Prevalence of Hepatitis B Virus Infection in the United States: The National Health and Nutrition Examination Surveys, 1976 Through 1994

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ABSTRACT

Objectives. Data from 2 National Health and Nutrition Examination Surveys (NHANES), NHANES II (1976–1980) and NHANES III (1988–1994), were analyzed to examine trends in the prevalence of hepatitis B infection in the United States.

Methods. Serum specimens were tested for markers of hepatitis B virus infection, and risk factors were determined from questionnaires.

Results. The overall age-adjusted prevalence of hepatitis B virus infection was 5.5% (95% confidence interval [CI] = 4.8, 6.2) in NHANES II, as compared with 4.9% (95% CI = 4.3, 5.6) in NHANES III. In both surveys, Black participants had the highest prevalence of infection (NHANES II, 15.8%; NHANES III, 11.9%). No differences in infection were found in the major racial groups between surveys, except for a decrease among those older than 50 years. Black race, increasing number of lifetime sexual partners, and foreign birth had the strongest independent associations with hepatitis B virus infection.

Conclusions. Testing of participants in 2 national surveys demonstrates no significant decrease in hepatitis B virus infection, despite the availability of hepatitis B vaccine. (*Am J Public Health*. 1999;89:14–18)

The acute and chronic consequences of hepatitis B virus infection continue to be a major public health problem in the United States, with an estimated 200 000 to 300 000 annual infections occurring over the past 2 decades.[1] However, because the majority of children and adults infected with hepatitis B virus do not develop clinical disease,[2] seroepidemiologic studies provide a more comprehensive picture of the distribution of this infection than does acute disease surveillance.[3] Trends in hepatitis B virus infection are important in evaluating the effectiveness of recommended routine vaccination of infants and younger adolescents, along with older adolescents and adults at high risk of infection.[1]

In this study, we determined the prevalence of serologic markers of resolved and chronic hepatitis B virus infection in 2 National Health and Nutrition Examination Surveys (NHANES) conducted approximately 10 years apart to determine trends in infection prevalence. In addition, we determined risk factors for infection in the most recent NHANES.

Methods

Study Populations and Sample Design

The NHANES are a series of cross-sectional national surveys designed to provide representative prevalence estimates for a variety of health measures and conditions. The sampling plan of each survey is a stratified, multistage, probability cluster design selecting a sample representative of the US civilian noninstitutionalized population.[4,5]

In NHANES II (n = 28 000), conducted from 1976 to 1980, selected subgroups were oversampled, including children aged 6 months to 5 years, adults aged 60 to 74 years, and persons living below the poverty level. The upper age limit was 74 years. Race was defined as White, Black, and other. As a means of making ethnic categories comparable across studies, respondents in NHANES II who listed their ancestry as Hispanic were excluded from the Black and White race categories and included in the total population along with respondents of other races.

In NHANES III (n = 40 000), conducted from 1988 to 1994, children under 5 years of age, persons aged 60 years and older, Mexican Americans, and Black Americans were sampled at a higher rate than other persons. Since there was no upper age limit in the survey, analyses that compared NHANES II and NHANES III were restricted to persons aged 6 to 74 years. Race/ethnicity was defined as non-Hispanic White, non-Hispanic Black, and Mexican American. Persons not fitting these categories were classified as "other" and included in the total population. Analysis of risk factors was generally restricted to NHANES III.

Response Rates

Because hepatitis B virus marker testing was not included in the original design of NHANES II, the availability of stored specimens was lower for children and Blacks.[3] In

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TABLE 1—Age-Adjusted Prevalence of Hepatitis B Virus Infection, by Age and Race: NHANES II and NHANES III Participants Aged 6–74 Years

	NHANES II (1976–1980)			NHANES III (1988–1994)		
	Sample Size	%	95% Confidence Interval	Sample Size	%	95% Confidence Interval
Gender						
Male	6213	6.2	5.3, 7.3	9267	5.7	4.9, 6.6
Female	6788	4.8	4.1, 5.6	10235	4.1	3.4, 5.0
Race/ethnicity						
Non-Hispanic White	10618	3.6	3.2, 4.2	6648	2.6	2.2, 3.1
6–49 y	6507	2.7	2.2, 3.4	4202	2.6	2.1, 3.2
50+ y	4111	6.5	5.7, 7.5	2446	4.1	3.2, 5.2
Non-Hispanic Black	1488	15.8	13.8, 18.1	5907	11.9	10.7, 13.3
6–49 y	1022	9.9	7.8, 12.6	4747	9.3	8.2, 10.5
50+ y	466	32.3	27.5, 37.8	1160	21.3	18.6, 24.5
Mexican American	...	...	...	6101	4.4	3.4, 5.6
6–49 y	...	...	...	4941	2.7	2.0, 3.6
50+ y	...	...	...	1160	9.7	6.6, 14.1
Other	895	14.5	11.5, 18.2	846	19.1	14.3, 25.5
6–49 y	696	10.3	6.7, 15.9	648	16.2	11.5, 22.8
50+ y	199	23.3	18.5, 29.2	198	25.2	18.2, 34.9
Total[a]	13001	5.5	4.8, 6.2	19502	4.9	4.3, 5.6

[a]Includes racial/ethnic groups not shown separately.

NHANES III, individuals aged 6 years and older were eligible for hepatitis B virus marker testing. Of the 32 233 respondents in this age range, 24 713 (77%) were examined, and from 21 265 (66%) a serum specimen was obtained for testing. However, persons in the youngest and oldest age groups had the lowest response rates (6–11 years, 55%; 70 years or older, 55%).

Laboratory Methods and Definitions

NHANES II specimens were tested (1) for antibody to hepatitis B surface antigen or hepatitis B core antigen and (2) for hepatitis B surface antigen by enzyme-linked immunoassay (AUSAB, CORZYME, and AUSZYME; Abbott Laboratories, North Chicago, Ill).[3]

NHANES III specimens were first tested for antibody to hepatitis B core antigen by radioimmunoassay (CORAB, Abbott Laboratories), and positive specimens were tested for hepatitis B surface antigen and antibody to the surface antigen (AUSRIA II and AUSAB, Abbott Laboratories). NHANES III participants with a medical occupation who were negative for the antibody to hepatitis B core antigen were tested for the antibody to hepatitis B surface antigen (AUSAB-EIA with a 10-mIU/mL standard included in triplicate) and considered immunized if the concentration was 10 mIU/mL or higher.[1]

For both surveys, chronic hepatitis B virus infection was defined as the presence of both hepatitis B surface antigen and antibody to hepatitis B core antigen. For NHANES II, any (past or present) hepatitis B virus infection was defined as the presence of any 2 serologic markers; for NHANES III, a positive or borderline antibody to hepatitis B core antigen assay was used to define the presence of any hepatitis B virus infection. The 102 individuals with antibody to hepatitis B core antigen and no other serologic marker of infection repeatedly tested positive. If these individuals had been excluded, the overall prevalence would have been reduced by 0.5%; therefore, they were included in the analysis.

Statistical Analysis

For each survey, prevalence estimates were weighted to represent the total United States population and to account for oversampling and nonresponse to the household interview and physical examination. Standard

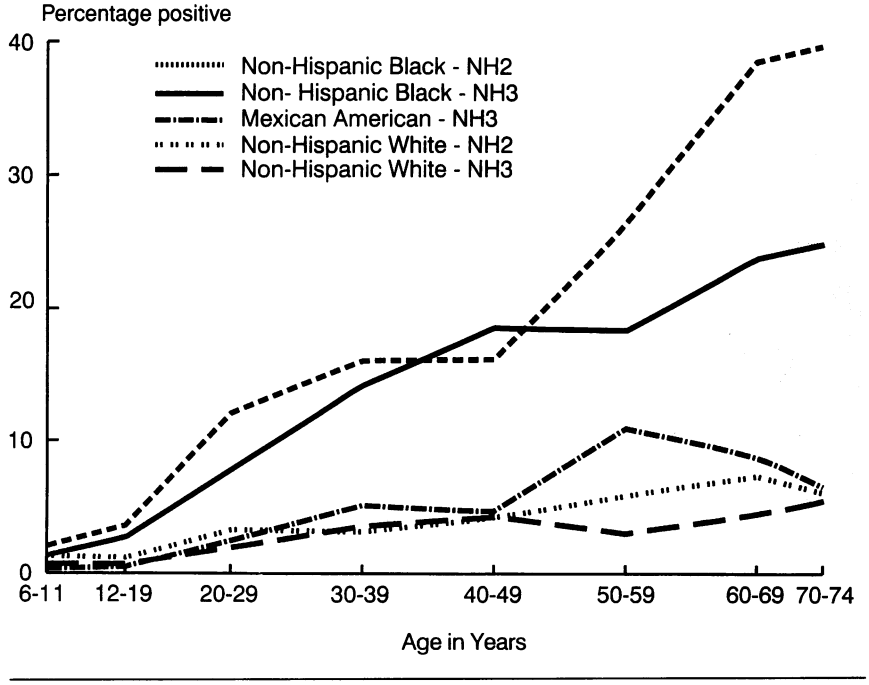

FIGURE 1—Age-specific prevalence of hepatitis B virus infection, by ethnicity: NHANES II (NH2) and NHANES III (NH3) participants aged 6–74 years.

TABLE 2—Age-Adjusted Prevalence of Hepatitis B Virus Infection, by Demographic Variables and Risk Behaviors: NHANES III Participants

	Sample Size	Total,[a] % (95% CI)	Non-Hispanic Whites (n = 3862), % (95% CI)	Non-Hispanic Blacks (n = 3625), % (95% CI)	Mexican Americans (n = 3643), % (95% CI)
Education					
Less than high school	6928	8.8 (6.9, 11.2)	5.1* (3.7, 7.2)	18.0* (15.8, 20.6)	6.1 (4.5, 8.1)
High school	5052	5.2* (4.5, 6.1)	3.1 (2.4, 3.9)	16.2 (13.9, 18.8)	4.7 (3.3, 6.6)
Some college	4532	4.6* (3.9, 5.4)	2.8 (2.1, 3.6)	12.4 (10.1, 15.3)	6.0 (3.6, 9.9)
Place of birth[b]					
United States	17305	3.6 (3.2, 4.1)	2.5 (2.1, 2.9)	12.0 (10.7, 13.6)	4.5 (3.5, 5.9)
Other	3902	15.7* (12.4, 19.7)	7.5* (4.7, 11.9)	22.8* (17.6, 29.5)	5.1 (3.7, 7.1)
Marital status[c]					
Married	9716	4.9 (4.2, 5.7)	2.9 (2.4, 3.6)	15.1 (12.6, 18.0)	6.0 (4.6, 7.8)
Widowed	1646	23.5 (13.3, 41.7)	1.4 (0.8, 2.6)	12.2 (9.1, 16.6)	5.2 (2.5, 10.9)
Divorced/separated	1774	7.8* (6.3, 9.6)	5.2* (3.6, 7.5)	16.2 (12.8, 20.4)	4.8 (2.9, 7.7)
Single	3449	8.7* (6.9, 11.0)	4.1 (2.8, 6.1)	17.6 (14.3, 21.6)	7.8 (4.5, 13.4)
Military service (17+ age group)[b]					
Yes	2401	5.3 (4.1, 6.9)	3.8* (2.5, 5.7)	18.8* (15.5, 22.7)	8.7 (5.3, 14.3)
No	14128	5.9 (5.1, 6.8)	3.0 (2.5, 3.6)	14.7 (13.2, 16.4)	5.5 (4.2, 7.1)
Lifetime sexual partners[d]					
0–1	2810	2.7 (2.1, 3.6)	0.9 (0.4, 1.8)	9.4 (6.4, 13.9)	2.8 (1.7, 4.6)
2–9	5550	4.4* (3.7, 5.2)	2.5* (1.8, 3.4)	12.2 (10.3, 14.5)	4.7* (3.4, 6.6)
10–49	2303	5.6* (4.5, 7.1)	3.6* (2.6, 5.1)	12.8 (10.3, 15.9)	8.0* (5.1, 12.5)
50+	455	12.2* (8.5, 17.6)	12.4* (7.7, 19.9)	14.7 (9.9, 21.9)	9.5* (4.5, 20.0)
Age at first intercourse,[b,d] y					
<18	6343	5.4* (4.6, 6.3)	3.4* (2.6, 4.5)	13.5* (11.8, 15.4)	6.4* (4.7, 8.7)
18	4131	3.7 (3.0, 4.5)	2.1 (1.5, 3.0)	8.8 (7.2, 10.8)	3.2 (2.1, 4.9)
Male-to-male sex[b,d]					
Yes	80	26.8* (18.4, 39.2)	26.1* (16.8, 40.6)	35.5* (22.0, 57.3)	26.9* (11.3, 64.0)
No	5299	5.7 (4.8, 6.8)	3.2 (2.4, 4.2)	14.3 (11.9, 17.2)	6.1 (4.7, 8.1)
Lifetime cocaine use[b,d]					
Never	10059	4.2 (3.6, 4.8)	2.5 (2.0, 3.1)	10.8 (9.5, 12.2)	4.3 (3.3, 5.7)
1–99 times	1081	7.8* (5.7, 10.8)	2.3* (1.3, 4.2)	25.8* (19.6, 33.9)	11.0* (6.0, 20.2)
100+ times	174	20.2* (11.7, 34.9)	13.6* (7.3, 25.1)	29.6* (18.7, 46.9)	16.0* (6.6, 38.6)
Medical occupation[c]					
Yes	769	6.2 (4.4, 8.8)	4.5 (2.7, 7.7)	13.4 (10.0, 18.1)	4.4 (1.8, 11.0)
No	15637	5.8 (5.0, 6.7)	3.2 (2.7, 3.8)	15.4 (13.9, 17.1)	5.8 (4.5, 7.5)
Total	21265	5.1 (4.4, 5.8)	2.8 (2.4, 3.2)	12.8 (11.5, 14.2)	4.8 (3.7, 6.2)

Note. CI = confidence interval.
[a]Includes racial/ethnic groups not shown separately.
[b]Examinees with missing data not included.
[c]Includes those aged 17 years and above.
[d]Includes those aged 17–59 years.
*$P \leq .05$.

errors were calculated with SUDAAN,[6] a family of statistical procedures for analysis of data from complex sample surveys. For comparisons between NHANES II and III and comparisons across population subgroups of NHANES III, data were age adjusted by the direct method to the 1980 US population.[7] Logistic regression was used to determine significant individual age-adjusted differences for the demographic and risk factor variables; a Satterthwaite-adjusted F statistic at $P < .05$ was considered significant.

Results

The prevalences of chronic hepatitis B virus infection (hepatitis B surface antigen–positive) were similar in NHANES II (0.33%, 95% confidence interval [CI] = 0.21, 0.51) and NHANES III (0.42%, 95% CI = 0.32, 0.55). Serologic markers of past and chronic infection were combined to estimate total prevalence, trends, and risk factors.

The age-adjusted prevalence of hepatitis B virus infection decreased from 5.5% in NHANES II to 4.9% in NHANES III (Table 1). Although the overall decrease between surveys was not significant, significant decreases did occur among non-Hispanic Whites (3.6% to 2.6%) and non-Hispanic Blacks (15.8% to 11.9%) but were restricted to persons older than 50 years (Table 1). The prevalence of infection between the 2 surveys increased among persons in the "other" race category. However, the composition of this category differed in NHANES II (77% Hispanic White, 0.1% Hispanic Black, 20% Asian or Pacific Islander, and 2.9% other) and NHANES III (29% Asian or Pacific Islander, 25% Hispanic Black, 35% Hispanic White, and 11% other).

In both surveys, the prevalence of hepatitis B virus infection was low until 12 years of age, when it increased in all racial groups (Figure 1). The age-specific prevalence among Mexican Americans was similar to that among non-Hispanic Whites until 50 years of age, when the prevalence increased to 11.0% (95% CI = 6.3, 18.9) among Mexican Americans, as compared with 3.1% (95% CI = 1.9, 4.8) among non-Hispanic Whites.

In comparison with persons with some college education, those with less than a high school education had an increased prevalence of infection in all ethnic groups except

TABLE 3—Relative Odds of Hepatitis B Virus Positivity From Logistic Regression Model for Adults Aged 17–59 Years, Controlled for Age: NHANES III Participants

	Odds Ratio (95% Confidence Interval)			
	Total	Non-Hispanic White	Non-Hispanic Black	Mexican American
Ethnicity				
Non-Hispanic Black	3.9 (2.9, 5.0)	...	...	...
Mexican American	0.7 (0.4, 1.3)	...	...	...
Non-Hispanic White	Reference	...	...	...
Lifetime sexual partners				
50+	6.5 (3.5, 12.2)	12.2 (5.1, 29.6)	1.3 (0.6, 2.9)	2.8 (0.9, 8.5)
10–49	2.9 (1.9, 4.3)	4.0 (2.0, 7.9)	1.3 (0.8, 2.1)	2.6 (1.7, 3.8)
2–9	2.1 (1.4, 3.2)	2.4 (1.2, 5.0)	1.4 (0.9, 2.1)	1.7 (0.9, 3.1)
0–1	Reference	Reference	Reference	Reference
Ever used cocaine				
Yes	1.8 (1.2, 2.7)	1.3 (0.7, 2.6)	3.1 (2.3, 4.1)	2.0 (1.3, 3.1)
No	Reference	Reference	Reference	Reference
Marital status				
Divorced/separated	1.6 (1.1, 2.2)	2.0 (1.2, 3.4)	0.9 (0.7, 1.3)	0.7 (0.5, 1.1)
Other	Reference	Reference	Reference	Reference
Age at first intercourse, y				
<18	1.2 (0.9, 1.6)	1.1 (0.7, 1.7)	1.3 (1.0, 1.7)	1.4 (0.8, 2.4)
18+	Reference	Reference	Reference	Reference
Education				
Less than high school	1.5 (1.1, 2.1)	1.8 (1.1, 2.8)	1.5 (1.1, 2.0)	1.3 (0.8, 2.3)
High school	1.1 (0.9, 1.5)	1.1 (0.7, 1.6)	1.4 (1.0, 1.9)	1.0 (0.5, 1.9)
Some college	Reference	Reference	Reference	Reference
Place of birth				
Other	3.4 (2.0, 5.8)	4.5 (2.1, 9.9)	3.2 (2.0, 5.2)	1.1 (0.5, 2.2)
United States	Reference	Reference	Reference	Reference

Mexican Americans. In addition, prevalence was significantly higher among non-Hispanic White and Black individuals who were foreign born or had prior military service (Table 2). Divorced or separated marital status significantly increased infection only among non-Hispanic Whites. An increasing number of sexual partners was associated with an increase in prevalence of infection in all except non-Hispanic Blacks. Early age at first intercourse, male-to-male sex, and cocaine use were also associated with an increase in hepatitis B virus prevalence. An increase in hepatitis B virus prevalence was not present among participants older than 17 years with a medical occupation (n = 769). Of the 654 health care workers who tested negative for the antibody to hepatitis B core antigen, 30.1% (95% CI = 24.1, 37.6) had concentrations of antibody to hepatitis B surface antigen greater than 10 mIU. A higher percentage of younger health care workers were immune (20–29-year-olds, 38.3%; 30–39-year-olds, 43.8%; 40–49-year-olds, 26.0%). The percentage of health care workers immune to hepatitis B virus differed by survey phase. In phase 1 (conducted from 1988–1991), 23.0% had protective antibody levels; in phase 2 (conducted from 1991–1994), 36.9% were immune.

Independent predictors of infection were identified by logistic regression analysis (Table 3). When predictors were modeled for the total population and adjusted for age, the strongest association was found between hepatitis B virus infection and non-Hispanic Black ethnicity and increasing number of sexual partners. Cocaine use, divorced or separated marital status, foreign birth, and having less than a high school education were also independent predictors of infection. No significant interactions were found between age and race, race and gender, or age, race, and gender, but variations in association across ethnic groups were seen with other sociodemographic and behavioral risk factors. For non-Hispanic Whites, increasing number of sexual partners, foreign birth, divorced or separated marital status, and less than a high school education were predictive of infection. In the non-Hispanic Black population, cocaine use, foreign birth, less than a high school education, and early age at first intercourse were associated with infection. In the Mexican American population, only cocaine use and increasing numbers of sexual partners were associated with infection.

Discussion

The NHANES are the only population-based surveys that provide nationally representative estimates of the prevalence—and therefore the lifetime risk—of hepatitis B virus infection. The 2 surveys described here demonstrated a relatively stable prevalence of hepatitis B virus infection in the United States during the 11-year interval. The reduction in hepatitis B virus prevalence in non-Hispanic Whites and Blacks older than 49 years most likely reflects a loss of an older cohort of infected persons.

In both surveys, non-Hispanic Blacks had a significantly elevated prevalence of hepatitis B virus infection relative to non-Hispanic Whites and Mexican Americans. In the logistic regression model, Black race remained an important risk factor for infection, independent of risk factors such as increasing number of sexual partners, cocaine use, and educational level. The inclusion of other risk factors for hepatitis B virus infection in the survey, such as injection drug use or transfusion, might reduce the effect of race.

In both surveys and in all racial/ethnic groups, the prevalence of hepatitis B virus infection did not begin to increase until puberty, suggesting that sexual transmission is the primary mode of spread in the United States. In NHANES II, hepatitis B virus infection was associated with a positive serologic test for syphilis.[3] Although cocaine use, divorced or separated marital status, less than a high school education, and foreign birth were all independently associated with hepatitis B virus infection, increasing number of sexual partners had the greatest influence

on infection risk, except in the non-Hispanic Black population.

That no large decrease in the prevalence of hepatitis B virus infection occurred during the 11-year interval between the 2 surveys is not surprising. Hepatitis B vaccine was first licensed in the United States in late 1981.[8] An immunization strategy to eliminate hepatitis B virus transmission was published in 1991.[1] Federal programs for routine hepatitis B vaccination of infants began in late 1992, and vaccination of adolescents was included in the Vaccines for Children program in 1995.[9] Vaccination of persons at occupational risk of infection began in 1981[8] but did not gain widespread coverage until 1991.[1] Data from NHANES demonstrate that children have a low but appreciable risk of hepatitis B virus infection that increases significantly at adolescence, presumably with the onset of sexual activity and other high-risk behaviors; this supports the need to routinely vaccinate. Future NHANES should provide a means to evaluate the age-specific effect of hepatitis B immunization on infection prevalence. □

Contributors

Dr McQuillan was the project officer for the NHANES laboratory component and was involved in every aspect of data collection. She coconceived and codeveloped the intellectual content for the paper, analyzed the data, and wrote the paper with input from the coauthors. Dr Coleman assisted with statistical input and hepatitis surveillance data. Ms Kruszon-Moran provided statistical advice and analysis. Ms Moyer was responsible for the laboratory data management over the course of the survey. Mr Lambert was the senior laboratory scientist responsible for the validity of the serologic testing done by other technicians in his laboratory. Dr Margolis coconceived and codeveloped the intellectual content for the paper and provided the framework for the discussion. A11 6 contributors commented on all drafts and are guarantors for the integrity of the paper.

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