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Drug Addiction and Related Clinical Problems



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The Pharmacological Rationale for Methadone Treatment of Narcotic Addiction

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Summary

Despite over a quarter-century of remarkably consistent reports from throughout the world of favorable results with the use of methadone to treat heroin addiction, this modality remains exceedingly controversial. Even among those who utilize methadone in caring for addicts, there is intense debate over optimal dosages, duration of treatment and other aspects of the medical care which is rendered. Ironically, the polarization seems to reflect a misunderstanding of the basis pharmacological rationale for methadone treatment.

In this paper the pharmacological principles which apply to narcotics in general, and to methadone in particular, are presented. It will be noted that the effects (and, in maintained patients, the lack of effect with respect to euphoria) of methadone are absolutely free of any controversy. Physicians and policy-makers must be guided by these straight-forward, unequivocal pharmacological properties in determining how methadone should be utilized in the management of patients with a chronic, potentially deadly illness.

Pharmacological Rationale for Methadone Treatment

I can not emphasize too strongly the fact that the pharmacology of methadone is not and never has been the subject of debate among knowledgeable professionals. There are moral issues, political issues, economic issues and pragmatic issues which can provoke respectful disagreement and thoughtful discussion, but the way methadone affects (and does not affect) the body is absolutely unequivocal.

Methadone is a narcotic medication, which merely means that it has a series of actions similar to those of morphine. Table 1 provides a partial listing of these actions. There are obviously many drugs which produce one or more of the individual effects listed, but unless they are capable of eliciting the entire spectrum, they are not classified as narcotics.

Table 1. Narcotic: a drug which has a series of actions similar to those of morphine

CENTRAL NERVOUS SYSTEM DEPRESSION
Respiratory depression (death)
Sleepiness
ANALGESIA
EUPHORIA
COUGH SUPPRESSION
PUPILLARY CONSTRICTION
NAUSEA AND VOMITING
INCREASED RESPIRATORY TRACT SECRETIONS
CONSTIPATION
DIAPHORESIS
ITCHING

You will note that nausea and vomiting are among the pharmacological effects of narcotics. And yet, it is obvious if addicts experienced these exceedingly unpleasant consequences daily, each time they inject heroin, we clearly would not be faced with a problem of narcotic addiction! But why does the addict not experience these effects, since they are listed - appropriately - among the pharmacological actions of narcotics? The answer is a simple one: repeated exposure to a narcotic (and indeed, to most substances) produces a tolerance to the drug's effects. Clinically, this is known to physicians and patients alike who experience the great frustration in treating pain, only to find that a tolerance to the analgesic properties of even the most potent narcotics develops quite quickly and soon reaches a stage where no relief is obtainable.

There are several characteristics of tolerance which must be stressed. First of all, tolerance does not develop to the same degree or with the same speed for each of the various actions of the drug. Thus, the addict soon develops tolerance to the adverse effects of nausea and vomiting, but is still able to achieve euphoria, and risks overdose due to the central nervous system depressant effect.

Secondly, although tolerance develops as a result of repeated exposure to a specific drug, it applies to all drugs in the same class. Thus, a patient whose pain has been treated exclusively with morphine, and who develops tolerance as a result, is unable to get analgesic relief from codeine, demerol or any other narcotic. Similarly, although the street addict's exclusive drug may have been heroin, he or she develops a tolerance to morphine, methadone and all other narcotics as well.

And thirdly, although tolerance is defined as a level of drug concentration in the body which must be exceeded before the pharmacological effect can be experienced (as shown in Fig. 1), that level may be so high that it is unreachable regardless of the amount of drug taken. A non-narcotic example of this phenomenon is the common decongestant nose drop. Initially the sufferer experiences great relief, but tolerance quickly develops and to such an extent that even an endless flow of the medicine will produce no effect whatsoever. As mentioned previously, precisely the same phenomenon precludes sustained analgesia through the administration of narcotics, even if they are given in progressively higher and higher dosages.

Along with tolerance, there is another consequence of repeated exposure to narcotics, and that is dependence. Dependence also refers to a level of drug concentration in the body, but it has nothing to do with the pharmacological actions of the drug. Rather, it is the level which must be exceeded in order to avoid the symptoms associated with the absence of the drug. As Fig. 2 indicates, when the concentration of narcotics in the body of a physically dependent individual falls below the dependence level, withdrawal symptoms result, while when the concentration is above this level there are no such symptoms.

As in the case of tolerance, dependence - even when a consequence of exposure to only a single specific drug - is in fact a dependence on the entire class of drugs. This means that withdrawal symptoms in an addict who has never taken anything but heroin can be treated effectively by the administration of any narcotic.

A range exists between the dependence level and the tolerance level which is critical to the understanding of the use of methadone in the treatment of addiction. As indicated in Fig. 3, as long as the concentration of narcotics in the body falls below the tolerance level (thus precluding the patient experiencing any of the narcotic effects), and yet is above the dependence level (thus precluding withdrawal symptoms), the patient will look and feel completely normal. The most astute clinical observer will be unable to distinguish the addict from the non-addict under these circumstances. Of course, the heroin-dependent user, if unable to obtain another fix, will experience withdrawal symptoms in a matter of hours as the drug from previous injections is metabolized and the concentration falls below the dependence level.

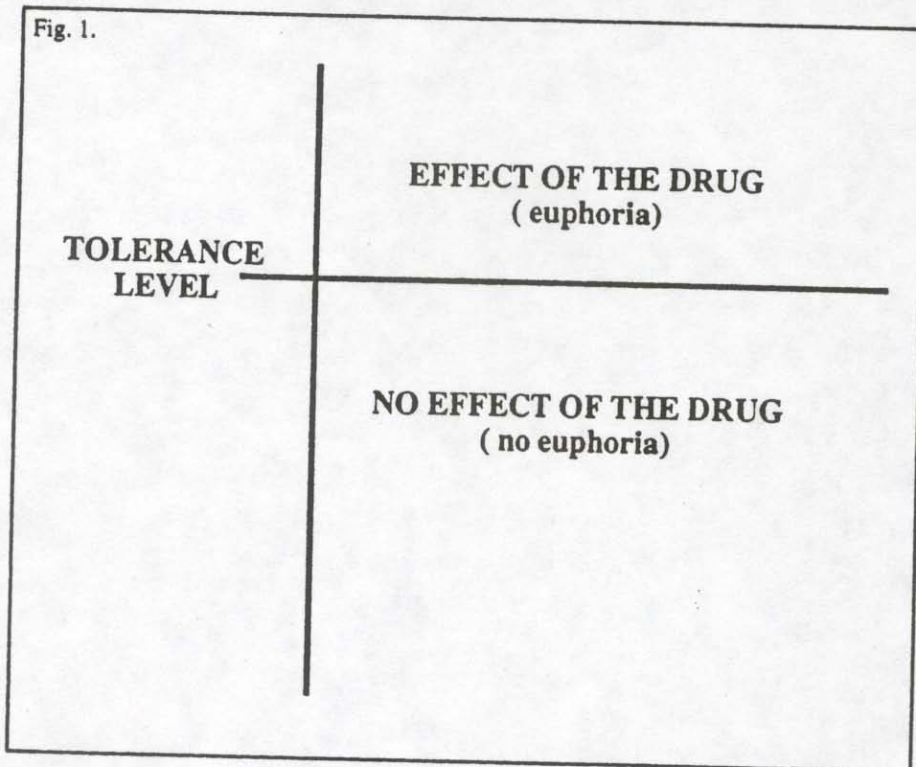


Fig. 2.

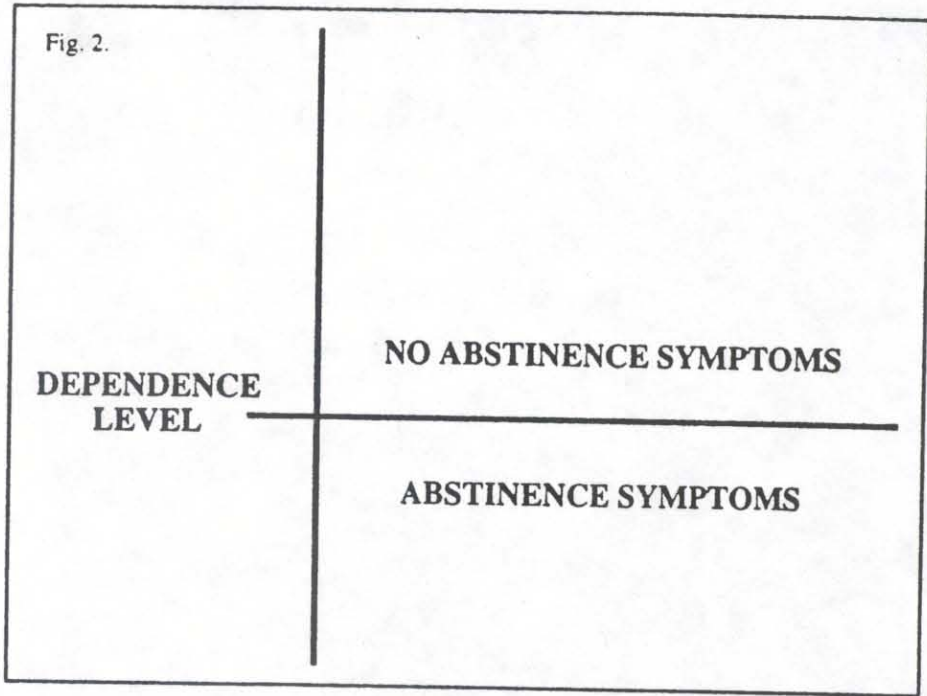
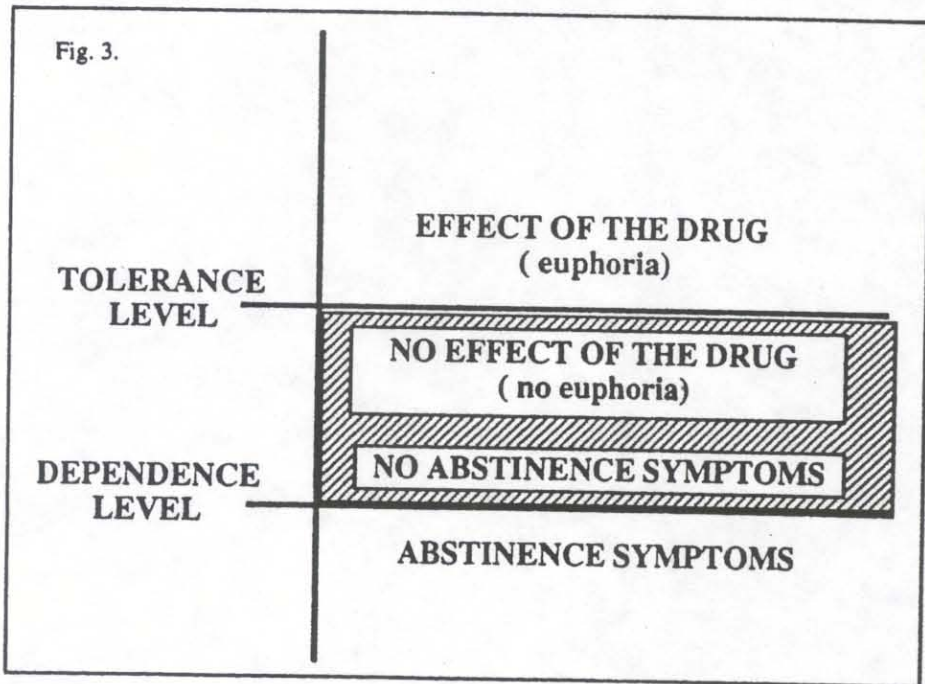
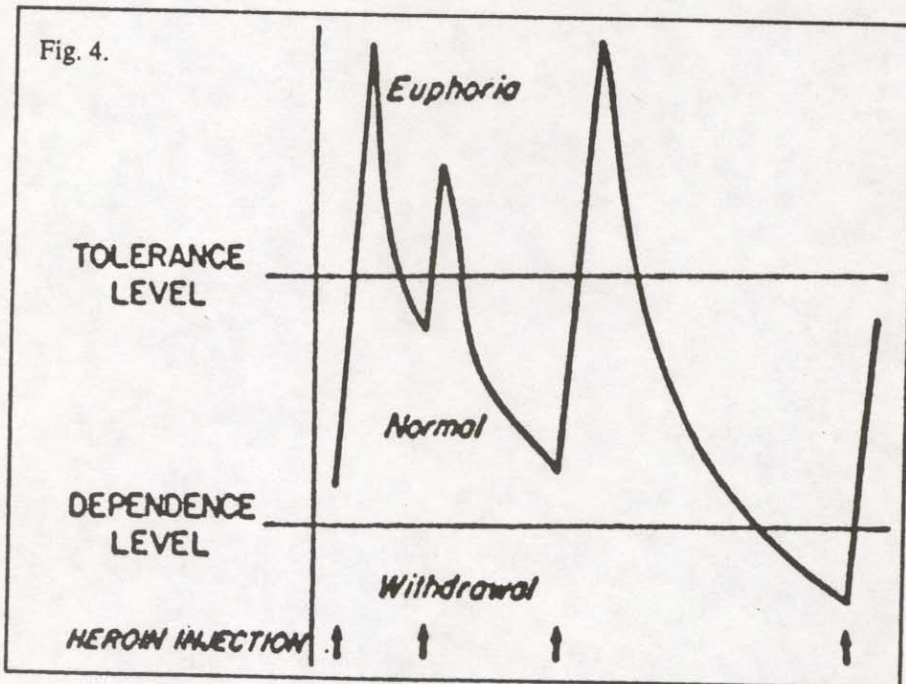


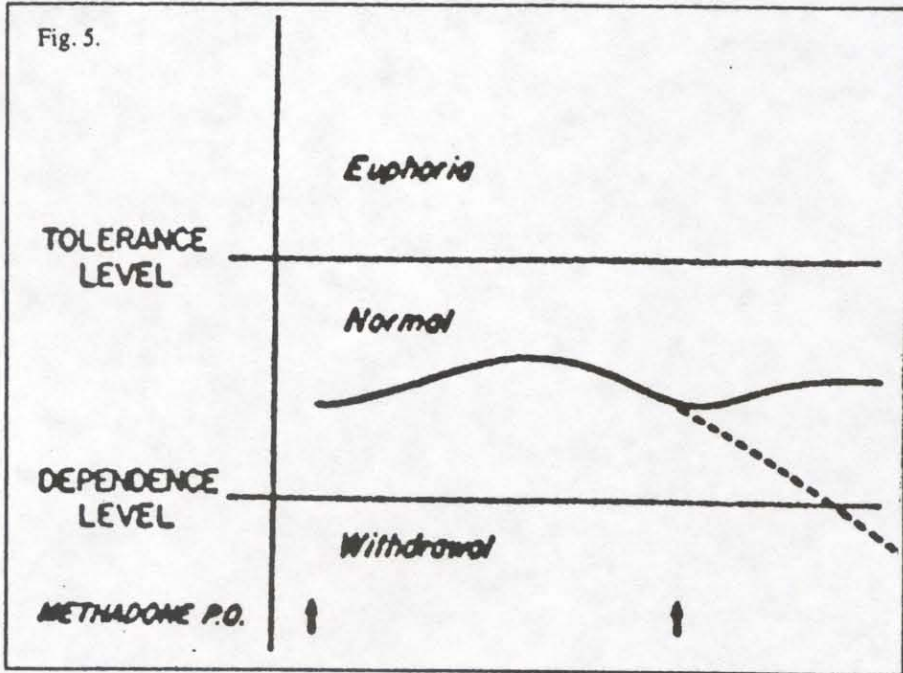
Fig. 3.



In the chemotherapeutic treatment of addiction, whether the goal is short-term detoxification or long-term maintenance, the objective is obvious: to maintain the patient in a state of physiological normalcy by keeping the narcotic concentration in the body in the range between the tolerance level and the dependence level. Theoretically, one could try to "stabilize" a patient with heroin or morphine, but this would require the administration of the drug at least four or five times each day, and by injection rather than by the oral route (Fig. 4). Obviously, such a treatment regimen would be impossible from a pragmatic standpoint. With methadone, on the other hand, this objective is relatively easy to achieve. Firstly, methadone has a very predictable effectiveness even when taken by mouth; and secondly, the duration of effectiveness is in the neighborhood of 24 to 36 hours, while that of virtually all other narcotics is no more than three to six hours (Fig. 5).

In countries throughout the world where methadone treatment has been employed, it has been demonstrated that an initial dose of methadone of 30 to 40 mgs. will prevent withdrawal symptoms without producing any significant untoward effects. This is true regardless of the amount of heroin being consumed by the individual addict, the purity of the drug or the route of administration. Once treatment has begun, the body quickly adjusts to the starting dosage such that the concentration of the narcotic in the body is maintained at approximately the mid-level between the dependence and the tolerance levels.





Methadone Used for Detoxification

Since we are dealing with a range between the two levels, and a relatively broad range at that, it is possible to increase or decrease the dosage by five or ten milligrams of methadone without crossing either of the two levels. Thus, in detoxification treatment, a decrease of five milligrams will not be accompanied by withdrawal symptoms, and after several days at the new reduced level, the dosage can be lowered once more, and this process can be repeated until methadone administration has been discontinued altogether (Fig. 6). In this way, generally in no more than 14 days, the physical dependence can be eliminated successfully without the patient experiencing withdrawal symptoms.

The benefits of such short-term addiction treatment with methadone are very substantial. It is a completely safe, very effective, relatively inexpensive (particularly when provided on an outpatient basis) medical intervention in the chronic problem of heroin addiction. It lends itself to very rapid and large-scale implementation - to the extent that virtually unlimited numbers of patients can be accommodated promptly. In this way, it can ease significantly the unconscionable situation in which addicts who desperately want treatment must remain on "waiting lists" because long-term rehabilitation programs are filled to capacity. In addition, we know from the experience in many parts of the world that no other form of treatment generates as much demand among the addict population. For example, in New York City, a network of only five ambulatory detoxification clinics admitted over 22,000 individuals yearly in the early 1970s - before the program was terminated by short-sighted government officials determined to reduce

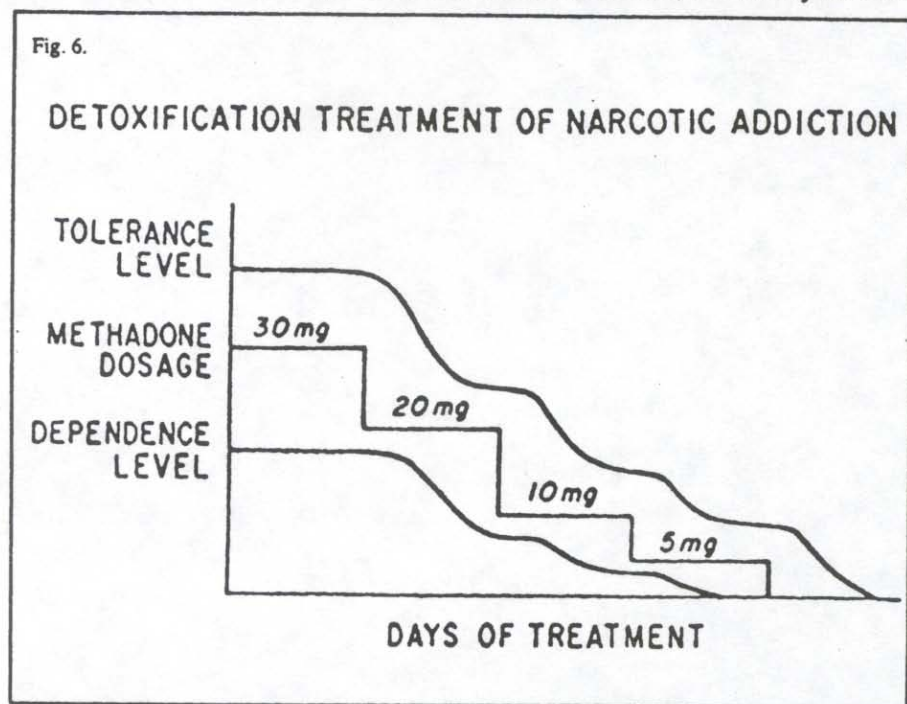
expenditures.

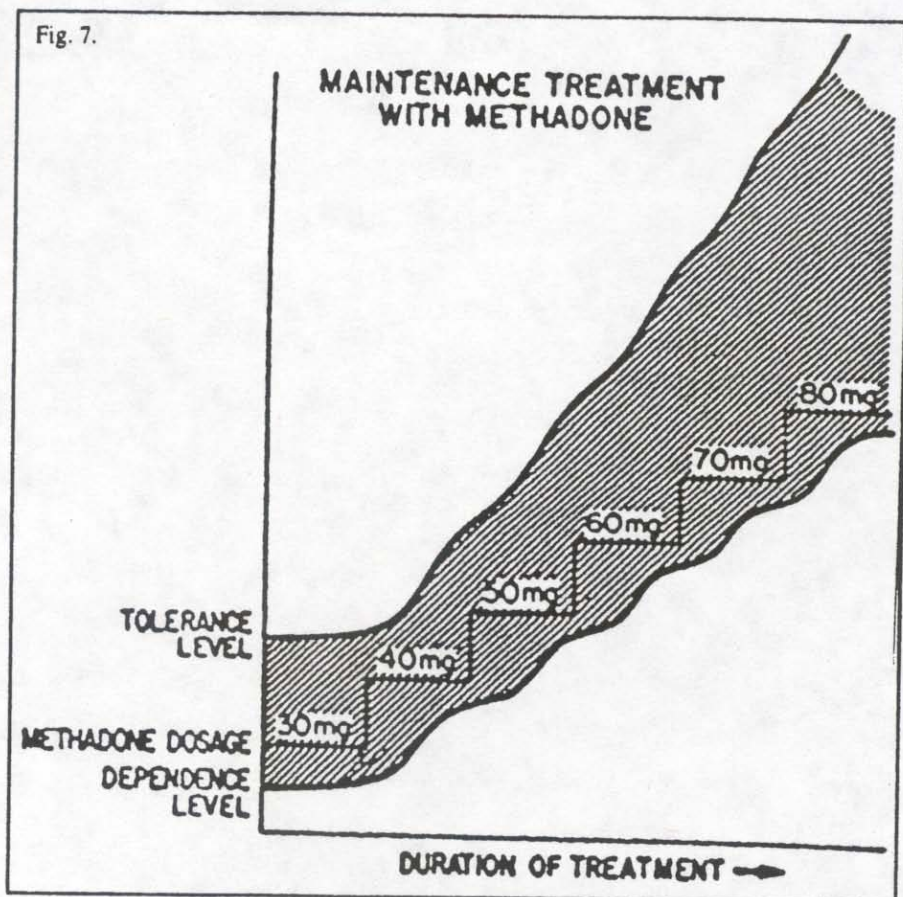
On the other hand, there is a major limitation of detoxification treatment: we know that once withdrawal from physical dependence has been accomplished, the former heroin user almost invariably will revert to illicit drug use. This might occur after a matter of days or, in some cases many months, but sooner or later relapse is the rule rather than the exception. For this reason, there is another application of methadone in the treatment of heroin addiction: as a maintenance medication for patients who are motivated to give up heroin use and the life style associated with it.

Methadone in the "Maintenance" Treatment of Addiction

Methadone "maintenance" is really a relative term and does not denote any specific duration of treatment. It should be clear from the pharmacological description above that any patient can be maintained - with any amount of methadone - for an indefinite period of time. Constant doses will maintain the concentration of methadone in the range between the dependence and the tolerance levels, and thus neither withdrawal symptoms nor narcotic effects will be experienced. It also should be obvious that any patient can be detoxified from methadone through a gradual reduction of dosage, in precisely the manner described previously, regardless of the dose and duration of methadone treatment.

A fundamental question is: why maintain a patient on methadone? The answer is simple: empirically, it has been demonstrated in countries throughout the world that individuals are able to give up illicit heroin use and to resume (and in many instances





assume for the first time) a normal, productive, socially acceptable and self-fulfilling life style while maintained on constant doses of methadone. Surely this is a compelling rationale for methadone maintenance!

Another question commonly raised is: how long should this treatment continue? The response, again, is both simple and empirical: as long as it is effective! As in any other form of medical treatment, the success of the treatment regimen is determined by how the patient responds, and the favorable assessment of a therapeutic outcome is not diminished in the slightest by the fact that the patient continues to receive medication.

What underlies the response to both of the above questions is the reality that heroin addicts, following treatment, have a tendency to relapse to illicit drug use regardless of the form of care which has been provided, its duration or its apparent effectiveness. This being the case, the conservative approach - and the common sense approach - is to continue treatment which is effective.

Some have rejected as nihilistic the notion that a persistent risk of recidivism is inevitable. Frankly, such rejection is nonsense, and ignores the experience of all addiction treatment specialists, regardless of their individual techniques, and regardless of their locale. It is worth considering the field of alcoholism, which in many respects is analogous. Alcoholics Anonymous, the most respected voice in the field of

alcoholism treatment, has as the cornerstone of its philosophy the premise that no alcoholic is ever cured, and that the illness of alcoholism persists even after a decade or more of total abstinence. The universal experience with narcotic addiction suggests most strongly that precisely the same premise applies to that form of substance abuse as well.

And finally, a word about dosages. One of the greatest absurdities in the field of addiction treatment is the perception that there is inherent goodness in prescribing the lowest possible dose of methadone. In fact, the only consideration that matters is the effectiveness of the medication; if the patient is comfortable at a particular dosage, reports no drug craving and clinically is doing well, it is inconsequential what dosage of medication is contributing to this outcome. Thus, the answer to the question of "optimal" dosage is once again an empirical one: whatever dosage is effective! Here, too, the conservative approach is to give more rather than less, as long as no side effects occur, and indeed there are no significant side effects which have been associated with methadone in either low or high dosages.

But there is a pharmacological rationale for relying, in general, on relatively higher amounts of medication. As demonstrated in Fig. 7, the tolerance level does not rise in parallel with the methadone dosage which is administered. The individual who is maintained at 30 or 40 mgs. of methadone has little difficulty through supplemental narcotics (methadone, heroin or any other drug in this class) in reaching and exceeding the tolerance level and thereby experiencing euphoria. As the maintenance dose increases, however, the proportionate increase in the tolerance level is much greater, so that it takes steadily more and more supplemental narcotics to achieve any effect. Ultimately, at a maintenance dose of approximately 80 to 90 mgs, the tolerance level is so exceedingly high that for practical purposes it is impossible for the patient to achieve euphoria or other central nervous system effects of narcotics, regardless of the amount of additional narcotics which might be taken. The sole exception is with respect to the analgesic effect; patients are tolerant to the analgesic action of the methadone dosage being taken, but this tolerance level can be exceeded by normal pain-killing doses of any narcotic medication. But again, with regard to euphoria, the patient is pharmacologically unable to achieve euphoria through misuse of narcotics, and ultimately will not be tempted to do so regardless of the circumstances or opportunities which might arise.

Conclusion

It must be stressed again that none of the above pharmacological phenomena are speculative or theoretical or the focus of controversy among knowledgeable individuals. They reflect what is known to every doctor, nurse and medical student who has prescribed narcotics for pain medication or for any other purpose. To summarize: methadone maintenance is associated with no euphoria whatsoever, and indeed at appropriate dosages renders the patient pharmacologically unable to achieve euphoria even with supplemental narcotics. It is safe, effective and in tremendous demand by addicts throughout the world who are motivated to give up illicit narcotic addiction and the associated life style, even though they will also give up the euphoria which they once enjoyed.

It is inappropriate to compare different treatments for narcotic addiction and to try to determine which is "better" than another. The problem is complex and difficult, and any treatment which offers help and which is acceptable to addicts should be made available. There is no question, however, that only methadone treatment lends itself to implementation on a massive scale. Any country which refuses to include methadone treatment as part of the therapeutic armamentarium is guaranteeing that only a tiny percentage of those who need and who want treatment will get it. Rejecting methadone treatment, therefore, amounts to dooming the vast majority of addicts, including those desperately motivated to give up the habit, to continued illicit drug use causing incalculable detriment to themselves and to the general society.