

Hepatitis C Virus Serosorting in People Who Inject Drugs: Sorting Out the Details

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(See the major article by Smith et al on pages 1934–42.)

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In developed countries such as the United States, hepatitis C virus (HCV) is primarily transmitted between people who inject drugs (PWID) due to the combination of high existing prevalence in the population, HCV's high infectivity, and repeated exposures to multiple potential contaminated sources of both drug preparation and administration equipment [1–3]. Although HCV incidence has declined since the 1990s in the United States, and several studies suggest it has been stable in the past decade [4], newly detected outbreaks of HCV in multiple areas of the United States, especially in suburban and rural (or “exurban”) settings, have been tied to increasing rates of opiate use in young adults [5, 6]. These new outbreaks raise serious concerns as HCV quickly reaches epidemic levels, as seen among adolescents and young adults in Massachusetts [7].

Further dissection of risk factors and behaviors that govern HCV risk related to injection practices in PWID is welcomed. In this issue of *The Journal of Infectious Diseases*, Smith et al present intriguing data that suggest that PWID throughout the United States are engaging in “serosorting,” defined as a decision to share or not to share injection equipment based on the partner's HCV serostatus [8]. A person injecting drugs who is HCV seropositive will worry less about acquisition if the sharing partner is also HCV positive; conversely, someone who perceives himself or herself to be HCV negative will seek HCV-negative partners to avoid acquisition.

For human immunodeficiency virus type 1 (HIV-1), serosorting has been previously described in men who have sex with men, as a seroadaptive strategy aimed at preventing HIV transmission—for instance, choosing sex partners with concordant HIV status [9, 10]. For HCV, less is known about serosorting. One study among young injection drug users found that knowledge about one's own serostatus correlated with higher knowledge about transmission of HCV but not with reduced distributive or receptive syringe sharing [11]; this study did not evaluate participants' knowledge or perception of their partner's serostatus. Results from subsequent single-center studies that

assessed seroadaptive behavior in PWID and examined perceived partner serostatus for HCV [12, 13] and HIV [14] do support that it influences whether to share or not share injecting equipment. In fact, in one of those studies [12], 39% of participants who reported sharing equipment said serosorting was an intentional strategy. The present study provides further evidence of seroadaptive behavior among PWID in association with HCV, and indicates that this behavior may be common on a national level. By asking about the testing history of last injection partner as a preface to participants' awareness of their partners' HCV status, the authors increase the potential for higher internal validity of this self-reported measure in their analyses. They found strong independent associations indicative of serosorting between both self-reported HCV-positive and -negative respondents: the former with higher, and the latter with lower, odds of sharing with HCV-positive partners compared to those with unknown HCV status. An additional strength of this study was the very large and well-sampled population of PWID from multiple urban centers.

As the authors point out, inference about intention is limited; this study, like others, was cross-sectional, and it cannot be determined if the participants made selective decisions about behavior or if

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the behavioral mixing influenced knowledge of and testing for HCV. To gain further knowledge, both prospective studies as well as measures regarding seroadaptive intention are needed. One important limitation of the current study was reliance of self-reported HCV infection status, as actual test results of the respondents and their partners were not present.

This study shows that HCV testing and counseling may influence injecting behavior of PWID. It is remarkable that up to 75% of PWID at these centers reported a perceived serostatus for themselves. Although almost half of the participants reported sharing injecting equipment, more than a third (37.7%) of those reported knowledge of their injecting partners' serostatus, based on testing history [8]. These numbers imply that testing has been widely applied in this population and that status is shared among injecting groups. What is not clear is whether testing is as widespread in nonurban settings, such as the "exurban" areas where opiate use and HCV cases may be rising.

Moreover, it remains unclear whether appropriate counseling about the meaning of a positive result and, specifically, regarding infectiousness has been communicated. PWID are infectious if they have HCV RNA in the blood compartment. Testing algorithms have suggested that all HCV antibody-positive persons receive confirmation of viremia via a nucleic acid test [15], not only because approximately 20% of those infected clear virus (and are not infectious), but also because of false-positive anti-HCV tests. Although there are alternative approaches, such as reflexive testing on a single sample (mostly for anti-HCV confirmation), in practice, 2-stage testing for HCV RNA following a positive screening enzyme-linked immunosorbent assay (ELISA) is the most widely utilized approach. For a variety of reasons, including competing priorities and the cost and time associated with multiple visits for counseling, it is not clear that nucleic

acid tests have been widely applied or that knowledge regarding the nuances of HCV results have been disseminated among PWID.

For someone choosing to avoid acquisition of HIV-1, serosorting to guide choice of sexual partners makes intuitive sense, as a positive result, when combined with an idea of treatment status (being off antiretrovirals), correlates with infectiousness. In contrast, HCV serostatus alone may not correlate with infectiousness, as a positive HCV antibody result simply indicates exposure without information regarding viremia in the bloodstream. This results in potential misclassification of infectious status between partners for at least 2 major reasons: (1) During acute HCV infection, there is a relatively long period averaging 6 weeks where HCV antibody is negative but viremia is present, when exposed individuals may perceive themselves to be negative; and (2) a significant proportion of untreated individuals infected with HCV, especially more women, will spontaneously clear the virus and, thus, be noninfectious [16]. Moreover, clearing virus does not eliminate susceptibility; seropositive individuals who have spontaneously cleared the virus remain at risk for reinfection. Counseling messages that accompany routine HCV testing are, therefore, more complex than for other infections such as HIV, and are parallel to those for human papillomavirus, another infection with a possibility of clearance. These complexities have the potential to result in incorrect perceptions or interpretations of HCV infectiousness. Thus, serosorting is even less likely to be effective as a preventive strategy among PWID to avoid HCV than the parallel sexual behaviors observed among MSM to avoid HIV-1.

Recent recommendations by the Centers for Disease Control and Prevention [17], endorsed by the US Preventive Services Task Force, call for more widespread HCV testing [18]. Among PWID, regular testing that is comprehensive and includes HCV RNA to confirm a positive screening ELISA test will have the benefit

of providing information about infectiousness, in addition to follow-up for clinical care to avoid long-term risks for premature death due to liver disease. The results may not only inform future behaviors, including seroadaptive ones, but also care seeking. In an ideal world, all results would be at the point of care and rapidly obtained to enhance the provider's ability to counsel and refer patients. The test would be less costly than current viral titer measurements to allow for greater implementation, especially when resources are limited. At present, the most recent-generation tests for HIV-1 combine antibody and antigen testing to capture the acute stage; parallel development of similar tests for HCV would obviate the 2-step testing algorithm currently recommended, but are currently not available.

Future studies should examine in more detail the consequences and potential utility of HCV testing and counseling, including the understanding that PWID and others have of their HCV testing results, and how they interpret and use these in decision making and risk assessments. Prospective studies in PWID are needed to assess the durability of counseling messages on individual behaviors and within injecting partnerships, which are often complex and vary significantly over time and arrangement (eg, cohabitating, sexual) [13]. Increasing "PWID's awareness of their HCV status will have important consequences for public health" [8] only if testing is both accurate and comprehensive, then accompanied by counseling that is truly informative of those at risk of and with infection, and finally followed by linkage to treatment.

Note

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