MAJOR ARTICLE

Seroprevalence of Herpes Simplex Virus Types 1 and 2—United States, 1999–2010

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(See the editorial commentary by Kimberlin on pages 315–7.)

Background. Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) are common infections with serious sequelae. HSV-1 is an increasingly important cause of genital herpes in industrialized countries.

Methods. Using nationally representative data from the National Health and Nutrition Examination Survey (NHANES), we examined HSV-1 and HSV-2 seroprevalence among 14- to 49-year-olds in the United States. We estimated seroprevalence in 1999–2004 and 2005–2010, stratified by sociodemographic characteristics and sexual behaviors. We also reviewed HSV-1 and HSV-2 seroprevalence from 1976–1980 to 2005–2010.

Results. In 2005–2010, the seroprevalence of HSV-1 was 53.9%, and the seroprevalence of HSV-2 was 15.7%. From 1999–2004 to 2005–2010, HSV-1 seroprevalence declined by nearly 7% ($P < .01$), but HSV-2 seroprevalence did not change significantly. The largest decline in HSV-1 seroprevalence from 1999–2004 to 2005–2010 was observed among adolescents aged 14–19 years, among whom seroprevalence declined by nearly 23%, from 39.0% to 30.1% ($P < .01$). In this age group, HSV-1 seroprevalence declined >29% from 1976–1980 to 2005–2010 ($P < .01$).

Conclusions. An increasing number of adolescents lack HSV-1 antibodies at sexual debut. In the absence of declines in HSV-2 infections, the prevalence of genital herpes may increase.

Keywords. HSV-1; HSV-2; herpes simplex virus; genital herpes; adolescents; NHANES.

Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) are lifelong infections. In 1999–2004, HSV-1 seroprevalence in the United States was 57.7% and HSV-2 seroprevalence was 17.0% [1]. HSV-2 is almost always transmitted sexually, whereas HSV-1 has typically been transmitted nonsexually during childhood. Because most HSV-1 and HSV-2 infections are subclinical, many people with these viruses do not know they are infected. When symptoms do occur, they consist primarily of episodic ulcerative lesions at the site of infection. HSV-1 infection typically causes orolabial lesions, and HSV-2 infection typically causes genital lesions. Although either HSV-1 or HSV-2 can cause genital herpes, HSV-1 infection is characterized by fewer recurrences of lesions and less viral shedding than HSV-2 infection. [2].

Although rare, HSV-1 and HSV-2 have several serious sequelae. Both can be transmitted perinatally from mother to child, and in some cases, cause fatal infection in infants. Other serious complications in adults include blindness, encephalitis, and aseptic meningitis [2]. Of major public health importance is the interaction of HSV-2 with human immunodeficiency virus (HIV). HSV-2 infection increases the risk of acquiring HIV infection 2- to 3-fold [3] and of transmitting HIV infection 4-fold [4].

Largely due to the synergy between HSV-2 and HIV infections, HSV-2 prevalence and epidemiology have been more frequently described than patterns of HSV-1 infection. However, HSV-1 seroprevalence is increasingly

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important to monitor. Two HSV vaccine trials found efficacy against symptomatic disease for HSV-2 among HSV-1–negative women only [5], although a follow-up trial did not find efficacy among this group [6]. HSV-1 seroprevalence data can be helpful for ongoing HSV vaccine development efforts, including for characterization of efficacy trial target populations and for vaccine policy considerations.

HSV-1 is a significant cause of genital herpes in industrialized countries [7]. In a study of US college students, the percentage of genital herpes specimens that were attributable to HSV-1 increased from 31% in 1993 to 78% in 2001 [8]. More recently, results from an HSV vaccine trial in the United States indicated that nearly 60% of incident genital herpes infections were attributable to HSV-1 [6, 9]. Similar trends have been observed in other industrialized countries [10–12]. One possible explanation for increasing genital HSV-1 infection is that HSV-1 acquisition may be declining prior to sexual debut, rendering young people without HSV-1 antibodies susceptible to genital HSV-1 acquisition if exposed.

In this study, we estimated the seroprevalence of HSV-1 and HSV-2 infection using the National Health and Nutrition Examination Survey (NHANES) data. We examined change in the seroprevalence of HSV-1 and HSV-2 across surveys. HSV-1 and HSV-2 are lifelong infections, and seroprevalence increases with age. Emergent change in population-level risk for HSV infections is most effectively detected in the youngest age groups.

METHODS

NHANES is a program of cross-sectional surveys that are designed to be representative of the noninstitutionalized US population. Surveys have been conducted by the National Center for Health Statistics (NCHS) since the 1960s to describe the health and nutritional status of adults and children. In addition to interviews, the NHANES survey methodology includes a physical examination, during which blood and urine specimens are collected for further testing. Previously, NHANES was a series of surveys conducted at predetermined time intervals. In 1999, the methodology was modified such that surveys are now administered continuously. Since NHANES' inception, the surveys have utilized a multistage, complex sampling scheme to produce nationally representative estimates. NHANES is approved by the NCHS/Centers for Disease Control and Prevention Research Ethics Review board. Informed consent was obtained from all participants. Permission from parents or legal guardians was obtained for participants aged <18 years.

Serologic testing for HSV-1 and HSV-2 has been conducted as part of NHANES since the 1988–1994 survey; stored serum samples from the 1976–1980 survey were previously tested. The same glycoprotein G–based assays have been used to detect type-specific HSV antibodies in all NHANES surveys. These assays have been previously described in detail; they are highly sensitive and specific, and discriminate well between HSV-1 and HSV-2 [13–15]. Demographic information was collected via face-to-face interview, and information about income and sexual behavior was collected via audio computer assisted self-interview.

For the main analyses, we used NHANES data from the period 1999–2010. To examine change in seroprevalence of HSV-1 and HSV-2 over time, we categorized these data into 2 groups including 6 years each: 1999–2004 and 2005–2010. We included respondents aged 14–49 years who were tested for HSV-1 and HSV-2. During 1999–2004, 82% of screened participants were interviewed, 78% were examined, and 72% were tested for HSV-1 and HSV-2. During 2005–2010, 80% of screened participants were interviewed, 78% were examined, and 71% were tested for HSV-1 and HSV-2. From 1999 to 2010, 0.2% of respondents had an indeterminate HSV-1 result, and 0.3% had an indeterminate HSV-2 result. These results were recoded as negative for analytic purposes.

To make the estimates nationally representative of the US noninstitutionalized population, we used NHANES participants' medical examination sample weights for all analyses. These weights are provided by NCHS and account for the differential probabilities of selection, nonresponse, and noncoverage. We used SAS version 9.3 software, which uses Taylor linearization to incorporate the survey's complex sample design and the weights [16, 17]. First, we calculated the percent change and corresponding 95% confidence intervals in age-specific seroprevalence of HSV-1 and HSV-2, from one time period to the next. The χ^2 test for independence was used to assess statistical differences in age-specific seroprevalence by time period. We used 2 criteria to evaluate potential statistical unreliability of prevalence estimates: having a relative standard error of >30% or having <10 cases in the numerator. None of our estimates met either of these criteria.

To better understand emerging change in HSV-1 seroprevalence, we examined seroprevalence among individuals aged 14–19 and 20–29 years in both time periods, stratified by respondents' sociodemographic characteristics and sexual behaviors. We calculated the percent change (and corresponding 95% confidence intervals) in the seroprevalence of HSV-1 and HSV-2 in each stratum and performed χ^2 tests to detect statistically significant change from one time period to the next. To assess potential confounding of the relationship between time period and HSV-1 prevalence, we examined associations between respondent characteristics and HSV-1 using prevalence ratios and χ^2 tests. We also tested potential differences between respondent characteristics in the 2 time periods (not shown).

Last, we examined HSV-1 and HSV-2 seroprevalence in every survey period for which NHANES conducted serosurveys. We estimated and compared overall and age-specific seroprevalence of HSV-1 and HSV-2 in 1976–1980, 1988–1994, 1999–2004, and 2005–2010. The 95% confidence intervals were calculated for each seroprevalence estimate, and tests for trend were conducted for overall samples and separately for each age group.

Table 1. Weighted Herpes Simplex Virus Type 1 Seroprevalence by Age Among Men and Women Aged 14–49 Years: NHANES, 1999–2004 and 2005–2010

	1999–2004			2005–2010				
		HSV-1 Seroprevalence			HSV-1 Seroprevalence			
Age Group, y	Sample Size	%	(95% CI)	Sample Size	%	(95% CI)	% Change	(95% CI)
14–19	4650	39.0	(36.7, 41.2)	3180	30.1	(27.3, 32.8)	−22.9	(−30.7, −14.2)**
20–29	2412	54.4	(51.8, 57.0)	2658	49.5	(46.0, 52.9)	−9.1	(−16.4, −1.1)*
30–39	2251	63.5	(60.7, 66.3)	2592	61.8	(58.6, 65.0)	−2.7	(−9.1, 4.1)
40–49	2195	65.3	(62.6, 67.9)	2670	63.6	(60.4, 66.7)	−2.6	(−8.6, 3.8)
Total	11 508	57.9	(56.1, 59.6)	11 100	53.9	(51.6, 56.1)	−6.9	(−11.6, −2.0)**

Abbreviations: CI, confidence interval; HSV-1, herpes simplex virus type 1; NHANES, National Health and Nutrition Examination Survey.

*$P \leq .05$.

**$P \leq .01$.

RESULTS

HSV-1 and HSV-2 Seroprevalence in 1999–2004 and 2005–2010

Overall, the seroprevalence of HSV-1 was 53.9% in 2005–2010 (Table 1). During this period, seroprevalence was 30.1% among 14- to 19-year-olds, 49.5% among 20- to 29-year-olds, 61.8% among 30- to 39-year-olds, and 63.6% among 40- to 49-year-olds. HSV-1 seroprevalence declined by nearly 7%, from 57.9% to 53.9%, from 1999–2004 to 2005–2010 ($P < .01$). Among 14- to 19-year-olds, HSV-1 seroprevalence declined by nearly 23%, from 39.0% to 30.1% ($P < .01$). Among 20- to 29-year-olds, HSV-1 seroprevalence declined by >9%, from 54.4% to 49.5% ($P < .05$). HSV-1 seroprevalence was stable over these 2 time periods in the 2 oldest age groups.

The overall seroprevalence of HSV-2 was 15.7% in 2005–2010 (Table 2). Seroprevalence was 1.2% among 14- to 19-year-olds, 9.9% among 20- to 29-year-olds, 19.3% among 30- to 39-year-olds, and 25.6% among 40- to 49-year-olds. From 1999–2004 and 2005–2010, HSV-2 seroprevalence did not change significantly overall or in any age group.

HSV-1 Seroprevalence in Demographic Subgroups

Among 14- to 19-year-olds, HSV-1 seroprevalence declined significantly from 1999–2004 to 2005–2010 in nearly every strata examined (Table 3). HSV-1 seroprevalence declined by >31% among non-Hispanic whites and nearly 29% among non-Hispanic blacks; however, HSV-1 seroprevalence did not change among Mexican Americans. Seroprevalence declined by 25% among US-born respondents but did not change significantly among foreign-born respondents. Seroprevalence declined among those living above and below the poverty level and in all sexual behavior groups.

Associations between respondent characteristics and HSV-1 were similar in the 2 time periods. In both time periods, HSV-1 seroprevalence was significantly higher among young women compared to young men and among non-Hispanic blacks and

Table 2. Weighted Herpes Simplex Virus Type 2 Seroprevalence by Age Among Men and Women Aged 14–49 Years: NHANES, 1999–2004 and 2005–2010

	1999–2004			2005–2010				
		HSV-2 Seroprevalence			HSV-2 Seroprevalence			
Age Group, y	Sample Size	%	(95% CI)	Sample Size	%	(95% CI)	% Change	(95% CI)
14–19	4650	1.6	(1.2, 1.9)	3180	1.2	(0.8, 1.5)	−24.0	(−47.2, 9.3)
20–29	2412	10.6	(8.8, 12.3)	2658	9.9	(8.7, 11.1)	−6.2	(−23.7, 15.3)
30–39	2251	22.1	(20.1, 24.1)	2592	19.3	(17.1, 21.5)	−12.8	(−24.7, 1.0)
40–49	2195	26.3	(24.1, 28.5)	2670	25.6	(23.1, 28.2)	−2.6	(−14.4, 10.8)
Total	11 508	17.2	(15.8, 18.6)	11 100	15.7	(14.6, 16.8)	−8.5	(−17.6, 1.8)

Abbreviations: CI, confidence interval; HSV-2, herpes simplex virus type 2; NHANES, National Health and Nutrition Examination Survey.

Table 3. Weighted Herpes Simplex Virus Type 1 Seroprevalence by Respondent Characteristics Among Men and Women Aged 14–19 Years: NHANES, 1999–2004 and 2005–2010

	1999–2004					2005–2010						
		Seroprevalence					Seroprevalence					
Characteristic	Sample Size	%	(95% CI)	Prevalence Ratio	*P* Value	Sample Size	%	(95% CI)	Prevalence Ratio	*P* Value	% Change	(95% CI)
Sex					.01					<.01		
Male	2368	36.7	(34.1, 39.2)	1.00		1660	27.1	(23.9, 30.4)	1.00		−26.0	(−35.6, −14.9)**
Female	2282	41.4	(38.2, 44.5)	1.13		1520	33.2	(29.8, 36.5)	1.23		−19.8	(−29.4, −9.0)**
Race					<.01					<.01		
Non-Hispanic white	1220	30.6	(27.4, 33.8)	1.00		951	21.0	(17.2, 24.7)	1.00		−31.5	(−44.4, −15.6)**
Non-Hispanic black	1470	55.7	(51.9, 59.5)	1.82		888	39.6	(35.9, 43.4)	1.89		−28.8	(−36.7, −20.0)**
Mexican American	1658	57.5	(54.7, 60.3)	1.88		919	58.3	(53.5, 63.2)	2.78		1.5	(−7.9, 11.8)
Foreign born					<.01					<.01		
No	3871	35.9	(33.4, 38.5)	1.00		2731	26.9	(24.3, 29.6)	1.00		−25.1	(−33.6, −15.5)**
Yes	778	65.8	(59.6, 72.1)	1.83		446	61.6	(52.6, 70.5)	2.29		−6.5	(−21.4, 11.3)
Income ≤ poverty level					<.01					<.01		
No	2829	32.2	(29.6, 34.8)	1.00		2017	25.3	(22.4, 28.3)	1.00		−21.3	(−31.6, −9.3)**
Yes	1436	53.9	(48.9, 58.9)	1.67		949	45.0	(40.1, 50.0)	1.78		−16.4	(−27.6, −3.7)*
Ever had sex					<.01					<.01		
No	2047	34.0	(30.8, 37.1)	1.00		1414	24.6	(21.5, 27.7)	1.00		−27.6	(−38.2, −15.3)**
Yes	2282	43.4	(40.0, 46.6)	1.28		1549	34.4	(30.3, 38.4)	1.40		−20.7	(−31.1, −8.8)**
≥3 lifetime sex partners					<.01					.02		
No	3589	36.8	(34.4, 39.2)	1.00		2555	28.8	(25.9, 31.7)	1.00		−25.7	(−34.5, −15.8)**
Yes	1055	46.9	(41.8, 51.9)	1.27		623	35.2	(29.6, 40.7)	1.22		−25.0	(−38.0, −9.2)**
Total	4650	39.0	(36.7, 41.2)			3180	30.1	(27.3, 32.8)			−22.9	(−30.7, −14.2)**

Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

*$P \leq .05$.

**$P \leq .01$.

Mexican Americans than among non-Hispanic whites. Seroprevalence was also higher among foreign-born respondents compared to those born in the United States, and among respondents living at or below the federal poverty level compared to those living above the poverty level. Last, seroprevalence was higher among respondents who had ever had sex compared to those who had never had sex and among those with ≥3 lifetime sex partners compared those with < 3 sex partners. We did not find significant differences in respondent characteristics by time period (not shown), indicating that none of the characteristics examined confounded the relationship between HSV-1 prevalence and time period.

Among 20- to 29-year-olds, there were fewer significant declines in HSV-1 seroprevalence from 1999–2004 and 2005–2010 when stratified by respondent characteristics (Table 4). Although HSV-1 seroprevalence declined in all strata, there were fewer significant changes than among 14- to 19-year-olds. Seroprevalence declined by >11% among US-born respondents from 1999–2004 to 2005–2010 ($P < .05$), but there was no significant decline among foreign-born respondents. Seroprevalence declined by >11% among those living above the poverty level ($P < .01$), whereas no significant decline was observed among those living at or below the poverty level. Last, HSV-1 seroprevalence declined by >12% among 20- to 29-year-olds who had ever had sex or had ≥3 lifetime sex partners ($P < .01$).

Similar associations between sociodemographic characteristics and HSV-1 are observed in both time periods; these associations are also similar to those seen among 14- to 19-year-olds. Seroprevalence was significantly higher among young women compared to young men, among non-Hispanic blacks and Mexican Americans than among non-Hispanic whites, among foreign-born compared to US-born respondents, and among respondents living at or below the federal poverty level compared to those living above the poverty level. Among 20- to 29-year-olds, however, there were no significant differences in HSV-1 seroprevalence by either sexual behavior variable.

HSV-1 and HSV-2 Seroprevalence During 1976–2010

Overall, HSV-1 seroprevalence decreased from 60.1% in 1976–1980 to 53.9% in 2005–2010 (Figure 1). Apart from a slight increase from 1976–1980 to 1988–1994, seroprevalence declined steadily in each time period, and the overall test for trend was significant ($P < .01$). Tests for trend were also significant for declines in every age group except 30- to 39-year-olds ($P < .01$). The largest decline from 1976–1980 to 2005–2010 was observed among 14- to 19-year-olds, among whom HSV-1 seroprevalence declined >29%, from 42.6% to 30.1%.

HSV-2 seroprevalence did not follow the linear trend observed for HSV-1 seroprevalence during this time period. HSV-2 increased from 13.4% to 15.7% from 1976–1980 to 2005–2010 ($P = .02$; Figure 2). HSV-2 seroprevalence increased >56% from 1976–1980 to 1988–1994. Seroprevalence has been steadily declining since 1988–1994 but has not yet declined to 1976–1980 levels. Tests for trend from 1976–1980 to 2005–2010 were not significant overall or in any age group.

DISCUSSION

In the United States, the seroepidemiology of HSV-1 and HSV-2 has been investigated through NHANES since 1976. In this report, we update data last published for these 2 infections (1999–2004) and evaluate trends through 2010. We found large declines in HSV-1 seroprevalence among 14- to 19-year-olds. In this age group, HSV-1 seroprevalence declined by nearly 23%, from 39.0% to 30.1%, from 1999–2004 to 2005–2010, and by >34% since peaking in 1988–1994. Among 14- to 49-year-olds, HSV-1 seroprevalence declined by nearly 7%, from 57.9% to 53.9%, from 1999–2004 to 2005–2010 and by nearly 13% since 1988–1994.

HSV-2 seroprevalence was 15.7% in 2005–2010, which was not significantly different from the estimate in 1999–2004. Since 1976–1980, HSV-2 seroprevalence has increased significantly, primarily due to a large increase from 1976–1980 to 1988–1994, which was previously described [18]. A statistically significant decline in HSV-2 seroprevalence was observed in the last review from 1988–1994 to 1999–2004, but since that time, findings suggest that seroprevalence has plateaued [1].

Declines in HSV-1 seroprevalence have also been observed in other industrialized countries during the past 2 decades [19–22]. Improvements in living conditions, better hygiene, and less crowding likely explain these declines. These data are consistent with the hypothesis that living conditions during childhood play an important role in HSV-1 serostatus. Significant declines in HSV-1 seroprevalence were not observed among respondents who were born outside the United States, >40% of whom were Mexican Americans. The sociodemographic disparities in HSV-1 seroprevalence seen in this study are consistent with previous findings [1, 23] and are also similar to disparities in HSV-2 seroprevalence [1, 24]. In both time periods, HSV-1 infection was more common among non-Hispanic blacks and Mexican Americans than among non-Hispanic whites and among respondents with lower vs higher incomes. Among 14- to 19-year-olds in 2005–2010, seroprevalence was 58.3% among Mexican Americans, 39.6% among non-Hispanic blacks, and 21.0% among non-Hispanic whites. However, the 39.6% seroprevalence among non-Hispanic blacks in this age group represents a nearly 29% decline from 1999–2004. No decline in HSV-1 seroprevalence was observed among Mexican Americans in either age group, which is largely attributable to the lack of decline seen among foreign-born respondents. Among 14- to 29-year-olds, 48.2% of Mexican Americans were born outside the United States, compared to 4.1% of whites and 6.9% of blacks.

Although we examined the association between 2 sexual behavior variables and HSV-1 in this analysis, we do not have

Table 4. Weighted Herpes Simplex Virus Type 1 Seroprevalence by Respondent Characteristics Among Men and Women Aged 20–29 Years: NHANES, 1999–2004 and 2005–2010

	1999–2004					2005–2010						
		Seroprevalence					Seroprevalence					
Characteristic	Sample Size	%	(95% CI)	Prevalence Ratio	*P* Value	Sample Size	%	(95% CI)	Prevalence Ratio	*P* Value	% Change	(95% CI)
Sex					.02					<.01		
Male	1044	51.7	(48.5, 54.9)	1.00		1197	46.6	(42.5, 50.8)	1.00		−9.8	(−19.1, .5)
Female	1368	57.1	(53.5, 60.7)	1.10		1461	52.3	(48.5, 56.1)	1.12		−8.5	(−16.8, .7)
Race					<.01					<.01		
Non-Hispanic white	1042	46.1	(42.1, 50.0)	1.00		1054	40.9	(36.8, 45.0)	1.00		−11.2	(−22.3, 1.4)
Non-Hispanic black	476	55.5	(49.7, 61.3)	1.20		543	52.2	(46.2, 58.1)	1.28		−6.1	(−19.5, 9.7)
Mexican American	678	80.0	(75.4, 84.6)	1.74		680	76.1	(71.9, 80.3)	1.86		−4.9	(−12.2, 3.1)
Foreign born					<.01					<.01		
No	1791	49.2	(46.2, 52.1)	1.00		1964	43.7	(40.2, 47.1)	1.00		−11.1	(−19.5, −1.8)*
Yes	621	78.2	(73.2, 83.1)	1.59		694	75.4	(70.8, 80.0)	1.73		−3.5	(−11.7, 5.4)
Income ≤ poverty level					<.01					<.01		
No	1636	51.6	(49.2, 54.0)	1.00		1713	45.7	(42.2, 49.3)	1.00		−11.4	(−19.1, −3.0)**
Yes	587	62.7	(56.9, 68.6)	1.22		753	58.5	(54.0, 63.0)	1.28		−6.7	(−17.4, 5.3)
Ever had sex					.65					.83		
No	155	52.5	(43.5, 61.5)	1.00		213	48.8	(40.5, 57.0)	1.00		−7.1	(−27.0, 18.2)
Yes	2026	54.5	(51.9, 57.2)	1.04		2185	47.9	(44.2, 51.5)	0.98		−12.2	(−19.8, −3.9)**
≥3 lifetime sex partners					.71					.89		
No	744	54.9	(50.0, 59.8)	1.00		684	47.8	(41.5, 54.2)	1.00		−12.8	(−25.7, 2.3)
Yes	1413	54.0	(51.5, 56.4)	0.98		1348	47.3	(42.9, 51.7)	0.99		−12.3	(−21.0, −2.8)**
Total	2412	54.4	(51.8, 57.0)			2658	49.5	(46.0, 52.9)			−9.1	(−16.4, −1.1)*

Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

*$P \leq .05$.

**$P \leq .01$.

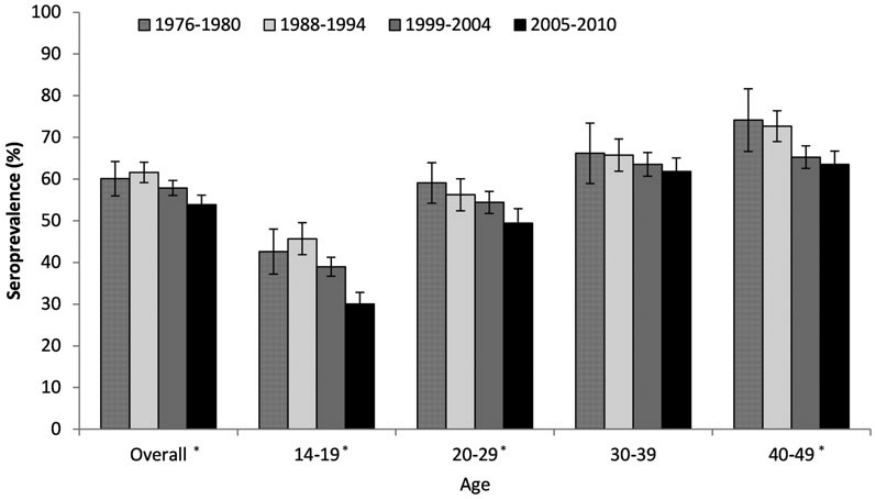

Figure 1. Herpes simplex virus type 1 seroprevalence by age and time period.

information about site of infection and are thus unable to draw inferences about genitally acquired vs non–genitally acquired HSV-1. We observed higher HSV-1 seroprevalence among 14- to 19-year-olds who had ever had sex compared to those who had never had sex, and among those who had ≥3 vs <3 sexual partners. There was no difference in HSV-1 seroprevalence by sexual behavior among 20- to 29-year-olds. The difference in HSV-1 seroprevalence by sexual behavior in the youngest age group is likely explained by the association between earlier sexual debut among non-Hispanic blacks compared to non-Hispanic whites [25]. Thus, the observed association between HSV-1 infection and sexual activity is likely to be confounded by race/ethnicity.

While many industrialized countries have experienced a decline in HSV-1 seroprevalence in recent years, the proportion of genital herpes disease caused by HSV-1 (vs HSV-2) has simultaneously increased as detected by culture and polymerase chain reaction collected from specimens [8–12]. An increasing number of adolescents lack HSV-1 antibodies at sexual debut and are therefore susceptible to genital herpes infection from either HSV-1 or HSV-2. In combination with increased oral sex behaviors among young people [26], this means that adolescents may be more likely than those in previous time periods to genitally acquire HSV-1.

Although we are unable to determine genitally acquired HSV-1 infection in this analysis, the increasing proportion of

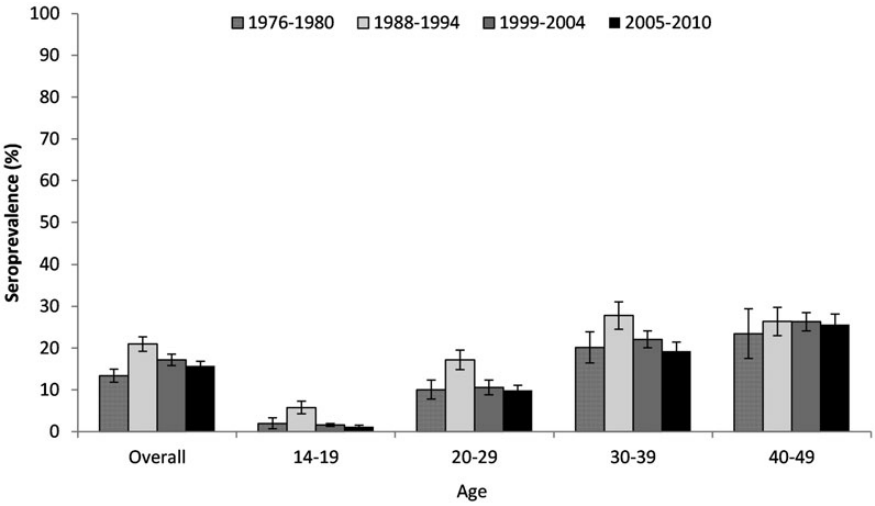

Figure 2. Herpes simplex virus type 2 seroprevalence by age and time period.

young people entering adolescence without HSV-1 antibodies merits careful and ongoing surveillance. In addition to potential increases in genitally acquired HSV-1, persons lacking HSV-1 antibodies are more likely to develop symptomatic disease if infected with HSV-2 [27].

This analysis has limitations. First, the data are cross-sectional, and cohorts of individuals represent different age groups in different surveys; we are unable to separate age and cohort effects. Furthermore, because HSV-1 and HSV-2 are lifelong infections, it is difficult to infer changes in seroincidence using seroprevalence data in older age groups.

Second, NHANES oversamples some demographic groups for precision purposes, and oversampling strategies differ over time. For example, 14- to 19-year-olds were oversampled in 1999–2006. The stratified HSV-1 seroprevalence estimates for this age group are more precise in 1999–2006 than in later years, and the larger sample size makes it easier to detect change in seroprevalence over time, especially in the stratified analysis. Similarly, because 20- to 29-year-olds were not oversampled, we had less statistical power to detect significant differences in stratified HSV-1 prevalence over time in this age group. The relative absence of statistically significant changes over time in this age group must be interpreted accordingly. Last, these analyses are based on HSV serologic testing, and we did not have information on site of infection. Therefore, it is impossible to draw inferences about change in prevalence of genitally acquired vs non–genitally acquired HSV-1.

HSV-1 epidemiology is rapidly changing, and these changes are important to monitor for several reasons. First, in the absence of declines in HSV-2, the decline in childhood-acquired, orolabial HSV-1 is likely to impact the prevalence of genital herpes. Declines in early childhood acquisition of HSV-1 means more young people are susceptible to genital HSV-1 infection, and symptomatic HSV-2 disease is more likely among persons lacking HSV-1 antibodies. Additionally, a population-level shift toward later acquisition of HSV-1 infection may inform HSV vaccine development and delivery strategies, such as optimal vaccine timing. Continued surveillance of HSV-1 and HSV-2, as well as associated symptomatic disease, will provide important information about the changing epidemiology of these infections in the United States.

Notes

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