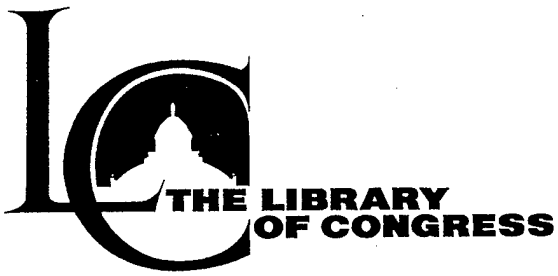

METHADONE MAINTENANCE TREATMENT AND HIV SEROPOSITIVITY

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Preface

The purpose of this study is to provide a perspective on key issues in methadone maintenance treatment for opiod dependence and its role in the containment of HIV transmission. The key issue addressed is the following: Is methadone maintenance treatment effective in reducing the rates of HIV seropositivity?

The study describes and analyzes the development of methadone maintenance as a treatment modality for opiod dependence and reviews the available observational research evidence on the effectiveness of methadone maintenance treatment, the basic facts about HIV and AIDS, and the epidemiology of HIV infection among injecting drug users. The limited amount of research literature that has evaluated the impact of methadone maintenance treatment on the transmission of HIV/AIDS among drug users is summarized. With the advent of HIV in the early 1980s and the rapid increase in its prevalence among injecting drug users in the United States, its containment has become a relevant outcome on which to assess the effectiveness of methadone maintenance treatment. As will be seen from the evidence, there is good reason to believe that methadone maintenance is the best available treatment option for preventing HIV seropositivity among opiod dependent drug users.

This study is based on scholarly articles, government reports, and monographs, largely retrieved from the general collections of the Library of Congress and the National Library of Medicine. Every effort has been made to incorporate as broad

and representative a sample of findings as possible. However, because of the nature of the subject, this study cannot be totally comprehensive in such an expanding field, where new areas of research and intervention appear daily. Where little or no research evidence is available, the study relies upon the plausibility and logic of the authors' views as expressed in the professional literature.

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Introduction

The human immune system disorder now known as Acquired Immune Deficiency Syndrome, or AIDS, was first reported in the United States in 1981, when physicians in New York City and San Francisco were confronted with the mysterious deaths of a growing number of young men who had illnesses usually held in check by the body's natural defenses. In the decade that followed, over 144,000 American men, women, and children lost their lives due to the Human Immunodeficiency Virus (HIV), the agent that causes AIDS.[1]

The Human Immunodeficiency Virus

The Human Immunodeficiency Virus, a retrovirus that replicates itself by invading and destroying cells of the body, attacks all of the body's immune system, gradually impairing the ability to fight illness and leaving a person vulnerable to a range of opportunistic infections. Transmission occurs primarily through five activities: (1) male-male sex; (2) male-female sex; (3) transplantation of infected organs or tissues, including the transfusion of blood and blood products; (4) use of unsterilized skin-piercing instruments, including needles shared during injection drug use or in health care setting; and (5) birth to an HIV-infected woman. The possibility of other modes of transmission such as insect bites has been proposed and investigated but there is considerable evidence against such forms of transmission and no evidence to support such theories.[2]

Although the brunt of the epidemic in the United States to

date has been borne by the homosexual and bisexual community, a closer examination of the statistics provided by the Center for Disease Control (CDC) reveals that the pattern of HIV/AIDS cases has begun to change significantly in the last few years. In addition, although the number of new HIV/AIDS cases among homosexual and bisexual men continues to increase, the rate of progression has begun to slow.

HIV Epidemiology

Before 1985, 63 percent of HIV/AIDS cases occurred among white, homosexual and bisexual men with no history of injection drug use. Further, prior to 1985, only 18 percent of the reported cases involved heterosexual injection drug users and only 2 percent were the sex partners or children of intravenous drug users (IDUs).[3]

Although the majority of newly reported cases of AIDS are still among white, homosexual-bisexual men, new infections among injecting drug users continues to climb at an alarming rate. Of the 46,052 AIDS cases reported in the 12-month period ending in February 1992, 53.1 percent were non-drug-injecting homosexual-bisexual males. However, the representation of heterosexual IDUs had increased to 23.8 percent and the incidence of disease among their sex partners and children more than doubled to 4.7 percent.[4] Hence, as the number of reported cases of AIDS has increased, so, too, has the proportion of cases related to injection drug use. In New York, New Jersey, Connecticut, and Puerto Rico, the number of newly reported cases of HIV/AIDS among

IDUs has equalled or exceeded new cases reported among non-IDU, homosexual-bisexual men.[5]

Intravenous drug users have become the second largest risk group for AIDS and the main route of transmission of HIV in heterosexual and perinatal cases.[6] HIV seropositivity is related to the frequency of drug injection, injection with used needles, sharing needles with strangers or acquaintances, injecting in a "shooting gallery," injecting with cocaine, and injecting with heroin.

The Surgeon General of the United States, the President's Commission on AIDS, the National Academy of Sciences, and the Center for Disease Control recognize drug abuse and injecting drug users as the most important factor today in the spread of HIV/AIDS in the United States. They predict that the trend will accelerate in the next few years as the HIV epidemic spreads to the general population in those areas with high concentrations of IDUs.

HIV Prevention Strategies

As there is no effective treatment or vaccine available either to cure AIDS or to curb the transmission of HIV, new targeted prevention and risk-reduction programs and strategies are viewed as the means to reduce further transmission. In the case of injecting drug users, these changes amount either to abstinence, altering the route of injection, or safer injecting practices. Efforts must be directed not only at changing attitudes but also at providing practical alternatives. Goals

should be realistic given that intravenous drug users are more likely to minimize risk rather than eliminate behavior, and programs must focus on changing the norms surrounding needle-sharing and sexual activity while at the same time fostering positive attitudes toward the adoption of risk-reduction behaviors.

Access to clean needles, "bleach and teaching kits," free condoms, medical care and substance abuse treatment are essential adjuncts to drug culture behavior and patterns of use. To effectively limit the number of HIV- infected persons, prevention must also be aimed at reducing the number of persons initiated into injection use, as well as reducing the number of sexual partners of injection drug users. Some parts of the nation, for example the South Bronx, are approaching HIV infection levels among young addicts comparable to those observed in central Africa[7].

The growing pervasiveness of HIV within the drug-injecting community and concomitant potential for perinatal and sexual transmission clearly indicate a need for acquired immune deficiency syndrome prevention efforts targeted to this population.

Illicit Drug Use

IDUs present a particular challenge to the treatment community. This population, frequently termed "hidden" because its illegal and stigmatized activities require concealment from society, is considered difficult to access. Unlike the gay

community, IDUs in the United States are not mobilized as a cohesive and effective advocacy movement promoting prevention among their ranks.[8] To combat the spread of HIV/AIDS among this population, public health officials have begun to integrate HIV/AIDS prevention and education efforts with drug treatment programs. It is estimated that at any given time there currently is no available treatment for 90 percent of the nation's IDUs. Without expanded AIDS prevention programs targeting addicts not in treatment, the battle against HIV contagion will be lost, particularly in cities already experiencing intermediate rates of HIV seroprevalence.

An objective review of the available clinical and sociological research data demonstrates that of the three modalities available for treatment of IV drug use and its relationship to HIV, that is, methadone maintenance, residential drug free, and outpatient drug free, the methadone maintenance modality, while not a panacea, promises to be the most effective preventive measure for reducing the risk of transmission of HIV seropositivity and AIDS.[9]

Methadone Maintenance Experience

The methadone maintenance program, founded in 1964 in New York City by Drs. Vincent Dole and Marie Nyswander, was originally implemented to provide a comprehensive medical and rehabilitative service to intravenous heroin addicts. It provided an orally ingested alternative to injected opiods, such as heroin, which made it an attractive option for heroin users who

were either ill-prepared or unable to become abstinent. With time and expansion of services, methadone maintenance changed from a medically supervised treatment for a designated population of heroin addicts to a more diversified form of treatment and rehabilitation provided to addict patients.[10]

The extent of change to the Dole-Nyswander methadone maintenance model has been extensive. Changes include variations in the number of patients treated in individual programs; qualifications of the directors; qualifications of staff; amount and type of counseling and medical services provided; methadone dose commonly prescribed; and policies relating to urine-testing, take home methadone, and many other facets of treatment. In the early 1990s, however, the methadone maintenance treatment program was still far from being a uniform entity.

Although the effect of the HIV/AIDS epidemic on methadone maintenance treatment in the long run remains to be seen, in 1994 it is the only effective means of slowing the spread of HIV infection among drug abusers and chronic heroin addicts.[11] Because methadone maintenance treatment is associated with reductions in frequencies of needle use and needle sharing--factors that compound the risk of HIV seropositivity--and because methadone maintenance treatment eliminates heroin abuse and affords the opportunity for social rehabilitation, successful methadone maintenance should effect a major risk reduction for HIV infection.[12]

The need for methadone maintenance programs is even more

evident when one considers a comparative study of street and treatment IDUs, which found that street IDUs were more likely to engage in high-risk sexual and drug using behaviors. A study of methadone maintenance programs found that prevalence of high-risk behaviors was greatly reduced among IDUs in treatment.[13]

Methadone Maintenance and Containment of HIV

The differences in behaviors may account for the disparity observed in a few cities between HIV seroprevalence rates of IDUs in methadone treatment programs and those recruited from the streets. For example, a 1987 San Francisco study found that IDUs enrolled in treatment had a 7 percent HIV seropositivity rate, compared with a community sample that had a 16 percent rate.[14] In Philadelphia, at 19 different sites, including prenatal care and sexually transmitted diseases clinics and ten alcohol and drug abuse treatment centers, data was collected on 2,287 IDUs who were tested between July 1989 and October 1990. Fourteen percent of the sample case were HIV positive; however, of the 110 street IDUs who were tested between the months of December 1988 and May 1990, 21 percent of the sample were seropositive.[15]

A Chicago-based study of street IDUs found seroprevalence rates ranging from 15 to 31 percent in different social environments. During roughly the same time frames, other research studies reported a 12.8 percent HIV seroprevalence rate among addicts in treatment programs and a 0 percent rate among long-term stable methadone maintenance patients in Chicago.[16] The Chicago-based study was conducted by A. Barthwell and associates

of the Addictions Research Institute of the Department of Alcoholism and Substance Abuse of the state of Illinois. A group of 95 subjects was tested for the presence of antibodies for the human immunodeficiency virus on a blind basis. Results from the random sample of 31 subjects tested with enzyme-linked immunosorbent assay (ELISA) showed that none of the subjects tested positive for HIV. Although the sample was drawn from a cohort group, half of the Chicago area methadone maintenance treatment programs were represented in the cohort.

The Chicago results suggest that methadone maintenance programs can be effective preventive instruments for the human immunodeficiency virus. The rsults of the study are impressive considering that rates of seropositivity among street population of IDUs not enrolled in any formal treatment program in the metropolitan Chicago area were approximately 20 percent, compared to the 12 percent rate of infection for IV drug users enrolled in methadone maintenance treatment.[17]

In another study undertaken by D.M. Novick and associates, 58 (85%) of 68 former heroin addicts agreed to participate in a study to measure antibody to HIV and hepatitis B virus markers. All of the subjects were long-term socially rehabilitated methadone maintenance patients who had completed five or more years of methadone maintenance, had a stable working history, lack of any major criminal activity, absence of alcohol or drug abuse, and a reliable clinic attendance record.[18] All of the subjects were provided pretest and post-test HIV counseling.

Antibody to HIV was determined in all subjects by both the enzyme-linked immunosorbent assay and indirect immunofluorescence. Enzyme-linked immunosorbent assay was used to determine hepatitis B surface antigen and antibody and core antibody.[19]

Results of the Novick study demonstrated that none of the 58 long-term methadone maintenance subjects had antibody to HIV. In 53 (91 percent) of the patients, one or more markers of hepatitis B virus infection was observed. Previously, all the patients had engaged in high risk practices for HIV seropositivity, such as needle sharing, long-term drug use, attendance in "shooting galleries" (sites where drugs are injected and needles rented), and promiscuous sexual practices with other drug abusers.[20] None of the patients, their spouses, or their children was diagnosed with acquired immunodeficiency syndrome or displayed other relevant evidence of HIV seropositivity. Novick concludes that, since these former heroin addicts had entered treatment before or at the start of the epidemic of HIV infection, and given that the current rate of HIV seroprevalence is in the range of 55 to 60 percent among New York City drug abusers, it is safe to assume that successful cessation of drug abuse during methadone maintenance treatment enabled them to avoid HIV seropositivity. It must be remembered that before their methadone maintenance treatment, these subjects were hard-core, long-term heroin users engaging in extremely high-risk behaviors and practices for HIV. The high prevalence of exposure to hepatitis B virus among study

members (53 of 58 patients--91 percent) attests to the high degree of past needle utilization.[21]

Novick's hypothesis that successful methadone maintenance treatment can protect parenteral drug abusers from HIV seropositivity is substantiated by his findings. However, as the study was performed under an uncontrolled setting, his hypothesis can not be proved.

Nonetheless, Novick's results are supported by a number of other findings. In a Swedish study that approximated a random selection procedure, nearly all the subjects who entered a methadone treatment program after 1983 had previously applied for admission and had been rejected. The applicants were accepted or rejected for treatment in an almost random fashion depending upon availability of space at a methadone center. Three percent of the patients who entered methadone maintenance treatment before 1983 were found to be HIV seropositive, compared with 16 percent of those who entered treatment during 1984-1986 and 57 percent of subjects who entered treatment after 1987. No seroconversions were detected in any of the subjects who had previously tested negative for HIV on admission since 1984.[22] This study, which appears to be independent of selection bias, provides strong evidence that methadone maintenance treatment shelters its recipients from HIV seropositivity.

Other retrospective studies have found a powerful association between the length of treatment in a methadone program and low seropositivity rates. In New York, patients who

had entered methadone treatment before 1982 were found less likely to be HIV seropositive than those clients who entered treatment after 1982.[23] Other researchers, for example, Abdul-Quader and Schoenbaum, have detected an inverse correlation between the duration of time involved in methadone treatment and the presence of HIV seropositivity among injecting drug users in New York City.[24] Two other studies have found that clients in methadone treatment programs were more likely to be HIV seronegative than clients in detoxification programs[25] and those not yet receiving methadone treatment.[26]

Similar results demonstrating the effectiveness of methadone maintenance in the prevention of HIV seroprevalence have been reported in Italy.[27] A group of 219 drug addicts residing in Bergamo, Italy were tested for HIV antibody by two different enzyme immunoassay methods (Abbot and Organon). The subjects were divided into four groups.

Results showed that the prevalence rate of HIV antibody was significantly lower among patients on methadone maintenance treatment than in any other group. The 74 methadone patients were divided into subgroups according to the time period in which they had been initiated into the program (October 1, 1981 to September 30, 1985). Higher incidence of HIV infection was observed in clients who originated treatment in the last semester as compared to patients in the other subgroups (8/13 positive vs 13/61, $p<.01$, chi-square analysis). The data confirms that a program of methadone maintenance assists in prevention of HIV virus

diffusion since patients on such programs usually desist intravenous heroin self-administration.[28]

Conclusions

Substance abuse is a major social problem with enormous human and economic costs against which the United States directs significant resources for law enforcement, interdiction, treatment, and prevention. Greatly increasing the costs of substance abuse is the problem of HIV infection among persons who inject illicit drugs. With the advent of HIV in the early 1980s and the rapid increase in its prevalence among injecting drug users in the United States and the rest of the world, containment has become a relevant outcome on which to assess the effectiveness of methadone maintenance.

Evidence from all major cities suggests that once HIV is introduced into the injecting drug use community it can spread rapidly with devastating results. The main mode of HIV transmission among drug injectors is the sharing of contaminated injecting equipment. HIV is also spread sexually and perinatally, thus putting at risk the sexual partners and children of injecting drug users. Because there is as of yet no cure for HIV, the only way in which the epidemic will be stemmed is through the behavior modification of known routes of transmission.

The dynamics of needle sharing have been identified. The frequency with which a person injects, the type of drugs individuals use, and a long history of injecting drug use have all been found to be significantly associated with HIV

seropositivity. The research to date on what is known about the specific risk behaviors associated with HIV transmission in the drug community and the evidence for the effectiveness of methadone maintenance treatment in preventing HIV infection clearly support with reasonable evidence and consistency, that methadone treatment is effective in reducing the HIV risk factor and seropositivity associated with injecting. In the absence of evidence to the contrary, it is reasonable to conclude that methadone maintenance treatment is an important HIV prevention measure among drug-dependent users.

However, in order to be effective, methadone maintenance programs must make greater risk-reduction opportunities available to the large population of intravenous drug users who request treatment. Maximum risk-reduction effectiveness will require maximum efficacy from methadone programs. Some of the recommended risk-reduction strategies, for example, counseling about HIV infection, safe sex education, and family planning, need to become integral services in methadone programs. State and local laws that prohibit methadone treatment or place arbitrary limits on the duration of treatment will work against AIDS risk-reduction efforts. State and local medical associations must provide assistance by educating patients as well as the public and policymakers about the special risks to the public health created by untreated intravenous drug users. In addition, physicians must be encouraged to become actively involved in the direct provision of methadone treatment.

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