Chapter 5
Treatment for Drug Abuse as a Strategy to Prevent HIV Infection

INTRODUCTION

The critical role of intravenous (IV) drug use in the spread of the human immunodeficiency virus (HIV) is well recognized and documented (216,239). Reflecting this reality, the Presidential Commission on the Human Immunodeficiency Virus Epidemic stated that the nation's ability to control the HIV epidemic depends on its ability to control the IV drug use problem (239). Providing treatment is indeed a cornerstone of any adequate strategy (105). Hubbard and colleagues proposed that treating drug abuse may have important direct (reduction of drug use) and indirect (improvement of immune function) effects on the HIV epidemic (see box 5-A) (148). Decreasing drug use for both HIV-positive and HIV-negative drug users is of great importance. In low prevalence areas, a window of opportunity exists to control the spread of the virus, so that the course of the epidemic will not parallel the past rises in seroprevalence rates seen among IV drug users in the already highly infected areas (25,28,68). In high prevalence areas, curtailing drug use could reduce further transmission of HIV.

This chapter briefly reviews the association between drug use and increased morbidity, addresses some of the methodological obstacles to the evaluation of drug abuse treatment as a strategy for HIV prevention, and reviews the relevant studies. Finally, the chapter examines other approaches to HIV prevention among IV drug users.

A decrease in drug use will most likely produce benefits besides decreasing the risk of spreading HIV. A threefold increase in overall mortality rates, AIDS incidence, and AIDS mortality rates was reported among IV drug users in methadone maintenance clinics in New York City between 1984 and 1987 (263). Similarly, from 1981 to 1986, narcotics-related deaths from AIDS and other causes, especially other infectious diseases, increased on average 32 percent. The investigators speculated that these deaths from other causes may also have been associated with HIV infection (286). For drug users in treatment, death rates were about 1.5 percent per year in contrast to the 3.5 to 8 percent for those not in treatment (88).

Box 5-A--Drugs of Abuse and the Immune System

There is evidence that opiates, as well as other drugs of abuse, exert immunosupressive effects on the immune system. These effects may be related to the drug itself, to some of the toxic substances used to process it, or to another factor associated with drug use (186,364). A related finding of importance is that methadone doses lower than 75 mg per day may reverse the immunosupressive effects of heroin, which suggests that methadone may in fact provide benefits besides curtailing heroin use to those in treatment (101). An effective dose is usually over 60 mg (257). Moreover, it has been reported that those in methadone maintenance treatment who are HIV positive and do not continue to inject drugs have a better functioning immune system than those who continue IV drug use (95).

A recent prospective study from Switzerland showed that cessation of IV drug use is associated with lower risk of disease progression among HIV positive subjects (365). For a median time of 19 months, researchers followed 355 HIV-positive patients who were not taking any antiretroviral therapy and fell into three categories: former IV drug users, enrollees in methadone maintenance during the study period, and continued users of IV drugs. Multivariate regression analysis showed that the latter group was almost 80 percent more likely to progress to acquired immunodeficiency syndrome (AIDS) than the groups who ceased IV drug use (odds ratio = 1.76). Lifetable analysis also revealed a significantly lower probability of disease progression among those who had stopped using IV drugs. After 3 years, the probability of progression to AIDS was 19 percent in former IV drug users, 24 percent in the methadone group, and 41 percent in the persistent IV drug use group (365).

Historically, IV drug users have had higher death rates from a variety of causes (overdoses, injuries, infections). They have suffered from an increased incidence of a range of infectious diseases, from all types of hepatitis and endocarditis to sexually transmitted diseases (gonorrhea, syphilis); central nervous system disorders; and skin, bone, and joint infections. All of these diseases have been reported to increase in recent years (139). Furthermore, recent studies indicate the presence of human T-lymphotropic viruses (HTLV-1 and HTLV-2) in some populations of IV drug users. These viruses have been associated with a necrologic disorder and with adult T-cell leukemia and lymphoma (139).

METHODOLOGICAL PROBLEMS

Any study of the effectiveness of treating drug abuse to prevent HIV infection involves a series of major methodological obstacles. The difficulty of establishing a cause-effect link in human studies, as discussed in chapter 4, is further exacerbated by the complex nature of HIV disease.

As is the case in other fields, the inclusion of an evaluation component in AIDS intervention programs is the exception rather than the norm (220,296). Despite the challenges that this type of evaluation poses, it is essential to conduct rigorously designed evaluation research with sufficient resources to provide policymakers with information necessary for the more effective and efficient use of resources.

Identifying the possible contribution of drug abuse treatment to the prevention of HIV infection relies on answering the following question: Did treating drug abuse with a particular modality have an effect in reducing the spread of the virus? The issue is whether the observed change was a direct consequence of the treatment or a result of one or more external, non-treatment related factors. The challenges that these question raise are discussed below.

Study Design Issues

Major difficulties in study design include the following: identifying members of a hard-to-reach population, such as drug users; recruiting them; and eliciting their cooperation for a study that could last several years. Such a study requires truthful answers about some compulsive and clandestine behaviors and practices, practices that may subject individuals to legal or social sanctions.

Random assignment to treatment modalities and control groups is not always possible. Many factors--personal, social, psychological, and legal--influence an addict's decision to enter and remain in treatment. The alternative to a randomized controlled experiment is the quasi-experimental design. Trade-offs between feasibility and the likelihood that the study will provide valid evidence of the treatment's effect become a necessity. Moreover, the more removed the study design is from a randomized clinical trial, the more prospects for a truly valid comparison fade. Subsequently, since the observed findings may not be attributed directly to treatment, alternative plausible explanations need to be considered to critically evaluate and perhaps explain any findings.

Study Outcome Issues

After the type of design option is settled, the next major question concerns choosing the types of outcomes that best demonstrate the effectiveness of the treatment. A number of potential outcomes exist and have been classified into three categories: biological, behavioral, and psychological (220).

Since, at present, preventing AIDS means halting the spread of the virus, the most direct measure of outcome is the actual seroconversion of abusers under treatment and not in treatment to HIV-positive status. Seroconversion, however, may be a rare event even among high risk-groups **(220).** On the other hand, annual rates up to 10 percent or more have been reported (145,203). Very low rates of seroconversion require that for researchers to be able to observe meaningful statistical differences, large numbers of subjects need to be recruited and retained for followup for a long time. Such a study is accompanied by the logistical and financial problems of testing and retesting people at frequent intervals for HIV infection (220).

An alternative option to the use of seroconversion or seroprevalence as an outcome measure in evaluation studies is the use of a surrogate disease with the same transmission patterns, such as hepatitis B. Another option is to use intermediate outcomes relating to behavior, such as sharing drug-injecting equipment or having unprotected sex, to measure the reduction of risk behaviors that lead to HIV infection. A last option is to use psychological outcomes that measure awareness or knowledge about the behaviors that lead to infection (220). It should be noted, however, that although awareness or knowledge may be important for some people, they do not necessarily induce behavior change (205). Which outcome measure to use is also a decision that involves trade-offs between feasibility and obtaining direct evidence. By employing behavioral and, even more so, psychological outcomes, researchers can examine more immediate impacts. On the other hand, the evidence for the treatment's effectiveness then becomes indirect.

Regardless of the outcome measure used, another serious question is the duration of the study. What is a sufficient time, not only to observe differences in behavior but also to maintain them, and how often should outcomes be measured during the study period?

Measurement Issues

Measurement of any type of outcome raises issues of reliability and validity (173,249). Reliability is the reproducibility of the results over repeated measurements and relates to the lack of random error over these repeated measurements. Validity refers to the lack of systematic error, that is, whether the measurement reflects what it is intended to measure. These common issues are of particular concern when self-reported data are used, in this case behaviors that may be private and illegal. In addition, the retrospective collection of information exacerbates problems of recall.

There is evidence that reliability maybe less of a concern than validity when people report drug-related behavior (220,296). In some studies, data collected from drug treatment centers under conditions of confidentiality have correlated well with urine testing results (200). In another study, however, the results were conflicting and produced evidence that several variables influence accurate self-reporting. In this study, the validity of self-reporting depended on the type of drug examined, with self-reporting for opiates less valid and for cocaine highly valid. Younger age and the use of paraprofessional staff were associated with a decreased rate of underreporting (199). Similarly, in an experiment at San Francisco General Hospital's methadone detoxification clinic, the rates of self-reported needle-sharing increased from 40 to 60 percent when the patients were interviewed by staff not affiliated with the clinic instead of clinic staff (189).

Another critical issue in these types of evaluations is whether to focus the measurement and the analysis on the individual or the total population of drug users and partners in a specified area. It is suggested that because the final outcome of transmission reduction is a function of the drug-using and sexual behaviors of both HIV-positive and HIV-negative individuals, the unit of measurement should be the community rather than the individual (296). However, it seems that both measures have a useful role to play in treatment evaluation. In addition, community-based research is a task with its own challenges.

Validity of the Results

The goal of a well-designed and thoroughly executed study is to eliminate or at least reduce possible sources of bias. Reducing biases ensures internal validity by decreasing the likelihood that the results are distorted and lead to misleading conclusions. But not all factors are amenable to control. Of particular concern in researching AIDS issues is the "background noise," which refers to the mass of information about the epidemic and its associated risk behaviors. This background noise has the potential to confound the outcome, thus making it almost impossible to attribute any effect solely to the treatment or other intervention under study (215). Randomized controlled trials usually can overcome these difficulties.

After the validity of the results is addressed, the task remains of extrapolating them to other populations (external validity). Those drug abusers who

were accessible, available, motivated, and willing to cooperate and complete the study may have some unique known or unknown characteristics that make them different from other abusers who did not participate. As in any study, caution should be exercised in generalizing the results to other groups in the same city, let alone to different regions of the country.

EFFECTIVENESS OF DRUG ABUSE TREATMENT TO PREVENT HIV INFECTION

There is a growing body of literature on programs to prevent HIV infection among IV drug users. The data demonstrate that drug users are capable of altering behavior to protect themselves and their partners (91,273). It is of concern, however, that drug users are less likely to change sexual practices than injection practices. A variety of studies indicate that a higher proportion of IV drug users change practices to reduce needle-sharing or clean equipment than practices related to heterosexual transmission (26,27,341).

Despite the relative availability of studies examining behavior changes for HIV prevention among IV drug users, few studies have examined the role of drug abuse treatment in preventing HIV infection. These few studies have employed different designs and different outcome measures. All but TOPS examine the effect of one treatment modality, methadone maintenance, on reducing IV drug use, and with varying strength of evidence, all point to the conclusion that methadone maintenance is beneficial in halting the spread of HIV.

Reduction in Drug Use and Risk Behaviors

The Treatment Outcome Prospective Study (TOPS) provided useful data for examining the effect that treatment regardless of modality had on behavior associated with HIV transmission, and more specifically, on IV drug use (149). During the year preceding admission, approximately 65 to 70 percent of all clients in the three admission cohorts who responded to the interview (80 percent of all clients entering treatment) were regular IV drug users. The proportion of IV drug users in various time periods (up to 3 to 5 years) after treatment was approximately 25 to 30 percent of the clients sampled for followup. This decline of IV drug use was similar for the three cohorts that entered treatment in 1979, 1980, and 1981.

The investigators suggest that this marked decline in IV drug use was a direct result of treatment and not of fear and awareness of AIDS, since these changes were similar across the three admission cohorts before and after widespread knowledge of AIDS. Treatment may exert a beneficial effect by reducing overall drug use, thus leading to reductions in IV drug use. The investigators suggest that treatment for drug abuse, "is an effective means of reducing the risk of exposure to HIV infection" (149). Without a comparison group of untreated IV drug users, however, the role of other factors is not clear.

It is troubling that those who remain regular IV drug users seem resistant to changing the route of drug administration (149). Although treatment improvements may reduce even further the number of these hard-core users, different approaches may be needed to reduce the risk of HIV infection among this group.

Ball and colleagues conducted a carefully designed 3-year study of 6 methadone clinics in 3 Eastern U.S. cities to evaluate the effectiveness of methadone maintenance not only in reducing drug use but also in reducing needle-sharing (20,21). In the winter of 1985-1986, 633 male methadone patients, including those already in treatment and new admissions, were interviewed, and 506 (80 percent) were reinterviewed 1 year later. Of those reinterviewed, 107 had ceased treatment at the time of followup. Although 98 percent of the patients had been IV users, the prevalence of IV drug use at admission was 81 percent because some abusers had been incarcerated or in another drug treatment program prior to their admission. For those who remained in treatment, the mean time in treatment was 45 months. Overall, among the 388 patients (61 percent) who remained in treatment for 1 year or more, the prevalence of IV drug use decreased by 71 percent. The largest drop in prevalence occurred during the admission period (from 81 percent with IV use to 63 percent), and subsequently the decline continued at a slower rate to 29 percent for those in

treatment 4 years or longer. In contrast, the annual relapse rate for those who ceased treatment was 82 percent, and the probability of relapse was directly related to the time out of treatment.

Patients were classified into 5 groups according to treatment status at last IV drug use (before current admission, at admission, during treatment, last year, and current IV drug use). A sizable proportion, 36.4 percent of the 324 patients for whom information was available on sharing practices, reported that they shared needles during their last or current, period of IV drug use; however, only 9 percent of all patients in treatment were currently sharing needles (2 I). The investigators also compared the frequency of needle-sharing among these groups. The results showed that the frequency of needle-sharing days per month was significantly lower for those patients whose last IV drug use occurred after admission to treatment compared with the needle-sharing days of those patients whose last IV drug use occurred at or before admission. This finding suggests that treatment had a positive effect in reducing this high-risk behavior even among those who continued IV drug use while in treatment. In grave contrast, for all those who had been out of treatment for 10 to 12 months, the proportion of needle-sharers was 48 percent (21).

A special methadone maintenance clinic for IV drug users who are infected with HIV, have symptoms of the disease, or have AIDS has been operating at the San Francisco General Hospital (23). An evaluation of 42 people enrolled in this program at 3 and 12 months showed that heroin use in the past 30 days had decreased from a mean of 28 days use to 7 days, a statistically significant difference. Cocaine use decreased, but to a lesser degree. Sexual activity had also decreased overall, but the rate of condom use remained the same. The 12-month results were quite similar to the 3-month findings (280).

HIV Infection and Entry Into Treatment

The next set of studies provide indirect evidence of methadone maintenance's protective effect. These studies looked at cohorts entering methadone maintenance at different times and observed that those who entered treatment earlier in the course of the epidemic and remained in treatment had lower HIV infection rates. This finding implies that methadone maintenance had a beneficial effect in preventing infection by reducing IV drug use, especially at the time of HIV spread. Although those who remain in treatment longer maybe self-selected, nevertheless these studies underscore the importance of having the drug user in treatment early in the spread of HIV in a specified area for treatment to exert its maximum protective effect.

A retrospective followup study of 995 patients entering methadone maintenance in the Bronx between 1978 and 1987 was conducted (132). The analysis showed that the year of entry into treatment was the strongest predictor of AIDS incidence: 11.4 per 1,000 person years for those entered before 1983 as opposed to 33.0 per 1,000 person years for later entrants. Regression analysis, which controlled for age, sex, race, entry selection factors, and length of treatment, showed that the year of entry was a stronger predictor of AIDS than race, with odds ratios of 2.6 and 1.1, respectively. One subgroup of 362 patients was enrolled in a longitudinal seroprevalence study to examine the association between methadone maintenance and HIV status. Data from this group showed an inverse relationship between the length of time in methadone maintenance and HIV seropositivity (132).

In a similar study, 239 methadone maintenance patients in a New York hospital were interviewed between 1986 and 1987 and classified into cohorts according to the year of entry into methadone maintenance. Among the three cohorts entering methadone maintenance before 1982, between 1982 and 1984, and after 1984, the HIV-seropositive rates at entry were 35 percent, 54 percent, and 57 percent, respectively (l). Lower seroprevalence rates among the earlier cohorts who continued methadone maintenance at a time of rapid spread of HIV in New York City testify to the protection offered by this modality.

Another study tested clients from 28 methadone maintenance centers in New York City for HIV from June 1988 to January 1989 and found that new entrants were 1.7 times more likely than longer-term clients to be HIV-positive (295).

In a similar analysis, 2,430 patients enrolled in methadone maintenance between 1972 and 1988 were studied to examine the relationship of IV cocaine use to HIV infection and AIDS. IV cocaine use was significantly associated with both HIV infection and AIDS mortality. Subsequent analysis revealed that entrance into methadone maintenance after 1980 was an independent predictor of HIV status and of AIDS and pneumonia deaths, with odds ratios exceeding 2.0 Low daily methadone dose (less than 60 mg) was also found to be associated with HIV antibody and with testing positive for heroin and cocaine use (376). In addition, those on 60 mg or more per day were less likely to relapse and more likely to remain in treatment (327).

A study of 454 people in drug abuse treatment clinics in New York City in 1989 examined demographic, behavioral, and clinical features of HIV infection. Multivariate analysis revealed that lower methadone dose and shorter period of drug treatment enrollment were significant predictors of HIV-positive status (40).

Also in New York City, Novick and colleagues in 1985 reported that the prevalence of HIV antibodies was 23 percent among patients in methadone maintenance as opposed to 47 percent among those not in treatment. The lowest rates were observed among those who had the longest treatment stays in methadone maintenance (228).

History of methadone maintenance treatment and HIV serostatus were examined in a cohort of 2,112 heterosexual IV drug users in San Francisco from 1985 to 1989. Those who had spent more than 60 months in methadone maintenance had half the risk of being HIV positive of those with less than 60 months (odds ratio = 0.5, confidence interval 0.35 to 0.70) (374).

The same pattern of lower seroprevalence rates among drug abusers who entered treatment early in the epidemic and remained in treatment has been observed in other countries. In Sweden, patients were tested at admission and retested during subsequent treatment. The prevalence of HIV-positive patients admitted before 1983 was 3 percent, but it was 16 percent for those admitted in 1984 and 1986 and 57 percent for those admitted in 1987 (36). There was no seroconversion to HIV-positive status among those who tested negative upon admission since 1984 and were still on the program in December 1987. Likewise in Italy, the HIV rate was 21 percent for the 1981 to 1985 entrants into methadone maintenance, and 62 percent for those entering after 1987 (291).

Medical Maintenance

The concept of medical maintenance has been described in chapter 3. Stable, non-drug using, socially rehabilitated methadone maintained subjects receive their methadone from a physician in intends as far apart as 28 days. It is reported that among the 58 respondents from the qualified group of socially rehabilitated and stable methadone maintenance clients who received their methadone at the office of a primary care physician, none was HIV-positive (229).

Interim Methadone Maintenance Program

The interim methadone maintenance program is a measure proposed by the National Institute on Drug Abuse and the Food and Drug Administration that is intended to curb the spread of HIV among IV drug users, especially among those on waiting lists for methadone maintenance. This concept calls for faster provision of methadone and HIV counseling without additional ancillary services (counseling, vocational and educational training, urine testing) until treatment space in a comprehensive program becomes available. This proposal by the U.S. Department of Health and Human Services in 1989 raised considerable debate and sharply divided the drug treatment community. The Department has since withdrawn the proposal for interim methadone. The issue nevertheless arises here because of its implications for preventing HIV infection among IV drug users.

Two relevant studies provided what seemed to be conflicting results with respect to the benefits of providing methadone alone. A closer examination of these studies, however, reveals that there is not necessarily a conflict between their findings, as they address different issues. The first study was conducted in New York City and provided evidence of a

beneficial effect (264). IV drug users on a waiting list to enter methadone maintenance were randomly assigned to two groups. One (36 subjects) received methadone daily, urine testing twice a week, and an interview, and the other (26 subjects) received only urine testing twice a week and an interview. At baseline, needle use averaged 95 times per month for both groups; at followup (after at least 30 days), needle use had decreased to 33 times per month for the methadone group but remained almost unchanged, 87 times per month, for the control group. The prevalence of heroin use for the experimental group dropped from 60 percent to 29 percent, while it remained almost stable from 62 to 60 percent for the control group. Cocaine use continued the same for both groups. It was also reported that the mean number of days since last drug injection was 33 days for the treatment group, significantly longer than the mean of 7 days for the control group. In addition, improvement in quality-of-life scores was observed for the methadone group.

Preliminary results from an ongoing study in Philadelphia have been used to argue against interim methadone. This study is designed to identify the "active ingredients" of a methadone maintenance program (59). To accomplish this, three levels of methadone maintenance services are being compared: 1) minimum methadone maintenance, with only methadone, emergency counseling, and referral services; 2) basic methadone maintenance, with counseling and urine testing, but no other additional services (family or employment counseling); and 3) enhanced methadone maintenance, with a more comprehensive set of services (medical and psychiatric care, social work, family therapy). Those who participate in the study are randomly assigned to one of these methadone maintenance levels. The followup time is 6 months, and outcome measures include IV drug use and high-risk behaviors for HIV infection.

This is an ongoing study, and data collection is in very early stages. One interim outcome measure is the proportion of patients who required "protective termination." According to the investigators, this outcome indicates an unacceptable level of illicit drug use. The criteria used were 1) either 8 total or 4 consecutive opiate-positive urine tests during the 24-week intervention, 2) either **12** total or 6 consecutive cocaine-positive urine tests during the same time period, or 3) 3 or more psychiatric emergencies. Investigators observed that more than half the participants in the minimum methadone maintenance group met the "protective termination [w] criteria, while none in the enhanced methadone maintenance did so. This finding pertains to a small number of patients but is statistically significant. Of the 15 patients assigned to minimum methadone maintenance so far, 9 met the protective termination criteria, while 2 of the 12 assigned to basic methadone maintenance did so. None of the 15 assigned to the enhanced methadone maintenance met the requirements. Although the interim report stated that blocking doses of methadone were offered, it did not report the mean dose or mention dose as a possible factor in interpreting the results. Because inadequate dosage can confound the results, evaluating the non-pharmacological components of methadone programs requires provision of an adequate dose and controlling for dose in data analysis.

When completed, this study is expected to provide useful insights regarding the relative effectiveness of methadone maintenance programs and their effects on HIV-related high-risk behaviors. If the results demonstrate the increased effectiveness of the more comprehensive methadone maintenance services, they will be in accordance with previous findings that program factors, more than client characteristics, play a major role in reducing IV drug use among methadone maintenance clients and in improving treatment effectiveness (21). On. the other hand, such findings and preliminary results would not provide evidence that an interim methadone program is ineffective, since at least 40 percent of those in the minimum methadone maintenance reduced or eliminated their IV drug use (6 out of 15 who remained on minimum methadone maintenance). From the public health perspective, it would be a gain if a similar proportion of IV drug users on a methadone maintenance waiting list in a highly infected area abstained from IV drug use and needle-sharing. Such a reduction would be another step in breaking the chain of HIV spread.

Those who support the interim concept argue that existing capacity cannot accommodate everyone

who seeks treatment. For those who want to enter methadone maintenance and are placed on a waiting list, the alternatives are limited. To the extent that their physical dependence on opiates leads them to continue shooting heroin intravenously to alleviate drug hunger and withdrawal symptoms, they continue to engage in the high-risk behavior of needle-sharing (225). The provision of interim methadone and HIV counselling to those individuals who cannot be admitted because no comprehensive treatment is available attempts to offer an immediate response to this urgent situation.

Opponents of interim methadone argue that the multiplicity of problems that drug abusers bring with them into treatment--psychiatric disorders, multiple drug abuses, other illnesses, limited or no education, unemployment, legal problems, and homelessness--calls for an uncompromised, comprehensive approach to the whole problem. During current efforts to expand treatment capacity and improve its quality, some have argued that relaxing drug treatment requirements through an interim program would send the wrong message and "undermine the foundation of treatment structure" (235,363). Moreover, there is the danger that the existence of an interim methadone program in a given treatment facility would increase pressure on the staff to discharge clients prematurely and to admit those who are on the waiting list. More importantly, opponents argue, despite the intention of patients to transfer to a more comprehensive setting, given the existing realities, they might remain on interim status indefinitely. Thus, the interim methadone program might evolve from a temporary substitute for comprehensive treatment to a "permanent and less costly part of the treatment system" (235,363).

All these concerns are worth considering. The HIV epidemic, however, adds an additional dimension to the problem and warrants a clear focus on societal priorities. Of the estimated 500,000 heroin users in the United States, approximately 400,000 are not currently in treatment (225). The increased outreach efforts initiated by the HIV threat are, and will continue, bringing more people to treatment. It is unclear whether and how the system is prepared to respond in a timely fashion. Interim methadone has been proposed exclusively as an alternative to continued heroin injection in the street by the hundreds of thousands of heroin users who do just that three or more times every day.

It is important to note that since methadone has no pharmacological action against cocaine, IV use of cocaine may continue. Thus, the argument is used that interim methadone will have a minimum impact on IV drug use, and will not protect against HIV spread. Not all heroin users, however, also abuse cocaine intravenously. Rates of IV cocaine use, are lower in most narcotics addicts than their rate of injecting heroin (9). A survey in 1989 of 24 methadone maintenance centers around the country revealed that the prevalence of concurrent use of cocaine varied from O to 40 percent (299). In 8 programs, the prevalence ranged from 20 to 40 percent; in the remaining 16, it ranged from O to 15 percent. In 5 methadone maintenance clinics surveyed in New York City, the proportion of cocaine users was between 8 and 21 percent in 4 of the programs and 40 percent in the fifth (299). It seems, however, that cocaine abuse may fall while heroin abusers attend methadone maintenance, most likely among those who use one drug to mitigate the effects of the other. TOPS data showed that the proportion of regular cocaine users decreased from 26.4 percent 1 year before methadone maintenance treatment to 9.4 percent at 3 months in treatment (149).

The potential for HIV spread exists each time needle-sharing and injection occur. These are practices in which people both outside the treatment milieu and those on waiting lists for methadone maintenance engage. With respect to the latter, findings from a still unpublished study are of particular concern, although the numbers are small. This study showed that of those opiate abusers seeking treatment in New Haven in 1988 who were not IV drug users at the time of clinic intake, 35 percent (6 of the 17 patients who were intranasal heroin users) either started or resumed IV drug use by the time of admission, 1 to 4 months later (256).

Pharmacologically, an adequately high dose of methadone addresses the biochemical aspects of heroin abuse by blocking drug hunger and the onset of opiate withdrawal symptoms. In practical terms, those individuals who respond to methadone will

stop the IV use of heroin, breaking one link in the transmission chain of HIV. Any sustained reduction in injection frequency reduces the rate of HIV transmission. In medical and epidemiologic terms, this is a very important step toward shrinking the pool of people at risk of spreading or contracting HIV infection. From a public health perspective, this is a need that cannot be ignored. It is possible that interim methadone maintenance programs may be more appropriate for certain areas, such as those with a large number of IV drug users and long waiting lists (for example, for New York City as opposed to a rural community) (see ch. 3). Concerns for deterioration of existing services because of interim methadone might be addressed by the "development of appropriate guidelines for both interim and comprehensive maintenance treatment and monitoring by an appropriate quality assurance agency" (9).

ADDITIONAL APPROACHES TO PREVENT HIV INFECTION

To understand better the contribution of drug abuse treatment as a strategy to prevent HIV infection, one must consider a framework of policies. These policies in turn should be based on consideration of the following facts: that the probability of contracting HIV is a function of many variables and that drug users in treatment may differ in attitudes and motivations from drug users not in treatment.

The probability of contracting HIV from drug use is a function of both the risk from needle use and the risk from sexual practices. In both cases risk depends on the prevalence of HIV infection among partners and their infectiousness. The risk from needle use also depends on the number of persons sharing equipment, the use of rented or borrowed needles, the frequency of injection, and the frequency and effectiveness of needle-cleaning behaviors. The risk from sexual practices depends on the type of practice, the number of partners, and the frequency of preventive measures, such as condom use.

Moreover, drug users differ widely in their attitudes and practices. Some drug users smoke or sniff heroin, cocaine, or amphetamines but do not yet inject them. In addition, of those who are using drugs intravenously, the vast majority are not currently in drug treatment; some have a desire to enter but cannot, due to the lack of available space, and some simply do not want to get treatment for their drug abuse (45,239,324,332a). Of those who are in treatment, some actively sought it and are motivated to complete it. Others are not personally motivated; although some kind of family, social, or legal pressure brought them into treatment, they also may respond to treatment. Finally, some enter treatment for temporary relief from the "hustle" of drug use or to reduce their tolerance to the abused drugs

This diversity makes it essential from a public policy perspective to distinguish between risk elimination and risk reduction, with the latter being a viable and vital public health objective. The justification for such a distinction is further reinforced by the reality that there is no immediate, effective way to treat cocaine abuse, a tragic reality that has direct consequences for the spread of HIV infection.

From the public heath perspective, the objective is to control the HIV epidemic. A comprehensive HIV prevention strategy needs to keep a sharp focus on this objective and to recognize all the above realities. Both the urgency of the epidemic and a realistic assessment of drug abuse dictate that there should be a hierarchical structure of tactics against HIV infection, and appropriate multiple policies should take account this structure. As Sorensen has stated with regard to drug use, tactics include total abstinence, not injecting drugs, not sharing needles, and, if sharing needles, then cleaning needles effectively. With regard to sexual activity, the hierarchy consists of abstinence, monogamous relationships, and safer sexual practices, including use of condoms with casual and regular partners (281).

The Importance of Preventing IV Initiation

Preventing drug sniffers and smokers from switching to injection can eventually reduce the pool of eligible people at risk of spreading HIV. The most common factors mentioned among heroin sniffers that promote initiation of IV use are fear of tolerance to sniffed heroin and social pressure from friends who inject drugs. Clearly, programs are

necessary to address these issues, perhaps by emphasizing techniques to cope with social pressure and providing counseling about HIV infection (93).

Risk Reduction Through Needle-Exchange Programs

To prevent HIV transmission, short of abstinence, risk reduction implies safer drug and sexual practices. One approach is to provide the means for safer practices, in an attempt to reduce the harm associated with IV drug use to both the user and society. The means for safer practices are clean needles, bleach to disinfect used equipment, and condoms. The provision, especially of materials related to safer IV drug use, is considered controversial because of the argument that the mere provision of injection equipment encourages drug use and consequently leads to increased use. There is no empirical support, however, for such an argument.

Needle exchange programs in which a person can exchange used needles for new ones have been operating in England, Holland, Australia, and a few sites in the United States. The premise is that scarcity of injection equipment contributes to sharing and multiple uses, thus increasing the chances of HIV transmission. Those who support these programs view them as one of the many HIV prevention strategies making up a comprehensive strategy to halt the spread of the infection. These programs are targeted specifically to the large numbers of drug users who are not in treatment and who continue to inject drugs and share needles. In fact, these programs may provide the vehicle for educating people not in treatment and for recruiting them into treatment. The underlying philosophy is that, "keeping drug users alive is more important than keeping them clean. Recovery is possible after relapse, but it is not possible after death" (278).

Opponents argue that providing injection equipment sends wrong messages, since abstinence from drug use is inconsistent with exchange of needles. They argue that these measures may be perceived as condoning drug use and that the provision and availability of needles will lead to increased drug use:

The evaluation of needle-exchange programs raises serious methodological problems and is often hard to conduct. Biased selection into the program and high turnover of this population with losses to followup are major obstacles to valid evaluations. Furthermore, even if these programs are shown to be effective in reducing high-risk behaviors that lead to HIV infection, it is even harder to identify their contribution to slowing HIV infection in a community. Nevertheless, advances in research methods have allowed rigorous research, including randomized controlled studies, to be conducted in areas, such as treatment for drug abuse, previously considered impractical. Methodological problems, therefore, should not stymie efforts to evaluate needle-exchange programs.

Despite methodological problems, studies have been performed both in Europe and the United States. An evaluation of a program in London found that in the year prior to the exchange scheme, 49 percent of 133 participants had shared needles (131). Seventy-six of the initial sample of 133 were reinterviewed for a second time. Approximately 1 month and 4 months into the program, 85 and 89 percent respectively, had not shared needles in the 4 weeks before the interview. An evaluation was also performed of a program in Tacoma, Washington (%). The evaluation examined the number of opportunities for HIV infection, i.e., the frequency of injection with used or borrowed equipment, among 106 participants. A statistically significant decline was observed from a frequency of 62 injections per month with used or borrowed equipment before the exchange to 44 per month after the exchange. Another analysis of drug use trends from the same program found no significant difference in the overall rate of drug injection before and after participation in the program (125). Findings from all these studies, however, come from self-reported behavior. None of the studies had a control group, and the representativeness of the IV drug users interviewed was not clear.

It is difficult to evaluate the effect of such programs in slowing the rate of HIV transmission in a particular community, especially because of the long latency period of HIV infection. Hepatitis B infection is transmitted among IV drug users through

the same routes as HIV and has a considerably shorter latency time. A 1989 evaluation of the Amsterdam needle-exchange program, which was initiated in 1984, included an assessment of the annual incidence of hepatitis B infection. The incidence of hepatitis B infection declined steadily from 49 per 10,000 drug users in 1984 to 9 per 10,000 in 1989. This decline, as the authors state, "indicates that a change in injecting behavior indeed seemed to occur among IV drug users in Amsterdam" (70).

Summarizing presentations at the Fifth International Conference on AIDS in 1989, Wohlfeiler commented that needle-exchange programs may serve as contact points for education and referral (Wohlfeiler 1990). In the recent "What Works" conference on drug abuse treatment, Stimpson examined strengths, limitations, and areas of further development with respect to these programs. Based on information from Europe and Australia, the author concluded that syringe exchange programs have attracted people with lower levels of risk behavior and have experienced high turnover and low retention rates. Stimpson found that injectors who attend syringe exchange programs reported desirable, although small, changes in behavior (272). A recent evaluation study was particularly enlightening in understanding needle-exchange programs (354). This study showed that needle-exchange programs did not automatically lead to sweeping changes in high-risk behaviors, although the proportion reporting borrowing or lending of syringes decreased over time among participating IV drug users (354). The authors speculated that a combination of providing the means to reduce risk and intense counseling may be needed to produce the necessary drastic changes in risk behavior. Their point underscores the importance of comprehensive strategies that consider the complexities of drug abuse.

Overall, available studies do not provide evidence to support claims that provision of needles makes non-IV drug users switch to IV use or that such provision leads to increased drug consumption. In fact, decreases in the frequency of sharing have been reported. On the other hand, available studies do not allow one to conclude that needle-exchange programs alone reduce risky behavior. The design of the studies so far has not allowed researchers to separate the effects of the program from other influences, such as the characteristics of the users who continue to participate. This situation has often characterized community intervention studies. Needle-exchange programs have raised heated debates. The urgency and threat of the HIV epidemic, however, make it even more important that innovative prevention approaches have a fair chance to be tested and evaluated.

Sale and Possession of Injection Equipment

Public policies in the United States limit availability of injection equipment. It is illegal in all but 11 States to sell syringes without a prescription (87). Furthermore, drug paraphernalia laws make possession of injection equipment illegal in almost all States (87).

Certain European countries do not have laws restricting the sale and possession of injection equipment. Research conducted in France, Austria, and Scotland, countries that allow over-the-counter sales of syringes, assessed the impact of programs that educate pharmacists about the need to prevent HIV. There were large increases in the number of drug users purchasing and using sterile injection equipment (87).

Paraphernalia laws that make it illegal to possess injection equipment are impeding evaluation of over-the-counter sale of syringes in those States permitting purchase without a prescription. The clear and present danger of the HIV epidemic increases the pressure for reevaluation of public policies with regard to the purchase and possession of syringes, especially since there is no empirical support to claims that mere availability of injection equipment leads to increased injections (27,87). Since sharing occurs because of scarce injection equipment and for social reasons, preventing the spread of HIV infection among IV drug users maybe enhanced by complementary measures to providing treatment or just providing the means for safer practices, such as interventions to change social patterns with regard to sharing. Wiebel states that "social networks of IV drug abusers as a whole should begin to discourage the sharing of drug injection equipment--including rinse water, cookers and

cottons--or at least the sharing of syringes that have not first been disinfected" (372).

The Role of Outreach Programs

Implementing effective strategies to prevent HIV infection calls for access to as many IV drug users as possible, both those who are in treatment and those who are not. Drug treatment programs provide the means for the former, while outreach programs may accomplish the latter.

An estimated 130,000 clients in drug and alcohol treatment facilities as of Sept. 30, 1989 were IV drug users at the time they started treatment (332a). On the other hand, the estimated number of IV drug users in the United States ranges from 1.1 to 1.8 million (45,64,324). That ***10 to*** 20 ***percent of IV drug users in the United States are in treatment at any time*** implies that at least one million or more are not in treatment. Since it is estimated that approximately 80 percent of IV drug users have sexual partners that are not using drugs, a target population of over 1.8 million may be engaging in high-risk behaviors for contracting HIV (318). Estimates of IV drug users and their sexual partners at risk of HIV infection have reached as high as 4.5 million (243).

Because so many IV drug users are not in treatment, outreach programs could make a substantial contribution. In Chicago, 42 percent of those contacted through an AIDS outreach project had never been in treatment (370). Similarly, in New Jersey, 40 percent of those persons redeeming vouchers for a free detoxification program had never been in treatment (152).

A variety of community-based programs in more than 50 cities in the United States are tailored to reach drug users not in treatment and their sexual partners. The majority of trained community outreach workers are ex-abusers themselves. The effort to reach those groups takes workers to shelters, street corners, and shooting galleries. The operating premise is first to reach the addict, next to gain his or her confidence, and then to provide a series of HIV-prevention activities. Such programs offer individual or group educational sessions with instructions on safer drug use and safer sexual practices, HIV testing and counseling, and referrals to drug treatment and other social services. Outreach programs through their contacts with drug users who are not in treatment are a key vehicle for applying measures that may be appropriate for successful risk reduction efforts, such as information on AIDS prevention, provision of the skills to accomplish desired behavior change, and reinforcement for long-term maintenance (92).

The National AIDS Demonstration Research Project, an ongoing program, is the largest U.S. intervention program relating to IV drug users not in treatment (340). As of July 1990, 41 community-based projects throughout the country have enrolled 38,635 IV drug users and their sexual partners (341). According to one of its principal investigators, it has already demonstrated that it is feasible to identify and educate active drug users in the community setting (369). Preliminary results show that IV drug users not in treatment can modify their behavior to reduce the risk of HIV infection (369). The data have indicated that 50 percent or more of those who received an intervention reduced the frequency of IV drug use. The intervention included intensive counselling, skills training, educational materials, and peer group support (37).

Preliminary data based on followup interviews of 1,584 IV drug users who were recruited between 1987 and 1989 and who had completed both the initial and first 6-month followup interviews are available from five cities: San Francisco, Chicago, Miami, Philadelphia, and Houston (341). Followup rates in all cities but Houston were greater than 65 percent (45 percent for Houston). Substantial proportions reported decreasing IV drug use, from 49 percent in San Francisco to 75 percent in Miami. These figures include complete cessation of all IV drug use from 16 percent of followup respondents in Chicago to 47 percent in Miami. Similarly, the proportion reporting either never sharing or never borrowing "works" increased between baseline and followup. Substantial percentages of respondents reported decreases in sharing or borrowing injection equipment. Of those respondents who continued to inject drugs at followup, except for those who reported always using new needles, 20 to 39 percent reported increased use of bleach. Reported use of condoms also increased in all five cities. Overall,

however, reported reductions in sexual behaviors (use of condoms with steady or multiple partners) lagged behind reduction of high-risk drug use behaviors.

There is also evidence that outreach programs,by encouraging drug abusers to seek treatment, have increased the demand for treatment (107). For example, in Tacoma, Washington, of 218 treatment vouchers distributed, 75 percent were redeemed and led to detoxification treatment. Almost half of those who entered detoxification treatment (48 percent) were subsequently transferred to methadone maintenance (244). Nearly 50 percent of 1,884 IV drug users in New Jersey redeemed their coupons for free and immediate entry to 21- or 90-day methadone treatment (341). The proportion of individuals in the National AIDS Demonstration Research project entering formal drug treatment varied from 14 to 35 percent, with the lowest rates in Miami and Houston (14 and 15 percent, respectively), where the capacity of publicly funded drug abuse treatment programs is reported to be limited (341).

Similarly encouraging results are reported by Watters and colleagues from a community-outreach program in San Francisco (361,362). Elements of the outreach program included provision of bleach and condoms and a clandestine needle-exchange program. A series of seven cross-sections of 2,114 heterosexual IV drug users, 57 percent of whom were not enrolled in treatment programs at the time of the interview,' between 1986 and 1989 revealed a change in HIV high-risk behaviors (362). The proportion reporting no needle-sharing gradually increased from 8.8 percent in 1986 to 53 percent by late 1989. Decreases in needle-sharing were also reported among IV drug users entering treatment in San Francisco (124). A combined measure of needle hygiene, which included frequency of use of bleach, no needle-sharing, and cleaning syringes with alcohol, increased nearly five times. At baseline in 1986, needle hygiene was reported 13 percent of the time, while in 1989 it was reported 80 percent of the time (362). Frequency of injection for both those in treatment and those not in treatment declined over time. Condom use increased significantly over time from 4 percent to nearly 30 percent by late 1989. Hepatitis B eases among injection drug users diagnosed at San Francisco General Hospital declined from 36 percent in 1987 to 23 percent in 1989. Although HIV seroprevalence almost doubled from 7 to 13 percent between 1986 and 1987, it thereafter remained at about the same level, 11.4 percent in 1989 (362). Overall, it has been reported that seroconversion in San Francisco has also leveled off at 2.4 percent annually (124). These reported major behavior changes of key risk behaviors coincided with the implementation of outreach efforts.

It should be noted that providing the means for IV drug users not in treatment to switch to safer behaviors (bleach, condoms) reaches those at high risk of contracting and transmitting HIV. These people may include those who want treatment and are on waiting lists, those who are contemplating and with some encouragement may seek treatment, and those who currently do not have a desire to stop using drugs. From the public health perspective, provision of material on safer practices is a justified action. Overall, these outreach programs may lead to behavior changes, perhaps not for all users and perhaps not each time they engage in drug or sexual activities. Because AIDS is such a lethal infectious disease, any gain in delaying the infection from spreading to more people is important. "Any decrease in injection frequency is likely to reduce the risk of further HIV spread.

SUMMARY

The findings of available studies are consistent, despite the various designs and outcome measures used. Methadone maintenance has a positive effect in reducing the spread of the HIV virus, because, if properly implemented, methadone maintenance can help reduce or even eliminate abusers' desire to inject drugs. Time spent in treatment and adequate methadone dosage have been consistently found to be important predictors of successful outcomes, in particular, reduction of drug use and needle-sharing practices.

No studies similar to the ones described above for methadone maintenance clinics have been performed among patients of therapeutic communities or outpatient drug-free programs. With an average stay of

18 to 24 months in traditional therapeutic communities, a study would require a long followup time.

Risk behaviors leading to HIV infection are not confined to IV drug users seeking methadone maintenance treatment. It has been reported that 20 percent to 75 percent of those entering therapeutic communities report either IV drug use or unprotected sex (22,33). It would be reasonable to assume that, given the substantial drug-free rates for those who complete treatment or even stay a substantial amount of time in treatment, this modality has the potential to reduce the high-risk behaviors associated with the spread of the HIV, at least among those who stay in treatment for a certain time.

From the public health perspective and for society's benefit, spread of HIV infection needs to be halted. Prevention and control of the HIV epidemic among IV drug users, their partners, and offspring require comprehensive strategies that reflect the epidemiological characteristics of HIV infection and the complexities of drug abuse. Drug treatment alone, despite its effectiveness in reducing IV drug use and needle-sharing is not sufficient. The fact is that an overwhelming majority of IV drug users are. not in treatment (45,218,332a,341). As many as 1 million or more not in treatment engage every day in behaviors that place them at high risk of contracting or transmitting HIV. Outreach programs are an integral component of intervention strategies aimed at those IV drug users not in treatment. Preliminary results from different parts of the country have found that IV drug users not in treatment are either stopping drug use or changing their behavior to reduce the risk of HIV infection (341). Outreach programs also generate demand for treatment (341). Experience from New Jersey and Washington has shown that when financial barriers to treatment are reduced, drug users who have never been in treatment come forth and enter treatment.

Finally, it is increasingly important to reconsider the desirability of additional interventions aimed at IV drug users not in treatment, such as needle-exchange programs and providing methadone and HIV counseling to those on waiting lists. Fears that exchange programs will lead to increased injection are not supported by empirical evidence. Providing blocking doses of methadone to heroin users on waiting lists seems to be a better public health measure than having them continue daily injections of heroin. In light of the urgency of the epidemic, it is reasonable to consider these and other programs to reduce drug users' risk of contracting HIV.

Overall, it should be emphasized that regardless of the intervention to prevent HIV spread, what is ultimately important in medical and epidemiologic terms is the fact that any sustained reduction in injection frequency is likely to reduce the rate of HIV transmission. Such efforts need to be consistent and persistent over time to break the chain of HIV transmission.