Hepatitis C Virus Infection in Young, Low-Income Women: The Role of Sexually Transmitted Infection as a Potential Cofactor for HCV Infection

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Objectives. We evaluated risk for hepatitis C virus (HCV) infection in women residing in low-income neighborhoods of northern California.

Methods. A population-based sample of 1707 women, aged 18 to 29, were surveyed and screened for sexually transmitted infections and HCV.

Results. Women infected with HCV (2.5%) were more likely to have a history of injection and noninjection drug use, to exchange sex for money or drugs, and to have sexually transmitted infections. HCV was independently associated with history of injection drug use, herpes simplex virus type 2 (HSV-2) infection, and heroin and cocaine use.

Conclusions. Injection drug use is the highest risk exposure for HCV, but HSV-2 and noninjection drug use contribute significantly to increased risk. HCV prevention programs in impoverished areas should integrate drug treatment and sexually transmitted infection control. (*Am J Public Health.* 2002; 92:670–676)

Hepatitis C virus (HCV) is the most important cause of acute and chronic liver disease in the United States. An estimated 4 million people, 1.8% of the US general population, are HCV infected.[1] Persistent infection develops in more than 85% of the persons exposed. Chronic hepatitis develops in 50% to 70% of the infected persons, and 10% to 20% of these may go on to develop cirrhosis.[2] Liver failure and hepatocellular carcinomas necessitating liver transplantation are some of the most severe consequences of HCV infection. An estimated 8000 to 10 000 deaths per year are attributed to HCV-associated liver disease, a figure expected to triple in the next 10 to 20 years.[3] Given the current low response to treatment (<50%),[4,5] primary prevention remains the most important public health control strategy to reduce HCV-related morbidity.

HCV infection is most easily acquired parenterally. As a result, prevalence is highest among injection drug users (IDUs) and hemophiliacs.[6–8] Nonparenteral transmission of HCV appears to be inefficient.[7–14] Past research has documented the cofactor role of sexually transmitted infections in amplifying the acquisition and transmission of HIV and hepatitis B virus (HBV),[15–17] but this interrelationship has not been well examined for HCV. High rates of sexually transmitted infections and HCV coinfection among IDUs suggest that ulcerative or nonulcerative urogenital infections may be cofactors for HCV transmission. However, investigation of sexually transmitted infections as potential cofactors for sexual transmission of HCV is hampered by the confounding effects of concomitant high-risk sexual behavior and injection practices.[18] Lack of data on the determinants of sexual transmission of HCV has limited the development of guidelines for sexual partners who may be at risk for transmitting or acquiring HCV.[9,19]

The current study examined HCV in the Young Women's Survey, a population-based sample of young women recruited in low-income, multiethnic neighborhoods of northern California.[20] Analysis focused on sexual behavior and sexually transmitted infections as risk factors for HCV and their associated population attributable fractions.

METHODS

Study Design

The Young Women's Survey was a single-stage, cluster-sample, population-based, door-to-door, cross-sectional survey designed to measure the prevalence of HIV, sexually transmitted diseases, and related risk behavior in young, low-income women in northern California. The Young Women's Survey study methods, study population, and primary outcomes have been described in detail elsewhere.[20] HCV testing was conducted on stored sera from participants in 4 counties: Alameda, San Francisco, San Joaquin, and San Mateo.

Study Subjects

The target population was young women residing in low-income neighborhoods. Eligibility criteria were being female, aged 18 to 29 years, fluent in English or Spanish, and a resident in the target area. The target area was defined as 1990 US census block groups below the 10th percentile for median household income. In the 4 counties included in the study of HCV, a total of 19 270 inhabited dwellings were enumerated in 276 randomly selected street blocks within the target area. Contact was made with a resident in each of 15 943 dwellings (82.7%). Of the 2828 eligible women identified, 2096 (74.1%) were enrolled from April 1996 to January 1998. Sera were available for 1707 (81.4%) of the women who were interviewed.

Measures

A structured interviewer-administered survey was conducted to gather data on sociodemographic characteristics, sexual behavior, substance use, medical history, and other health-related factors. Response rates for most variables were greater than 99%. Blood and urine samples were obtained to test for

HIV, syphilis, herpes simplex virus types 1 and 2 (HSV-1, HSV-2), HBV, gonorrhea, and chlamydia.

Laboratory Methods

Antibody to HCV (anti-HCV) was detected with a third-generation enzyme immunoassay (EIA-3.0; Ortho Diagnostics Systems, Raritan, NJ). Specimens reactive by initial EIA-3.0 were confirmed with a strip recombinant immunoblot assay (RIBA 2.0; Chiron, Emeryville, Calif). Discrepant results (EIA+, RIBA–) were considered negative. HIV testing was conducted with enzyme immunoassay (EIA; Abbott Laboratories, Abbott Park, Ill) and confirmed by immunofluorescent antibody (IFA; Neufeld, Vienna, Austria). Antibody to hepatitis B core antigen (anti-HBc) was detected by EIA (Abbott Laboratories, Abbott Park, Ill), and hepatitis B surface antigen (HBsAg) was detected by microparticle EIA (Abbott Laboratories, Abbott Park, Ill). HSV-1 and HSV-2 specific antibodies were differentiated based on recombinant antigen bands for gG1, gB1, gG2, and gD2 with a strip recombinant immunoblot assay (RIBA HSV Type 1/Type 2 SIA; Chiron, Emeryville, Calif). Blood samples were tested for syphilis by rapid plasma reagin or VDRL tests; reactive specimens were confirmed by microhemagglutination test for *Treponema pallidum*. Ligase chain reaction (LCx; Abbott Laboratories, Abbott Park, Ill) was used to detect gonococcal and chlamydial DNA in urine specimens.

Statistical Methods

To account for the single-stage, cluster-sample survey design, we used Stata, Version 6.0, Survey (SVY) procedures to construct point prevalences, 95% confidence intervals (CIs), and odds ratios (ORs).[21] Ninety-five-percent confidence intervals were adjusted to account for homogeneity within the primary sampling units (i.e., city blocks). Because crude prevalence estimates in the sample differed from the survey-adjusted estimates, we present only weighted percentages.

Multiple logistic regression analysis, adjusting for the survey design, was used to identify independent correlates of HCV infection based on factors significant in bivariate analyses, a priori hypotheses (such as coinfection with HIV or HBV), and other variables of interest or potential confounders (such as age, race/ethnicity, and county). Models were examined with both a backward and a forward stepwise process. Variables were retained in the models if they reached a significance level of .05 or less. The final multiple logistic model and *aflogit* procedures[21] employing Stata statistical software were used to obtain estimates of adjusted population attributable fraction and corresponding 95% confidence intervals with an approach based on unconditional logistic regression.[22,23] The 95% confidence intervals associated with the population attributable fraction estimates were adjusted for probability weights but not for the cluster weights.

RESULTS

Prevalence of Anti-HCV, by Social and Demographic Characteristics

The population-based estimate of HCV prevalence among women aged 18 to 29 years in low-income neighborhoods of the 4-county target area was 2.5% (95% CI=1.4, 3.6) (Table 1). The estimate is based on the

TABLE 1—Prevalence of Hepatitis C Virus (HCV) Infection, by Demographic Characteristics, in Women Aged 18 to 29 Years From Low-Income Neighborhoods of 4 Northern California Counties, April 1996–January 1998

	Population Prevalence of Variable, %[a]	Population Prevalence of HCV Antibody, % (95% CI)[a,b]	OR (95% CI)[a]
Total		2.5 (1.4, 3.6)[b]	
County of residence			
Alameda	30.0	3.8 (1.7, 6.0)	8.9 (2.6, 29.7)*
San Francisco	27.9	4.3 (1.4, 7.1)	10.0 (2.8, 35.4)*
San Joaquin	13.2	1.4 (0.1, 2.7)	Referent
San Mateo	28.9	0 (NA[c])	NA[c]
Monthly household income, $			
0–499	25.9	5.1 (2.4, 7.8)	5.6 (2.1, 14.7)*
500–999	33.7	2.2 (0.8, 3.7)	2.4 (0.9, 6.2)
1000–2999	33.0	1.1 (0.2, 2.1)	Referent
≥3000	7.3	0 (NA[c])	NA[c]
Race/ethnicity			
White	15.4	3.8 (1.1, 6.4)	5.3 (1.3, 21.5)***
African American	39.2	4.0 (2.0, 5.9)	5.6 (1.8, 17.5)**
Asian or Pacific Islander	6.7	0.9 (0, 2.5)	1.2 (0.1, 11.6)
Other	6.7	1.7 (0, 4.0)	2.3 (0.4, 15.0)
Latina	31.9	0.7 (0, 1.6)	Referent
Education			
<High school	40.6	3.1 (1.4, 4.8)	5.7 (0.9, 36.8)
High school graduate	27.0	2.6 (1.1, 4.1)	4.7 (0.7, 32.1)
Vocational or some college	22.2	2.4 (0.7, 4.0)	4.3 (0.5, 35.0)
≥College degree	10.2	0.6 (0, 1.7)	Referent
Marital status			
Currently married	19.4	1.9 (0, 4.1)	0.7 (0.2, 2.2)
Previously married	8.4	4.9 (1.1, 8.6)	1.8 (0.8, 4.3)
Unmarried partnership	10.1	0.6 (0, 1.7)	0.2 (0.3, 1.4)
Single	62.1	2.7 (1.4, 4.0)	Referent

Note. CI = confidence interval; OR = odds ratio.
[a]All prevalence estimates, 95% CIs, and ORs are adjusted for the survey design.
[b]Anti-HCV confirmed in n = 40.
[c]Not able to calculate survey-adjusted CIs or ORs when no infections were detected.
*$P \leq .001$; **$P \leq .01$; ***$P \leq .05$.

40 HCV RIBA-confirmed specimens of a total of 63 found to be positive with EIA-3.0. More than a third (39.2%) of the subjects were African American, 31.9% were Latina, 15.4% were White, 6.7% were Asian or Pacific Islander, and 6.7% indicated *other* or *mixed* race/ethnicity. Most women (70.5%) were born in the United States; 16.9% were born in Mexico, and 12.5% were born in other countries. The median age was 23.9 years (interquartile range=21.0–26.7).

The prevalence of HCV varied significantly by county of residence, income level, and race/ethnicity. HCV prevalence was highest in the 2 most urban counties: San Francisco (4.3%; 95% CI=1.4, 7.1) and Alameda (3.8%; 95% CI=1.7, 6.0). HCV prevalence increased with decreasing income, reaching 5.1% (95% CI=2.4, 7.8) among women in the lowest income category (<$500 per month). By race/ethnicity, HCV prevalence was highest among African Americans (4.0%; 95% CI=2.0, 5.9).

Women for whom sera were not available did not differ significantly from women with sera with respect to age, education, income, or injection drug use history. However, women without sera available were more likely to be single and to have 2 or more male sex partners and less likely to be Latina (χ^2 test, $P<.05$). The latter finding resulted from sera not being available for a disproportionate number of subjects from San Joaquin County.

Prevalence of Anti-HCV, by Sexually Transmitted Infections and Sexual Behavior

Prevalence of HCV was significantly higher among women with serologic markers for infection with syphilis (18.3%; 95% CI=0, 41.7), HSV-2 (4.2%; 95% CI=1.9, 6.4), HBV (8.3%; 95% CI=3.2, 13.5), and HIV (63.5%; 95% CI=0.8, 119.5) (Table 2). Prevalence of HCV increased with increasing number of lifetime male sexual partners, from 0.4% (95% CI=0, 1.3) among women with 1 partner to 3.9% (95% CI=2.2, 5.7) among women with 5 or more partners. Only 2 women (0.1%) reported no male sexual partners, and 1 of these women had HCV infection. Other sexual risk behaviors associated with increased HCV prevalence were sex with an IDU (12.6%; 95% CI=7.2, 18.0), exchange sex (trading sex for money, drugs, or other needs) (13.6%; 95% CI=5.6, 18.6), and ever having anal sex (4.5%; 95% CI=2.1, 7.0).

TABLE 2—Prevalence of Hepatitis C Virus (HCV) Infection, by Sexually Transmitted Infections and Reported Sexual Behavior, in Women Aged 18 to 29 Years From Low-Income Neighborhoods of 4 Northern California Counties, April 1996–January 1998

	Population Prevalence of Variable, %[a]	Population Prevalence of HCV Antibody, % (95% CI)[a,b]	Bivariate OR (95% CI)[a]
Chlamydia	3.2	2.1 (2.0, 6.2)	0.8 (0.1, 6.0)
Syphilis	0.8	18.3 (0, 41.7)	9.1 (1.7, 46.8)**
Gonorrhea	0.8	0 (NA[c])	NA[c]
Herpes simplex virus type 2	34.2	4.2 (1.9, 6.4)	10.4 (3.2, 34.3)*
Hepatitis B (core antibody or surface antigen)	8.8	8.3 (3.2, 13.5)	4.1 (1.9, 8.8)*
HIV	0.2	63.5 (0.8, 119.5)	69.6 (6.1, 788.0)*
Lifetime male sex partners			
1	19.8	0.4 (0, 1.3)	Referent
2–4	26.2	1.0 (0, 2.2)	1.4 (0.2, 8.5)
≥5	53.9	3.9 (2.2, 5.7)	5.6 (1.3, 23.8)**
Sex with injection drug user	10.3	12.6 (7.2, 18.0)	10.4 (5.8, 18.6)*
Traded sex for money or drugs	12.1	13.6 (5.6, 18.6)	14.5 (7.1, 29.7)*
Anal sex	22.9	4.5 (2.1, 7.0)	2.3 (1.3, 4.1)**

Note. CI = confidence interval; OR = odds ratio.
[a]All prevalence estimates, 95% CIs, and ORs are adjusted for the survey design.
[b]Anti-HCV confirmed in n = 40.
[c]Not able to calculate survey-adjusted CIs or ORs when no infections were detected.
*$P \leq .001$; **$P \leq .01$.

Prevalence of Anti-HCV, by Injection and Noninjection Drug Use

Table 3 shows the prevalence of HCV among women by reported alcohol, noninjection drug, and injection drug use. Of note, the estimate of lifetime injection drug use in the target population was 4.4% (95% CI=2.9, 5.9). HCV infection was strongly associated with a history of injecting any drug (OR=64.6; 95% CI=33.0, 126.2, $P<.001$). HCV infection was significantly more likely among women who reported sharing needles in the past 6 months compared with those who did not (66.7% vs 37.1%; OR=3.3; 95% CI=1.0, 11.0) but not among women who reported having ever shared a needle compared with those who did not (OR=2.7; 95% CI=0.8, 10.1). Among women with a history of injection drug use, the prevalence of HCV increased significantly with age: 19.7% (95% CI=5.5, 34.2) among those younger than 24 years and 55% (95% CI=38.0, 72.0) among those 24 years and older (data not shown).

Ever and recent use of alcohol was not associated with increased HCV prevalence, but having had sex while high on alcohol was (OR=2.6; 95% CI=1.3, 5.3). HCV prevalence was significantly higher among women reporting use of amphetamine, cocaine, or heroin compared with women not using these drugs. For each of these drugs, HCV prevalence was higher among those reporting recent use compared with ever use and among those reporting injecting compared with those not injecting. Of any risk factor measured, HCV prevalence was highest among women reporting recent cocaine injection (72.6%; 95% CI=51.0, 94.2), followed by those reporting recent heroin injection (66.7%; 95% CI=56.1, 77.2).

Independent Risk Factors for HCV Infection

In multivariate analyses (Table 4), the strongest independent associations with HCV infection were history of injection drug use

TABLE 3—Prevalence of Hepatitis C Virus (HCV) Infection, by Alcohol, Noninjection Drug, and Injection Drug Use, in Women Aged 18 to 29 Years From Low-Income Neighborhoods of 4 Northern California Counties, April 1996–January 1998

	Population Prevalence of Variable, %[a]	Population Prevalence of HCV Antibody, % (95% CI)[a,b]	OR (95% CI)[a]
History of injection drug use	4.4	37.5 (26.4, 48.6)	64.6 (33.0, 126.2)*
Shared needles (among those with a history of injection drug use)			
Ever	56.0	51.4 (38.8, 63.9)	2.7 (0.8, 10.1)
Last 6 mo	38.5	66.7 (47.2, 86.1)	3.3 (1.0, 11.0)***
Alcohol			
Ever	78.0	2.8 (1.6, 4.2)	2.2 (0.8, 6.3)
Last 6 mo	60.3	2.8 (1.5, 4.1)	1.3 (0.7, 2.7)
Sex while high on	30.7	4.3 (2.3, 6.4)	2.6 (1.3, 5.3)**
Amphetamine			
Ever	12.3	9.3 (4.7, 13.8)	7.1 (4.0, 12.6)*
Last 6 mo	5.0	15.6 (8.3, 22.9)	9.8 (5.6, 17.4)*
Sex while high on	2.8	19.7 (9.0, 30.3)	11.8 (6.0, 23.3)*
Injected amphetamine			
Ever	2.2	42.2 (26.5, 57.8)	43.8 (18.8, 102.0)*
Last 6 mo	1.0	55.8 (34.8, 76.7)	61.9 (21.9, 174.7)*
Sex while high on	0.6	50.0 (28.1, 71.9)	44.0 (15.7, 123.5)*
Cocaine			
Ever	17.5	12.1 (7.8, 16.4)	27.6 (11.2, 67.9)*
Last 6 mo	8.5	21.1 (14.5, 27.7)	32.9 (15.8, 68.5)*
Sex while high on	5.2	24.5 (15.4, 33.7)	24.3 (11.2, 52.5)*
Injected cocaine			
Ever	1.6	51.2 (33.2, 69.2)	59.9 (25.5, 140.8)*
Last 6 mo	0.9	72.6 (51.0, 94.2)	135.5 (40.7, 451.2)*
Sex while high on	0.2	100 (NA[c])	NA[c]
Heroin			
Ever	5.1	28.9 (18.8, 38.9)	36.2 (18.8, 68.9)*
Last 6 mo	2.2	50.4 (36.9, 64.1)	68.4 (32.7, 143.1)*
Sex while high on	1.5	51.7 (34.3, 69.1)	59.2 (25.9, 135.0)*
Injected heroin			
Ever	2.8	44.5 (32.5, 56.5)	59.5 (28.5, 124.2)*
Last 6 mo	1.7	66.7 (56.1, 77.2)	140.6 (71.4, 276.6)*
Sex while high on	1.2	62.8 (51.2, 74.3)	93.4 (47.7, 182.8)*
Ever on methadone treatment	1.2	45.5 (21.3, 69.8)	41.0 (13.0, 129.8)*

Note. CI = confidence interval; OR = odds ratio.
[a]All prevalence estimates, 95% CIs, and ORs are adjusted for the survey design.
[b]Anti-HCV confirmed in n = 40.
[c]Not able to calculate survey-adjusted CIs or ORs when the point estimate is 0 or 100%.
*$P \leq .001$; **$P \leq .01$; ***$P \leq .05$.

(adjusted OR=4.9; 95% CI=2.7, 9.2), serological evidence of HSV-2 infection (OR=3.7; 95% CI=1.2, 11.5), any use of heroin (OR=5.6; 95% CI=3.1, 10.2), any use of cocaine (OR=3.4; 95% CI=1.2, 9.5), and very low income (adjusted OR for income<$500 per month=4.2; 95% CI=1.2, 14.4) after adjustment for age. Sexual risk behavior did not reach statistical significance in the model. The associations found between HCV infection and race/ethnicity were confounded by income and reported sexual risk behavior. African American women were most likely to have HSV-2 infection, to have lower income, and to report a history of trading sex for drugs or money and thus were at highest risk for HCV infection. No significant interactions were found between age, racial/ethnic group, and sexual risk behaviors. HIV infection was a significant risk factor for HCV in this study but was excluded from the model because of small numbers and the observation that parameter estimates of the other variables were not significantly changed by its inclusion. The adjusted odds ratio for HCV infection associated with HIV infection was 7.5 (95% CI=1.5, 37.0).

Analyses among women with no history of injection drug use were conducted to evaluate risk factors associated with nonparenteral acquisition of HCV infection. In this subset, 12 women (0.9%) were positive for anti-HCV. Factors associated with HCV among women non-IDUs were African American race/ethnicity, noninjection cocaine use, and lower income (Table 5). Cocaine use and exchange sex (e.g., trading sex for money or drugs) were highly collinear; however, cocaine use had a stronger association. Among women non-IDUs, African Americans were significantly more likely (OR=27.5; 95% CI=3.4, 221.5) to be positive for HCV than were non–African American women, an association confounded by income level (the unadjusted OR was 36.0).

Population Attributable Fraction Estimates

Adjusted population attributable fraction estimates and 95% confidence intervals for risk factors for HCV are shown in Table 4. History of injection drug use had an associated population attributable fraction of 33.2%. The population attributable fraction for HSV-2 infection was the highest (50.6%), reflecting the high prevalence of the risk factor (34.2%). Both noninjection heroin use and noninjection cocaine use had higher population attributable fraction estimates than did injection history (39.4% and 44.2%, respectively), also because of their higher prevalence. In analyses excluding the effects of socioeconomic status and age, the summary population attributable fraction for these 4 factors accounted for 91.0% of the HCV cases. The summary population attributable

TABLE 4—Independent Associations With Hepatitis C Virus Infection (Multivariate Analysis) and Associated Population Attributable Fractions for Women Aged 18 to 29 Years From Low-Income Neighborhoods of 4 Northern California Counties, April 1996–January 1998

	Adjusted OR (95% CI)	Adjusted Population Attributable Fraction (95% CI)
History of injection drug use	4.9 (2.7, 9.2)	0.332 (–0.9, 0.8)
Herpes simplex virus type 2	3.7 (1.2, 11.5)	0.506 (–13.8, 1.0)
Heroin use (ever)	5.6 (3.1, 10.2)	0.394 (–1.1, 0.8)
Cocaine use (ever)	3.4 (1.2, 9.5)	0.442 (–9.2, 1.0)
Age (< 24 vs ≥ 24)	2.5 (0.9, 7.2)	
Monthly income, $		
< 500	4.2 (1.2, 14.4)	0.400 (–6.4, 1.0)
500–999	1.5 (0.3, 6.9)	0.695 (–2.3, 0.7)
≥ 1000	Referent	

Note. CI = confidence interval; OR = odds ratio.

TABLE 5—Independent Associations With Hepatitis C Virus Infection Among Women Noninjection Drug Users (Multivariate Analysis) Aged 18 to 29 Years From Low-Income Neighborhoods of 4 Northern California Counties, April 1996–January 1998

	Adjusted OR (95% CI)
Cocaine use (ever vs never)	6.6 (2.1, 20.9)
African American (vs other race/ethnicity)	27.5 (3.4, 221.5)
Monthly income, $	
< 500	3.5 (0.4, 30.3)
500–999	3.1 (0.3, 27.5)
≥ 1000	Referent

Note. CI = confidence interval; OR = odds ratio.

fraction for all of the risk factors in the logistic model was 96.3%.

DISCUSSION

The 2.5% prevalence of HCV infection in this population-based survey of young, low-income women was higher than that reported in a national sample of women, in which prevalence was of 1.2% overall[1] and 0.6% among women aged 20 to 29 years (M. Alter, PhD, personal communication, 2000). HCV infection was most highly associated with a history of injection drug use, although noninjection use of heroin and cocaine persisted as independent risk factors. HCV transmission has been hypothesized to occur through sharing of straws or other devices that deliver the virus to hyperemic and traumatized nasal mucosa.[7] Very low income was the strongest socioeconomic correlate of HCV infection. Of particular note, HSV-2 infection was independently associated with HCV infection.

The independent association of anti-HCV with HSV-2 infection suggests a possible cofactor for sexual transmission or acquisition of HCV. As has been hypothesized with HIV, HSV-2 infection may serve to increase the efficiency of sexual acquisition of HCV infection through enhanced viral reproduction or by providing a portal of entry through ulceration or inflammation. The cross-sectional design of this study, however, precludes confirmation of this hypothesis and limits causal inference.

A similar association between HCV and HSV-2 was shown in a study of heterosexual couples who were HCV serodiscordant.[24] Alter et al.[1] found that HCV infection was associated with HSV-2 infection in the National Health and Nutrition Examination Survey III study in analyses controlling for age but not for drug use and high-risk sexual behaviors. Similarly, in a recent study among drug users in treatment, Hwang et al.[25] found no association between HCV and HSV-2 after controlling for the confounding effects of injection history and sexual risk.

We recognize that HSV-2 seropositivity may simply serve as a biological marker for underreported sexual risk in our study. However, understanding the role HSV-2 plays in HCV infection could help reduce the potential sexual risk further and clarify prevention messages regarding sexual transmission.[6,26] Furthermore, the high attributable risk suggests, first, that if a causal link is established, HSV-2 infection may be an important determinant of sexually acquired HCV, and second, that reducing exposure through condom use and treatment of symptomatic genital herpes infections could avert many infections.

Attributable fraction estimates, which combine information on the prevalence of the exposure with an associated measure of excess risk, provide an estimate of the potential effect of preventive interventions.[27] Our study suggested that although injection drug use had a significant excess risk associated with HCV infection, the higher prevalence of HSV-2 infection and noninjection drug use resulted in a larger population attributable fraction estimate for these nonparenteral exposures. Results further implied that prevention and control of HCV infection must focus not only on reducing injection drug use, which has a moderately low prevalence, but also on reducing sexually transmitted infections and noninjection drug exposures. However, the etiologic interpretation of population attributable fraction estimates must be approached with caution because of the wide confidence intervals and potential noncausal associations. Given the modest sample size and the limited focus of the population under study (young women from low-income neighborhoods), the reader must not overinterpret the population attributable fraction estimates, which may be subject to both variability and the bias inherent in observational data. Measures of attributable risk provide an important tool for public

health planning and should not be considered alternatives to measures of effect.[27,28]

We recognize other possible limitations of the data. Only women for whom sera were available were included in the analyses, and although these women constituted 81.4% of the participating sample, they represented only 60% of all the eligible women identified. No observations were made of nonparticipants; thus, nonresponse bias is possible. Comparisons of women with and without sera detected some differences; the most significant was due to lack of sera from some women from San Joaquin County. Nonetheless, omitting San Joaquin from the analyses did not substantially change the principal findings of the study. Readers are also cautioned not to overinterpret results based on 40 confirmed HCV infections.

Despite these limitations, our data provide rare population-based estimates of HCV prevalence and related risk factors among young, low-income women. Understanding the epidemiology of HCV infection among women in low-income neighborhoods is a critical first step in designing primary and secondary interventions to mitigate the morbidity and mortality of this emerging infection. The growing evidence linking HSV-2 to HIV and HBV[15–17,29] points to a potential role for HSV-2 as a cofactor in sexual transmission of HCV as well. Strong empirical evidence supports the efficacy of sexually transmitted infection control as a means of reducing HIV risk through clinical and behavioral intervention.[15] Prevention of sexual transmission of HCV should be considered from a similar public health perspective. Although the per-contact likelihood of HCV transmission may be lower than through syringe sharing, a large and growing pool of carriers may generate significant numbers of new infections through sexual intercourse. Because many of the risk factors responsible for HCV infection are also related to risk of other adverse health outcomes, public health efforts aimed at reducing drug use and sexual risk vulnerability in very-low-income women should have multiple positive results. ■

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K.A. Page-Shafer conceptualized and designed the study, analyzed and interpreted the data, and drafted the paper. B. Cahoon-Young helped design the study and conducted laboratory analyses. J.D. Klausner contributed to interpretation of the data and to the writing and critical revisions of the paper. S. Morrow and F. Molitor participated in acquisition of the data, administrative and technical support, and revisions of the paper. J. Ruiz contributed to obtaining funding, acquisition of the data, administrative and material support, and revisions of the paper. W. McFarland contributed to conceptualizing the study, designing the questionnaire, analyzing the data, and the writing and revisions of the paper. The Young Women's Survey Team contributed to the conception of the parent study, acquisition of the data, and technical and material support.

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The California Department of Health Services Institutional Review Board and local institutional review boards, when available, approved all study protocols and materials.

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