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Methadone and Its Rationale in the Treatment of Narcotic Dependency*

Walter J. Cassidy, MD**

An effective methadone maintenance program must do more than dispense measured doses in a well-organized clinic. It should attempt to effect changes in the patient's personality and coping mechanisms, social situation, and other conditioning factors which maintain his involvement in narcotics.

An effective narcotic treatment program requires assessment and intervention along four dimensions. First is the user's pre-narcotic dependency personality; secondly, the changes in his personality and life style, which have resulted from interaction between the effects of the narcotic and the environment of the user; thirdly, the influence of the conditioning factors which have served to make these changes and maintain his involvement in narcotic addiction; and fourthly, his changed social pattern. Most effective narcotic treatment programs include some individual and/or group psychotherapy to deal with the user's personality problems, along with vocational counselling, supportive psychotherapy, and similar endeavors that the social worker and rehabilitation worker bring to bear on the user's social problems. The conditioning factors are often ignored and, at times, more unwittingly dealt with than deliberately. By significantly affecting the addiction pattern, I believe that methadone maintenance programs now offer the most effective broad scale programs for the treatment of narcotic dependent persons.

An alternative rationale for the use of methadone was proposed with the introduction of large scale methadone maintenance treatment by Dole and Nyswander, who postulated that narcotic dependency is a metabolic disorder. Two versions of the biochemical theory have been advanced. The first suggests that the user has a pre-existing deficit


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Cassidy which prevents him from feeling normal. He reacts in much the same way as a diabetic suddenly exposed to insulin feels better. There is very little empirical evidence to substantiate this theory. Introduction to opiates seems to begin with exposure, opportunity for use, and willingness to try them. Unfortunately, we do not know how many people try drugs such as heroin, continue regular use, stop, or go on to infrequent use. It seems fairly clear that most people who try it do so, not because they feel abnormal in some sense, but out of a spirit of adventure or for "thrill-seeking". From available facts, it appears that a fairly high proportion of people exposed in this way to drugs like heroin continue their usage. It is also interesting to note that a very small percentage of people exposed to opiates through iatrogenic means go on to continued abuse of the drug, when the conditions for which they were originally prescribed no longer exist. It appears that the attitude with which the user approaches his first experimentation with narcotics, and whether the effect of the drug usage is euphoria or the relief of a distressing condition, are much more relevant to continued usage of the drug than any supposed pre-existing genetic defect.

The second version of this metabolic disorder theory is that permanent derangement of the metabolic system of the user occurs upon extended utilization of narcotics. This theory, also, receives relatively little support from medical use of narcotics, even though there is little doubt that wide-spread prescribing of narcotics, for conditions which are not of great seriousness, results in more persons continuing to abuse narcotics. Similarly, the length of treatment with narcotics for a chronic condition is positively correlated with the use of narcotics upon termination of medical necessity. Evidence has been advanced by Martin and his associates that continued narcotic administration creates a physiological disorder that attains for at least four to six months after narcotic withdrawal. Physiological dysfunction during protracted abstinence has been suggested to be related to relapse, and studies with animals such as rats have similarly shown an association of physiological changes with relapse. Similar studies with humans have suggested an association between protracted abstinence and increased responsivity to stress. Clinical experience similarly identifies the symptoms of protracted abstinence. The important issue is that this physiological disturbance is protracted as opposed to permanent. This suggests that a methadone maintenance program would last for specific periods of time rather than the idea of life-long dependency upon the substitute narcotic. The theory also fails to explain the fact that abstinent ex-addicts would be expected to function poorly without a narcotic, but this is not proven — in fact, many examples to the contrary are known. Also, an adequate dosage of methadone or other narcotic would be expected to eliminate narcotic craving, although this seems to be present in various programs, regardless of the dosage of maintenance methadone. Studies by Garbutt and Goldstien, in which the dosage varied from 40 to 200 milligrams without the patients' knowledge, appeared not to alter their psychological state as reported by their desire for changes in dosage, or in behavior, as estimated by their actual experimentation with heroin usage while on the maintenance methadone program.

The suggestion that methadone's major role in the treatment of narcotic dependency is in permitting the effective intervention in the conditioning factors which maintain narcotic dependency can be developed more clearly, if first we examine the role of conditioning factors.
In heroin dependency there is a
three-stage cycle which usually lasts ap­
proximately six hours. The three stages
are (1) euphoria, which can vary from a
pharmacogenic orgasm to a general feel­
ing of well-being or relative lack of con­
cern with the environment; (2) normal­
ity, or the drug user's usual state when
not affected by the other stages; (3)
withdrawal.

The user may take an injection of
heroin at any point in the cycle. This is
significant because the relative effects of
learning may be dependent upon the
point in the cycle when the drug is
taken. The more marked the euphoria,
the stronger the positive reinforcement.
An injection while still in the state of
euphoria adds only the positive rein­
forcement afforded by the increment, if
any, in the euphoria. At the user's stage
of "normality" the factor of avoidance
comes into significance. As
withdrawal develops, escape becomes
the most important factor. The simple
contiguity of classical conditioning acts
throughout the cycle.

Although conditioning factors have
been generally accepted as important in
the problem of drug dependency, there
has been little discussion of how they
operate. Wickler has stressed the aver­
sive factors, stating that the variables re­
sponsible for relapse of the user after
withdrawal from drug usage are, first,
"the constant reinforcement of drug­
seeking behavior as a result of relieving
the disturbing and frightening symptoms
of the abstinent syndrome by means of in­
jection of narcotics; and secondly, con­
tioned symptoms of the abstinent syn­
drome, precipitated by stimuli, especially
environmental and interpersonal, that
have been associated with the activity of
the user previous to acquiring drugs."

I feel the factors of avoidance and es­
cape, although important, are over­
ridden by the positive reinforcement of
euphoria. In the first place, initial con­
tact with heroin is often unpleasant, due
to low tolerance. In some individuals
this prevents further involvement. More
generally, the euphoric effects of the
drug lure the user back again and again.
During this initial phase there is estab­
lished no third stage of withdrawal, so
that the pattern of dependency upon
heroin is incomplete. However, as the
user continues taking drugs, withdrawal
only later assumes its importance in per­
petuating dependency. Similarly, drug
dependency which develops with the
amphetamines does not involve the fac­
tor of physical withdrawal. However,
one the dependency is firmly estab­
lished, it is similarly very difficult to
eradicate. Thus, the initial effects of the
drug must be the most important in es­
tablishing the pattern of drug use.

The state of withdrawal is a variable
amalgam of psychological and physical
components. According to my clinical
experience, it is greatly aggravated by
anticipation, which changes an uncom­
fortable state into an agonizing one. This
fear is a tradition of the "junky". It ap­
pears to hark back to when heroin was of
a much higher strength and capable of
greater acute physical distress. The
present day levels are inconsistent and
generally weak — consequently, they
are not generally associated with severe
withdrawal states on a physical basis.
One can see this effect in vivo in the
jailed user; he goes through his "cold
turkey" withdrawal without marked dis­
tress if he is sure he will get no treat­
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The same user attempting, as he often has, this withdrawal outside of jail where he could have access to drugs, experiences excruciating symptoms which result in drug-seeking behavior.

Where no withdrawal syndrome is established, conditioned stimuli (CS) act directly to elicit the conditioned response of drug-seeking behavior (DSB). Once a withdrawal syndrome is established, it becomes incorporated into the person's behavior pattern, not only as a physiological occurrence, but also as a conditioned response (CR). Hence, once heroin dependency is established, we can depict it as follows:

<table>
<thead>
<tr>
<th>CS</th>
<th>Maintained by</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Euphoria and</td>
</tr>
<tr>
<td></td>
<td>Absence of Dysphoria</td>
</tr>
</tbody>
</table>

Figure 2.

The conditioned stimuli can be of two varieties: first, originally neutral stimuli like the sight of a connection or the smell of a match; second, original aversive stimuli arising from intrapsychic and interpersonal conflicts. The extent and significance of the latter varies widely and refers back to the predependency personality and, together with withdrawal symptoms, provides the dysphoric elements in the dependency pattern. The withdrawal is induced psychologically rather than physiologically. However, withdrawal symptoms regardless of cause also act as stimuli, since they are followed by an increased occurrence of drug-seeking behavior. The whole pattern is kept intact by effects of the drug, euphoria, and, where appropriate, the absence of dysphoria.

There is a "natural" experiment bearing on the above discussion. It is generally well accepted that users in their late thirties and forties, after many years of dependency, stop entirely. Now, it seems unreasonable to expect that they had somehow become mature and socially adept as a result of their dependency. In the outline above, the only factors which significantly vary are the effects of the drug — dysphoric factors are seldom changed. With prolonged use, developed tolerance often reaches such a point that the euphoria is so decreased that the user merely tries to stay "normal" and avoid sickness. He is, nonetheless, as prone to withdrawal symptoms as ever. Still, since the drug-seeking behavior is no longer reinforced by euphoria, the pattern initiated by this effect is now capable of extinction. Once again this suggests that the positive reinforcement of euphoria is of prime importance in the maintenance of drug dependency. Where the user quits, the absence of euphoria is likely to be the only significant change. This could be seen reasonably as the change permitting extinction to occur.

Methadone's utilization in a maintenance program would appear to be justified over the simple utilization of other opiates due to two properties of the drug — the first being that methadone is longer-acting and withdrawal symptoms do not normally become evident for 24 to 48 hours. Secondly, on a fixed dosage, the euphoric effects of taking methadone quickly dissipate — the patient is able to function in his normal or usual state. In a program where methadone is administered daily in a fixed dosage, the patient is soon no longer euphoric, and is in his state of usual normality. He is not faced with the imminent pressure of withdrawal symptoms if he shows up daily for his medication. Cross-tolerance develops between methadone and short-lasting opiates, limiting the user's ability to get "high" if he tries heroin again. With the blockage of euphoria, and delayed withdrawal, the cycle of
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euphoria to normality to withdrawal is thus eliminated. The patient remains in his normal environment but with significant changes — he no longer has to concentrate his attention on drug-seeking behavior; he is able to function normally and thus able to become employed; he is able to re-establish normal social contacts, and family relations; and his medical health is no longer markedly endangered. Furthermore, he has available to him, through his maintenance program, assistance for the increased anxiety which can be anticipated from a patient whose defense mechanisms have been disrupted by dependency on drugs, and who must now re-establish an effective set of coping mechanisms.

It is clear that the accomplishment of all of the objectives does not occur quickly. In cooperative patients, one can expect them to occur within six months to a year after getting into a program. Some persons may require less and certain persons more time in the program, depending on the assessment of other factors besides the conditioning factors. Over a period of time the patient, having established a stable way of life, has extinguished all of his conditioned responses, because of his exposure to his previous environment, even if it is of different quality and different quantity.

There is, however, one area to which he is not exposed while on the program, and that is the experience of withdrawal symptoms. Usually one sees a crisis in a patient on a maintenance program via the occurrence of a situation which simulates withdrawal symptoms. This is characterized by a severe flu-like illness with diarrhea, coryza, etc., and an occasional anxiety crisis. When withdrawing patients from a methadone program, one has to face a final stage in the conditioning cycle. A very slow and gradual reduction is mandatory, since withdrawal symptoms from methadone are much longer lasting and have greater severity than the shorter term opiates. This is probably because the dosage that the patient takes in the maintenance program is equivalently much higher than he would have used in illegal opiates. A sudden stoppage of methadone is usually accompanied by acute symptoms, becoming marked by 72 hours, and only slowly receding over a two-week period. Even with slow withdrawal, symptoms such as diarrhea, may occur, lasting several months. On occasion hospitalization is necessary for the final stages of the withdrawal cycle. Additional supportive psychotherapy is necessary at this point, but knowing precisely when to do this remains to be determined.

The World Health Expert Committee's definition of methadone maintenance is:

the continuing daily oral administration of methadone, under adequate medical supervision, with the dose being adjusted to prevent:
  a) the occurrence of abstinence phenomenon;
  b) to suppress partially or completely any preoccupation with the taking of drugs of a morphine type;
  c) to establish a sufficient degree of tolerance or cross-tolerance to blunt or suppress the effects of such agent.

It appears to me that this definition is inadequate in that it includes two types of programs which are similar, but have significant differences. The first of these types of programs is very closely tied to the concept of substituting a legal narcotic addiction pattern for an illegal narcotic addiction pattern. Here, the patient is being dispensed methadone in a supposed fixed dose, but the control over when and how it is taken is entrusted to the user himself. The patient tends to take the methadone in relationship to previous conditioned stimuli: to take a varying dose, often with the deliberate
intention to get "high"; and then to anticipate withdrawal symptoms much sooner than they would occur physiologically. In examining some narcotic treatment programs in England, I noted that methadone was often used as a precise substitute for heroin, and was given by injection even on a six-to-eight-hour cycle. Patients in these circumstances complained of feeling "sick" near the end of the cycle, and despite the absence of marked withdrawal symptoms, drug-seeking behavior was initiated.\textsuperscript{17}

Methadone, when given in a blind injection, has been found to be indistinguishable from heroin or dilaudid.\textsuperscript{18} It has the capacity to produce the previously experienced narcotic euphoria. Any narcotic taken by mouth will produce less of this, but given in widely varying doses, eg, from zero one day to 200 mg the next, euphoria can be expected to occur. Methadone is not an ideal drug of abuse because tolerance to the euphoric effects apparently occurs more rapidly, perhaps because of the long-acting effect of the drug. However, methadone has the advantage of being cheap, readily available, and somewhat freer of the impurities and other risks that usually accompany the ingestion of illegal drugs. Although it would seem that some degree of flexibility is appropriate in any methadone maintenance program, the greater control a patient has of the drug, and the greater the number of patients that have this control, the more the drug will be used to attempt to re-establish addiction patterns, in as close a facsimile to the original as is possible. Although no hard figures are available on this point, it is nevertheless a very real and significant complication.

If a patient were to receive methadone in association with life conflicts, and experienced euphoria regularly as a result of taking methadone, he would not have eliminated the narcotic cycle of heroin, but altered its length of operation. I re-emphasize the importance of withdrawal symptoms, but still maintain the critical importance of the euphoric component. No clinic would deliberately set out to establish doses of methadone that would vary from as little as zero to an indefinite maximum, in a somewhat random manner. I clearly recognize that because of the length of time it takes to develop withdrawal symptoms, such a schedule could be arranged, but it would produce in the patient the effects that he previously experienced in his illegal narcotic habit. Yet, a number of programs make the rather obvious mistake of prematurely giving control of the time, and thus, indirectly, the dosage of the methadone that the patient takes, by prescribing the drug either in tablet form or by letting the patient take the drug away from the clinic with him. If this is permitted, it is reasonable to expect that an indeterminate percentage of patients will utilize the methadone to replace the narcotic cycle previously experienced, including euphoria. Patients on methadone do not lose their desire to be "high", and their fond memories of their "high" experiences. They generally lose pre-occupation with the desire to get "high". They lose this because they are not getting "high" with methadone, and partly because methadone has been established in their minds as an agent which will prevent them from becoming "high" if they used an illegal drug such as heroin. They are thereby able to concentrate on the dimensions of an effective rehabilitation program.

In other words, it seems necessary, for an effective methadone maintenance program, to establish a dependency upon a hospital or clinic setting that is maintained by the necessity of returning daily for the methadone, in order to avoid facing severe withdrawal symptoms. Thus, with the patient coming to
the clinic daily, controlled dosage remains in the hands of the physician, permitting a rapid elimination of euphoria, and establishing a setting under which the elimination of the conditioning factors can occur. Periodic urinalyses, regular contact with the patient, and more formalized involvement such as group therapy give an adequate assessment of the patient's cooperation. With well-motivated patients, the maintenance dosage level of methadone need not be as high as was originally thought. Probably a dosage of 50 mg per day completely eliminates the dysphoric effects of being off heroin, and keeps the patient in a relatively settled state of health and mind. Dosages even at this level develop a cross-tolerance, blocking the average dose of street strength heroin. A lower dose allows for a shorter and easier withdrawal from methadone at the time when the patient should give up his dependency on the hospital or clinic.

Some patients' experimentations with heroin appear to require the use of higher doses of methadone. This would be justified to stabilize the patient in a pattern of non-abuse of other narcotics. The use of blind dosages allows reduction in total amount of methadone at an earlier stage, with less concentration in contact between the physician and patient on the dosage of methadone per se. Questions remain about precise dosages and precise patterns of using these drugs, whether the dosages relate more directly to the patient's previous length and intensity of involvement with narcotics, or to the patient's personality. At least it should be eventually related to these factors, rather than to the personality of the therapist. To deviate from this program, at least initially, is to establish the opportunity for a significant number of patients to produce a substitute addiction, not only in the physiological sense, but also in the psychological sense. I suggest it would make the eventual removal of the patient from the program more difficult, interfere with his present functioning, and may even lead to an increase in periodic heroin usage.

Summary

Hence, a maintenance methadone program is more than maintaining a patient on methadone, but is the utilization of methadone by continual administration, in relatively fixed dosages, obtained on a daily basis, under supervision, together with the assistance of an organized clinic, to aid in effective changes in the patient's personality and coping mechanisms, in improving his social situation — thus allowing eventually for the elimination of the conditioning factors which maintain his involvement in narcotics. The dependency upon the hospital for methadone may become eventually unwelcome and an aid in the total rehabilitation of the addict to a functioning member of society at or near his original potential, before involvement in narcotics.

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