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Spontaneous Clearance of the Hepatitis C Virus Among Men Who Have Sex With Men

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Background. The probability of spontaneous hepatitis C virus (HCV) clearance ranges from 11% to 49%. Our previous cross-sectional study suggests that mode of acquisition explains some of this heterogeneity. We performed this prospective study to determine factors associated with spontaneous HCV clearance among men who have sex with men (MSM).

Methods. A mixture-cure model was used to evaluate the probability of spontaneous HCV clearance among 101 MSM in the Multicenter AIDS Cohort Study with acute HCV infection between 1984 and 2012.

Results. Spontaneous HCV clearance occurred in 46% of MSM (49% in non-injection drug users [IDUs] and 23% in IDUs). In the multivariable analysis, age <30 years (clearance ratio [CR] = 2.43; 95% confidence interval [CI], 1.53–3.87) and being human immunodeficiency virus (HIV) uninfected (CR = 2.97; 95% CI, 1.98–4.46) were independently associated with spontaneous clearance. Among men aged ≥30 years, being HIV uninfected, not having unprotected anal intercourse, older age, and being on highly active antiretroviral therapy were independently associated with higher clearance. The interferon lambda rs12979860 single nucleotide polymorphism (SNP) was not associated with spontaneous clearance among the 88 MSM who were not active IDUs (CR = 0.74; 95% CI, .46–1.21 for CC vs CT/TT genotype).

Conclusions. The high probability of spontaneous HCV clearance together with the lack of an association between the rs12979860 SNP and spontaneous clearance among MSM who do not use injection drugs suggests that the immune mechanisms involved with a successful response to acute HCV differ by mode of virus acquisition. Understanding potential mechanistic differences could be important for HCV vaccine development.

Keywords. hepatitis C virus; HIV; IL28B; injection drug use; MSM.

Spontaneous hepatitis C virus (HCV) clearance without antiviral drug treatment occurs in approximately 25% of people [1, 2]; however, reports that show a range from 11% to 49% [3–7] demonstrate substantial heterogeneity for successful host control of acute HCV infection. In our recent cross-sectional study, spontaneous clearance was significantly higher among men who have sex with men (MSM) with no history of injection drug use (IDU; 34.5%) compared with men who had used injection drugs (11.5%) [8]. Better understanding of the mechanisms that lead to higher rates of spontaneous clearance among non-IDUs could aid development of a vaccine to prevent new HCV infections and reinfections after successful treatment with expensive direct-acting antiviral medications [9].

Characteristics associated with a lower probability of spontaneous HCV clearance include black race [3],

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male gender [2], human immunodeficiency virus (HIV) infection [10], and age >40 years [11], while hepatitis B virus infection [4, 8, 12, 13], heterosexual transmission [13], and homozygosity for the C allele of the single nucleotide polymorphism (SNP) rs12979860 [8, 11], which is located within intron 1 of the interferon lambda 4 (IFN-λ4) gene but is also near IFN-λ3 (IL28B) [14], have been associated with a higher probability of spontaneous clearance. However, these results were obtained from studies that focused mainly on IDUs, so it remains unknown whether these characteristics are independently associated with spontaneous clearance of sexually acquired HCV. Furthermore, many of these studies were cross sectional and, thus, were unable to determine which characteristics were present at the time of acute HCV infection and temporally related to spontaneous clearance.

The objective of this study was to determine the factors associated with spontaneous clearance of incident HCV infection among MSM from the Multicenter AIDS Cohort Study (MACS) [15]. The MACS, comprised of MSM who have been followed prospectively at protocol-defined semiannual study visits for 30 years, is an ideal cohort for achieving this objective.

METHODS

Study Population

The MACS is an ongoing observational cohort study of MSM in 4 metropolitan areas of the United States (Baltimore, Maryland/Washington, DC; Chicago, Illinois; Pittsburgh, Pennsylvania; and Los Angeles, California) that enrolled 6972 participants during the following 3 periods: 1984–1985, 1987–1995, and 2001–2003 [16–18]. Data were collected at study entry and semiannual visits via interviewer-administered and computer-assisted questionnaires and physical examinations. Biological specimens were obtained at each visit for laboratory testing and repository storage. HIV status was determined at baseline and during follow-up for HIV-uninfected participants using enzyme-linked immunosorbent assays and confirmed with Western blot [16]. The institutional review board at each site approved the MACS protocol and data collection forms (available at http://statepi.jhsph.edu/macs/macs.html), and all participants gave written informed consent.

Hepatitis C Testing

The MACS HCV testing protocol and the laboratory testing methods for HCV antibody, RNA, and genotype, and the INF-λ rs12979860 SNP have been described elsewhere [8, 15]. Briefly, for men enrolled in the MACS prior to 2001, we tested for HCV antibody (anti-HCV; ADVIA Centaur HCV assay, Siemens Healthcare Diagnostics, Tarrytown, New York) in cryopreserved serum samples that were obtained at enrollment and at the last study visit. A prospective HCV testing protocol was implemented for men enrolled in 2001 or later where anti-HCV was tested at the time of enrollment, and anti-HCV negative men were retested every 2 years while they remained negative. For all HCV seroconverters, we iteratively tested for anti-HCV in samples obtained at interim visits to determine the first anti-HCV–positive visit. Next, we tested for HCV RNA by real-time polymerase chain reaction (COBAS AmpliPrep TaqMan HCV assay, Roche Molecular Systems, Pleasanton, California; lower limit of detection, 43 IU/mL) at the last anti-HCV–negative, first anti-HCV–positive, and last follow-up visits. If HCV RNA was detected at the last anti-HCV–negative visit, we repeatedly tested for HCV RNA at earlier visits until the last HCV RNA–negative visit was determined. Men who were HCV RNA positive at the first anti-HCV–positive and last follow-up visits were classified as having chronic HCV (CHC) infection, and no further testing was performed. For those who cleared HCV by the last study visit, we iteratively tested for HCV RNA at interim visits until we identified the last HCV RNA–positive and first HCV RNA–negative visits.

Study Outcome

The study outcome was spontaneous HCV clearance within 2 years of infection. We selected a 2-year follow-up period because the longest observed time to clearance in this cohort was 1.3 years but also to account for the semiannual timing of MACS visits. Men with sufficient follow-up had clearance confirmed with 2 consecutive HCV RNA positive or negative results obtained at least 6 months apart. Those who were infected with HCV shortly before their last MACS visit and remained HCV RNA positive with less than 2 years of follow-up had their follow-up time censored at the last HCV RNA–positive visit. Because we focused on spontaneous clearance, we censored the follow-up time for 4 men who initiated anti-HCV therapy within 2 years of infection at the time of the last pretreatment HCV RNA test.

Participant Characteristics

The characteristics and exposures examined in this study included recruitment period, MACS site, race/ethnicity, age, cigarette use, alcohol consumption, IDU, non-injection recreational drug use, number of male sex partners during the prior 6 months, use of condoms (protection) during anal intercourse, presence of sexually transmitted infections, HIV infection status, HIV RNA level, $CD4^+$ T-cell count, use of highly active antiretroviral therapy (HAART), hepatitis B surface antigen (HBsAg) status, rs12979860 genotype (ABI TaqMan allelic discrimination kit; Applied Biosystems, Foster City, California), and HCV genotype (Inno-LiPA HCV II, Innogenetics, Ghent, Belgium). All risk factors were ascertained by participant self-report except HIV status, RNA level, $CD4^+$ T-cell count, HBsAg status, rs12979860

genotype, and HCV genotype. All time-varying risk factors except drug use and sexual exposures were determined at the last pre-HCV infection visit. For drug use and sexual exposures, we combined the data obtained at visits immediately before and after incident HCV infection to characterize these HCV risk measures during the interval in which each participant was infected with HCV.

Statistical Analyses

Time to spontaneous HCV clearance was described using a Kaplan–Meier (KM) curve. To generate the KM curve we assumed that the HCV incidence and clearance dates occurred at the midpoints between consecutive MACS visits. If both events occurred within the same interval, we assumed that incidence occurred one-third of the way and clearance occurred two-thirds of the way through the interval.

Standard methods for comparing time-to-event data, including KM curves and the Cox proportional hazards model, assume all individuals experience the outcome eventually and that the baseline time point (ie, time = 0) is known. Because HCV infection occurred during a time interval and many participants did not spontaneously clear HCV, we determined the factors associated with spontaneous clearance using a parametric mixture-cure model [19, 20] that was developed to address these limitations using a competing risks framework [21]. Specifically, we assumed that spontaneous HCV clearance occurred within 2 years of infection and that men who remained infected for more than 2 years developed CHC. We accounted for left-censoring when HCV infection and clearance both occurred between the same MACS visits and for interval-censoring when HCV infection occurred during 1 interval and clearance during a later interval. Finally, we modeled the probability of HCV clearance using a log-binomial distribution that incorporated covariates and assumed that time to HCV clearance followed a homogeneous log-normal distribution. As defined, this mixture-cure model allowed us to examine the effect of covariates on the probability of HCV clearance but not on the time to clearance.

Comparisons of the spontaneous clearance probabilities are reported as clearance ratios (CRs) with 95% confidence intervals (CIs). All characteristics were examined in the multivariable analysis, but only those remaining independently associated with spontaneous clearance at the 0.1 level were retained in the final models. SAS PROC NLMIXED (SAS version 9.3, SAS Institute, Cary, North Carolina) was used to estimate the model parameters. Statistical significance was inferred from a 2-sided P value <.05.

RESULTS

One hundred twenty-five MACS participants became infected with HCV between April 1984 and September 2012. We excluded 24 (19%) men whose last pre-HCV infection visit and first visit following HCV infection were >2 years apart because of the lack of precision about the timing of HCV infection and, hence, their risk factor status at the time of infection. Eleven (46%) of these 24 men subsequently cleared HCV, but only 1 (20%) of the 5 IDUs cleared HCV compared with 10 (53%) of the 19 non-IDUs.

At the time of HCV infection, the mean age for the 101 men included in the analysis was 40.5 (standard deviation = 9.4) years, 78% were white, 85% reported having had sex with multiple men during the prior 6 months, and only 13% reported recent IDU (Table 1). The majority (82%) of men were recruited before 1996, and 85% were infected with HIV.

The estimated time to spontaneous HCV clearance in the 2 years following infection is depicted in Figure 1. Accounting for censored follow-up, spontaneous clearance occurred in 46% (95% CI, 37%–57%) of this MSM study population. Among the 45 men who cleared HCV, 40 (89%) did so within 6 months and 44 (98%) within 1 year.

In unadjusted analyses, the characteristics significantly associated with a higher probability of spontaneous HCV clearance were age <30 years, consuming fewer than 4 alcohol-containing drinks per week, no unprotected anal intercourse during the prior 6 months, being HIV uninfected, and, among HIV-infected men, having undetectable HIV RNA (Table 1). Spontaneous clearance also occurred more frequently among HIV-infected men taking vs not taking HAART (59% vs 35%, respectively; $P = .054$) and among men who had not used injection drugs within 6 months of infection (49% vs 23% among active IDUs; $P = .15$). In preliminary analyses, we also examined the association of spontaneous clearance with the use of marijuana, poppers, crack/cocaine, uppers, erectile dysfunction drugs, ecstasy, heroine/opiates, speedball, phencyclidine, downers, and gamma hydroxyl butyrate, but none of these were found to be significantly associated with clearance following adjustment for the use of injection drugs (data not shown). Data about the use of intranasal and intrarectal drugs were not available for analysis.

HCV genotype was determined for 65 of the 101 participants; no HCV RNA–positive samples were available to determine genotype for the remaining 36 men, all of whom cleared HCV. A similar proportion of men with and without spontaneous HCV clearance were infected with genotype 1 HCV (88% and 86%, respectively).

The INF-λ rs12979860 SNP was not significantly associated with spontaneous HCV clearance in the unadjusted analysis. Stratifying by IDU status, men with this protective CC genotype had a higher probability of spontaneous clearance among active IDUs (CR = 2.00; 95% CI, .12–32.18) but not among nonactive IDUs (CR = 0.74; 95% CI, .46–1.21). However, this differential effect was not statistically significant

Table 1. Characteristics of Men With Incident Hepatitis C Virus (HCV) Infection, and Unadjusted Associations With Spontaneous HCV Clearance

		Spontaneous HCV Clearance	
Participant Characteristic	N (%)	Percent Cleared	Clearance Ratio (95% Confidence Interval)
All	101 (100)	45.8	
Age, y			
18–29	12 (11.9)	91.7	1
30–49	72 (71.3)	34.3	0.37 (.26, .55)*
≥50	17 (16.8)	58.8	0.64 (.41, .99)*
Mean (standard deviation)	40.5 (9.4)		
Median (interquartile range)	39.5 (34.0,46.4)		
Race			
White	79 (78.2)	48.7	1
Black	12 (11.9)	36.4	0.75 (.33, 1.70)
All others	10 (9.9)	33	0.68 (.26, 1.80)
Site			
Baltimore	18 (17.8)	26.7	1
Chicago	25 (24.8)	48	1.80 (.70, 4.56)
Pittsburgh	23 (22.8)	54.5	2.04 (.80, 5.22)
Los Angeles	35 (34.7)	47.1	1.76 (.70, 4.46)
Multicenter AIDS Cohort Study recruitment period			
1984–1995	83 (82.2)	43.2	1
2001–2003	18 (17.8)	60	1.39 (.85, 2.26)
Year infected with HCV			
1985–1994	60 (59.4)	45.8	1
1995–2004	22 (21.8)	33.3	0.73 (.37, 1.43)
2005–2012	19 (18.8)	62.5	1.37 (.85, 2.20)
Smoking history			
Never	27 (27.6)	41.6	1
Former	26 (26.5)	53.9	1.29 (.71, 2.36)
Current (past 6 mo)	45 (45.9)	40.9	0.98 (.54, 1.79)
Alcohol consumption past 6 mo			
Fewer than 4 drinks/week	42 (42.4)	56.1	1
4–13 drinks/week	28 (28.3)	46.2	0.82 (.50, 1.36)
At least 14 drinks/week	29 (29.3)	28.6	0.51 (.27, .98)*
Non-injection recreational drugs use past 6 mo			
No	33 (35.1)	43.8	1
Yes	61 (64.9)	47.5	1.08 (.67, 1.76)
IDU history			
Never	72 (71.3)	49.3	1
Prior use	16 (15.8)	50	1.02 (.57, 1.82)
Current use (past 6 mo)	13 (12.9)	23.1	0.47 (.17, 1.32)
Had a sexually transmitted infection during past 6 mo			
No	60 (60.6)	43.9	1
Yes	39 (39.4)	47.4	1.08 (.69, 1.70)
Number of male sex partners past 6 mo			
0–1	15 (15.5)	57.1	1
2–5	31 (32.0)	46.7	0.82 (.45, 1.49)
6–15	27 (27.8)	46.2	0.81 (.43, 1.51)
>15	24 (24.7)	37.5	0.66 (.33, 1.32)
Had anal intercourse past 6 mo			
No	13 (13.4)	83.3	1
Yes, always used protection	21 (21.7)	52.4	0.63 (.39, 1.02)
Yes, did not always use protection	63 (64.9)	36.1	0.43 (.28, .66)*

Table 1 continued.

Participant Characteristic	N (%)	Spontaneous HCV Clearance	
		Percent Cleared	Clearance Ratio (95% Confidence Interval)
Hepatitis B surface antigen status			
Negative	92 (91.1)	43.7	1
Positive	9 (8.9)	66.7	1.53 (.90, 2.58)
rs12979860 (IL28B/interferon-λ4) genotype			
CC	42 (42.9)	40.6	1
CT	40 (40.8)	46.2	1.15 (.69, 1.93)
TT	16 (16.3)	53.3	1.33 (.72, 2.47)
HCV Risk group			
Current IDU	13 (12.9)	23.1	1
Sex with men, prior IDU	16 (15.8)	50	2.17 (.69, 6.80)
Sex with men, never IDU	67 (66.3)	47.7	2.07 (.73, 5.87)
Undetermined	5 (5.0)	60	. . .
HIV status			
Uninfected	16 (15.8)	75	1
Infected	85 (84.2)	40	0.53 (.36, .79)*
$CD4^+$ T-cell count (cells/mm^3) (HIV+ only)			
<300	19 (22.3)	38.9	1
300–500	26 (30.6)	44	1.13 (.54, 2.37)
>500	40 (47.1)	37.8	0.97 (.47, 2.00)
HIV RNA (cp/mL) (HIV+ only)			
Undetectable (<400)	17 (20.0)	64.1	1
400–9999	14 (16.5)	28.6	0.45 (.18, 1.13)
≥10 000	54 (63.5)	36.5	0.57 (.33, .97)*
Currently taking highly active antiretroviral therapy (HIV+ only)			
No	66 (77.7)	34.9	1
Yes	19 (22.3)	58.7	1.68 (.99, 2.56)

The unadjusted clearance estimates, ratios, and confidence intervals were estimated using the mixture-cure model.

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug use.

* $P < .05$.

($P = .45$), likely due to the small number of IDUs in the study population.

In the multivariable analysis among all 101 men with incident HCV infection (Table 2, model 1), spontaneous clearance occurred significantly more often among HIV-uninfected vs HIV-infected men (CR = 2.43; 95% CI, 1.53–3.87) and among men aged <30 years compared with men ≥30 years (CR = 2.97; 95% CI, 1.98–4.46). Notably, the men aged <30 years were significantly less likely to be HIV infected than their older counterparts (58% vs 88%; $P = .02$), but no other significant differences between these 2 age groups were observed (data not shown). Additional covariates could not be added to the model because 11 of the 12 men aged <30 years cleared HCV, resulting in unstable statistical models when other covariates were added.

To examine other covariates, we restricted the analysis to the 89 men aged ≥30 years. Consistent with the whole cohort, spontaneous clearance occurred significantly more often among HIV-uninfected vs HIV-infected men (CR = 4.35; 95% CI, 1.84–10.22; Table 2, model 2). The probability of HCV clearance was also significantly higher among older men (CR = 1.47 per 10 years; 95% CI, 1.02–2.10) and among men who did not have unprotected anal intercourse during the prior 6 months (CR = 3.59; 95% CI, 1.59–8.11).

Finally, to evaluate the effect of HAART on spontaneous clearance, we examined the 78 HIV-infected men aged ≥30 years (Table 2; model 3). The effects of unprotected anal intercourse and age were similar to those reported in model 2. Adjusted for these factors, HIV-infected men taking HAART at the time of incident HCV were more than twice as likely to spontaneously clear HCV as men not taking HAART (CR = 2.10; 95% CI, 1.15–3.82). Further adjustment for $CD4^+$ T-cell count did not alter this effect of HAART (data not shown).

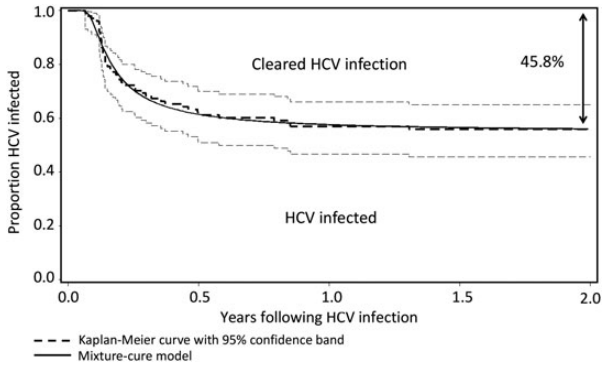

Figure 1. Time to spontaneous hepatitis C virus (HCV) clearance in the Multicenter AIDS Cohort Study. This figure compares the time to HCV clearance curves using the Kaplan–Meier method and the mixture-cure model. For both curves, incident HCV infection was assumed to have occurred at the midpoint between the last HCV-negative and first HCV-positive visits.

DISCUSSION

This is the first study to examine spontaneous HCV clearance prospectively in a cohort of HIV-infected and HIV-uninfected MSM with incident HCV infection acquired predominantly by sexual contact. In this cohort, 46% of men spontaneously cleared HCV, which is nearly twice the average HCV clearance rate reported in the literature [2]. Spontaneous clearance was higher in men who were younger, HIV uninfected, and non-IDUs, but men who had unprotected anal intercourse during the 6 months before infection were less likely to clear HCV. Among HIV-infected men, those who were receiving HAART were also more likely to clear HCV. Surprisingly, the INF-λ rs12979860 SNP was not associated with spontaneous clearance among these MSM, and this finding was most evident among non-IDUs.

An increased probability of spontaneous HCV clearance has been observed among men [4, 8, 12, 13] and women [6, 7] who acquired HCV through routes other than IDU. Our data from MSM extend those observations to acquisition of HCV through the rectal mucosa. Specifically, spontaneous clearance among the 88 non-IDU MSM in our study was 49%, which is twice as high as that reported from predominately IDU cohorts [1, 2] and also compared with the 13 active IDUs in our study. Possible explanations for lower spontaneous clearance among IDUs include higher viral inoculum [13] or repeated HCV exposures and reinfections that decrease effective HCV-specific immunity [13, 22]. Alternatively, mucosal immunity [13] might play a protective role against sexual exposures to HCV that is not available against percutaneous exposures, and this might explain the higher probability of clearance in women that has been attributed to hormonal differences between women and men [23]. Understanding the immune mechanisms that increase the probability of spontaneously clearing sexually acquired HCV infections could provide insights useful for vaccine development.

An intriguing finding from the present study was that men with the favorable rs12979860-CC genotype were not more likely to clear HCV spontaneously than those without this genotype, which differs from the strong association between rs12979860 genotype and spontaneous clearance in individuals who acquired HCV percutaneously [11]. Because most men in this study acquired HCV via male–male sex, this finding suggests that rs12979860-CC does not confer an immune advantage when HCV is acquired by this mode of transmission. The results are consistent with our previous cross-sectional study in which the impact of this genotype on spontaneous HCV clearance was significantly larger among IDUs than non-IDUs [8]. Together, these studies imply that an effect of IFN-λ4 activity on IFN-stimulated gene expression [24] does not substantially alter the anti-HCV immune response to infections acquired through the rectal mucosa.

Consistent with the results from Thomas et al [11], spontaneous clearance was highest among the youngest MSM in the

Table 2. Multivariable Analyses of Spontaneous Hepatitis C Virus Clearance

	Model 1: Full Cohort (N = 101)		Model 2: Men Aged ≥30 Years (N = 89)		Model 3: HIV-infected Men Aged ≥30 Years (N = 78)	
Covariate	CR	95% CI	CR	95% CI	CR	95% CI
HIV-uninfected	2.43	(1.53,3.87)	4.35	(1.84, 10.31)		
Taking highly active antiretroviral therapy					2.10	(1.15, 3.82)
Aged <30 vs ≥30 y	2.97	(1.98,4.46)				
Age (continuous per 10 y)			1.47	(1.02, 2.10)	1.53	(.96, 2.45)
No unprotected anal intercourse during the past 6 mo			3.59	(1.59, 8.11)	2.53	(1.34, 4.76)

The adjusted clearance ratios and confidence intervals were estimated using the mixture-cure model.

Abbreviations: CI, confidence interval; CR, clearance ratio; HIV, human immunodeficiency virus.

present study. Although men aged <30 years were more likely to be HIV uninfected, the association of clearance with age <30 years remained statistically significant following adjustment for HIV infection, suggesting that a more effective anti-HCV immune response is generated in younger men.

HIV infection is associated with a lower probability of spontaneous HCV clearance among IDUs [8, 10], and the present study confirmed this association for sexually acquired HCV infections among MSM. Notably, we also found that HAART significantly attenuated the adverse effect of HIV, suggesting that HAART can restore the HCV-specific immune response important for clearance [5, 25, 26]. Further studies are needed to determine whether HIV-infected individuals with CHC who initiate HAART can generate an HCV-specific immune response that might lead to spontaneous HCV clearance.

The inverse association between unprotected anal intercourse and spontaneous HCV clearance may be related to more risky sex behaviors, including having multiple partners, resulting in higher rates of HCV reinfection and cumulative risk of developing CHC [27]. On the other hand, it could also be explained by traumatic sex practices that allow for a larger inoculum of HCV or allow it to overcome the mucosal immune response [28].

Two important strengths of this study are that factors preceding incident HCV infection were examined for association with spontaneous HCV clearance and that this MSM cohort had little active IDU. However, the small number of IDUs may have limited our ability to demonstrate a significant difference between route of HCV acquisition and spontaneous clearance, and we lacked data about rough sex practices and the frequency of IDU, which precluded our examination of these recognized risk factors for HCV acquisition. This study was also limited by the use of self-report data to determine IDU status. However, this would most likely result in a conservative bias because misclassification of IDUs as non-IDUs is more probable than the reverse, which would lead to underestimation of the HCV clearance rate among non-IDUs and, thus, the difference between IDUs and non-IDUs. Although we excluded 19% of participants with incident HCV from this analysis, this was unlikely to have affected our conclusions because the percentage of excluded men who cleared HCV (46%) was identical to that of the study cohort, as were the clearance probabilities when the excluded men were stratified by IDU status. Finally, we could not definitively distinguish between persistence of HCV and rapid reinfection with HCV, a limitation that might be important because many of the factors we found to be associated with HCV persistence (eg, unprotected anal intercourse, HIV infection, and IDU) are also associated with an increased risk of acquiring HCV infection.

Given that nearly half of the men who acquired HCV through male-to-male sex spontaneously cleared the virus in this study, MSM who develop acute HCV infections should be carefully monitored for spontaneous clearance before treatment is initiated. Furthermore, discovering immune mechanisms that might explain an increased probability of spontaneous HCV clearance among MSM who acquired HCV through sexual contact compared with those who acquired HCV percutaneously could aid HCV vaccine development.

Notes

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Potential conflicts of interest. S. Y. is on the advisory board for Roche Molecular Systems and Quidel. L. P. J. has consulted on an outcomes advisory panel for Bristol Myers Squibb. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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