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Fifteen Years of Research on  
Preventing HIV Infection among  
Injecting Drug Users: What We  
Have Learned, What We Have Not  
Learned, What We Have Done,  
What We Have Not Done

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**S Y N O P S I S**

**Objective.** Acquired immunodeficiency syndrome (AIDS) was formally identified among injecting drug users (IDUs) in 1981, and research on preventing human immunodeficiency virus (HIV) infection among drug injectors began shortly thereafter. At the time this research was begun, there was a general assumption that drug users (who were called drug *abusers* at that time) were too self-destructive and their behavior too chaotic for them to change their behavior to avoid infection with HIV. This chapter reviews the history of research on implementation of programs for prevention of HIV infection among IDUs.

**Methods.** Reviews of both research and program implementation research were conducted. Consultative discussions of issues and findings were conducted with researchers in the United States and other countries.

**Results.** An extremely large amount of useful information has accumulated during the past 15 years. We now know that the great majority of IDUs will change their injecting behavior in response to the threat of AIDS and that these behavior changes are effective in reducing HIV transmission among drug injectors. Additional insight is needed regarding the apparent insufficiency of

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some prevention programs to control HIV, the transmission dynamics of rapid HIV spread, and the persistence of moderate to high incidence of HIV infection in high seroprevalence populations. Despite the current research knowledge base, implementation of effective prevention programs in many countries is nonexistent to incomplete.

**Conclusion.** The most important barrier to reducing HIV transmission among drug injectors is not a lack of knowledge but the failure to implement effective prevention programs in many parts of the world.

The disease that is now called acquired immunodeficiency syndrome (AIDS) was formally identified in injecting drug users (IDUs) in late 1981.<sup>1</sup> Since then there has been a substantial amount of research on the problems of human immunodeficiency virus (HIV) infection among drug users; research support has reached hundreds of millions of dollars. The National Institute on Drug Abuse (NIDA) has been the primary funding source for this research, with important contributions from the Centers for Disease Control and Prevention (CDC) and other Federal agencies; European, Canadian, and Australian government research agencies; some developing country governments; and private foundations such as the American Foundation for AIDS Research (AmFAR). By our personal estimate, the number of published studies and abstracts on HIV infection among IDUs is in the tens of thousands. As we are now halfway into the second decade of research on AIDS and psychoactive drug use, it is appropriate to summarize what we have and have not learned through this tremendous research effort.

This review concentrates on issues related to behavioral and social prevention of needle-borne HIV infection among IDUs. Topics such as sexual transmission among drug users (including noninjecting drug users), outcomes of HIV infection among IDUs (including the effects of psychoactive drug use on the immune system), providing anti-HIV treatments for IDUs, and the development of vaccines against parenteral transmission have been omitted due to time and space limitations. The review is organized into five research issues and a section on prevention policy.

### Research Issues

**The international diffusion of injecting drug use and HIV among IDUs.** The first cases of full-blown AIDS among IDUs were highly concentrated in the New York City area,<sup>2</sup> leading to a false impression that the problem was concentrated geographically in this area. The development of the HIV antibody tests in 1985 showed HIV infection among drug injectors in many other U.S. and European cities, though at widely varying seroprevalence levels. (Note that this discovery occurred prior to the adoption of the name "human immunodeficiency virus" and prior to the long-term outcome studies showing the long latency period and extremely high fatality rate for HIV infection.) By the middle 1980s, HIV infection among IDUs was seen as an important problem in many parts of North America and Western Europe.

The spread of HIV among IDUs in Bangkok in 1988 was the first definitive indication of severe problems of HIV infection among IDUs in developing countries. According to the most recent estimates, injecting drug use occurs in 124 different countries, and HIV infection among IDUs has been found in 97 different countries.<sup>3</sup> The problem has truly been "globalized." The reasons for the rapid diffusion of injecting drug use have not been well studied.<sup>4</sup> The same factors, such as improved communication, improved transportation, and reduced barriers to financial transactions, which have facilitated the globalization of trade in licit goods, are probably important in the globalization of trade in illicit drugs. While international efforts like the work of the United Nations International Drug Control Program probably do limit the overall trade in illicit drugs, we clearly do not have effective means for halting the international diffusion of illicit drugs.

The international spread of HIV among drug injectors can occur several ways. "Bridge populations," such as men who have sex with men and who also inject drugs, may introduce HIV into a local drug-injecting population. This appears to be the way in which HIV was introduced into the IDU population in New York City.<sup>5</sup> International travel by IDUs who are infected with HIV also is a common method for the international spread of HIV among IDUs.<sup>6</sup> Such travel may be particularly common along drug distribution routes. Again, since the international spread of HIV infection among IDUs has not been well studied, we do not yet know how to reduce this spread.

Once HIV is introduced into a population of IDUs, very rapid transmission can occur. Increases in HIV seroprevalence of 20% or more per year have been noted among IDUs in both industrialized and developing countries. Very rapid transmission has occurred in New York City;<sup>5</sup> Edinburgh, Scotland;<sup>7</sup> Bangkok, Thailand;<sup>8</sup> and Manipur, India.<sup>9</sup> (See review by Friedman and Des Jarlais, 1991.<sup>10</sup>)

**The "first generation" questions on AIDS risk reduction among IDUs.** When HIV infection was first noted among IDUs, it was widely assumed that they would not be capable of changing their behavior in response to this new threat. Research studies, however, showed behavior change and risk reduction in response to a wide variety of HIV prevention programs, including basic HIV education, community outreach, bleach distribution, syringe exchange, pharmacy sales, drug user organization programs, and treatment for drug dependence. (See review by Des Jarlais et al. 1992.<sup>11</sup>) Drug users have

also changed their risk behavior in response to mass media and oral communication network information, in the absence of formal HIV prevention programs.<sup>12</sup>

Studies that have used HIV infection as the outcome measure have confirmed the validity of the reported risk reductions. Lower rates of HIV infection have been associated with participation in street outreach programs,<sup>13</sup> syringe exchange,<sup>14</sup> drug abuse treatment,<sup>15</sup> and generalized risk reduction.<sup>16</sup>

It is now clear that a large majority of IDUs will change their risk behavior in response to the threat of AIDS and that these behavior changes can lead to reduced rates of HIV infection.

**The "second generation" questions on AIDS risk reduction among IDUs.** While the majority of IDUs will change their risk behaviors, there are still several very important questions to be addressed. If demonstrating that effective risk reduction occurs among IDUs was the "first generation" research problem, these remaining questions can be termed "second generation" research problems.

*Characteristics of "insufficient" programs.* While the great majority of studies of HIV prevention programs have shown dramatic reductions in risk behavior, there are also studies that have identified programs that have not been sufficient to control HIV infection among their participants or potential participants. To cite two examples, HIV incidence among participants in the Amsterdam methadone treatment programs is estimated to be 4/100 person-years at risk (PYAR),<sup>17</sup> and HIV incidence among participants in the Vancouver syringe exchange program (SEP) has been estimated at 18/100 PYAR.<sup>18</sup> These relatively high HIV incidence rates do not mean that these programs are totally ineffective. IDUs who self-select to participate in syringe exchange and drug abuse treatment also may be at generally higher risk than those who do not select to participate in such programs, and incidence rates may be higher if the programs are not implemented. Nevertheless, the incidence rates in the Amsterdam methadone program and in the Vancouver SEP cannot be considered acceptable from a public health perspective.

While there is still much to be learned about why some programs are not sufficient to control HIV infection, three working hypotheses can be offered at this point. First, some HIV prevention programs can be considered "user friendly." They have hours of operation and locations that are convenient for drug users, they do not impose heavy restrictions on participants, and, perhaps most importantly, participants are treated with dignity and

respect. Nonuser-friendly programs tend to attract and retain few participants; indeed some programs have been closed because they could not attract sufficient participants to justify continued operation.<sup>19</sup> Programs that do not attract and retain large numbers of individuals at risk for HIV infection are not likely to be sufficient for controlling HIV transmission.

A "dose-response" relationship can be considered as a second working hypothesis regarding "sufficient-insufficient" HIV prevention programs. Methadone programs that utilize only low doses of medication have substantially less effect in reducing drug injection than programs that utilize higher dosages.<sup>20</sup> SEPs that limit the number of syringes that can be exchanged per visit also may be less effective in reducing the sharing of injection equipment than programs that permit large numbers of syringes to be exchanged per visit and that encourage "secondary" exchanging to other IDUs who do not personally attend the exchange.<sup>19</sup>

A third hypothesis is that "insufficient" programs do not address the mixing patterns of IDUs who engage in risk behavior. As discussed below, mixing patterns that lead to rapid partner change may be critical in the spread of HIV among local populations of IDUs.

Full determination of the reasons why some HIV prevention programs are not sufficient to control HIV transmission within local populations of IDUs will require cross-site research that includes measurement of both the local "context" of drug injection behavior and potential risk behaviors.

*Characteristics of and programs for difficult-to-change drug injectors.* While participation in various HIV prevention programs is reliably associated with risk reduction among IDUs, there are still substantial numbers of IDUs who either do not participate in such programs or who participate and still engage in relatively high levels of risk behavior. Studies of participants in SEPs<sup>18,21</sup> and in drug abuse treatment<sup>20,22</sup> suggest that these drug users have "individual and social disadvantages" that can make effective risk reduction more difficult. These disadvantages can include high rates of drug use, dependence on multiple drugs, homelessness, severe stigmatization, and psychiatric comorbidity such as concurrent depression. Occupational disadvantages, such as roles within street drug distribution systems, also may serve to facilitate high risk behavior among some IDUs.

While this "personal and social disadvantage" finding must still be considered a preliminary conclusion, the implications for HIV prevention are quite serious. First,

we do not have a well-developed set of programs to address these types of disability and disadvantage problems. Second, new programs that do address these types of problems are likely to be very resource intensive.

*The naturally occurring limits of HIV risk reduction among IDUs.* During the past 15 years, literally thousands of HIV prevention efforts for IDUs have been implemented in different locations throughout the world. To our knowledge, no individual program or set of programs has led to complete risk elimination in any population of IDUs. (In addition, we know of no programs that have achieved elimination of risk behavior for any other population at risk for HIV infection.) This suggests that there are some naturally occurring limits to HIV risk reduction among IDUs, at least in regard to the current set of HIV prevention programs. Determining these naturally occurring limitations on risk reduction and the relationships between residual risk behavior, local conditions, and rates of HIV transmission will be important for establishing control over HIV epidemics among IDUs in many areas.

**Dynamics of HIV transmission.** As noted earlier, HIV has spread rapidly in many populations of IDUs. Factors associated with rapid spread include lack of knowledge about HIV and AIDS as a local threat to the IDU population, restrictions on the effective availability of sterile injection equipment, and mechanisms that facilitate rapid partner change among IDUs who are sharing injection equipment.<sup>11</sup> Examples of mechanisms that facilitate rapid partner change include shooting galleries, where many IDUs can rent injection equipment, and dealers' works, where a drug seller may lend injection equipment to many different drug purchasers.

In contrast to areas with rapid transmission of HIV in the local population of IDUs, some areas where the virus was introduced into the local IDU population have experienced minimal HIV transmission. In populations of IDUs where HIV seroprevalence has remained low (less than 5%) for extended periods (a minimum of five years), public health officials began HIV prevention efforts early, utilized community outreach to establish trusted communication between IDUs and health workers, and provided good access to sterile injection equipment.<sup>23</sup> HIV risk behavior was not eliminated in populations of IDUs with stable, low seroprevalence. Indeed, at least one-third of IDUs in these five cities reported injecting with equipment that had been used by others (in the six-month period prior to interview).

At present, we do not have effective measures to differentiate patterns of risk behavior that permit stable, low seroprevalence from patterns of risk behavior that fuel rapid transmission of HIV within a population of IDUs. It is clear that the standard variable of "any sharing in the  $x$  months prior to interview" is not an adequate variable for distinguishing between these different epidemiological conditions. Variables that describe mixing patterns among risk partners are more likely to be important in this differentiation.

**High seroprevalence HIV epidemics.** Once HIV becomes well established in a large, at-risk population, the epidemic has a strong tendency for self-perpetuation. With large numbers of individuals capable of transmitting the virus, modest rates of risk behavior can lead to substantial rates of new infections. HIV incidence rates in IDU populations with 20% or greater seroprevalence are typically 4/100 PYAR or higher.<sup>24</sup> In the United States and in other industrialized countries, the great majority of new HIV infections are occurring in high seroprevalence populations, despite the effects of prevention programs.<sup>25,26</sup> HIV seroprevalence is typically stable in these areas, with the new infections balanced by loss to the population of HIV seropositives (often through death or disease) and the entry of new individuals into the population (almost all of whom are seronegative when entering the high risk population).

Amsterdam is a good example of the problem of persistent HIV incidence in a high seroprevalence IDU population. Beginning in 1984, the city implemented a "full set" of HIV prevention programs for IDUs, including readily available drug treatment, syringe exchange, community outreach, and drug user organizations. Both risk behaviors and HIV incidence were reduced after the implementation of these programs, and both have since stabilized.<sup>27</sup> In recent research interviews, approximately 30% of IDUs report that, in the six months prior to the interview, they injected with equipment used by others; the current incidence rate is 3–4/100 PYAR. Incidence rates of 3–4/100 PYAR (or higher in many other high seroprevalence cities) cannot be considered acceptable from a public health perspective.

Current data from New York City indicate that the large HIV epidemic among IDUs may be entering a truly declining (rather than merely stable) phase. We compiled seroprevalence data from IDUs at five different sites—a large detoxification program, a large methadone maintenance program, two street research storefronts, and city-operated sexually transmitted disease (STD) clinics.<sup>28</sup>

Subjects were volunteers at the detoxification program and research storefronts; blinded seroprevalence studies were conducted at the methadone program and at the STD clinics. At all of the sites, HIV seroprevalence declined significantly during the five years from 1991 to 1996. Seroprevalence across the five sites declined by an average of 2.67% per year, from slightly less than half of the IDUs infected with HIV in 1991 to slightly less than a third of the IDUs infected with HIV in 1996.

We also have compiled data from 12 recent (post-1992) HIV incidence studies among IDUs in New York City (results are still in preparation). These include cohort studies and studies of repeat users of services such as individuals who used STD clinics multiple times, individuals who used SEPs multiple times, and individuals who sought HIV counseling and testing multiple times at drug treatment programs. All of the HIV incidence rates from these studies were in a narrow range, from 0 to 3/100 PYAR. All of the incidence rates were below the 4.3/100 PYAR mean incidence rate for HIV infection during the period of stable HIV seroprevalence.<sup>25</sup>

Comparison of specific HIV incidence studies also suggests that the situation among IDUs in New York City is improving compared with that in Amsterdam. Incidence among participants in New York City methadone programs is 0.7/100 PYAR<sup>29</sup> compared with 4/100 PYAR among participants in the Amsterdam methadone program,<sup>17</sup> and incidence among participants in the New York City SEPs is 1.5/100 PYAR<sup>14</sup> compared with 4/100 PYAR among participants in the Amsterdam SEP.<sup>17</sup> To date, other high HIV seroprevalence epidemics among IDUs (and also among other populations at high risk for HIV) have followed the pattern seen in Amsterdam, with stable seroprevalence and reduced but still unacceptably high seroincidence. Whether the apparent new decline in the HIV epidemic among IDUs in New York City will continue and whether similar declines can be achieved in other high seroprevalence HIV epidemics will be key questions for future research.

**Summary of research issues.** Injecting drug use and HIV infection among IDUs continue to spread throughout the world, with wide variations in HIV transmission patterns among IDUs. In some areas, HIV has spread extremely quickly among IDUs, while in other areas prevalence has remained low with very few new infections. Rapid transmission appears to be linked to high rates of partner change, but we do not have good measures of partner change nor an understanding of the determinants of different rates of partner change. The great

majority of HIV prevention programs appear to reduce injection risk behavior substantially, though some programs clearly have not been able to control HIV transmission among IDUs. Once seroprevalence reaches high levels among populations of IDUs, seroincidence tends to stabilize at unacceptably high levels. Recent data from New York City, however, suggest that it may be possible to achieve declines in high seroprevalence epidemics. Research to address these problems will require many cross-site comparisons. Mechanisms to increase multisite studies of HIV prevention among IDUs are urgently needed.

### Policy Issues: What Has and What Has Not Been Done

HIV infection among IDUs has been a public health catastrophe in many countries. Present trends suggest that the catastrophe will continue in many high seroprevalence areas and will be repeated in many new areas. As discussed earlier, while additional research is needed to reduce risk behaviors and HIV transmission among IDUs, present knowledge is clearly sufficient to limit HIV transmission among IDUs. However, in many parts of the world, implementing HIV prevention programs for IDUs is far from optimal.

For some areas, a lack of resources is the major difficulty. If sufficient resources are not available to provide sterile injection equipment for medical care, it will be difficult to provide sterile injection equipment for illicit drug injection. Given the potential for cross-national transmission of blood-borne pathogens among IDUs, it would be appropriate for countries with adequate resources to support HIV prevention efforts in resource-poor countries.

For most of the countries that have not implemented appropriate HIV prevention programs, however, the

problem is not one of resources but of political attitudes. Application of present knowledge and implementation of effective HIV prevention programs require taking a modern public health perspective toward drug use and HIV infection among drug users. Modern public health perspectives emphasize pragmatic activities and the treatment and prevention of illness without condemnation of people at risk for acquiring the illness. Modern public health perspectives often require active collaboration between health workers and those at risk for disease. Specific applications of public health approaches to preventing HIV infection among IDUs have been developed under the concepts of "harm reduction" and "harm minimization."<sup>30-34</sup>

Rather than taking a public health approach to the problems of HIV infection among IDUs, many countries have applied moralistic approaches coupled with law enforcement, or have attempted to prevent health problems primarily by eliciting fear about using drugs. Within these approaches, drug users are heavily stigmatized and frequently incarcerated. The activities to prevent HIV infection are assessed mainly in terms of the messages they send about drug use; in other words, HIV prevention activities must discourage drug use and must not appear to condone drug use. Thus it becomes difficult to implement a variety of potentially effective prevention programs that target active drug users, including agonist chemotherapy treatment for addiction, SEPs, condom distribution, and support for drug users' organizations.

Research on potential improvements in health benefits through encouraging community and political leaders to adopt public health perspectives on the problem of HIV infection among IDUs may be equally as important as additional research on prevention programs.

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