject and to a non-DS, noninstitutionalized mentally normal child or young adult living in the Greater Madison, Wis., area. Of the DS subjects, 70 from NWC and 29 from CWC were matched to equal numbers of non-DS subjects for age at first admission and duration of institutionalization. Informed consent was obtained from the parents or legal guardian before each subject was investigated.

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Serum samples, obtained by venipuncture, were stored frozen until tested for HBsAg or anti-HBs. Serums (1965 and 1972) used in the investigation of HBsAg and anti-HBs persistence were obtained from the CWC serum bank.

Testing for HBsAg was done by solid-phase radioimmunoassay (Ausria II-125, Abbott Laboratories). Results were calculated as suggested by the manufacturer (positive $\geqq$ 2.1 times the mean of 7 simultaneous tests with a standard negative control). Positive test specificity was confirmed by counter-immunoelectrophoresis (*6*). Anti-HBs was also determined by solid-phase radioimmunoassay (Ausab, Abbott Laboratories). The specificity of positive tests was confirmed by the passive hemagglutination technique (*7*).

Liver function tests (total bilirubin, serum glutamic-oxaloacetic-transaminase, serum glutamic-pyruvic-transaminase), performed immediately after sample acquisition, were within normal limits in the HBsAg positive subjects.

Table 1. Prevalence of hepatitis-B antigen at Central Wisconsin Center and Northern Wisconsin Center

| Age group (years) | Down's syndrome subjects | | Non-Down's syndrome subjects | | P value |
|---|---|---|---|---|---|
| | Number positive | Percent positive | Number positive | Percent positive | |
| **Central Wisconsin Center** | | | | | |
| 5–9 | 7/12 | 58.3 | 0/12 | 0.0 | <0.01 |
| 10–14 | 12/20 | 60.0 | 6/20 | 30.0 | 0.06 |
| 15–19 | 7/9 | 77.8 | 1/9 | 11.1 | <0.01 |
| Total | 26/41 | 63.4 | 7/41 | 17.1 | <0.01 |
| **Northern Wisconsin Center** | | | | | |
| 5–9 | 2/5 | 40.0 | 1/5 | 20.0 | >0.10 |
| 10–14 | 23/40 | 57.5 | 4/40 | 10.0 | <0.01 |
| 15–19 | 13/32 | 40.6 | 2/32 | 6.2 | <0.01 |
| 20–24 | 8/24 | 33.3 | 11/24 | 45.8 | >0.10 |
| Total | 46/101 | 45.5 | 18/101 | 17.8 | <0.01 |

## Results

**HBsAg prevalence at CWC.** An age-related increase in HBsAg prevalence occurred among DS subjects resident at CWC (table 1). The highest HBsAg prevalence (77.8 percent) was among the age group 15–19 years, and antigen prevalence among their age- and sex-matched institutionalized peers was 11.1 percent. Subjects with DS had significantly higher HBsAg prevalences at ages 5–9 and 15–19 years than similarly aged institutionalized non-DS subjects. The difference in HBsAg prevalence among DS and non-DS institutionalized subjects of the 10–14 age group was of questionable significance ($P=0.06$).

**HBsAg prevalence at NWC.** The HBsAg prevalences for DS and non-DS subjects at NWC are shown in table 1. DS and non-DS institutionalized children of the 5–9 age group had similar HBsAg prevalences ($P>0.10$); however, the number in this age group was small. Among the 10–14 age group, DS children had HBs-antigenemia more frequently than their institutionalized non-DS peers ($P<0.01$).

The age 15–19 DS subjects had a higher HBsAg prevalence than institutionalized non-DS subjects. HBsAg occurred less frequently among DS subjects aged 20–24 than in comparably aged non-DS subjects.

**HBsAg and anti-HBs prevalence among noninstitutionalized subjects.** None of the 142 non-DS, non-institutionalized subjects exhibited HBsAg in their serums. However, three subjects had anti-HBs. One anti-HBs positive subject was a 17-year-old female; the other two subjects with antibody to HBsAg were males aged 20–24. Overall, the prevalence of anti-HBs in this noninstitutionalized, non-DS population was 2.1 percent.

**Anti-HBs prevalence at CWC and NWC.** Age-specific anti-HBs prevalences for DS and non-DS children at CWC are shown in table 2. Children with DS and other institutionalized children at CWC had similar anti-HBs prevalences in all age groups. The highest anti-HBs prevalence (35.0 percent) at CWC occurred in non-DS children aged 10–14.

Prevalences of anti-HBs at NWC are shown in table 2. The prevalences of anti-HBs were statistically similar among DS and non-DS subjects in the 5–9, 10–14, and 15–19 age groups. However, anti-HBs was more prevalent among DS subjects of the 20–24 age group than among non-DS subjects of the same age. The highest anti-HBs prevalence (46.9 percent) at NWC was in DS subjects aged 15–19.

Antibody to HBsAg was more prevalent among DS subjects at NWC (38.6 percent) than among DS subjects at CWC (19.5 percent). However, anti-HBs prevalences were similar among non-DS subjects at CWC and non-DS subjects at NWC.

Table 2. Prevalence of hepatitis-B antibody at Central Wisconsin Center and Northern Wisconsin Center

| Age group (years) | Down's syndrome subjects | | Non-Down's syndrome subjects | | P value |
|---|---|---|---|---|---|
| | Number with antibody | Percent with antibody | Number with antibody | Percent with antibody | |
| | Central Wisconsin Center | | | | |
| 5–9 | 1/12 | 8.3 | 5/12 | 41.7 | 0.07 |
| 10–14 | 6/20 | 30.0 | 7/20 | 35.0 | 0.89 |
| 15–19 | 1/9 | 11.1 | 1/9 | 11.1 | 1.00 |
| Total | 8/41 | 19.5 | 13/41 | 31.7 | >0.10 |
| | Northern Wisconsin Center | | | | |
| 5–9 | 2/5 | 40.0 | 2/5 | 40.0 | 1.00 |
| 10–14 | 12/40 | 30.0 | 17/40 | 42.5 | >0.10 |
| 15–19 | 15/32 | 46.9 | 14/32 | 43.7 | >0.10 |
| 20–24 | 10/24 | 41.6 | 1/24 | 4.2 | <0.01 |
| Total | 39/101 | 38.6 | 34/101 | 33.6 | >0.10 |

Table 3. Evidence of hepatitis-B infections at Central Wisconsin Center and Northern Wisconsin Center

| Subjects | Hepatitis-B antigen | | Hepatitis-B antibody | | Total infected with hepatitis-B | |
|---|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | Frequency | Percent |
| With Down's syndrome: | | | | | | |
| Central Wisconsin Center | 26/41 | 63.4 | 8/41 | 19.5 | 34/41 | 82.9 |
| Northern Wisconsin Center | 46/101 | 45.5 | 39/101 | 38.6 | 85/101 | 84.1 |
| Without Down's syndrome: | | | | | | |
| Central Wisconsin Center | 7/41 | 17.1 | 13/41 | 31.7 | 20/41 | 48.8 |
| Northern Wisconsin Center | 18/101 | 17.8 | 34/101 | 33.6 | 52/101 | 51.4 |

**Prevalence of hepatitis-B infection at CWC and NWC.** The occurrence of infection with hepatitis-B virus, as measured by the presence of HBsAg or anti-HBs in subjects' serums is shown in the last column of table 3. The hepatitis-B infection rates among persons with DS at CWC and NWC were similar. In addition, the hepatitis-B infection rates among non-DS persons at CWC and NWC were analogous. However, significantly more subjects with DS, at both institutions, had evidence of hepatitis-B infection than non-DS subjects ($P<0.01$ for CWC; $P<0.01$ for NWC). The prevalence of anti-HBs among those subjects with evidence of hepatitis-B virus infection was significantly lower in DS subjects than in non-DS subjects ($P<0.001$).

**Effects of age at admission and duration of institutionalization on HBsAg and anti-HBs prevalence.** We were able to match 29 DS subjects at CWC and 70 DS subjects at NWC with equal numbers of non-DS subjects based on age at first admission to an institution and duration of institutionalization.

Significantly more people with DS at CWC and NWC had HB-antigenemia than their non-DS peers ($P<0.001$ at both CWC and NWC). However, no such difference was found between DS and non-DS subjects with regard to the prevalence of anti-HBs ($P=0.76$ at CWC; $P=0.75$ at NWC).

**Persistence of HBsAg and anti-HBs.** Paired serums were available for 23 DS subjects at CWC. As shown in table 4, 69.7 percent of the DS subjects had HBsAg in 1965. HBsAg persisted in 93.7 percent (15/16) of these subjects until 1975. Sometime between 1965 and 1972 one DS subject, No. 146, became negative for HBsAg. However, this subject did not develop detectable antibody to HBsAg as a result of infection.

Table 4 also gives the prevalence of anti-HBs among the 23 DS subjects. Two of the DS subjects (Nos. 178 and 179) lost detectable antibody to HBsAg during the 10-year period. On the other hand, two DS subjects (Nos. 160 and 185) seroconverted to become anti-HBs positive during the period.

The persistence of HBsAg and anti-HBs among 15 non-DS subjects institutionalized at CWC from 1965

Table 4. Persistence of hepatitis-B surface antigen and antibody in institutionalized subjects with Down's syndrome

| Subject No. | Hepatitis surface antigen | | | Hepatitis surface antibody | | |
|---|---|---|---|---|---|---|
| | 1965 | 1972 | 1975 | 1965 | 1972 | 1975 |
| 101 | + | + | + | − | − | − |
| 104 | − | − | − | + | + | + |
| 111 | + | + | + | − | − | − |
| 113 | + | + | + | − | − | − |
| 114 | + | + | + | − | − | − |
| 120 | + | + | + | − | − | − |
| 121 | + | + | + | − | − | − |
| 125 | + | + | + | − | − | − |
| 142 | + | + | + | − | − | − |
| 146 | + | − | − | − | − | − |
| 155 | − | − | − | − | − | − |
| 159 | − | + | + | − | − | − |
| 160 | − | − | − | − | − | + |
| 176 | + | + | + | − | − | − |
| 178 | − | − | − | + | + | − |
| 179 | − | − | − | + | + | − |
| 183 | + | + | + | − | − | − |
| 185 | − | − | − | − | + | + |
| 201 | + | + | + | − | − | − |
| 210 | + | + | + | − | − | − |
| 211 | + | + | + | − | − | − |
| 214 | + | + | + | − | − | − |
| 242 | + | + | + | − | − | − |
| Total: | | | | | | |
| Number | 16/23 | 16/23 | 16/23 | 3/23 | 4/23 | 3/23 |
| Percent | 69.7 | 69.7 | 69.7 | 13.0 | 17.4 | 13.0 |

to 1975 is shown in table 5. Overall, 26.6 percent (4/15) of the subjects had HBsAg in 1965. The same subjects were still HBsAg positive in 1975. One subject, No. 119, had HBsAg in the presence of anti-HBs in 1975.

In 1965, 13.3 percent (2/15) of the non-DS subjects had anti-HBs. Between 1965 and 1975, 40 percent (6/15) of the non-DS subjects seroconverted, making the prevalence of anti-HBs 53.2 percent in 1975. Unlike the DS subjects, none of the non-DS subjects lost detectable anti-HBs during the 10 years.

## Discussion

In this study, higher HBsAg prevalences among DS subjects were seen than in previously reported studies. The reason for this high prevalence is conjectural, but it may be related to admission of patients at young ages, the persistence of the infection, or the presence of a susceptibility factor among people with DS (*8*). However, the increased HBsAg prevalence at CWC and NWC does not appear to be related to hygienic conditions or to dietary quality in these institutions, since both foster excellent personal hygiene practices, have immaculate living and play areas, and provide nutritious meals to their residents.

Investigations into the prevalence of HBsAg among noninstitutionalized DS subjects indicate that substantially fewer are infected with hepatitis-B virus than those in institutions (*9*).

The dominant feature of an institutional environment that could account for high prevalences of HBsAg among interned DS subjects is the pooling of susceptibles. If, as is suggested by Sutnick and associates, people with DS represent a group who are genetically predisposed to persistent hepatitis-B antigenemia (*8*), then institutionalizing such persons could result in high prevalences of HBsAg.

The persistence of HBsAg may not be lifelong, but as our data indicate, it usually continues for many years among most people with DS. Longer persistence of HBsAg could result in the increased HBsAg prevalences seen in DS subjects, but the possibility that HBsAg carriers promote the infection of other DS subjects should not be discounted as a contributory factor. However, the HBsAg prevalence data gathered from matching DS and non-DS subjects with regard to age at first admission and length of institutionalization indicate that the higher prevalence seen in DS subjects is not related to those variables.

We have shown that anti-HBs prevalences are, with the exception of subjects aged 20–24 years at NWC, essentially the same in people with DS as they are in other institutionalized subjects. This relationship suggests that persons with DS respond to hepatitis-B infection with the production of anti-HBs commensurately with non-DS persons. Our anti-HBs prevalence data from DS and non-DS subjects paired for age at admission and duration of institutionalization support this hypothesis. However, when DS and non-DS subjects who were infected with hepatitis-B virus (indicated by the presence of HBsAg or anti-HBs) were considered, it was evident that significantly more non-DS subjects had anti-HBs than DS subjects. Thus, when hepatitis-B infection is manifest as a chronic carrier state, it is apparent that anti-HBs prevalence does not accurately reflect the response of the population to infection.

Children and young adults with and without DS are housed at CWC and NWC on the basis of ability, mobility, and social awareness. The residents are also intermingled when they attend school and other social functions. Szmuness and co-workers have asserted that in closed institutions all patients have equal exposure and equal susceptibility (*5*). Our data show an excess of hepatitis-B infections among subjects with DS. This excess of infection is not related to age at first admission, duration of institutionalization, or the age or the sex of the DS subject. However, it may be related to

Table 5. Persistence of hepatitis-B surface antigen and antibody in institutionalized children who did not have Down's syndrome

| Subject No. | Hepatitis surface antigen | | | Hepatitis surface antibody | | |
|---|---|---|---|---|---|---|
| | 1965 | 1972 | 1975 | 1965 | 1972 | 1975 |
| 109 | − | − | − | − | − | − |
| 112 | − | − | − | − | + | + |
| 119 | + | + | + | − | − | − |
| 127 | − | − | − | − | + | + |
| 129 | − | − | − | + | + | + |
| 132 | + | + | + | − | − | − |
| 141 | + | + | + | − | − | − |
| 144 | − | − | − | − | − | − |
| 145 | − | − | − | + | + | + |
| 164 | − | − | − | − | + | + |
| 166 | + | + | + | − | − | − |
| 174 | − | − | − | − | + | + |
| 177 | − | − | − | − | − | − |
| 212 | − | − | − | + | + | + |
| 251 | − | − | − | − | − | − |
| Total: | | | | | | |
| Number | 4/15 | 4/15 | 4/15 | 2/15 | 7/15 | 8/15 |
| Percent | 26.6 | 26.6 | 26.6 | 13.3 | 46.6 | 53.2 |

an increased susceptibility among people with DS to hepatitis-B virus infection.

One DS subject (No. 146) either did not produce antibody to HBsAg as a result of a 1965 infection, or produced antibody that persisted less than 7 years. The results of antibody tests with two other DS subjects demonstrate that while anti-HBs was present in 1972, it was not present 3 years later. These data indicate transient anti-HBs production among DS subjects. Thus, a plausible hypothesis is that persons with DS are not only more susceptible to infection with hepatitis-B virus initially, but they may also become reinfected and thereby increase the prevalence of HBsAg.

HBsAg persisted among a few non-DS subjects for many years. This persistence of HBsAg among non-DS institutionalized subjects is enigmatic, but may be the result of clustering genetically predisposed subjects into the institution. It is interesting that in our study the four non-DS subjects who were HBsAg carriers were each mentally retarded due to a congenital infection or other congenital anomaly, but none had a genetic defect.

The persistence of antibody to HBsAg has been shown to be as short as 9 months (*10*). However, other investigators have shown that anti-HBs can persist for 1 year (*11*). Our results show that anti-HBs can persist for 10 years. Thus, reinfection with hepatitis-B virus should be a rather uncommon event, provided serologic response to HBsAg can be interpreted as "protective."

The observations reported here indicate that the high prevalence of HBsAg seen in institutionalized persons, especially those with DS, may be a result of clustering genetically susceptible persons in whom hepatitis-B virus persists.

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# SYNOPSIS


McMILLAN, B. C. (Central Wisconsin Center, Madison), HANSON, R. P., GOLUBJATNIKOV, R., and SINHA, S. K.: *Hepatitis-B surface antigen and antibody: prevalence and persistence in institutionalized and noninstitutionalized persons. Public Health Reports, Vol. 94, May–June 1979, pp. 262–267.*

A total of 426 persons were studied in an attempt to more clearly define the high prevalence of hepatitis-B surface antigen (HBsAg) seen among institutionalized persons.

HBsAg was found in 63.4 percent of the children and young adults with Down's syndrome (DS) at the Central Wisconsin Center (CWC) and in 45.5 percent of those at the Northern Wisconsin Center (NWC). Significantly more subjects with DS had hepatitis-B antigenemia than age- and sex-matched non-DS institutionalized subjects.

Antibody (anti-HBs) to HBsAg was found in 19.5 percent of the DS subjects at CWC and in 38.6 percent of those at NWC. The prevalence of anti-HBs was similar among DS and non-DS institutionalized subjects. None of the noninstitutionalized subjects had HBsAg in their serums and their anti-HBs prevalence was low (2.1 percent).

HBsAg was found to persist for at least 10 years in both DS and non-DS institutionalized subjects. However, persistence occurred more frequently among DS subjects. Anti-HBs persisted at least 10 years among non-DS subjects, but DS subjects tended to lose antibody sooner.

The study findings indicated that the high prevalence of HBsAg seen in institutionalized DS subjects at CWC and NWC were not related to the age of the subject at admission nor to the duration of institutionalization.