Effective Medical Treatment of Opiate Addiction

National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction

Objective.—To provide clinicians, patients, and the general public with a responsible assessment of the effective approaches to treat opiate dependence.

Participants.—A nonfederal, nonadvocate, 12-member panel representing the fields of psychology, psychiatry, behavioral medicine, family medicine, drug abuse, epidemiology, and the public. In addition, 25 experts from these same fields presented data to the panel and a conference audience of 600. Presentations and discussions were divided into 3 phases over 2½ days: (1) presentations by investigators working in the areas relevant to the consensus questions during a 2-day public session; (2) questions and statements from conference attendees during open discussion periods that are part of the public session; and (3) closed deliberations by the panel during the remainder of the second day and morning of a third day. The conference was organized and supported by the Office of Medical Applications of Research, National Institutes of Health.

Evidence.—The literature was searched through MEDLINE and other National Library of Medicine and online databases from January 1994 through September 1997 and an extensive bibliography of 941 references was provided to the panel and the conference audience. Experts prepared abstracts for their presentations as speakers at the conference with relevant citations from the literature. Scientific evidence was given precedence over clinical anecdotal experience.

Consensus Process.—The panel, answering predefined questions, developed its conclusions based on the scientific evidence presented in open forum and the scientific literature. The panel composed a draft statement that was read in its entirety and circulated to the experts and the audience for comment. Thereafter, the panel resolved conflicting recommendations and released a revised statement at the end of the conference. The panel finalized the revisions within a few weeks after the conference. The draft statement was made available on the World Wide Web immediately following its release at the conference and was updated with the panel's final revisions.

Conclusions.—Opiate dependence is a brain-related medical disorder that can be effectively treated with significant benefits for the patient and society, and society must make a commitment to offer effective treatment for opiate dependence to all who need it. All persons dependent on opiates should have access to methadone hydrochloride maintenance therapy under legal supervision, and the US Office of National Drug Control Policy and the US Department of Justice should take the necessary steps to implement this recommendation. There is a need for improved training for physicians and other health care professionals. Training to determine diagnosis and treatment of opiate dependence should also be improved in medical schools. The unnecessary regulations of methadone maintenance therapy and other long-acting opiate agonist treatment programs should be reduced, and coverage for these programs should be a required benefit in public and private insurance programs.

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IN THE UNITED STATES, before 1914, it was relatively common for private physicians to treat patients dependent on opiates in their practices by prescribing narcotic medications. Although the passage of the Harrison Act did not prohibit the prescribing of a narcotic by a physician to treat an addicted patient, this practice was viewed as problematic by US Treasury officials charged with enforcing the law. Physicians who continued to prescribe were indicted and prosecuted. Because of withdrawal of treatment by physicians, various local governments and communities established formal morphine clinics for treating opiate addiction. These clinics were eventually closed when in 1920 the American Medical Association stated that there was unanimity that prescribing opiates to addicts for self-administration (ambulatory treatment) was not an acceptable medical practice. For the next 50 years, opiate addiction was basically managed in this country by the criminal justice system and the 2 federal

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This statement is an independent report of the panel and is not a policy statement of the NIH or the federal government.

The abstract is prepared by the conference organizers and added to the consensus panel's statement as service for *JAMA* readers.

This Consensus Development Conference was held on November 17-19, 1997, and the Consensus Statement was posted on the Web site on November 19, 1997.

NIH Consensus Statements, NIH Technology Assessment Statements, and related materials are available by writing to the NIH Consensus Program Information Center, PO Box 2577, Kensington, MD 20891, by calling (888) 644-2667, or by visiting the NIH Consensus Development Program Web site at http://consensus.nih.gov.

public health hospitals in Lexington, Ky, and Fort Worth, Tex. The relapse rate for opiate use from this approach was close to 100%. During the 1960s opiate use reached epidemic proportions in the United States, spawning significant increases in crime and deaths from opiate overdose. The increasing number of younger people entering an addiction lifestyle indicated that a major societal problem was emerging. This stimulated a search for innovative and more effective methods to treat the growing number of individuals dependent on opiates. This search resulted in the emergence of drug-free therapeutic communities and the use of the opiate agonist methadone hydrochloride to maintain those with opiate dependence. Furthermore, a multimodality treatment strategy was designed to meet the needs of patients who were addicted. These 3 approaches remain the main treatment strategies being used to treat opiate dependence in the United States today.

Opiate dependence has long been associated with increased criminal activity. For example, in 1993 more than one quarter of the inmates in state and federal prisons were incarcerated for drug offenses (234 600), and prisoners serving drug sentences were the largest single group (60%) in federal prisons.

During the past 10 years, the prevalence of human immunodeficiency virus (HIV), hepatitis B and C viruses, and tuberculosis has dramatically increased among intravenous opiate users. From 1991 to 1995, in major metropolitan areas, the annual number of opiate-related emergency department visits increased from 36 000 to 76 000, and the annual number of opiate-related deaths increased from 2300 to 4000. This associated morbidity and mortality further underscore the human, economic, and societal costs of opiate dependence.

During the last 2 decades, evidence has accumulated on the neurobiological aspects of opiate dependence. Whatever conditions may lead to opiate exposure, opiate dependence is a brain-related disorder with the requisite characteristics of a medical illness. Thus, opiate dependence as a medical illness will have varying causative mechanisms. Discrete subgroups of persons dependent on opiates along with the most relevant and effective treatments for each subgroup should be identified. The safety and efficacy of narcotic agonist (methadone) maintenance treatment has been unequivocally established. Although other medications (eg, levo alpha acetylmethadol [levomethadyl acetate hydrochloride] and naltrexone, an opiate antagonist) are safe and effective in the treatment of opiate addicts, the focus of this Consensus Development Conference was primarily on methadone maintenance treatment (MMT), which is effective in reducing illicit opiate drug use, reducing crime, enhancing social productivity, and reducing the spread of viral diseases such as acquired immunodeficiency syndrome (AIDS) and hepatitis.

Approximately 115 000 of the estimated 600 000 persons dependent on opiates in the United States are in MMT. Science has not yet overcome the stigma of addiction and the negative public perception of MMT. Some leaders in the federal government, public health officials, members of the medical community, and the general public frequently consider opiate dependence a self-inflicted disease of the will or a moral flaw. They also regard MMT as an ineffective narcotic substitution and believe that a drug-free state is the only valid treatment goal. Other obstacles to MMT include federal and state governmental regulations that restrict patient access and the number of treatment providers. Some of these federal and state regulations are driven by a disproportionate amount of concern among some state and federal legislators and members of law enforcement agencies about methadone diversion, premature (eg, 12-year-olds) initiation of maintenance treatment, and provision of methadone without any other psychosocial services.

Although a drug-free state represents an optimal treatment goal, research has demonstrated that this goal cannot be achieved or sustained by the majority of persons dependent on opiates. However, other laudable treatment goals including decreased drug use, reduced criminal activity, and gainful employment can be achieved by most MMT patients.

To address the most important issues surrounding effective medical treatment of persons dependent on opiates, the National Institutes of Health (NIH) organized this 2½-day conference to present data on opiate agonist treatment for those dependent on opiates. The conference brought together national and international experts in the fields of the basic and clinical medical sciences, epidemiology, natural history, prevention and treatment of opiate dependence, and broad representation from the public.

After 1½ days of presentations and audience discussion, an independent, nonfederal consensus panel chaired by Lewis L. Judd, MD, Mary Gilman Marston professor and chair of the Department of Psychiatry, University of California, San Diego School of Medicine, weighed the scientific evidence and wrote a draft statement that was presented to the audience on the third day. The consensus statement addressed the following key questions:

1. What is the scientific evidence that supports a conceptualization of opiate addiction as a medical disorder, including natural history, genetics and risk factors, and pathophysiology, and how is diagnosis established?
2. What are the consequences of untreated opiate addiction to individuals, families, and society?
3. What is the efficacy of current treatment modalities in the management of opiate addiction, including detoxification alone, nonpharmacological/psychosocial treatment, treatment with opiate antagonists, and treatment with opiate agonists (short-term and long-term)? Also, what is the scientific evidence for the most effective use of opiate agonists in the treatment of opiate addiction?
4. What are the barriers to effective use of opiate agonists in the treatment of opiate addiction in the United States, including perceptions and the adverse consequences of opiate agonist use and legal, regulatory, financial, and programmatic barriers?
5. What are the future research areas and recommendations for improving opiate agonist treatment and improving patient access to treatment?

1. WHAT IS THE SCIENTIFIC EVIDENCE THAT SUPPORTS A CONCEPTUALIZATION OF OPIATE DEPENDENCE AS A MEDICAL DISORDER INCLUDING NATURAL HISTORY, GENETICS AND RISK FACTORS, AND PATHOPHYSIOLOGY, AND HOW IS DIAGNOSIS ESTABLISHED?

The Natural History of Opiate Dependence

Persons addicted to opiates often become dependent on these drugs by their early 20s and remain intermittently dependent for decades. Biological, psychological, sociological, and economic factors determine when a person will start taking opiates. However, it is clear that when use begins, it often escalates to abuse (repeated use with adverse consequences) and then to dependence (opioid tolerance, withdrawal symptoms, compulsive drug-taking). Once dependence is established, there are usually repeated cycles of cessation and relapse extending over decades. This "addiction career" is often accompanied by periods of imprisonment.

Treatment can alter the natural history of opiate dependence, most commonly by prolonging periods of abstinence from illicit opiate abuse. Of the various treatments available, MMT, combined with attention to medical, psychiatric, and socioeconomic issues, as

well as drug counseling, has the highest probability of being effective.

Addiction-related deaths, including unintentional overdose, drug-related injuries, and many illnesses directly attributable to chronic drug dependence, explain one fourth to one third of the mortality in an opiate-addicted population. As a population of persons addicted to opiates ages, the percentage who are still addicted decreases.

There is clearly a natural history of opiate dependence, but causative factors are poorly understood. It is especially unclear for a given individual whether repeated use begins as a medical disorder (eg, a genetic predisposition) or whether socioeconomic and psychological factors lead an individual to try and then later to use opiates compulsively. However, undoubtedly once an individual is dependent on opiates, such dependence constitutes a medical disorder.

Molecular Neurobiology and Pathogenesis of Opiate Dependence: Genetic and Other Risk Factors for Opiate Dependence

Studies of twins, families, and persons who have been adopted show that vulnerability to drug abuse may be a partially inherited condition with strong influences from environmental factors. Cross-fostering adoption studies have demonstrated that both inherited and environmental factors operate in the etiology of drug abuse. These cross-fostering adoption studies identified 2 distinct genetic pathways to drug abuse or dependence. The first is a direct effect of substance abuse in a biologic parent. The second is an indirect effect from antisocial personality disorder in a biologic parent, leading to both antisocial personality disorder and drug abuse or dependence in the adopted person. Family studies report significantly increased relative risk for substance abuse (6.7-fold increased risk), alcoholism (3.5-fold), antisocial personality (7.6-fold), and unipolar depression (5.1-fold) among the first-degree relatives of patients dependent on opiates compared with relatives of controls. The siblings of patients dependent on opiates have very high susceptibility to abuse and dependence after initial use of illicit opioids. Studies of twins indicate substantial heritability for substance abuse and dependence, with half the risk attributable to additive genetic factors.

Neurobiological Substrates of Opiate Dependence

Dopaminergic pathways from the ventral tegmentum to the nucleus accumbens and medial frontal cortex are activated during rewarding behaviors. Opiates exert their rewarding properties by binding to the "μ" opioid receptor at several distinct anatomical locations in the brain, including the ventral tegmentum, the nucleus accumbens, the medial frontal cortex, and possibly the locus ceruleus. Opiate agonist administration causes inhibition of the locus ceruleus. Chronic administration of opioid agonists causes adaptation to the locus ceruleus inhibition. Rapid discontinuation of opioid agonists (or administration of antagonists) results in excessive locus ceruleus neuronal excitation and the appearance of withdrawal symptoms. Abnormal locus ceruleus excitation is thought to underlie many of the physical symptoms of withdrawal, and this hypothesis is consistent with the ability of clonidine hydrochloride, an α2-noradrenergic agonist, to ameliorate opiate withdrawal.

Regional Cerebral Glucose Metabolism in Opiate Abusers

Two independent human studies (using positron emission tomography) suggest that opiates reduce cerebral glucose metabolism in a global manner, with no regions showing increased glucose use. A third study demonstrates decreased D_2 receptor availability in patients dependent on opiates compared with controls. Opiate antagonist administration produced an intense withdrawal experience but did not change D_2 receptor availability.

Diagnosis of Opioid Dependence

Opioid dependence (addiction) is defined as a cluster of cognitive, behavioral, and physiological symptoms in which the individual continues use of opiates despite significant opiate-induced problems. Opioid dependence is characterized by repeated self-administration that usually results in opioid tolerance, withdrawal symptoms, and compulsive drug-taking. Dependence may occur with or without the physiological symptoms of tolerance and withdrawal. Usually, there is a long history of opioid self-administration, typically via intravenous injection in the arms or legs, although recently, the intranasal route or smoking also is used. Often there is a history of drug-related crimes, drug overdoses, and family, psychological, and employment problems. There may be a history of physical problems including skin infections, hepatitis, HIV infection, or irritation of the nasal and pulmonary mucosa. Physical examination usually reveals puncture marks along veins in the arms and legs and "tracks" secondary to sclerosis of veins. If the patient has not taken opiates recently, he or she may also demonstrate symptoms of withdrawal, including anxiety, restlessness, runny nose, tearing, nausea, and vomiting. Tests for opioids in saliva and urine can help support a diagnosis of dependence. However, by itself, neither a positive nor a negative test result can rule dependence in or out. Further evidence for opioid dependence can be obtained by a naloxone hydrochloride (Narcan) challenge test to induce withdrawal symptoms.

Evidence That Opioid Dependence Is a Medical Disorder

For decades, opioid dependence was viewed as a problem of motivation, willpower, or strength of character. Through careful study of its natural history and through research at the genetic, molecular, neuronal, and epidemiological levels, it has been proven that opiate addiction is a medical disorder characterized by predictable signs and symptoms. Other arguments for classifying opioid dependence as a medical disorder include: (1) consistent medical history, signs, and symptoms among those who are dependent on opiates despite varying cultural, ethnic, and socioeconomic backgrounds; (2) a strong tendency to relapse after long periods of abstinence; (3) cravings for opiates that induce continual self-administration despite powerful social consequences and an expressed and demonstrated strong motivation to stop; (4) and pathophysiologic changes in the brain following continuous exposure to opioids.

2. WHAT ARE THE CONSEQUENCES OF UNTREATED OPIATE DEPENDENCE TO INDIVIDUALS, FAMILIES, AND SOCIETY?

Of the estimated total opiate-dependent population of 600 000 individuals, only 115 000 are known to be in MMT programs. Research surveys indicate that the untreated population of opiate-addicted people is younger than those in treatment. Untreated patients are typically in their late teens and early to mid-20s, during their formative, early occupational, and reproductive years. The financial costs of untreated opiate dependence to the individual, the family, and society are estimated to be approximately $20 billion per year. The costs in human suffering are incalculable.

What is currently known about the consequences of untreated opiate dependence to individuals, families, and society?

Mortality

Before the introduction of MMT, annual death rates reported in 4 US studies of opiate dependence varied from 13 per 1000 to 44 per 1000, with a median of 21 per 1000. Although it cannot be causally attributed, it is interesting that af-

ter the introduction of MMT, the death rates of opiate-dependent persons in 4 US studies had a narrower range, from 11 per 1000 to 15 per 1000, and a median of 13 per 1000. The most striking evidence of the effectiveness of MMT on death rates is from studies directly comparing these rates in persons dependent on opiates who are receiving methadone with those who are not. Every study showed that death rates were lower in those who were receiving methadone than for those who were not. The median death rate for persons dependent on opiates who are in MMT was 30% of the death rate of those not in treatment. A clear consequence of not treating those who are dependent on opiates, therefore, is a death rate that is more than 3 times greater than that experienced by those engaged in MMT.

Illicit Drug Use

Multiple studies conducted over several decades and in different countries demonstrate clearly that MMT results in a marked decrease in illicit opiate use. Furthermore, MMT programs significantly and consistently reduce the use of other illicit drugs, including cocaine and marijuana, and the abuse of alcohol, benzodiazepines, barbiturates, and amphetamines.

Criminal Activity

Opiate dependence in the United States is unequivocally associated with high rates of criminal behavior. More than 95% of opiate-dependent persons report committing crimes during an 11-year at-risk interval. These crimes range in severity from homicides to other crimes against people and property. Stealing to purchase drugs is the most common criminal offense. Over the past 2 decades, clear and convincing evidence has been collected from multiple studies that effective treatment of opiate dependence markedly reduces the rates of criminal activity. Therefore, it is clear that significant amounts of crime perpetrated by persons dependent on opiates are a direct consequence of untreated opiate dependence.

Health Care Costs

Although the general health status of persons dependent on opiates is substantially worse than that of their nondependent contemporaries, they do not routinely use medical services. Typically, they seek medical care in hospital emergency departments only after their medical conditions are seriously advanced. The consequences of untreated opiate dependence include much higher incidence of bacterial infections including endocarditis, thrombophlebitis, skin and soft tissue infections, and tuberculosis; hepatitis B and C; AIDS and sexually transmitted diseases; and alcohol abuse. Because those who are dependent on opiates seek medical care in late stages of their diseases, medical care is generally more expensive. Health care costs related to opiate dependence have been estimated to be $1.2 billion per year.

Joblessness

Opiate dependence prevents many users from maintaining steady employment. Much of their time each day is spent seeking and taking drugs. Therefore, many seek public assistance because they are unable to generate the income needed to support themselves and their families. Long-term outcome data show that persons dependent on opiates who are in MMT earn more than twice as much money annually as those not in treatment.

Outcomes of Pregnancy

A substantial number of pregnant women dependent on opiates also have been diagnosed as having HIV or AIDS. On the basis of preliminary data, women who receive MMT are more likely to be treated with zidovudine. It has been well established that administration of zidovudine to HIV-positive pregnant women reduces by two thirds the rate of HIV transmission to their newborns. Comprehensive MMT, along with sound prenatal care, has been shown to decrease obstetrical and fetal complications as well.

3. WHAT IS THE EFFICACY OF CURRENT TREATMENT MODALITIES IN THE MANAGEMENT OF OPIATE DEPENDENCE INCLUDING DETOXIFICATION ALONE, NONPHARMACOLOGICAL/ PSYCHOSOCIAL TREATMENT, TREATMENT WITH OPIATE ANTAGONISTS, AND TREATMENT WITH OPIATE AGONISTS (SHORT-TERM AND LONG-TERM)? AND, WHAT IS THE SCIENTIFIC EVIDENCE FOR THE MOST EFFECTIVE USE OF OPIATE AGONISTS IN THE TREATMENT OF OPIATE DEPENDENCE?

The Pharmacology of Commonly Prescribed Opiate Agonists and Antagonists

The most frequently used agent in medically supervised opiate withdrawal and maintenance treatment is methadone. Methadone's half-life is approximately 24 hours and leads to a long duration of action and once-a-day dosing. This feature, coupled with its slow onset of action, blunts its euphoric effect, making it unattractive as a principal drug of abuse. Levo alpha acetylmethadol, a less commonly used opiate agonist, has a longer half-life and may prevent withdrawal symptoms for up to 96 hours. An emerging treatment option, buprenorphine hydrochloride, a partial opioid agonist, appears also to be effective for detoxification and maintenance.

Naltrexone is a nonaddicting specific μ antagonist with a long half-life permitting once-a-day administration. It effectively blocks the cognitive and behavioral effects of opioids, and its prescription does not require special registration. Persons dependent on opiates considering treatment should be informed of the availability of naltrexone maintenance treatment. However, naltrexone produces immediate withdrawal symptoms with potentially serious effects for those actively using opiates.

Medically Supervised Withdrawal

Methadone can also be used for detoxification, which can be accomplished over several weeks after a period of illicit opiate use or methadone maintenance. If methadone withdrawal progresses too rapidly, abstinence symptoms are likely, which may lead to illicit drug use and relapse into another cycle of abuse. Buprenorphine holds promise as an option for medically supervised withdrawal because its prolonged occupation of μ receptors attenuates withdrawal symptoms.

More rapid detoxification options include use of opiate antagonists alone; the alpha$_2$ agonist clonidine hydrochloride alone; or clonidine followed by naltrexone. Clonidine reduces many of the autonomic signs and symptoms of opioid withdrawal. These strategies may be used in both inpatient and outpatient settings and allow medically supervised withdrawal from opioids in as little as 3 days. Most patients successfully complete detoxification using these strategies, but information concerning relapse rates is not available.

The Role of Psychosocial Treatments

Nonpharmacologic supportive services are pivotal to successful MMT. The immediate introduction of these services as patients apply for MMT leads to significantly higher retention and more comprehensive and effective treatment. Comorbid psychiatric disorders require treatment. Other behavioral strategies have been used successfully in substance abuse treatment. Ongoing substance abuse counseling and other psychosocial therapies enhance program retention and positive outcome. Stable employment is an excellent predictor of clinical outcome. Therefore, vocational rehabilitation is a useful adjunct.

Efficacy of Opiate Agonists

It is now generally agreed that opiate dependence is a medical disorder and that pharmacologic agents are effective in its treatment. Evidence presented to the panel indicates that availability of these agents is severely limited and that large numbers of patients with this disorder have no access to treatment.

The greatest experience with such agents has been with the opiate agonist methadone. Prolonged oral treatment with this medication diminishes and often eliminates opiate use, reduces transmission of many infections, including HIV and hepatitis B and C, and reduces criminal activity. Evidence is now accumulating that suggests the effectiveness in such patients of levo alpha acetylmethadol and buprenorphine.

For more than 30 years, the daily oral administration of methadone has been used to treat tens of thousands of individuals dependent on opiates in the United States and abroad. The effectiveness of MMT is dependent on many factors, including adequate dosage, duration plus continuity of treatment, and accompanying psychosocial services. A dosage of 60 mg/d may achieve the desired treatment goal: abstinence from opiates. But higher doses are often required by many patients. Continuity of treatment is crucial—patients who are treated for less than 3 months generally show little or no improvement, and most, if not all, patients require continuous treatment for many years, and perhaps for life. Therefore, the program has come to be termed methadone "maintenance" treatment. Patient attributes that have sometimes been linked to better outcomes include older age, later age of dependence onset, lesser abuse of other substances including cocaine and alcohol, and lesser criminal activity. Recently, it has been reported that high motivation for change has been associated with positive outcomes. The effectiveness of MMT is often dependent on the involvement of a knowledgeable and empathetic staff and the availability of psychotherapy and other counseling services. The latter are especially important since individuals with opiate dependence are often afflicted with comorbid mental and personality disorders.

Because methadone-treated patients generally are exposed to much less or no intravenous opiates, they are much less likely to contract and transmit HIV and hepatitis. This is especially important since recent data have shown that up to 75% of new instances of HIV infection are attributable to intravenous drug use. Since many patients finance their opiate habit through criminal behavior, MMT generally leads to reduced crime.

Although methadone is the primary opioid agonist used, other full and partial opioid agonists have been developed for treatment of opiate dependence. An analog of methadone, levo alpha acetylmethadol, has a longer half-life than methadone and so can be administered less frequently. A single dose of levo alpha acetylmethadol can prevent withdrawal symptoms and drug craving for 2 to 4 days. Buprenorphine, a recently developed partial opiate agonist, has an advantage over methadone because its discontinuation leads to much less severe withdrawal symptoms. The use of these medications is at an early stage, and it may be some time before their usefulness has been adequately evaluated.

4. WHAT ARE THE BARRIERS TO EFFECTIVE USE OF OPIATE AGONISTS IN THE TREATMENT OF OPIATE ADDICTION IN THE UNITED STATES, INCLUDING PERCEPTIONS AND THE ADVERSE CONSEQUENCES OF OPIATE AGONIST USE AND LEGAL, REGULATORY, FINANCIAL, AND PROGRAMMATIC BARRIERS?

Misperceptions and Stigmas

Many of the barriers to effective use of MMT in the treatment of opiate dependence stem from misperceptions and stigmas attached to opiate dependence, the people who are addicted, those who treat them, and the settings in which services are provided. Persons dependent on opiates are often perceived not as individuals with a disease, but as "other" or "different." Factors such as racism play a large role but so does the popular image of dependence itself. Many people believe that dependence is self-induced or is a failure of willpower and that efforts to treat it will inevitably fail. Vigorous and effective leadership is needed to inform the public that dependence is a medical disorder that can be effectively treated with significant benefits for the patient and society.

Increasing Availability of Effective Services

Unfortunately, MMT programs are not readily available to all who could and wish to benefit from them. We as a society must make a commitment to offer effective treatment for opiate dependence to all who need it. Accomplishing that goal will require

- making treatment as cost-effective as possible without sacrificing quality,
- increasing the availability and variety of treatment services,
- including and ensuring wider participation by physicians trained in substance abuse who will oversee the medical care, and
- providing additional funding for opiate dependence treatments and coordinating these services with other necessary social services and medical care.

Training Physicians and Other Health Care Professionals

One barrier to availability of MMT is the shortage of physicians and other health care professionals prepared to provide treatment for opiate dependence. All primary care medical specialties (including general practice, internal medicine, family practice, obstetrics and gynecology, geriatrics, pediatrics, and adolescent medicine) should be taught the principles of diagnosing and treating patients with opiate dependence. Nurses, social workers, psychologists, physician assistants, and other health care professionals should also be trained. The greater the number of trained physicians and other health care professionals, the greater the supply not only of professionals who can competently treat those dependent on opiates but also of members of the community who are equipped to provide leadership and public education on these issues.

Reducing Unnecessary Regulation

Of critical importance in improving MMT of opiate dependence is the recognition that, as in every other area of medicine, treatment must be tailored to the needs of the individual patient. Current federal regulations make this difficult if not impossible. By prescribing MMT procedures in minute detail, US Food and Drug Administration (FDA) regulations limit the flexibility and responsiveness of the programs, require unproductive paperwork, and impose administrative and oversight costs greater than those necessary for many patients. Yet these regulations seem to have little if any effect on quality of MMT care. We know of no other area into which the federal government intrudes so deeply and coercively as the practice of medicine. For example, although providing a therapeutic dose is central to effective treatment and the therapeutic dose is now known to be higher than previously understood, FDA regulations discourage such higher doses. However well-intended the FDA's treatment regulations were when written in 1972, they are no longer helpful. We recommend that these regulations be eliminated. Alternative means, such as accreditation, for improving quality of MMT programs should be instituted. The US Department of Health and Human Services can more effectively, less coercively, and much more inexpensively discharge its statutory obligation to provide treatment guidance to MMT programs, physicians, and staff by means of publications, seminars, Web sites, continuing medical education, and the like.

We also believe current laws and regulations should be revised to eliminate the extra level of regulation on methadone compared with other Schedule II narcotics. Currently, methadone can be dispensed only from facilities that obtain an extra license and comply with extensive extra regulatory requirements. These extra requirements are unnecessary for a medication that is not often diverted for recreational or casual use but rather to individuals with opiate dependence who lack access to MMT programs.

If extra levels of regulation were eliminated, many more physicians and pharmacies could prescribe and dispense methadone, making treatment available in many more locations than is now the case. Not every physician will choose to treat patients dependent on opiates, and not every patient treated would prefer to receive services from an individual physician rather than in a clinic setting. But if some additional physicians and groups treat a few patients each, aggregate access to MMT would be expanded.

We also believe that state and local regulations and enforcement efforts should be coordinated. We see little purpose to having separate state and federal inspections of MMT programs. State and federal regulators should coordinate their efforts, agree which programs each will inspect to avoid duplication, and target "poor performers" for the most intensive scrutiny while reducing scrutiny for MMT programs that consistently perform well. The states should address the problem of slow approval (at the state level) of FDA-approved medications. Levo alpha acetylmethadol, for example, has not yet been approved by many states. States should harmonize their requirements with those of the federal government.

We would expect these changes in the current regulatory system to reduce unnecessary costs both to MMT programs and to enforcement agencies at all levels. The savings could be used to treat more patients.

In the end, an infusion of additional funding will be needed—funding sufficient to provide access to treatment for all who require it. We strongly recommend that legislators and regulators recognize that providing MMT is both cost-effective and compassionate and that it constitutes a health benefit that should be a component of public and private health care.

5. WHAT ARE THE FUTURE RESEARCH AREAS AND RECOMMENDATIONS FOR IMPROVING OPIATE AGONIST TREATMENT AND IMPROVING ACCESS?

To improve opiate agonist treatment and patient access to treatment, researchers should consider investigating such questions as what initiates opiate use. In so doing, they should define what types of genetic predispositions contribute to such a person's predilection for addiction. They should try to determine whether persons take opiates to treat a preexisting disorder, the extent to which of the multiple psychological, sociological, and economic factors believed to predispose individuals to try opiates are most important as causative factors, and whether answers to these questions can prevent opiate dependence. Other research should include determining

- the changes in the human brain that result in dependence when individuals repeatedly use opiates,
- the underlying anatomical and neurophysiological substrates of craving,
- the differences between individuals who can successfully terminate opiate dependence and those who cannot,
- the prevalence of opiate dependence in the United States through a scientifically credible national epidemiological study, which is strongly recommended,
- the economic costs of opiate dependence in the United States and the cost-effectiveness of MMT,
- effects of complete rapid detoxification on patients followed up in longer-term studies,
- the feasibility of alternative routes of administration for agonist and antagonist therapy,
- systematic pharmacokinetic studies of methadone during MMT maintenance therapy,
- definition of physiologic factors that may influence adequate methadone dose in pregnant women,
- the effects of reduction of entitlement programs for those patients receiving MMT,
- the effects of the early and systematic introduction of rehabilitation services in MMT,
- variables that result in treatment barriers,
- what sorts of educational strategies would successfully change the attitudes of members of the public, health professions, and legislators,
- ways of improving educational methods for health professionals,
- improved methods for preventing addiction, and
- the efficacy of other opiate agonists or antagonists compared with methadone.

CONCLUSIONS AND RECOMMENDATIONS

Vigorous and effective leadership is needed within the Office of National Drug Control Policy (and related federal and state agencies) to inform the public that opiate dependence is a medical disorder that can be effectively treated with significant benefits for the patient and society.

- Our society must make a commitment to offering effective treatment for opiate dependence to all who need it.
- The panel calls attention to the need for opiate-dependent persons under legal supervision to have access to MMT. The Office of National Drug Control Policy and the US Department of Justice should implement this recommendation.
- The panel recommends improved training of physicians and other health care professionals in diagnosis and treatment of opiate dependence. For example, we encourage the National Institute on Drug Abuse and other agencies to provide funds to improve training for diagnosis and treatment of opiate dependence in medical schools.
- The panel recommends that unnecessary regulation of MMT and all long-acting agonist treatment programs be reduced.
- Funding for MMT should be increased.
- We advocate that MMT be considered as a benefit in public and private insurance programs, with parity of coverage for all medical and mental disorders.
- We recommend targeting opiate-dependent pregnant women for MMT.
- Furthermore, MMT must be culturally sensitive to enhance a favorable outcome for participating African American and Hispanic persons.
- Patients, underrepresented minorities, and consumers should be included in bodies charged with policy development guiding opiate dependence treatment.
- We recommend expanding the availability of opiate agonist treatment in those states and programs where this treatment option is currently unavailable.

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Bibliography

The speakers listed above identified the following key references in developing their presentations for the consensus conference. A more complete bibliography prepared by the National Library of Medicine at NIH, along with the references below, were provided to the consensus panel for their consideration. The full bibliography is available at the following Web site: http://www.nlm.nih.gov/pubs/cbm/heroin_addiction.html.

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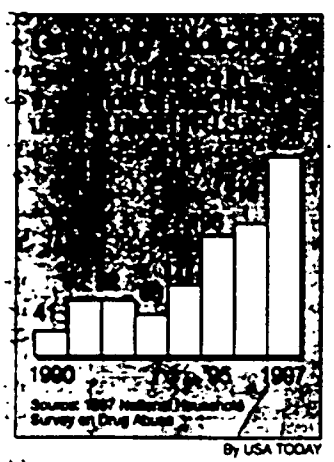
Heroin access spurs need for methadone

By Barry R. McCaffrey

Although the number of American adolescents using heroin is still relatively low, it is cause for concern. Because heroin is cheaper and purer than in the past, it's more accessible to young people who can smoke or snort the drug rather than inject it intravenously. A University of Michigan study called "Monitoring the Future" shows roughly one in 200 youths age 12-17 is a current user of heroin.

A new article in the journal *Pediatrics* also expresses concern. It maintains the age at which youths first try heroin may have dropped and the number of high school seniors using the drug could be higher than was previously thought. We are proud that the author, Dr. Richard Schwartz, encourages other pediatricians and parents to confront the fact that teens in their community could be using heroin.



The impact of heroin on our communities is one reason the debate over drug treatment engages many people. Several months ago, New York's Mayor Rudy Giuliani, a strong advocate of programs that reduce illegal drug use, made statements about methadone therapy for opiate addiction that were at odds with the conclusions of the nation's medical community and New York City's own experience.

There are too many methadone programs, Giuliani contended. On the contrary, there are too few. Only about 115,000 out of a national estimate of 810,000 heroin addicts participate in methadone programs. The National Academy of Sciences has said that "methadone treatment helps heroin addicts free themselves from drug dependency, a life of crime in support of their habit and the risk of adding to the AIDS population by sharing dirty needles."

The mayor objected to methadone treatment because he considered it simply the substitution of one addictive drug for another. However, as Dr. Avram Goldstein explains in his book *Addiction: From Biology to Drug Policy*, not only does orally taken methadone do away with syringes, but methadone also has "no adverse effects" on motor skills or memory. In other words, methadone doesn't make patients "high."

Methadone not just another addiction

Goldstein likens use of methadone for recovering heroin addicts to the use of insulin by people with severe diabetes. Recovering addicts need methadone because once heroin has changed the neurochemistry of the brain, the body is unable to synthesize certain chemicals without opiates.

People who have medical problems needn't feel stigmatized because some must take daily medication to live normal lives. The nature of a drug, not the frequency with which it is administered, is what distinguishes miraculous medicines from dangerous toxins.

Methadone therapy is one of the longest-established, most thoroughly evaluated forms of drug treatment. Scientific findings are overwhelmingly in favor of it. A "National Institute on Drug Abuse Treatment Outcome Study" found that methadone treatment reduced heroin use by 70% and criminal activity by 57%, while increasing full-time employment among former addicts by 24%. A 1998 General Accounting Office review says research provides "strong evidence to support methadone maintenance as the most effective treatment for heroin addiction."

Methadone therapy helps keep more than 100,000 young and old addicts off heroin. If we close down methadone programs, these human beings would be back on the streets, back on drugs and back on welfare at enormous cost to society.

As government agencies reform oversight of these programs, our goal is greater flexibility for medical practitioners in prescribing methadone as part of comprehensive drug treatment. Of course, the Drug Enforcement Administration would have to continue preventing the drug's diversion. Methadone is extremely dangerous if not used in a supervised medical setting. We asked Congress to provide $3.4 billion for the entire drug treatment program in fiscal 1999, up 38% since 1993.

Heroin addicts have a brain disease

Surely all those who consider the national and youth statistics agree the entire nation would be better off with less addiction. Drug use is a choice, and a bad one at that. Heroin addiction, however, is a brain disease that frequently responds to a combination of drug-treatment measures that may include physician-supervised use of methadone and other drugs.

The suffering that 800,000 heroin addicts cause themselves, their families and communities is nearly unbelievable. Our medical profession needs the skill and authority to use methadone appropriately as a tool in comprehensive drug treatment.

Barry R. McCaffrey is director of the Office of National Drug Control Policy.