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Can HIV and HCV Infection be Eliminated among Persons who Inject Drugs?

David C. Perlman[1,2,*], **Don C. Des Jarlais**[2], and **Jonathan Feelemyer**[2]

[1]Department of Medicine, Mount Sinai Beth Israel, New York, NY

[2]Baron Edmond de Rothschild Chemical Dependency Institute, Mount Sinai Beth Israel, New York, NY

Abstract

HIV and HCV infection are readily transmitted among persons who inject drugs (PWID). The epidemics have expanded rapidly, becoming a global health issue. Combined prevention (simultaneously implementing multiple interventions) has been implemented to reduce injection and sexual transmission of HIV and HCV among PWID. Reductions in risky injection and sexual behavior have led to dramatic reductions in HIV in many countries. Whether comparable reductions in HCV transmission can be achieved has yet to be determined. Eliminating HIV and HCV among PWID will require considerable resources and commitment, particularly in low and middle income countries.

Keywords

HIV; hepatitis c virus; drug injection; combined prevention; persons who inject drugs

Introduction

Both HIV and hepatitis C virus (HCV) are transmitted through the multi-person use ("sharing") of equipment for injecting illicit psychoactive drugs.[1] The injection of illicit narcotic drugs was once so geographically concentrated that it was known as "the American disease."[2] When HIV was first observed among persons who inject drugs (PWID) in 1981[3]

[*]**Contact Author Information:** David C. Perlman, MD, Mount Sinai Beth Israel, First Avenue at 16th Street, New York, New York 10003, (p) 212-844-8556, (f) 212-844-8556, dperlman@chpnet.org.

there were probably only several hundred thousand injectors infected with HIV. In the most recent estimate, injecting drug use exists in 148 countries; HIV infection exists among persons who inject drugs (PWID) in 61 countries, and HCV infection exists among PWID in 57 countries.[4, 5] Injecting drug use is driving HIV epidemics in Eastern Europe and Central and Southeast Asia [6, 7] and epidemics of HCV in most countries in the world.[4] The same factors that have led to the globalization of trade in licit goods (improved communications, improved transportation, reduced restrictions on the flow of capital)[8] have led to the worldwide diffusion of injecting drug use. HIV and HCV infection frequently follow drug distribution routes.[9] More recently, the mass commercial marketing of prescription opioid drugs has led to an epidemic of opioid dependence,[10] to a vastly increased pool of persons at risk for transition to opioid use, and consequently of people at risk for HIV and HCV infection.[11]

Thus, the overall situation of HIV and HCV among PWID has clearly become a global public health catastrophe over the last thirty years. In this paper we will consider the prospects for eliminating HIV and HCV among persons who inject drugs.

HIV

Potential for rapid spread—HIV is not transmitted nearly as efficiently as HCV, but there still are far too many examples of very rapid spread of the virus in PWID populations. HIV incidence rates greater than 10/100 person-years have been reported in New York,[12] Bangkok,[13] Manipur, India,[14] and other countries including China, Estonia, and Russia.[15–17] Common components in very rapid spread of HIV among PWID include: 1) lack of knowledge about HIV as a threat to the local PWID population,[18] 2) mechanisms for sharing with many partners within short time periods, e.g, injecting in “shooting galleries, use of “dealer's works,”[19] and 3) restrictions on access to sterile injection equipment, including law enforcement activities.[20]

Potential for averting HIV epidemics among PWID—There are a number of evidence based interventions that have been shown to reduce HIV transmission among PWID. Needle/syringe programs (NSPs),[21, 22] medication-assisted treatment (MAT) for substance use disorder, particularly methadone maintenance treatment,[23] and antiretroviral treatment (ART) for HIV infection [24] reduce HIV transmission among PWID.[25] If effective prevention programs are implemented *prior* to outbreaks of HIV among PWID, then it is possible to avert HIV epidemics. Australia[26] and the United Kingdom [27] are notable examples of countries that implemented large-scale effective HIV prevention programs early and never experienced national epidemics of HIV among PWID, but already had established high prevalence HCV epidemics.

It is important to note that it is not necessary to achieve risk elimination to avert HIV epidemics among PWID. In areas in which HIV prevalence is low (< 5%) and stable among PWID, typically 10% to 20% of PWID report current sharing of needles and syringes.[28] Prevalence stays low because almost all of the sharing is among persons who are HIV seronegative and because the sharing is typically confined within small, stable groups, without mechanisms for rapid injecting risk partner change.

Potential for Reversing and Ending High Seroprevalence HIV epidemics— When HIV prevalence is high in a PWID population there will be more opportunities for HIV seronegative persons to share needles and syringes with HIV seropositive persons generating higher incidence than in low prevalence situations. Over the last several years, however, we have seen evidence that with "combined prevention" (implementation of NSP, MAT, and ART at high levels of coverage) it is possible to "reverse" high HIV prevalence epidemics—with both incidence and prevalence declining and that it is possible to "end" HIV epidemics among PWID. Examples include Vancouver,[29] Amsterdam,[30] New York City,[31] and France.[32] Again, elimination of risk behavior in the PWID population is not necessary. Rather sharing is typically confined to small, stable groups and transmission risk behavior (passing on used needles and syringes by HIV seropositives) is greatly reduced [33] and because ART reduces the infectiousness of the HIV seropositives who do pass on their used needles and syringes. The process of reducing HIV transmission within a PWID population with high HIV prevalence can be viewed as a positive feedback loop. First, the numbers of HIV seronegative PWID engaging in receptive sharing is reduced, and the great majority of those who do engage in receptive sharing do so within small, stable groups. Then there is a progressive reduction in the numbers of HIV seropositive injectors who engage in distributive sharing (passing on needles and syringes that they have used to others). This reduction occurs through behavior change (HIV seropositives reducing distributive sharing), HIV seropositives leaving the active injecting population (through death or disability, or through ceasing to inject whether via MAT or otherwise), and through HIV seropositives receiving antiretroviral therapy and becoming much less infectious. This reduces the number of new HIV infections, and thus further reduces the numbers of HIV infectious persons engaged in distributive sharing. This feedback loop can continuously reduce new HIV infections, though we do not yet know just how far the reduction continues before a floor effect occurs.

Sexual HIV transmission among PWID—There is also the possibility of sexually transmitted HIV infections among PWID, including persons becoming infected through sexual transmission prior to beginning to inject. This possibility, combined with racial and ethnic disparities in Herpes simplex virus -2 (HSV-2) prevalence, reinforce the need for combined prevention programming for PWID to include efforts to reduce sexual HIV risks [34] and that addressing sexual transmission among PWID may be particularly important in efforts to reduce racial and ethnic disparities in HIV.[35]

It may not be possible to totally eliminate HIV in large populations of PWID, but with combined prevention, we now have the tools for getting close to zero new HIV infections among PWID.

Hepatitis C

Potential for rapid spread and mature HCV epidemics—Chronic HCV infections cause substantial mortality and morbidity, including cirrhosis and hepatocellular carcinoma, and is the leading indication for liver transplantation.[36,37,38] The medical risks of transplantation, as well as the costs of transplantation and limitations in numbers of

available livers reinforce the need for the primary prevention of HCV, and for those already infected, early detection and treatment before significant morbidity develops.

HCV is transmitted very efficiently through non-sterile injection practices, contamination of needles and syringes, as well as contaminated injection paraphernalia, creating a need for both more stringent adherence to safe injection techniques, and adequate supplies of clean, unshared, paraphernalia and syringes. In addition, HCV has been in circulation among PWID for many more years than HIV.[39, 40]

It is likely that considerations related to proportions of PWID engaging in receptive or distributive sharing, as discussed with respect to HIV, apply as well for HCV, but the degree of risk reduction required for population level impact appears to be greater. These biological, social, behavioral, and historical-epidemiologic factors combine to create a situation in which 1) recent initiates to injection have a very high average HCV incidence, ranging from 2.7/100 person years −66/100 person years of observation in some settings [41] 2) there is a higher prevalence of HCV than of HIV in virtually all PWID populations, and in which between 43–48% of lifetime PWID have HCV infection,[42, 43] and 3) compared with HIV, there are more settings with established high HCV seroprevalence epidemics (with or without high prevalence HIV epidemics) and fewer opportunities (or shorter lived opportunities) to avert HCV epidemics.

Sexual transmission of HCV—HCV is less readily sexually transmitted than HIV, but recent outbreaks of acute HCV among HIV positive men who have sex with men, often in conjunction with injection and non-injection drug use, demonstrate the potential for sexual transmission.[44] HIV-HCV co-infection is an important issue as HIV infection enhances the progression of HCV induced liver fibrosis, is a leading cause of death in HIV infected persons, and the potential for interactions between ART and HCV treatments can complicate the choice of therapeutic agents and increase adverse event rates.[45] Such overlapping epidemics of HCV, HIV and drug use, and densely connected social networks in which unprotected sex is frequent, may complicate efforts to control HCV epidemics.

Potential for averting epidemics of HCV among PWID—The rapidity with which PWID may acquire HCV creates a need to reduce risk among PWID very early in injection careers. Current HCV prevention efforts are poorly developed and insufficiently implemented to control the HCV epidemic among PWID. HCV vaccine development has been thwarted by the degree of viral diversity, multiple mechanisms of viral persistence, poorly protective host immune response, and lack of robust models.[46–49] Systematic reviews have concluded that it is unlikely that educational, counseling and peer-education interventions can have a significant effects on HCV transmission,[50] and that drug treatment programs that do not contain MAT show no preventive benefit.[51]

Published data, reviews and meta-analyses have identified some possible preventive benefit of MAT and broad coverage NSPs in reducing HCV acquisition among PWID, but the evidence has been mixed and considered to be “tentative” for MAT and “inconclusive” for NSP.[51–53] Further, neither MAT nor NSP are currently sufficiently scaled up in most settings to prevent emerging HCV epidemics, and neither intervention consistently draws

people who have recently initiated injection; hence both improved program designs and scale up may be needed to avert HCV epidemics.

Potential for reversing and ending High seroprevalence HCV epidemics— There is some evidence that we may have the strategies to reverse existing HCV epidemics among PWID. "Combination prevention" analagous to that discussed for HIV may already have impacted the HCV epidemic in New York City [54] and elsewhere.

Very significant scale up of these interventions, possibly in combination with even more dramatic increases in HCV treatment as prevention may be required to reverse high prevalence HCV epidemics. Modeling studies suggest that to reduce the prevalence of HCV by 75% within 15 years, treatment as prevention would have to be significantly scaled up.[55, 56] Among the potential barriers to doing so are 1) the very significant gaps in the HCV Care continuum that reduce the real world population-level effectiveness of HCV treatment, and 2) the suboptimal prevention of HCV infection and re-infection; combined these barriers contribute to the persistence of a high community HCV viral load fueling ongoing transmission.[57]

Among PWID with HCV infection, most are unaware they are infected, many are not HCV tested, are tested for HCV antibody (Ab) but not HCV viral load to confirm active infection, not evaluated for treatment, not offered or do not initiate treatment, or do not complete treatment.[58–60] The recent development of potent oral direct antiviral agents (DAAs) has resulted in treatment regimens that are both more efficacious, better tolerated, and shorter (currently 12–24 weeks, and possibly 8 weeks)[61] yielding sustained virologic responses (SVRs) in up to 90% of those completing therapy. There are at least 11 genotypes of HCV. Genotypes 1a and 1b account for approximately 60% of global infections. Specific genotypes respond differently to treatment and different agents and treatment durations may be required; however, some newer agents have pan-genotypic activity and fewer data exist for certain genotypes in general and with respect to certain agents.[61] The new DAA agents are highly efficacious, and regimens may still have significant adverse effects in some patients; further, pricing is quite variable by country, with costs of approximately $1000 USD per pill in the United States, where treatment courses may therefore cost $80,000 or more. As a consequence, in the United States, there is considerable state by state and payer variability regarding coverage, creating a situation with both promise and uncertainty about the implications for the treatment of HCV infected drug users and the potential impact of treatment as prevention on the HCV epidemic. When PWID (ever or active injectors) are treated, SVR rates obtained have been comparable to those obtained among non-injectors (56% (95%CI:50–61%)[62] yet despite the high efficacy of new HCV treatments, recent estimates are that 1%–9.5% of PWID initiate treatment.[60, 63] Interventions to link PWID with HCV from methadone maintenance treatment to HCV care show promise as a strategy increase the proportion of progressing through the HCV care continuum.[64]

Implementation—Predicting the Future—Given that we now have the tools needed to essentially eliminate injecting related transmission of HIV, the question becomes whether the global public health community with undertake this goal. Whether we clearly have the relevant tools to reduce, let alone eliminate HCV is less clear, but modeling does suggest

that dramatic scale up of combined prevention may be promising. Most injecting related transmission is occurring in low and middle -income countries, where the resources needed for large-scale implementation of harm reduction programs are often lacking. ART is being increasingly rolled out in many countries, but the promise of treatment as prevention (TasP) and HIV pre-exposure prophylaxis are far from realized. With the global economic recession, international support for addressing HIV/AIDS is being reduced.[65] Only recently have truly effective HCV treatment been available, but treatment is substantially less scaled up for HCV than for HIV, and cost remains a very substantial barrier. Drug users are a highly stigmatized group, so that the political will to utilize evidence-based interventions is often lacking. [66] Eliminating HIV and HCV among PWID will require resources and commitment to identify optimally effective evidence based strategies, and the resources, societal and global commitment to implement evidenced based public health efforts.

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