Injection Drug Users: The Overlooked Core of the Hepatitis C Epidemic

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(See the article by Hagan et al. on pages 669–72)

Injection drug users (IDUs) constitute the core of the hepatitis C epidemic in the developed world. Four times more prevalent than HIV infection, hepatitis C virus (HCV) has been acquired by at least 5 million Americans and an estimated 170 million people worldwide. In developed countries, people who use illegal drugs by injection are the largest group of persons with HCV infection and the group among whom most new infections occur. Viral transmission is uncontrolled among IDUs, with incidence rates ranging from 16%–42% per year [1–4], and yet, our efforts to control this pandemic have largely ignored the population in whom its biology and epidemiology are being played out with the most devastating effects.

Disease control depends on epidemiology, basic science, treatment, and prevention. In each of these spheres, work on HCV has focused on convenient populations—patients who come to our clinics and offices of their own accord—rather than the more challenged and stigmatized populations in whom the epidemic continues to rage out of control. The ubiquitously quoted estimate of the number of Americans infected with HCV—4 million—was derived from the National Health and Nutrition Examination Survey, a study of the housed, noninstitutionalized, civilian population of the United States [5]. But the populations most severely affected by HCV are poorly captured by this study. Disproportionately low response rates can be expected in government surveys from persons engaged in illegal activities, disclosure of which could result in incarceration or deportation. In addition, the National Health and Nutrition Examination Survey sampling frame, by design, explicitly excluded several large groups known to have high prevalences of injection drug use and HCV infection: people who are homeless, incarcerated, hospitalized, or institutionalized. Available estimates of the sizes and HCV prevalences of these populations suggest that at least a million more Americans have been infected with HCV than estimated by the National Health and Nutrition Examination Survey data [6].

New HCV infections in persons who inject illicit drugs are probably not well-represented in official estimates of HCV incidence in the United States, either. National estimates of the number of new HCV infections—about 30,000 per year—are based on data from cases of acute HCV infection reported to health departments in the 4 US counties (recently expanded to 6) participating in the Sentinel Counties Study of Acute Viral Hepatitis [7]. The calculations rely on the estimate that 1 in 6 new infections come to medical attention. HCV infections in IDUs, however, are rarely symptomatic, and probably <1% come to medical attention and are diagnosed [8, 9]. Thus, the true incidence of HCV infection among IDUs may be even less accurately ascertained by our surveillance system than the prevalence. The official estimates of these numbers tell us about infections in those of us who are stably housed, have nothing to fear from the criminal justice system, and go to the doctor when sick, but tell us little about those at the core of the epidemic.

If epidemiologists overlook IDUs when studying HCV, it is little wonder that basic scientists and treatment researchers do the same. Critical lessons about effective human immune responses to HCV infection can be learned from persons who clear the virus during the acute phase of infection. But although tens of thousands of IDUs in the United States become infected every year, most of our insights about the biology of acute HCV infection have come from less representative but more accessible sources—rare cases of symptomatic acute HCV infection that come to medi-
cal attention and occupationally exposed health care workers [10, 11]. And even as considerable progress has been achieved in developing new effective antiviral regimens for HCV infection, persons who inject illegal drugs, even former IDUs receiving methadone maintenance treatment, are routinely excluded from clinical trials of new HCV therapies.

Because, even by official estimates, most HCV transmission in developed countries occurs through the use of contaminated injection equipment during illicit drug injection, one might expect that prevention efforts would, of necessity, focus on stopping transmission among IDUs, even if other clinical or scientific efforts focused on more accessible populations. Most official publications on the prevention and control of HCV infection [12–14], however, have avoided directly recommending the central strategies for preventing bloodborne disease transmission among IDUs: accessible substance abuse treatment, syringe exchange programs, removal of the legal barriers to syringe access and possession, community-based outreach, and HCV testing and treatment programs for IDUs and incarcerated persons [15]. Prisons offer an unparalleled opportunity for HCV prevention and treatment [16], because an estimated 29%–43% of HCV-infected persons in the United States pass through the corrections system annually [17], but the opportunity is almost universally squandered [18]. Despite their centrality in the epidemic, IDUs all too often seem invisible to epidemiologists, basic scientists, clinicians, and public health authorities alike.

One official document that illuminated this blind spot was the 2002 National Institutes of Health consensus statement on the management of HCV [19]. Departing from previous guidelines, this document recommended that drug users be considered for HCV treatment on a case-by-case basis, just like other patients, and that drug use in and of itself not be considered a contraindication. This change was based on the recognition that data did not exist to support the previous recommendation, made in 1997 [20], that drug users not be treated for HCV infection until they had abstained from all illicit drug use for at least 6 months [21]. Nonetheless, few data exist to guide physicians considering treating active drug users for HCV infection outside of special targeted programs [22–38], and most hepatologists still adhere to the old guidelines on this matter. As a consequence, despite the new guidelines, very few drug users have access to treatment for HCV infection [39].

Current treatment regimens for HCV infection appear to eradicate the virus from 50% of patients [40], averting the risk of liver failure or liver cancer [41]. When restrictive criteria are applied to substance users with HCV infection, however, the proportion that remains eligible for antiviral therapy quickly evaporates, as reported by Hagan and her colleagues in this issue of Clinical Infectious Diseases [42]. Four-hundred four IDUs were drawn from the more than 1 million active IDUs in the United States with HCV infection. Of these 404, only 4% would be offered treatment if those with problem drinking, moderate-to-severe depression, or recent injection drug use are considered ineligible. If this is the best we can do—if the “incredible shrinking” pool of patients depicted in their figure is all we can hope to treat—we will forever remain consigned to treating patients at the peripheries of the epidemic, and the burden of liver disease will continue to rise.

But can patients with these problems be treated for HCV infection? A growing number of studies suggest that they can. Reports from Munich [22–24], Oakland [25], Chicago [26], Rhode Island [27], New York [28], Vancouver [29], England [30], France [31], Italy [32], Belgium [33], Dusseldorf [34], Switzerland [35], Austria [36], Norway [37], and Australia [38], reviewed elsewhere [43–45], have suggested that drug users treated for HCV infection can achieve sustained virologic response rates similar to those in other populations, even if they have psychiatric comorbidity, and even if they continue to use drugs while receiving treatment, although more frequent drug use may be associated with less success [25]. Many of these studies, however, reported on small, diverse groups of sometimes highly selected patients recruited and treated in different settings with differing strategies. Data are sparse on the characteristics that distinguish those who can be successfully treated and the programmatic elements that are critical for success. Larger studies that carefully characterize patient and program characteristics and outcomes are needed to provide this information. The need for such research is urgent, in view of the overwhelming prevalence of HCV infection in this population [46, 47], the increasing morbidity and mortality of the disease [48], and the limited access that IDUs have to liver transplantation [49]. In the meantime, these same considerations demand that we use what we know already to expand and replicate existing programs that have been successful [50].

Cultural and behavioral barriers encumber work with IDUs, whether in research, clinical care, disease prevention, or public health. Nonetheless, until these barriers are overcome, the HCV epidemic will continue to spread unabated, and morbidity and mortality from liver disease will continue to rise. Fortunately, experience working effectively with IDUs is available from a relatively large community of professionals serving substance-using populations, including those working in substance abuse treatment, HIV prevention, harm reduction, HIV care, primary medical care, social services, and other areas. Knowledge and experience with HCV infection and its treatment, however, are needed in these circles. Dialogue and collaboration between experts in HCV treatment and practitioners who have experience with IDUs will be needed to bring the unseen core of the HCV epidemic into view, so that progress can be made toward effective prevention of infection and effective treatment and care of those with HCV infection at the core of the epidemic.
The Ryan White CARE Act has provided resources for productive collaboration among providers serving patients with HIV infection. Advocacy for the needs of persons with HCV infection may be required to get needed resources allocated to support similar work on HCV. The all-too-frequently overlooked core of the epidemic is the battleground on which efforts to control HCV infection in the developed world will be won or lost.

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References

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