WE WANT TO KNOW ABOUT YOUR CLINIC. SEE PAGE 3

Methadone Today

The official newsletter of DONT--by patients, for patients **June 2006** **Volume XI Number IV**

Origins of Opioid Maintenance Therapy--

Development of Medications to Treat Opioid Addiction

From TIP #43, "Medication-Assisted Treatment For Opioid Addiction in Opioid Treatment Programs," CSAT. [CSAT is a government agency--Call 1-800-SAYNOTO to order free TIP/TAP publications.]

Early rationale for methadone maintenance treatment

In 1962, Dr. Vincent P. Dole, a specialist in metabolism at The Rockefeller University, became chair of the Narcotics Committee of the Health Research Council of New York City. After studying the scientific, public health, and social ramifications of addiction in the city, he received a grant to establish a research unit to investigate the feasibility of opioid maintenance. In preparing for this research, he read 'The Drug Addict as a Patient' by Dr. Marie E. Nyswander (Nyswander 1956), a psychiatrist with extensive experience treating patients who were addicted to opioids. She was convinced that these individuals could be treated within general medical practice. She also believed that many would have to be maintained on opioids for extended periods to function because a significant number of people who attempted abstinence without medication relapse, in spite of detoxifications, hospitalizations, and psychotherapy (Brecher and Editors 1972; Courtwright et al. 1989). Dr. Nyswander joined Dr. Dole's research staff in 1964. Among others joining the team was clinical investigator Dr. Mary Jeanne Kreek.

These researchers realized that morphine, which is related to heroin, was not a good choice as an opioid maintenance drug because patients' social functioning was impaired by morphine's sedating effects (White 1998). Also, the short half-life of morphine required several injections per day, and, as tolerance developed, increasing amounts were needed over a short time for patients to remain stable (Brecher and Editors 1972). Other short-acting opioids, such as heroin, codeine, oxycodone, and meperidine (Demerol), showed similar results (Dole 1980, 1988).

Development of methadone

With short-acting opioids eliminated as options for maintenance therapy, research focused on ***(Cont. p. 3)***

The Development of Treatment Medications

In spite of, or because of, all the hoopla surrounding FDA approval of buprenorphine for the treatment of opiate addiction, seemingly little progress has been made in the development of alternative opiate addiction treatment medications. One likely reason for this is that there are few economic incentives for pharmaceutical companies to develop such medications. But perhaps there are also ideological reasons for this.

Economically, there just is not as much profit potential for pharmaceutical companies in researching and selling medications for addiction treatment as for heart or allergy medications, for example. One issue is that, on average, drug addicted individuals may be less able to afford very expensive brand name prescriptions, if no other reason, because insurance companies are generally stingy when it comes to substance abuse treatment coverage--especially of the long term outpatient variety. The only reason that buprenorphine is now approved and available for opiate addiction treatment is that the pharmaceutical company was confident that policymakers would allow doctors to prescribe it outside of the accredited opiate treatment provider (OTP) setting (e.g., methadone clinics). The experience with LAAM taught pharmaceutical companies that few opiate addicts willing to attend a clinic were either able or willing to pay considerably more for an alternate medication. Plough Scherring, who has the patent on buprenorphine, determined that most opiate addicts who would be able to afford the cost of buprenorphine are unwilling to go to a methadone clinic; conversely, they may be willing to pay extra for their medication in order to get treated at a private doctor's office in a less strictly regulated setting.

Some of the most promising leads in the search for additional opiate addiction treatment medications are drugs that have already been on the market for years--already approved by the FDA, for a purpose other than opiate addiction treatment (i.e., pain relief). Even buprenorphine had already been approved by the government for pain management , generally in an inpatient setting. The problem is that there is little economic incentive for pharmaceutical companies to conduct or fund research involving medications that have already been approved and on ***(Cont. p. 4)***

Dear Methadone Today,

I have a question, I was on Oxycontin for over a year. Just a week ago I was able to get some 10 mg methadone. I took my first dose which was 10 mg, and I couldn't believe how good I felt. My brain was thinking so straight and clear and I had all my energy back and I was in a good mood... and I continued to take this amount for a couple days. Then I went down to 5 mg for a couple days and still felt wonderful and had no urge to even think about Oxycontin. When I wasn't taking methadone, all I could think of was how to make money to get more Oxycontin. So the methadone was working wonders! I want to take it to wean off Oxycontin and not raise my dose but keep lowering it instead. I am not out to abuse the methadone; I know exactly what I am suppose to do with them. The problem is my last dose of methadone was yesterday and that was 2.5 mg... I can't get any more from where I was getting it before. I don't want to go to a clinic... I am just not one to go to one of those places. I wouldn't be comfortable.

If I call my regular doctor, can he actually prescribe me methadone if I was able to explain my story to him. I just want to be trusted where if I was able to get them that my intentions are good and I am not out to over use them at any point. I just don't want to waste my time going to a primary doctor if they are just going to tell me to see someone at a clinic. Do you think I am going at this the correct way with wanting to get more of the 5 mg methadone and wean down? **-Amy**

Dear Amy,

We are glad to see that you are making a serious effort to overcome your Oxycontin addiction, although we cannot condone self-medicating with illegally obtained methadone--and if you increase the dosage of methadone too fast or you mix it with other drugs, you could overdose, though 10 mg/day is less than what methadone patients are typically started on. Unfortunately, you will not be able to get methadone from a primary care physician. The federal regulations only permit accredited opiate treatment providers (OTPs) to provide methadone for the treatment of ***(Cont p. 2)***

Dear Amy (from p. 1).

opiate addiction, with an exception for medical maintenance treatment, which would only be available for long term, stable patients.

We should point out that not all methadone clinics are like what we think you envision, but we certainly do not want to push you to do something you are not comfortable with. Fortunately, for opiate addicts who are not comfortable going to a methadone clinic, there is an alternative opiate agonist treatment that is available in an office-based setting--buprenorphine treatment. Buprenorphine treatment is not the best choice or suitable for all opiate addicts, but it may be a good option for you. If you decide to seek buprenorphine treatment, be prepared to pay more than you would for methadone treatment.

As indicated above, buprenorphine treatment is not subject to many of the rules and regulations associated with methadone treatment. One of the most important differences in regulations is with the provision of take-home medication. Methadone patients have to dose in front of treatment provider staff a minimum of 6 days a week for at least the first 90 days in treatment. There are no such government regulations attached to buprenorphine treatment.

If you are interested in obtaining buprenorphine treatment, you are going to have to find a doctor in your area that can provide it. Not every doctor is permitted to provide buprenorphine treatment--they have to have taken a course and passed a test indicating some basic knowledge about opiate addiction and buprenorphine treatment. You should be able to find a physician willing and able to provide buprenorphine treatment out of their office.

Finally, you should understand that after tapering off of methadone or buprenorphine, a large percentage of patients will relapse—that is simply the nature of opiate addiction. Opiate agonist therapy with methadone or buprenorphine is highly effective treatment but not a permanent cure. The most common analogy is insulin as a treatment for diabetes--insulin treats diabetes, but it only works as long as the patient continues taking it. You stated that you felt good while taking methadone--'good' meaning feeling well and functional but not intoxicated or 'high'; it is possible that you will continue to feel good once you taper off methadone or buprenorphine and are no longer physically dependent on opiates, but there is also the possibility that you will never feel 100% normal and free of strong opiate cravings without being in opiate agonist treatment. Right now you are only interested in using methadone or buprenorphine for a short term taper. If that helps you achieve long term opiate abstinence, that is great.

You should ask your prescribing physician for his/her opinion about how best to withdraw from opiates--sometimes, a more gradual taper works better. If you attempt to withdraw from methadone or buprenorphine 2-3 times and find that once you stop the medication you start abusing Oxycontin or other illicit opiates again, you might want to consider a longer term course of buprenorphine or methadone maintenance treatment. You may not like the idea of being on opiate agonist treatment long term, but it is definitely preferable to continued opiate abuse and the legal, financial, and health consequences associated with it.

AATOD Conference–Treatment of Inmates

by Dr. Andrew Byrne, Dependency Medicine (New South Wales, Australia)

American Association for the Treatment of Opioid Dependence (AATOD) meeting. April , 2006, Atlanta, GA

In one [Monday] session, we had James Carleton speaking about his experience with the Rhode Island penal system where there is one large jail for men and two smaller ones for women. When inmates had been on methadone prior to incarceration, this could be continued whilst in holding cells, but only for a limited period. We were told that primary medical care of inmates was quite separate and only those who were already on treatment were able to receive the methadone, albeit on reducing doses, on the authority of their original legal prescription. When pressed, Dr Carleton said that 30 to 60 and sometimes to 90 days treatment could be arranged in that state's lock-ups.

A perceptive participant asked whether a person who developed or redeveloped an opioid habit in jail could be treated by his team in this way. He told us that the prison administration would probably not physically allow such a person to attend for methadone treatment, but that indeed drugs were available in Rhode Island jails. Very recently there had been an overdose leading to hospitalization of the inmate, with a stay in intensive care, presumably at the jail's expense. It would appear that all around the world a drug-free jail is just about as realistic as a drug-free society. Yet US jails allowing methadone are still exceptional.

The [Tuesday] morning plenary was on treatment in the penal system, chaired by Paul Samuels, a long time advocate for rational approaches to the field of addictions and crime. ***(Cont. p. 3)***

NOTICE--Funding of Treatment in Jeopardy

It seems that there are some in the Michigan Legislature (i.e. Representative Bruce Caswell) who would like to end public funding of addiction treatment (i.e., Medicaid). We believe this would be both inhumane and foolish--especially foolish since cutting treatment would cost the state far more money in crime, incarceration, etc. than it would save. Methadone is proven to save several dollars for each dollar spent on the treatment.

Drug addiction is a medical condition, and those in need of publicly funded healthcare deserve substance abuse treatment as much as any other medical treatment. We urge you to send letters to Representative Caswell opposing eliminating public funding of addiction treatment, including how you or your family has benefitted from treatment, and send a copy to your own state representative.

Sample Letter:

The Honorable Bruce Caswell, State Representative
Chair
House Appropriation Subcommittee on Community Health
State Capitol
PO Box 30014
Lansing, MI 48909-7514

Dear Sir:

It has come to my attention that some of our Representatives have concluded that Public Funding for Alcohol and Drug Abuse Treatment Programs is a "waste" of time.

I am a 55-year-old woman and mother of two who has been in a Methadone Maintenance Program for the past 11 years. I had been addicted to prescription pain killers since I was 13 years old and had tried to stop using three different times over the next 30 years and have always relapsed back into drug use. Methadone Maintenance has been the only thing that has worked for me. We must remember that addiction is a disease and not a life choice, which is what some people actually think. I have a disease just as a Diabetic has a disease. I do not get "high" on the medicine I take for my disease, I am dependent on it to make my life as normal as anyone else's, just as I take medicine for my high blood pressure.

Beside the fact that I am an addict, my life is as normal as yours. I am a taxpayer and voter and I will not support any Representative who advocates cutting Public Funds for these vitally important programs. Cordially,

Opioid Maintenance Therapy (p. 1).

methadone. Methadone appeared to be longer acting and effective when administered orally. It also was selected on the basis of observations of its use in patients withdrawing from heroin and as an analgesic in the experimental treatment of pain (Dole 1980, 1988). In 1964, technology was not available to measure blood levels of heroin, morphine, or methadone to assess duration of action. Proof of the efficacy of methadone maintenance treatment depended on observation and recognition by researchers. In an initial study, methadone was administered to two patients previously maintained on morphine. Once tolerance for daily doses of 50 to 120 mg was established, patients could function normally without the anxiety associated with drug craving (White 1998). During this research, the following important findings about methadone maintenance were noted, all supporting its efficacy and benefits (Dole 1980, 1988):

➛Patients did not experience euphoric, tranquilizing, or analgesic effects. Their affect and consciousness were normal. Therefore, they could socialize and work normally without the incapacitating effects of short-acting opioids such as morphine or heroin.

➛A therapeutic, appropriate dose of methadone reduced or blocked the euphoric and tranquilizing effects of all opioid drugs examined (e.g., morphine, heroin, meperidine, and opium), regardless of whether a patient injected or smoked the drugs.

➛No change usually occurred in tolerance levels for methadone over time, unlike for morphine and other opioids; therefore, a dose could be held constant for extended periods (more than 20 years in some cases).

➛Methadone was effective when administered orally. Because it has a half-life of 24 to 36 hours, patients could take it once a day without using a syringe.

➛Methadone relieved the opioid craving or hunger that patients with addiction described as a major factor in relapse and continued illegal use.

➛Methadone, like most opioid-class drugs, caused what were considered minimal side effects, and research indicated that methadone was medically safe and nontoxic.

Expansion of methadone maintenance from research project to public health program

In 1965, the initial research project on methadone safety and efficacy was transferred to Manhattan General Hospital in New York City (Brecher and Editors 1972). Because Dole and his colleagues knew that an independent evaluation of this new treatment would be necessary, a team headed by Dr. Frances Rowe Gearing was formed at Columbgia University School of Public Health to evaluate patient progress as this treatment expanded. In general, the team found that patients' social functioning improved with time in treatment, as measured by elimination of illicit-opioid use and better outcomes in employment, school attendance, and homemaking. Most patients were stabilized on methadone doses of 80 to 120 mg/day. Most patients who remained in treatment subsequently eliminated illicit-opioid use. However, 20 percent or more of these patients also had entered treatment with alcohol and polysubstance abuse problems, despite intake screening that attempted to eliminate these patients from treatment (Gearing and Schweitzer 1974). Methadone treatment was continued for these patients, along with attempts to treat their alcoholism and polysubstance abuse. Further evaluation, research, and expansion of the program ultimately were recommended (Joseph and Dole 1970) and instituted. Methadone maintenance became a major public health initiative to treat opioid addiction under the leadership of Dr. Jerome Jaffe, who headed the Special Action Office for Drug Abuse Prevention in the Executive Office of the White House in the early 1970s. Dr. Jaffe's office oversaw the creation of a nationwide, publicly funded system of treatment programs for opioid addiction.

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- ❑ Name
- ❑ City, State
- ❑ Price per week
- ❑ Highest dose/Average dose
- ❑ Highest number of take home doses allowed?
- ❑ How many compulsory counseling and/or group sessions?
- ❑ Staff attitude toward patients
- ❑ Waiting list?
- ❑ Additional comments

Treatment of Inmates (from p. 2).

We heard at length from the Atlanta District Attorney, Paul Howard, about the incarceration statistics, progress with the need for treatment and prevention programs.

On any one day, 4-7% of prisoners in New York City are getting high on drugs. When he was commissioner in Pennsylvania, the rate was allegedly 10% which dropped to 1% after a concerted effort at interdiction. Various parts of the country are now moving to allow limited methadone treatment in jails. These include San Francisco; Orange County, Seattle; Orlando, Florida; New York City (not up-state where most prisoners are housed); Rhode Island.

Timothy Ryan spoke eloquently about their implementation of a system of methadone in Florida which gave methadone to existing patients under certain strict rules. He pointed out that one needs to tread lightly as there are 'no absolutes in this area'. I countered afterward to him privately that surely giving correct treatment to all inmates is an appropriate absolute goal. And since drug use is such a high priority issue and methadone treatment is so cheap and effective, there is no excuse for denying such treatment to prisoners on any basis except to punish them twice (like solitary cells and interstate transfers). As Commissioner Martin Horn from New York pointed out to the audience, they work for the Department of Corrections, not the department of punishment.

Editor's Note: The provision of methadone treatment in U.S. prisons is still a rarity, and as far as we know, Nassau County Prison in NY is still the only prison providing methadone on a maintenance basis to some inmates. (*Methadone maintenance is provided to opiate dependent inmates who are pregnant at many prisons and jails.)

The U.S. lags behind many other countries in the provision of methadone treatment in prison. Other countries have already realized that providing methadone treatment to opiate dependent inmates is not only the most humane course, but also the most sensible way of greatly reducing the probability, after release, of the inmate returning to crime and winding up back in prison. Some countries have wisely even made methadone maintenance treatment available to any opiate addict that is eligible for methadone treatment.

Development of Medications (from p. 1).

the market for a period of time. After a number of years on the market, the patent the pharmaceutical company has on the prescription medication expires; once the patent expires, they cannot charge nearly as much for the medication as they face competition from other manufacturers putting out their own formulations. Buprenorphine is expensive because the drug company still has a patent on it, whereas the patent on methadone ran out many years ago. So obviously, there is little incentive for a pharmaceutical company to spend time and money on researching another medical use for a medication that has already been on the market for awhile. The ultimate solution may be to get funding from a source other than pharmaceutical companies.

One non-economic factor that may be coming into play are concerns about potential abuse and diversion of treatment medication. Diversion control is one of the main reasons for all the rules and regulations surrounding methadone treatment. The most extreme form of diversion control was adopted for LAAM treatment. Until the adoption of the new federal regulations in 2001, no LAAM take-homes were permitted. In contrast, the manufacturer of buprenorphine was able to convince policymakers that buprenorphine is less abusable--and thus, less of a diversion concern than methadone so that they would permit buprenorphine treatment to be provided out of doctors offices without all the restrictions that apply to methadone treatment.

One development that has potential application in opiate addiction treatment is transdermal administration (e.g., administration through the skin) of medication. One of the most commonly used examples of transdermal medications is the nicotine patch. Transdermal fentanyl in the form of a patch is now used for pain management. One of the advantages of a patch is that the medication is slowly absorbed--making it far longer acting than oral, sublingual or i.v. ingestion of shorter acting opiates like fentanyl or morphine. A patch may be useful in opiate addiction treatment for opiate addicts that metabolize methadone very rapidly.

It may be that concerns about abuse and diversion are one of the reasons transdermal patches have not been considered for opiate addiction treatment. Fentanyl patches are not 'tamper-proof', and supervised dosing in front of a doctor or clinic staff is not possible (e.g., the patch has to be kept on much of the time to work). Fentanyl is considered a highly abusable drug. Although we believe that concerns about diversion should not be nearly as big a factor as it is, the temptation by new, unstable patients to deliberately abuse a treatment medication should be a factor in the choice of treatment medication. In contrast to methadone, which is not generally a preferred drug of abuse for opiate addicts, there would be a temptation for new patients to find a way to get the fentanyl out of a transdermal patch and inject it. Thus, the fentanyl patch wouldn't be feasible in addiction treatment.

However, there is also the potential to manufacture transdermal patches with opioids other than fentanyl. For methadone patients who metabolize their medication very rapidly to the point that they have problems despite splitting their daily doses, transdermal administration of methadone or some other opioid may reduce these problems. Although supervised dosing is not possible with a patch, deliberate abuse and diversion could be deterred to a large extent by requiring patients to return all used patches. Used patches would be inspected by treatment provider staff, as tampering with the patch to extract the drug for the purpose of injecting it or diverting it would result in apparent damage. If the patient failed to return patches or returned patches that had been tampered with, s/he could be taken off of the patch, and transferred to traditional methadone or buprenorphine treatment.

Finally, U.S. researchers and policymakers should look into two opiate agonists that have already been used to at least a small extent elsewhere. Codeine has been used in opiate addiction treatment in Germany and other countries. Anecdotal evidence suggests that codeine may be useful in opiate addiction treatment. Some of the use of codeine for this purpose, is informal and, for better or worse, with little doctor supervision. In many countries, a weak strength of codeine is available over-the-counter, so opiate addicts self-medicate or are treated by a doctor informally. Codeine is considered less-than-ideal for opiate agonist treatment because it is too short acting, but it may be useful for opiate addicts who, for various reasons, do not do well on buprenorphine or methadone. Also, long acting morphine, not to be confused with the usual shorter acting version, has been used in certain clinical settings, and researchers should investigate, what if any potential it has in the treatment of opiate addiction.

Researching and developing medication alternatives to the current opiate agonist treatments available (methadone and buprenorphine treatment) is going to take time and money, but it is important for those who do not do well on the currently available treatments for opiate addiction. Methadone maintenance treatment is highly effective, but with any treatment or medication there is at least a very small percentage of patients that do not do well in treatment. In the case of methadone treatment, a small percentage of patients have difficulty tolerating the side effects or metabolize the medication too rapidly. The proportion of methadone patients that have Hepatitis C is very high, and this disease affects the liver. Sometimes the result is rapid metabolism of methadone.

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