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研究報告の概要

○ワクチン接種世代の米国におけるB型肝炎ウイルス(HBV)感染の状況
目的:広範なB型肝炎ワクチン接種後の、米国におけるHBV感染の状況について傾向を評価すること。
方法:HBV感染と免疫の状況を調べるため、1999-2006年と1988-1994年の期間、米国健康・栄養調査の6歳以上の参加者で、HBc抗体、HBs抗原及びHBs抗体を検査した。罹患率の概算は加重及び年齢調整された。
結果:1999-2006年の期間中の、年齢調整後のHBc抗体(4.7%)とHBs抗原(0.27%)の保有率は、1988-1994年(それぞれ5.4%及び0.38%)と統計学的に違いはなかった。HBc抗体の保有率は、6-19歳(1.9%→0.6%;P<0.01)及び20-49歳(5.9%→4.6%;P<0.05)の間で減少したが、50歳以上(7.2%対7.7%)では変化がなかった。1999-2006年では、HBc抗体の保有率は、非ラテンアメリカ系白人(2.8%)やメキシコ系アメリカ人(2.9%)より、非ラテンアメリカ系黒人(12.2%)と他の人種(13.3%)で高く、そして、米国生まれ(3.5%)より外国生まれ(12.2%)の方が高かった。米国生まれの6-19歳の子供(0.5%)では、人種や民族性による違いがなかった。米国生まれと外国生まれの子供の相違は1988-1994年(1.0%対12.8%)より、1999-2006年(0.5%対2.0%)の方が小さかった。また、6-19歳では、56.7%がワクチンによる獲得免疫を持っていた。
結論:HBVの罹患率は米国の子供で減少した。それは世界的及び国内のワクチン接種の効果を反映している。しかし、成人の状況はほとんど変わらず、およそ730万人(95%信頼区間、550万-940万人)の米国在住者は慢性的に感染している。

使用上の注意記載状況・その他参考事項等

赤十字アルブミン20
赤十字アルブミン25
赤十字アルブミン20%静注4g/20mL
赤十字アルブミン20%静注10g/50mL
赤十字アルブミン25%静注12.5g/50mL

血液を原料とすることに由来する感染症伝播等

報告企業の意見	今後の対応
広範なB型肝炎ワクチン接種後の米国におけるB型肝炎ウイルス罹患率を評価したところ、子供で罹患率が減少しており、ワクチン接種の効果を反映していることが分かったとの報告である。 これまで、本剤によるHBV感染の報告はない。また本剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれている。さらに最終製品についてHBV-NAT陰性であることを確認しており、安全性は確保されていると考える。	これまでの使用実績やバリデーション成績に鑑み本製剤の安全性は確保されており、特別の対応を必要としないが、HBV感染に関する新たな知見等について今後も情報の収集に努める。なお、日本赤十字社では献血時のスクリーニング法としてより感度の高い化学発光酵素免疫測定法(CLEIA)および新NATシステムを導入した。

MAJOR ARTICLE

The Prevalence of Hepatitis B Virus Infection in the United States in the Era of Vaccination

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Background. Our objective was to assess trends in the prevalence of hepatitis B virus (HBV) infection in the United States after widespread hepatitis B vaccination.

Methods. The prevalence of HBV infection and immunity was determined in a representative sample of the US population for the periods 1999–2006 and 1988–1994. National Health and Nutrition Examination Surveys participants ≥6 years of age were tested for antibody to hepatitis B core antigen (anti-HBc), hepatitis B surface antigen (HBsAg), and antibody to hepatitis B surface antigen (anti-HBs). Prevalence estimates were weighted and age-adjusted.

Results. During the period 1999–2006, age-adjusted prevalences of anti-HBc (4.7%) and HBsAg (0.27%) were not statistically different from what they were during 1988–1994 (5.4% and 0.38%, respectively). The prevalence of anti-HBc decreased among persons 6–19 years of age (from 1.9% to 0.6%; $P<.01$) and 20–49 years of age (from 5.9% to 4.6%; $P<.05$) but not among persons ≥50 years of age (7.2% vs 7.7%). During 1999–2006, the prevalence of anti-HBc was higher among non-Hispanic blacks (12.2%) and persons of "Other" race (13.3%) than it was among non-Hispanic whites (2.8%) or Mexican Americans (2.9%), and it was higher among foreign-born participants (12.2%) than it was among US-born participants (3.5%). Prevalence among US-born children 6–19 years of age (0.5%) did not differ by race or ethnicity. Disparities between US-born and foreign-born children were smaller during 1999–1996 (0.5% vs 2.0%) than during 1988–1994 (1.0% vs 12.8%). Among children 6–19 years of age, 56.7% had markers of vaccine-induced immunity.

Conclusions. HBV prevalence decreased among US children, which reflected the impact of global and domestic vaccination, but it changed little among adults, and ~730,000 US residents (95% confidence interval, 550,000–940,000) are chronically infected.

Hepatitis B virus (HBV) is a bloodborne and sexually transmitted virus. Each year, ~600,000 HBV-related deaths occur worldwide [1, 2], most of which result from the chronic sequelae of HBV infection [3–5]. Approximately 25% of persons who become chronically infected during childhood and ~15% of those who become chronically infected after childhood die from cirrhosis or liver cancer [2]. In the United States, before hepatitis B vaccines were licensed in 1982, 200,000–300,000 persons each year became infected with HBV [6]. Hepatitis B vaccination is the most effective measure to prevent HBV infection and its consequences. However, for persons already infected with HBV, antiviral agents are available that may prevent the serious sequelae of chronic liver disease, which highlights the importance of identifying infected individuals [7].

Patterns of HBV infection vary worldwide. Approximately 45% of the world's population live in regions that are highly endemic for HBV infection, where most infections are acquired perinatally or during early childhood [2, 8]. Another 43% live in regions of intermediate endemicity, where multiple modes of transmission (ie, perinatal, household, sexual, injection drug use associated, and health care associated) are important. In

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countries of low endemicity, most infections occur among adolescents and adults and are attributable to sexual and injection drug use exposures. In 1992, the World Health Organization set a goal for all countries to integrate hepatitis B vaccine into their childhood vaccination programs by 1997 [9].

In the United States, a country of low endemicity, a strategy to eliminate HBV transmission [10] was initiated in 1991, which includes universal vaccination of infants; screening of all pregnant women for HBV, with postexposure prophylaxis provided to infants born to infected women; catch-up vaccination of adolescents; and vaccination of adults who are at increased risk of infection [11, 12]. To assess US trends in the burden of HBV and to provide the first nationally representative analysis of the impact of hepatitis B vaccination, we compared the prevalence of HBV infection among National Health and Nutrition Examination Survey (NHANES) participants during 1999–2006 to that during 1988–1994 and measured the prevalence of vaccine-induced immunity among participants during 1999–2006.

METHODS

Study populations and sample design. NHANES is a series of surveys conducted periodically to obtain representative data on the health status of the US population. Participants are chosen using a complex, stratified, multistage sampling design to obtain a representative sample of the civilian, noninstitutionalized population. Our analyses include data from 1999–2006 (NHANES 1999–2006) and 1988–1994 (NHANES 1988–1994). Further details on the design and implementation of these surveys are described elsewhere [13, 14].

During the years evaluated, all ages were eligible to participate. Participants were interviewed at home and then visited a mobile examination center for additional interviews and a physical examination. Blood samples were collected for participants aged ≥6 years in NHANES 1988–1994 and aged >2 years in NHANES 1999–2006. Informed consent was obtained. Efforts were made to ensure participation; respondents were nominally remunerated for their time and travel expenses.

Laboratory methods. Serum samples from participants aged ≥6 years were tested for antibody to hepatitis B core antigen (anti-HBc) (NHANES 1988–1994: Corab radioimmunoassay [Abbott Laboratories]; NHANES 1999–2006: Ortho HBc ELISA [Ortho Clinical Diagnostics]) and, if results were positive, were tested for hepatitis B surface antigen (HBsAg) (NHANES 1988–1994: Ausria II [Abbott Laboratories]; NHANES 1999–2006: Auszyme [Abbott Laboratories]). Starting with NHANES 1999–2006, serum samples from participants aged >2 years were tested for antibody to hepatitis B surface antigen (anti-HBs) (Ausab [Abbott Laboratories]).

Definitions. Past or present HBV infection was defined as the presence of anti-HBc. Chronic HBV infection was defined as the presence of anti-HBc and HBsAg. For NHANES 1999–2006, persons with test results positive for anti-HBs and negative for anti-HBc were considered to have vaccine-induced immunity.

In NHANES 1988–1994, 25,733 (83.2%) of the participants aged ≥6 years were interviewed, of whom 23,527 (91.4% of those interviewed) were examined and 21,260 (90.4% of those examined) were tested for anti-HBc and HBsAg. In NHANES 1999–2006, 34,338 (79.8%) were interviewed, 32,534 (94.7% of those interviewed) were examined, and 29,828 (91.7% of those examined) provided serum samples. Analysis of vaccine-induced immunity included NHANES 1999–2006 participants aged ≥2 years tested for anti-HBs. Samples for participants aged 2–5 years were collected starting in NHANES 1999; participation rates in this age group were low, with samples available for 55.8% of 3592 examined children. In NHANES, race and ethnicity is categorized as non-Hispanic white (hereafter "NH-white"), non-Hispanic black (hereafter "NH-black"), Mexican American, or Other (which includes all other racial and ethnic groups, including Asians and other Hispanics). Age groups were 6–11, 12–19, 20–29, 30–39, 40–49, 50–59, and ≥60 years of age.

Statistical analyses. Prevalence estimates were weighted to represent the US population and to account for oversampling and nonresponse to the household interview and physical examination. Standard errors were calculated in SUDANN Statistical Analysis Software (Research Triangle Institute). Prevalence estimates were age-adjusted by the direct method using the age groups listed above to the 2000 US census population for comparisons across subgroups and between surveys [15]. Prevalence of vaccine-induced immunity was compared between the periods 1999–2002 and 2003–2006. Prevalence estimates of HBV infection and chronic infection for some subgroups, where noted in the tables, are based on a small number of persons with positive results and may be unstable. Statistical comparisons were evaluated using a t test for linear contrast procedure in SUDAAN. No adjustments for multiple comparisons were made.

RESULTS

Overall prevalence of past and present HBV infection and markers of immunity. The prevalence of past and present infection during the period 1999–2006 was 4.8% (95% confidence interval [CI], 4.3%–5.3%). Prevalence of chronic HBV infection was 0.28% (95% CI, 0.21–0.36%), which represents ~730,000 infected persons (95% CI, 550,000–940,000). Prevalence of markers of vaccine-induced immunity was 22.2% (95% CI, 21.3%–23.1%).

Prevalence of HBV infection increased with age, from 0.6%

(95% CI, 0.2%–1.4%) among persons 6–11 years of age to 7.3% (95% CI, 6.2%–8.5%) among persons ⩾60 years of age (Figure 1). Prevalence of vaccine-induced immunity was negatively correlated with age, ranging from 53.5% (95% CI, 50.8%–56.3%) among persons aged 6–11 years to 5.1% (95% CI, 4.3%–6.0%) among persons ⩾60 years of age. Among the 2003 children 2–5 years of age who were tested, 57.3% (95% CI, 54.1%–60.4%) had test results that were positive for anti-HBs; the representativeness of that estimate is uncertain because of the low response rate in this age group.

Age-adjusted estimates of the prevalence of past and present HBV infection. The overall age-adjusted prevalence of past and present infection in NHANES 1999–2006 (4.7%) was lower than but was not statistically different from the prevalence in NHANES 1988–1994 (5.4%) (Table 1). However, among children 6–19 years of age, prevalence decreased significantly, from 1.9% to 0.6% ($P<.01$). Among adults, prevalence decreased significantly among those 20–49 years of age, from 5.9% to 4.6% ($P<.05$) but was unchanged among those ⩾50 years of age.

In NHANES 1999–2006, age-adjusted prevalence of past and present infection was significantly higher among NH-blacks (12.2%; $P<.001$) and Others (13.3%; $P<.001$) than it was among NH-whites and Mexican Americans, and it was significantly higher among foreign-born persons (12.2%; $P<.001$) than it was among US-born persons (3.5%). Compared with NHANES 1988–1994, prevalence decreased significantly only among the Other (from 20.1% to 13.3%) and Mexican American (from 5.1% to 2.9%) race and ethnic groups. No significant change in sex-specific prevalence occurred; in NHANES 1999–2006, prevalence among male participants remained significantly ($P<.001$) higher than it was among female participants.

The age-adjusted prevalence of chronic HBV infection in NHANES 1999–2006 (0.27%) was lower but not statistically different than it was in NHANES 1988–1994 (0.38%) (Table 1). Among children 6–19 years of age, there was a 79% decrease in the age-adjusted prevalence of chronic infection, from 0.24% to 0.05%, which was not statistically significant. In NHANES 1999–2006, prevalence of chronic infection was lower among persons 6–19 years of age (0.05%) ($P<.001$) than it was among those 20–49 years of age (0.30%) or ⩾50 years of age (0.38%), and it was lower among female participants (0.19%) ($P<.05$) than it was among male participants (0.35%). Chronic infection was more common among persons classified as Other (0.98%; $P<.001$) or NH-black (0.89%; $P<.001$) than it was among NH-whites (0.09%) and Mexican Americans (0.07%). Chronic infection among foreign-born participants (0.89%) decreased significantly ($P<.05$), compared with NHANES 1988–1994 (1.75%), but remained >5-fold higher than it was among US-born participants (0.16%; $P<.001$). The number of chronically infected persons identified in NHANES was small; estimates for some sparsely populated strata, where noted in the tables, have large confidence intervals and may be unstable.

Trends among children in past and present HBV infection. Among children, the age-adjusted prevalence of past and present infection among NH-blacks ($P<.05$) and Others ($P<.01$) decreased significantly across surveys. The decreases in these groups, which both had significantly ($P<.01$) higher prevalence than did NH-whites and Mexican Americans in NHANES 1988–1994, resulted in a narrowing of racial and ethnic disparities in NHANES 1999–2006, although the difference between the highest (NH-black) and lowest 2 groups (Mexican Americans and Other) remained significant ($P<.01$ and $P<.05$ respectively) (Table 2). Differences in prevalence between

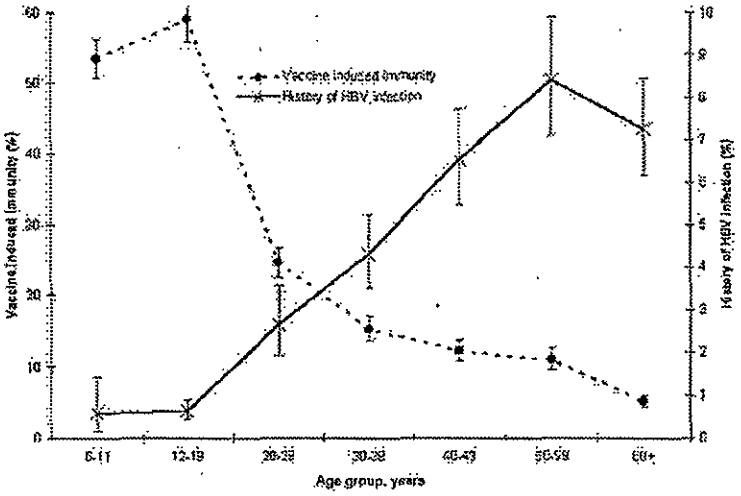

Figure 1. Crude prevalence of markers of hepatitis B virus (HBV) infection and vaccine-induced immunity by age, 1999–2006.

Table 1. Age Adjusted Prevalence of Hepatitis B Virus (HBV) Infection, by Selected Demographic Characteristics

	Past or present HBV infection					Chronic HBV infection		
	NHANES III (1988–1994)		NHANES 1999–2006			NHANES III (1988–1994): Prevalence, % (95% CI)	NHANES 1999–2006: Prevalence, % (95% CI)	P^b
Variable	Sample size[a]	Prevalence, % (95% CI)	Sample size[a]	Prevalence, % (95% CI)	P^b			
Overall	21,260	5.4 (4.8–6.1)	29,828	4.7 (4.2–5.2)	NS	0.38 (0.29–0.49)	0.27 (0.20–0.35)	NS
Age, years								
6–19	5679	1.9 (1.2–2.7)	12,004	0.6 (0.4–0.9)	<.01	0.24 (0.07–0.56)[c]	0.05 (0.02–0.11)[c,d]	NS
20–49	8857	5.9 (5.1–6.9)	9465	4.6 (3.9–5.3)	<.05	0.39 (0.25–0.60)	0.30 (0.21–0.42)	NS
≥50	6724	7.2 (6.2–8.3)	8359	7.7 (6.8–8.7)	NS	0.45 (0.21–0.84)	0.38 (0.25–0.55)	NS
Race/ethnicity								
White, non-Hispanic	7963	3.0 (2.6–3.5)	12,075	2.8 (2.5–3.1)	NS	0.21 (0.09–0.41)[c]	0.09 (0.05–0.14)	NS
Black, non-Hispanic	6133	13.8 (12.4–15.3)	7302	12.2 (11.1–13.5)	NS	0.83 (0.59–1.14)	0.89 (0.57–1.33)	NS
Mexican American	6275	5.1 (3.8–6.6)	8094	2.9 (2.4–3.5)	<.01	0.15 (0.05–0.37)[c,d]	0.07 (0.01–0.25)[c,d]	NS
Other	889	20.1 (15.4–25.5)	2357	13.3 (10.9–16.0)	<.05	1.51 (0.83–2.51)	0.98 (0.57–1.56)	NS
Country of birth								
United States	17,301	3.9 (3.5–4.4)	24,291	3.5 (3.1–3.9)	NS	0.20 (0.12–0.30)	0.16 (0.11–0.23)	NS
Foreign born	3901	16.2 (12.8–19.9)	5528	12.2 (10.7–13.9)	<.05	1.75 (1.26–2.36)	0.89 (0.55–1.35)	<.05
Sex								
Male	10,088	6.4 (5.5–7.3)	14,523	5.6 (4.9–6.3)	NS	0.52 (0.35–0.74)	0.35 (0.25–0.48)	NS
Female	11,172	4.5 (3.8–5.4)	15,305	3.8 (3.2–4.4)	NS	0.23 (0.14–0.36)	0.19 (0.11–0.30)	NS

NOTE. CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NS, not significant.

[a] Stratum-specific sample sizes may not sum to total because of missing data.

[b] Determined by *t* test evaluating change across surveys.

[c] Estimate is small relative to its standard error (relative standard error >30%) and therefore may be unstable.

[d] Estimate based on <10 individuals with positive samples.

US and foreign-born children diminished as a result of greater decreases in prevalence among foreign-born children. The prevalence among foreign-born children (12.8%) in NHANES 1988–1994, which was almost 13-fold higher than that among US-born children (1.0%; $P < .01$), decreased to 2.0% in NHANES 1999–2006, compared with 0.5% ($P < .01$) among US-born children. Most notable was a >90% decrease among foreign-born Other children ($P < .001$).

Among US-born children, racial and ethnic disparities were reduced. In NHANES 1988–1994, prevalence was significantly higher among US-born NH-black children (2.1%; $P < .05$), compared with NH-whites (0.7%) and Mexican Americans (0.5%). In comparison, in NHANES 1999–2006, prevalence was similar among US-born children by race and ethnicity, ranging from 0.1% (Other) to 0.6% (NH-white). Race-specific estimates for some subgroups, as noted in Table 2, are based on <10 positive samples and may be unstable.

Trends among adults. The significant decrease in prevalence across surveys among persons 20–49 years of age ($P < .05$) reflected decreases among US-born and foreign-born participants, although only the decrease among US-born participants was statistically significant ($P < .05$). Prevalence remained significantly higher among foreign-born participants (10.3%) in NHANES 1999–2006 than among US-born participants (3.4%; $P < .001$) (Table 3). Among US-born adults, a pattern of decreasing prevalence was noted in all racial and ethnic groups, but only the decrease in prevalence among NH-blacks was statistically significant ($P < .05$). In NHANES 1999–2006, prevalence among US-born non-Hispanic NH-blacks (9.6%) remained higher ($P < .001$) than the prevalence among NH-whites and Mexican Americans. In contrast, prevalence among US-born Others no longer differed from that among US-born NH-whites or Mexican Americans. The decrease among foreign-born participants 20–49 years of age ($P < .05$) was seen among several racial and ethnic groups but was statistically significant only among Mexicans Americans ($P < .05$). The prevalence was ~3-fold higher among foreign-born Others (16.1%) than it was among US-born Others (5.6%; $P < .001$), a gap that appeared to widen, compared with NHANES 1988–1994, when prevalences among foreign-born and US-born Others were 21.3% and 17.4%, respectively.

In contrast to the trends among younger adults, the prevalence among persons ≥50 years of age in NHANES 1999–2006 (7.7%; 95% CI, 6.8%–8.7%) did not differ from that in NHANES 1988–1994 (7.2%; 95% CI, 6.2%–8.3%). Disparities by race and country of birth that were present in NHANES 1988–1994 (data not shown) remained unchanged in NHANES 1999–2006. In particular, prevalence remained unchanged and significantly higher among NH-blacks (21.7%; 95% CI, 19.2%–24.3%; $P < .001$) and Others (25.5%; 95% CI, 19.6%–32.1%;

Table 2. Age-Adjusted Prevalence of Past and Present Hepatitis B Virus Infection among Children 6–19 Years of Age, by Selected Demographic Characteristics

Variable	NHANES III (1988–1994)			NHANES 1999–2006			
	Sample size[a]	No. of children with positive results	Prevalence, % (95% CI)	Sample size[a]	No. of children with positive results	Prevalence, % (95% CI)	P[b]
Overall	5679	77	1.9 (1.2–2.7)	12,004	81	0.6 (0.4–0.9)	<.01
Race and ethnicity							
White, non-Hispanic	1478	13	0.7 (0.4–1.9)[c]	3058	15	0.6 (0.3–1.2)[c]	NS
Black, non-Hispanic	1921	35	2.2 (1.4–3.3)	3830	44	1.0 (0.7–1.4)	<.05
Mexican American	2011	6	0.5 (0.1–1.3)[c]	4148	17	0.4 (0.2–0.7)[c]	NS
Other	269	23	10.3 (5.2–17.7)	968	5	0.4 (0.1–1.1)[c]	<.01
US born							
All	5022	50	1.0 (0.6–1.4)	10,474	44	0.5 (0.2–0.8)	<.05
White, non-Hispanic	1448	13	0.7 (0.4–1.3)	2963	13	0.6 (0.2–1.2)[c]	NS
Black, non-Hispanic	1840	31	2.1 (1.2–3.2)	3644	18	0.5 (0.3–0.7)	<.01
Mexican American	1581	4	0.5 (0.1–1.8)[c]	3079	12	0.4 (0.1–0.7)[c]	NS
Other	153	2	0.9 (0.0–5.8)[c]	788	1	0.1 (0.0–0.6)[c]	NS
Foreign born							
All	639	27	12.8 (6.7–21.4)	1529	37	2.0 (1.2–3.2)	<.01
White, non-Hispanic	28	0	0.0 (0.0–97.5)[c]	95	2	1.8 (0.3–5.9)[c]	NS
Black, non-Hispanic	74	4	5.3 (0.9–16.0)[c]	185	26	11.8 (5.9–20.3)	NS
Mexican American	421	2	0.5 (0.1–2.1)[c]	1069	5	0.3 (0.1–0.8)[c]	NS
Other	116	21	22.9 (12.6–36.3)	180	4	1.4 (0.3–3.9)[c]	<.001

NOTES. CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NS, not significant.

[a] Stratum-specific sample sizes may not sum to total because of missing data.

[b] Determined by t test evaluating change across surveys.

[c] Estimate is small relative to its standard error (relative standard error >30%) and therefore may be unstable.

$P<.001$), compared with NH-whites (4.7%; 95% CI, 3.9%–5.5%) and Mexican Americans (mean value, 6.0%; 95% CI, 5.0%–7.2%), and was significantly higher among foreign-born persons (22.8%; 95% CI, 19.4%–26.5%), compared with US-born persons (5.9%; 95% CI, 5.0%–6.9%; $P<.001$).

Age-adjusted prevalence of vaccine-induced immunity in NHANES 1999–2006. The age-adjusted prevalence of markers of vaccine-induced immunity in NHANES 1999–2006 was 22.9% (95% CI, 21.9%–24.0%), ranging from 56.7% (95% CI, 54.0%–59.3%) among children 6–19 years of age to 17.0% (95% CI, 15.8%–18.2%) among those 20–49 years of age to 7.5% (95% CI, 6.7%–8.3%) among persons ⩾50 years of age (Table 4). Prevalence of vaccine-induced immunity increased significantly, from 20.5% during 1999–2002 to 25.2% during 2003–2006 ($P<.001$). This reflected significant increases in all age and racial and ethnic groups and among foreign-born and US-born participants. Comparing data from 1999–2002 with that from 2003–2006, the age-adjusted prevalence of vaccine-induced immunity increased from 52.7% to 60.5% among those 6–19 years of age, from 14.3% to 19.6% among those 20–49 years of age, and from 6.6% to 8.2% among those ⩾50 years of age.

The prevalence of vaccine-induced immunity during 1999–2006 among children 6–19 years of age varied little by race and ethnicity, ranging from 53.6% (95% CI, 49.7%–57.6%) among NH-blacks to 59.7% (95% CI, 54.2%–65.0%) among Others and did not differ by sex. A significantly higher proportion of foreign-born children (63.7%; 95% CI, 59.3%–67.9.0%; $P<.01$) had evidence of vaccine-induced immunity, compared with US-born children (56.3%; 95% CI, 53.5%–59.1%), although the lowest prevalence in this age group occurred among foreign-born NH-blacks (51.2%; 95% CI, 41.7%–60.6%) (data not shown).

Among adults 20–49 years of age, prevalence was significantly higher among US-born persons (17.9%; 95% CI, 16.5%–19.4%; $P<.001$) than foreign-born persons (12.7%; 95% CI, 10.9%–14.6%) and higher among women (20.1%; 95% CI, 18.2%–22.0%; $P<.001$) than among men (13.8%; 95% CI, 12.6%–15.0%). Among adults ⩾50 years of age, the age-adjusted prevalence of vaccine-induced immunity (7.5%; 95% CI, 6.7%–8.3%) did not differ by race and ethnicity or country of birth (data not shown) but was significantly higher among women (8.7%; 95% CI, 7.6%–9.9%; $P<.001$) than among men (6.1%; 95% CI, 5.2%–7.0%).

DISCUSSION

In this analysis of the most recent NHANES, conducted a decade after universal vaccination of US children against hepatitis

Table 3. Age-Adjusted Prevalence of Past and Present Hepatitis B Virus Infection among Persons 20–49 Years of Age by Selected Demographic Characteristics

Variable	NHANES III (1988–1994) Sample size[a]	NHANES III (1988–1994) Prevalence, % (95% CI)	NHANES 1999–2006 Sample size[a]	NHANES 1999–2006 Prevalence, % (95% CI)	P[b]
Overall	8857	5.9 (5.1–6.9)	9465	4.6 (3.9–5.3)	<.05
Race/ethnicity					
White, non-Hispanic	2724	3.3 (2.6–4.2)	4176	2.6 (2.2–3.1)	NS
Black, non-Hispanic	2825	13.8 (12.2–15.5)	2018	11.5 (9.6–13.6)	NS
Mexican American	2929	4.2 (3.1–5.6)	2398	2.2 (1.5–3.1)	<.01
Other	379	20.0 (14.4–26.7)	873	11.5 (8.8–14.8)	<.05
US born					
All	6564	4.5 (3.8–5.3)	6935	3.4 (2.9–4.0)	<.05
White, non-Hispanic	2604	3.2 (2.4–4.1)	3941	2.3 (1.9–2.8)	NS
Black, non-Hispanic	2601	12.5 (10.8–14.5)	1804	9.6 (8.0–11.4)	<.05
Mexican American	1283	4.3 (2.8–6.1)	826	2.3 (1.2–3.9)	NS
Other	76	17.4 (6.7–34.1)[c,d]	364	5.6 (2.6–10.2)[d]	NS
Foreign born					
All	2269	14.4 (11.0–18.3)	2530	10.3 (8.2–12.6)	NS
White, non-Hispanic	118	7.5 (3.4–14.1)[c]	236	8.1 (4.8–12.6)	NS
Black, non-Hispanic	207	28.1 (20.4–36.9)	214	25.9 (19.2–33.5)	NS
Mexican American	1645	4.3 (2.7–6.5)	1572	2.2 (1.4–3.3)	<.05
Other	299	21.3 (14.4–29.7)	509	16.1 (12.2–20.6)	NS

NOTE. CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NS, not significant.

[a] Stratum-specific sample sizes may not sum to total because of missing data.

[b] Determined by t test evaluating change across surveys.

[c] Estimate is small relative to its standard error (relative standard error >30%) and therefore may be unstable.

[d] Estimate based on <10 individuals with positive samples.

B began in 1991, we demonstrate a significant reduction of 68% in HBV infection prevalence among children, including those born in the United States and elsewhere. In addition, a 79% decrease in the prevalence of chronic infection in this age group, although based on a small number of children and not statistically significant, further suggests that substantial progress has been made in reducing the disease burden among children. NHANES, the only source of nationally representative information on the seroprevalence of hepatitis virus infections in the United States, has been critical to describing the burden of HBV infection and, for the first time with this report, determining how it is changing after implementation of a comprehensive national strategy to eliminate HBV transmission in the United States. Keeping in mind the limitations of estimates that are based on small numbers, extrapolation from these data suggests that the number of chronically infected children during 1999–2006 was ~29,000 (95% CI, 11,000–63,000), compared with ~122,000 (95% CI, 36,000–290,000) during 1988–1994. These decreases among children are likely due, in large part, to the incorporation of hepatitis B vaccination into domestic and global routine infant and childhood vaccination programs. A smaller yet significant decrease in the prevalence of HBV infection occurred among US-born adults 20–49 years of age. Among US-born and foreign-born adults aged ≥50 years, HBV infection prevalence changed little over the decade. An estimated 730,000 US residents, mostly adults, had chronic HBV infection, which demonstrates the ongoing burden of HBV-associated disease.

The decrease in the prevalence of infection among children, which was primarily the result of large decreases among US-born NH-black and Other children and among foreign-born Other children, resulted in the elimination or narrowing of many disparities. Among US-born children, prevalence of HBV infection was uniformly low. Although the prevalence among foreign-born children continued to be higher than that among US-born children, it decreased by 84%, compared with data from the previous survey. Most strikingly, there was a >90% decrease among the foreign-born Other group, and the disparity between US-born and foreign-born children was reduced from 13-fold to 4-fold. These data provide a sense of the impact of vaccination here and abroad on preventing HBV infections among children living in the United States.

In the United States, the first recommendations for universal vaccination of children against hepatitis B were made in 1991 [10]. To prevent perinatal transmission of HBV, screening of pregnant women for HBsAg was recommended with the follow-up of infants born to infected women to ensure that they receive postexposure prophylaxis. "Catchup" vaccination of unvacci-

Table 4. Age-Adjusted Prevalence of Vaccine-Induced Immunity to Hepatitis B Virus (HBV) Infection by Selected Demographic Characteristics, 1999–2006

Variable	NHANES 1999–2006		NHANES 1999–2002		NHANES 2003–2006		
	Sample size[a]	Prevalence, % (95% CI)	Sample size[a]	Prevalence, % (95% CI)	Sample size[a]	Prevalence, % (95% CI)	P^b
Overall	29,828	22.9 (21.9–24.0)	15,051	20.5 (18.7–22.4)	14,777	25.2 (24.2–26.3)	<.001
Sex							
Male	14,523	20.8 (19.8–21.8)	7290	18.8 (17.2–20.5)	7233	22.7 (21.7–23.8)	<.001
Female	15,305	25.0 (23.6–26.3)	7761	22.2 (20.0–24.5)	7544	27.6 (26.2–29.1)	<.001
Age, years							
6–19	12,004	56.7 (54.0–59.3)	6202	52.7 (48.1–57.3)	5802	60.5 (57.9–63.0)	<.01
20–49	9465	17.0 (15.8–18.2)	4701	14.3 (12.5–16.2)	4764	19.6 (18.1–21.2)	<.001
≥50	8359	7.5 (6.7–8.3)	4148	6.6 (5.5–7.9)	4211	8.2 (7.3–9.3)	<.05
Race and ethnicity							
White, non-Hispanic, by age in years							
Overall	12,075	23.5 (22.2–24.8)	5910	21.0 (18.9–23.3)	6165	25.7 (24.4–27.0)	<.001
6–19	3058	56.7 (53.4–59.8)	1556	53.6 (48.5–58.7)	1502	59.3 (55.6–62.9)	NS
20–49	4176	18.0 (16.5–19.6)	2020	15.0 (12.8–17.4)	2156	20.9 (18.9–23.0)	<.001
≥50	4841	7.7 (6.8–8.6)	2334	6.6 (5.3–8.2)	2507	8.5 (7.4–9.8)	<.05
Black, non-Hispanic, by age in years							
Overall	7302	21.4 (20.0–22.8)	3461	18.5 (16.5–20.6)	3841	24.0 (22.4–25.7)	<.001
6–19	3830	53.6 (49.7–57.6)	1849	46.5 (40.7–52.4)	1981	60.3 (56.6–64.0)	<.001
20–49	2018	15.5 (13.7–17.5)	934	13.1 (10.6–16.0)	1084	17.5 (15.1–20.2)	<.05
≥50	1454	6.9 (5.6–8.5)	678	6.3 (4.5–8.5)	776	7.4 (5.5–9.8)	NS
Mexican American, by age in years							
Overall	8094	19.8 (18.3–21.3)	4408	17.9 (16.0–20.0)	3686	21.5 (19.5–23.6)	<.05
6–19	4148	57.0 (53.2–60.6)	2275	49.9 (44.5–55.3)	1873	63.5 (59.3–67.6)	<.001
20–49	2398	11.3 (9.6–13.3)	1291	10.7 (8.7–13.1)	1107	11.9 (9.3–14.9)	NS
≥50	1548	5.8 (4.2–7.7)	842	5.7 (4.0–7.8)	706	5.8 (3.5–9.1)	NS
Other, by age in years							
Overall	2357	24.1 (21.9–26.4)	1272	21.9 (18.6–25.4)	1085	27.0 (24.5–29.7)	<.05
6–19	968	59.7 (54.2–65.0)	522	57.8 (49.1–66.2)	446	63.3 (57.7–68.6)	<.001
20–49	873	18.2 (15.0–21.6)	456	14.2 (10.1–19.3)	417	22.7 (18.7–27.1)	<.01
≥50	516	7.4 (5.4–9.8)	294	7.5 (5.4–10.1)	222	7.1 (4.0–11.6)	NS
Country of birth							
US born	24,291	23.3 (22.1–24.6)	12,103	20.9 (18.8–23.1)	12,188	25.7 (24.6–26.8)	<.001
Foreign born	5528	22.1 (20.7–23.6)	2941	19.5 (17.6–21.5)	2587	24.8 (22.7–27.1)	<.001

NOTES. CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NS, not significant.

[a] Stratum-specific sample sizes may not sum to total because of missing data.

[b] Determined by *t* test evaluating change from 1999–2002 to 2003–2006.

nated adolescents was recommended in 1995 [16]. Vaccine coverage data indicate that, between 1993 and 2006, the percentage of children 19–35 months of age who received hepatitis B vaccine increased from 16% to 93% [17]. Coverage rates among adolescents 13–17 years of age have also increased substantially, to 81% in 2006 [18].

Considerable progress also has been made in implementing hepatitis B vaccination programs for children in other countries. As of December 2006, 164 (85%) of 193 World Health Organization member countries had introduced hepatitis B vaccination into their infant immunization schedules [19]. Of the 27 countries in the western Pacific, where HBV infection is endemic, 55% introduced infant hepatitis B vaccination by 1992 and, to date, 96% have integrated hepatitis B vaccine into their childhood immunization programs. Studies from Asian countries have documented the impact of these programs, including decreases in the prevalence of chronic infection and the incidence of hepatocellular carcinoma among children [20–22]. Of the 29 countries that have not yet integrated hepatitis B vaccination, 12 (41%) are in Africa, where endemicity remains high. The prevalence patterns among foreign-born children in NHANES appear to correlate with these global patterns of vaccination implementation, with dramatic decreases among the Other group, which includes those born in Asia.

Although patterns of markers of vaccine-induced immunity in NHANES 1999–2006 reflect the implementation of domestic and international vaccination programs, the results undoubtedly underestimate the true prevalence of vaccine-induced immunity, particularly that among children. Among persons who were vaccinated as infants or young children and responded to vaccination, 15%–45% have low or undetectable concentrations of anti-HBs 5–22 years after vaccination [8, 23–26]. However, evidence indicates that immunocompetent persons who respond to the vaccine remain protected against HBV even as anti-HBs levels become undetectable [27, 28]. Thus, prevalence of anti-HBs in NHANES underestimates the population level of vaccine-induced immunity by misclassifying participants who lost detectable anti-HBs as susceptible to HBV. Results from the National Immunization Survey and other surveys, which indicate high coverage among 19–35-month-old children and adolescents, provide a more complete reflection of coverage and immunity among US-born children [17].

The decreases in prevalence among younger US-born adults likely reflect the impact of several factors. Over the 18 years spanned by these NHANES surveys, the risk of HBV transmission has decreased, as evidenced by an 80% reduction in the incidence of acute hepatitis B cases since 1990[29]. This likely reflects the implementation of prevention strategies, such as improvements in infection control and screening of the blood supply, modified risk taking practices among high-risk groups, and the impact of targeted vaccination of adults at risk because of occupational or behavioral factors [30–32]. This decrease may also reflect the impact of programs to vaccinate adolescents [16]. This effect recently was documented among US military recruits, among whom anti-HBs prevalence ranged from 62% among those born during 1987–1988 to 27% among those born before 1982 [33].

Although substantial progress has been made in preventing HBV infection among children and young adults, NHANES indicates that the burden of chronic hepatitis B among adults remains large. Many disparities persist that reflect infections acquired over the participants' lifetimes. Among US-born adults, prevalence increased with age and was higher among NH-black and Other races and ethnicities. Of interest, prevalence decreased among young US-born adult Others, which could reflect an impact of vaccination programs targeting Asians of all ages [34–36]. As in previous surveys, HBV infection prevalence was significantly higher among foreign-born adults than it was among US-born adults, which reflected the level of endemicity in participants' countries or regions of origin. Foreign-born persons accounted for ~14% of the NHANES 1999–2006 population, which is similar to estimates from the US Census [37] that indicated that 12% of the US population was foreign-born. In NHANES 1999–2006, this group accounted for 43% of all chronic infections or ~317,000 (95% CI, 202,000–479,000) infections among foreign-born persons in the United States in 1999–2006.

The large burden of chronic HBV infection among adults demonstrated by NHANES highlights the need to improve screening programs and other efforts to identify chronically infected persons, most of whom remain asymptomatic until cirrhosis or end-stage liver disease develops. Limited data indicate that many persons with chronic infection are unaware of their infection status [38–40]. Screening and counseling programs are important to educate and medically manage infected patients to prevent liver disease progression and to identify and vaccinate susceptible contacts to interrupt further transmission [7].

There are limitations to the use of NHANES data to assess HBV prevalence. In NHANES, participants classify themselves with regard to race and ethnicity, but because the numbers of persons belonging to specific racial and ethnic groups other than non-Hispanic white, non-Hispanic black, or Mexican-American are not large enough to make stable prevalence estimates, the National Center for Health Statistics (NCHS), which oversees NHANES, groups these persons into a category of Other nonspecified race and does not release self-reported race data. Thus, the calculation of specific estimates for subgroups, such as Asians and Native Americans, is not possible. It is likely that prevalence among Asians is considerably higher than that reflected by the overall Other category, which includes populations which have lower prevalence of disease. Nevertheless, these groups are sampled in the NHANES population, and overall NHANES estimates reflect and are greatly influenced by the prevalence in these subgroups. A summary analysis provided by NCHS of unedited data, not publicly released, of participants' self-reported race and country of origin suggests that persons likely to be Asian represent ~3.3% (95% CI, 2.8%–3.8%) of the overall NHANES weighted sample and that ~71% of that group are foreign-born. These results may be subject to some error because of misclassification of Asian ethnicity based on unedited data but appear similar to US Census estimates [37], which characterize 4.4% of the US population as Asian, with 68% of this Asian population being born overseas. In addition, although composition of the Other category is not specified and varies somewhat across surveys, an estimated 30% of the group were classified as Asian based on the analysis of raw ethnicity and country of origin data, and the trends and patterns expected among the Asian population appear to be discernible in the results for the Other race and ethnic group.

Another limitation of NHANES is that it samples only from the noninstitutionalized civilian population of the United States. Thus, the overall estimate does not reflect infections among populations that include incarcerated persons, among whom HBV prevalence is known to be high. The prevalence of chronic HBV infection among the estimated 2.2 million

persons in US jails and prisons is ~2.0% [41], resulting in an estimated 44,000 persons with HBV infection in these settings and increasing the estimated number of chronically infected persons in the United States by 6%, to 774,000. Homeless persons, who also may have increased prevalence of infection, are also not included in NHANES [7].

In summary, this analysis of unique population-based data provides new evidence of the impact of domestic and global childhood hepatitis B vaccination programs on preventing HBV infections, while illustrating the remaining large burden of chronic HBV infection in the United States, which consists of ~730,0000 persons. These results are relevant to public health policy makers and highlight the importance of ongoing hepatitis B vaccination programs and of programs to identify persons with chronic HBV infection.

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