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## Present Status of Narcotic Addiction

With Particular Reference to Medical Indications and Comparative  
Addiction Liability of the Newer and Older Analgesic Drugs

abstinence from various drugs  
& time to develop addiction probably much  
greater of abstinence of 70

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## PRESENT STATUS OF NARCOTIC ADDICTION

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When the Harrison Narcotic Act was passed in 1914 there were perhaps 150,000 to 200,000 narcotic addicts, mostly women, in the United States.<sup>1</sup> Now, according to a recent estimate by Mr. H. J. Anslinger, Commissioner of Narcotics,<sup>2</sup> there is about 1 addict per 3,000 of population, or a total of approximately 48,000, mostly men. This reduction in addiction has been largely due to the vigorous enforcement of the Harrison Narcotic Act and to federal facilities for the treatment of addicts. Compared with the problems arising from the abuse of drugs such as the barbiturates and alcohol, narcotic addiction is not a great public health hazard. However, to the person and his family, narcotic addiction is a tragedy which often brings about complete ruin. Without the preventive influence of legal control and the treatment of identified addicts, narcotic addiction would spread somewhat like the infectious diseases which are public health problems.

If one listens to the inveterate narcotic addict, the question immediately arises as to why addiction should be controlled and discouraged, since the addict describes

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This article was edited previous to the date on which the Council on Pharmacy and Chemistry announced in *THE JOURNAL* the addition of a second "e" in the spelling of "methadone."

1. Kolb, L.: Drug Addiction as a Public Health Problem, *Scient. Monthly* 48:391 (May) 1939.

2. Anslinger, H. J.: Testimony Given Before the Subcommittee of the Committee on Appropriations, House of Representatives, Eightieth Congress, Second Session, Supplemental Federal Security Agency Appropriation Bill for 1949, Printed for the Use of the Committee on Appropriations, Washington, D. C., Government Printing Office, 1948.

"God's medicine" as the agent which makes him at ease, contented, ambitious and of such improved efficiency that he can compete on normal terms with his fellowman. This effect is not seen in the majority of cases. After mentioning the exceptional persons who may adapt to life's difficulties better with narcotic drugs, Kolb said of morphine and morphine-like drugs<sup>3</sup>:

. . . when taken in large doses, [they] sap the physical and mental energy; lethargy is produced, ambition is lessened, and the pleasurable feeling already described—that all is well—makes the addicts contented. These various effects cause them to pay less attention to work than formerly; consequently, they tend to become idlers by this means alone. Those who depend upon the illegitimate traffic are sometimes unable to work because of discomfort and weakness due to insufficient narcotics, and at other times they stay away from their work in order to look for the drug. There are cases . . . who have gone to distant cities regularly to get an ounce of heroin or morphine, and others who have lost as many as a dozen jobs through neglecting work to meet their peddlers, or through lying in bed in the morning instead of going to work because the dose that would have put energy into them was not available. Often, when these cases secure a supply, after their short periods of deprivation, they take more than is actually necessary to keep them comfortable. The result is that they alternate between physical and mental irritability and physical and mental lethargy. Both extremes make for emaciation, physical inefficiency, and unusual mental reactions.

The dreamy satisfaction and the pleasurable physical thrill produced by opium in many addicts in their early experiences with it are of themselves forms of dissipation that tend to cause moral deterioration. Addicts, as a rule, are compelled to associate with persons of low moral character in order to continue their addiction. Financial embarrassment resulting from idleness or the high price of peddled narcotics impels them to beg money from their friends, obtain it from members of their families by subterfuge, or steal, in order to supply themselves with drugs; they suffer in manliness through feeling what they often consider the just contempt of the public; they suffer through their constant fear of arrest, or because of a term in the penitentiary served for having narcotics in their possession. This train of events brings about unfavorable character changes and gradual moral deterioration, and converts what might have been fairly useful citizens into outcasts, idlers, or dependents.

In spite of the fact that there is no consistent organic damage seen in the body following prolonged and exces-

3. Kolb, L.: Pleasure and Deterioration from Narcotic Addiction, *Ment. Hyg.* 9: 699 (Oct.) 1925.

sive use of narcotic drugs, character deterioration is real and great, as evidenced by the deliberate policy of the Japanese in the late war to make addicts of large segments of the alien populations under their control.

#### DEFINITION OF DRUG ADDICTION

Drug addiction may be defined as a state in which a person has lost the power of self control with reference to a drug and abuses the drug to such an extent that the person or society is harmed. In the United States, only derivatives of opium (including morphine, heroin, dihydromorphinone hydrochloride ["dilaudid hydrochloride"], codeine and metopon), the morphine-like synthetic drugs (including meperidine hydrochloride ["demerol hydrochloride"], methadon [amidone, "dolphine," 10820] and isomethadon), cocaine and marijuana are under control of the Harrison Narcotic Act and similar acts. There are other drugs which, according to our definition, are addicting, including the barbiturates, bromides, alcohol, peyote (mescaline) and amphetamine, but none of these are subject to legal control. However, users of peyote are eligible for treatment at the federal hospitals for drug addicts.

Himmelsbach and Small<sup>4</sup> described addiction to opium and similar drugs as embracing three intimately related but distinct phenomena: (1) tolerance, (2) physical dependence and (3) habituation.

Tolerance is defined as a diminishing effect on repetition of the same dose of the drug or, conversely, a necessity to increase the dose to obtain an effect equivalent to the original dose when the drug is administered repeatedly over a period of time. Physical dependence refers to an altered physiologic state, brought about by the repeated administration of a drug over a long period of time, which necessitates the continued use of the drug to prevent the appearance of the characteristic illness which is termed an abstinence syndrome. Habituation refers to emotional or psychologic dependence on the drug—the substitution of the drug for other types of adaptive behavior. Habituation is closely related to a drug's euphoric effect, i. e., relief of pain or emotional discomfort.<sup>3</sup>

4. Himmelsbach, C. K., and Small, L. F.: *Clinical Studies of Drug Addiction: II. "Rossium" Treatment of Drug Addiction; with a Report on the Chemistry of "Rossium,"* Supplement 125 to the Public Health Reports, United States Treasury Department, Public Health Service, 1937, p. 1.

The comparative importance of these three qualities in the total picture of addiction is still a matter of dispute. The role of tolerance in addiction is obscure and difficult to evaluate. Tolerance, however, has been shown to develop to all morphine-like drugs. It is empirically included as one of the qualities of the addicting drug. Physical dependence has been regarded by many persons, particularly by pharmacologists, as the primary and only distinguishing characteristic of an addicting drug. Other persons, particularly psychiatrists, regard emotional dependence or habituation as the all-important factor in addiction. Some have gone so far as to claim that withdrawal symptoms are psychic and not of physiologic origin. A view intermediate between these two extremes is probably correct. Both physical and emotional dependence are important in addiction to morphine. Wikler<sup>5</sup> has shown that physical dependence on morphine and methadon develops in the isolated segments of the spinal cord in chronic spinal dogs, and also that physical dependence occurs in chronic decorticated dogs. Wikler's observation proves beyond doubt that physical dependence is a real physiologic entity and is not psychic in origin. On the other hand, physical dependence does not explain why addicts begin the use of drugs, continually increase the dose and number of doses until they are dependent. Nor does physical dependence explain why so many addicts repeatedly relapse to the use of drugs long after the withdrawal illness has subsided. Some addicts begin to use drugs for the alleviation of pain caused by organic lesions; others take up the habit to relieve emotional tension; all continue to use the drug because they enjoy the sensation it produces when taken in amounts beyond that necessary to alleviate or to prevent the appearance of the withdrawal illness.

Barbiturates fulfil all three criteria of addiction: tolerance is developed; habituation is developed; physical dependence, although not seen as consistently as with morphine, has been repeatedly observed among our patients who have used barbiturates alone or with

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5. Wikler, A.: Hindlimb Reflexes in Chronic Spinal Dogs During a Cycle of Morphine Addiction, *Federation Proc.* **4**: 141 (March) 1945. Wikler, A., and Frank, K.: Tolerance and Physical Dependence in Intact and Chronic Spinal Dogs During Addiction to 10820 (4-4-diphenyl-6-dimethylamino-3-heptanone), *ibid.* **6**: 384 (March) 1947. Wikler, A.: Reactions of Chronic Decorticated Dogs During a Cycle of Addiction to Methadon, *ibid.* **7**: 265 (March) 1948.

morphine. If barbiturates are withdrawn abruptly from patients who have been taking 12 grains (0.78 Gm.) or more daily for several weeks, convulsions may develop in three to four days and acute psychotic reactions may be seen after seven to ten days. Both of these conditions can be avoided by gradual reduction of the daily dose of barbiturates over a period of three weeks.

Bromide addicts show habituation but not physical dependence, as demonstrated by the fact that withdrawal is best accomplished abruptly and by elimination procedures. Tolerance to bromides is doubtful.

Amphetamine fulfils the most important qualification, that of habituation, but neither physical dependence nor tolerance develops. The best treatment is abrupt withdrawal of the drug.

Cocaine produces habituation but does not induce physical dependence or tolerance. Cocaine, when taken intravenously, produces an orgasmic sensation, and addicts repeat their doses at very short intervals in order to experience this feeling of ecstasy as often as possible. As the dose is repeated, the toxic effects of cocaine accumulate and the users have hallucinations and paranoid delusions, which may be dangerous. The toxic effects of cocaine are so unpleasant that there are few pure cocaine addicts in the United States. Ordinarily the drug is used in conjunction with some physiologic antidote, particularly morphine.

Marihuana causes a mild form of intoxication which is popular among maladjusted adolescents and others, including musicians. Neither tolerance nor physical dependence develops with this drug.<sup>6</sup> The greatest danger of smoking marihuana appears to be possible precipitation of disturbed behavior in persons with incipient psychoses.<sup>6c</sup>

With alcohol, tolerance and habituation definitely develop. It is possible that delirium tremens, alcoholic "epilepsy" and other phenomena sometimes attributed to toxic effects of alcohol represent abstinence syndromes based on physical dependence on this drug.

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6. (a) Wallace, G. B.: *The Marihuana Problem in the City of New York: Sociological, Medical, Psychological and Pharmacological Studies*, Lancaster, Pa., Jacques Cattell Press, 1945. (b) Reichard, J. D.: *Some Myths About Marihuana*, *Federal Probation*, 10:15 (Dec.) 1946. (c) Williams, E. G.; Himmelsbach, C. K.; Wikler, A.; Ruble, D. C., and Lloyd, B. J.: *Studies on Marihuana and Pyrahexyl Compound*, *Pub. Health Rep.* 61:1059 (July 19) 1946.

## ETIOLOGIC ASPECTS

Drug addiction should be regarded as a symptom of a basic underlying personality maladjustment. These personality disorders run the gamut of the standard psychiatric nomenclature from the simple anxiety states to the major psychoses. A vast majority of narcotic drug addict patients are fundamentally emotionally immature childlike persons, who have never made a proper adaptation to the problems of living. Many of our patients are former alcoholic addicts who found that narcotic drugs relieved their inner emotional tension as effectively as alcohol but, at the same time, did not produce obvious signs of intoxication. After changing from alcohol to narcotic drugs, alcoholic addicts may be able, for a period of time, to deceive themselves and their associates into believing that they are making a satisfactory adjustment.

The kinds of personality disorders which underlie drug addiction have been well described by Kolb<sup>7</sup> and by Felix,<sup>8</sup> who lists four general personality types.

The first group is made up of normal persons accidentally addicted. It consists of patients who in the course of an illness have received drugs over an extended period of time and, following relief of their ailments, have continued the use of drugs. These persons are frequently termed "accidental" or "medical" addicts. Such persons are regarded by some authors as constituting a special group of addicts who are different from those persons who began the use of drugs as a result of association with persons who were already addicted. In our experience, all "medical" addicts have some fundamental emotional problem which causes them to continue the use of drugs beyond the period of medical need. There is, then, no basic difference between "medical" and "nonmedical" addicts except in the mode of the original contact with drugs. In persons with stable personalities, social pressure, conscience and a well balanced emotional makeup negate the pleasure produced by drugs sufficiently to prevent their continued use.

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7. Kolb, L.: Types and Characteristics of Drug Addicts, *Ment. Hyg.* **9**: 300 (April) 1925.

8. (a) Felix, R. H.: Some Comments on the Psychopathology of Drug Addiction, *Ment. Hyg.* **23**: 567 (Oct.) 1939; (b) An Appraisal of the Personality Types of the Addict, *Am. J. Psychiat.* **100**: 462 (Jan.) 1944.

The second group consists of persons with all kinds of psychoneurotic disorders who, as Felix<sup>5a</sup> said, take drugs to relieve whatever symptoms they may have. The manifestation of the neurosis may be anxiety, an obsession or compulsion or any of the great group of psychosomatic disorders.

The third and largest group consists of psychopathic persons, who ordinarily become addicted through contact and association with persons already addicted. They are generally emotionally undeveloped aggressive hostile persons who take drugs merely for pleasure arising from the unconscious relief of inner tension, as shown by this statement of an addict:

I was always getting into trouble before I got on drugs—never could seem to get comfortable; I had to go somewhere and do something all the time. I was always in trouble with the law. Some fellows told me about drugs and how good they made you feel, and I tried them. From then on I was content as long as I had my drugs—I didn't care to do anything but to sit around, talk to my friends occasionally, listen to the radio, and only be concerned with the problem of getting money for drugs. This I usually did by picking pockets or other such petty stuff.

The fourth and smallest group is characterized by drug addiction with psychosis. The persons in this group, many of whom have borderline mental illness and sometimes frank mental illness, are seemingly able to make a better adjustment while taking drugs. Sometimes it is difficult to establish the diagnosis and not until drugs are withheld does the psychosis become apparent.

There is a category of patients not included in the aforementioned groups. Kolb<sup>7</sup> originally listed these as patients with psychopathic diathesis. While it is true that some of these exhibit much of the overt behavior pattern of psychopathic persons, when studied carefully they usually fall into a milder behavior or character disorder group, which has characteristics of both the psychoneurotic and the psychopathic groups. Included are persons with severe dependency problems, withdrawn schizoid types, emotionally immature adults, as well as those suffering with the milder degrees of maladjustment and inadaptiveness to the complications of living. Felix<sup>5a</sup> stated that most of the persons falling into this



group were making a marginal adjustment to life before becoming acquainted with narcotics. After their first few experiences with narcotics they felt an exhilaration and a sense of relief comparable to the solution of a difficult problem or the shaking off of a heavy responsibility. Many of them also felt an increase in efficiency which, in some cases, appeared to have been actual improvement.

In general, persons who never have been able to make a satisfactory adjustment to life, whose adaptive patterns of behavior have been inadequate, frequently find in morphine, much as the tired business man finds in the preprandial cocktail, a means of return to "normal." This is a false situation which may be recognized by the tired business man but is not recognized by the drug addict. Our studies indicate that patients who have made a marginal degree of emotional adjustment to life, and then have begun to use drugs, lose some of their normal adaptive patterns of adjustment. This regression in personality represents the greatest danger of drug addiction.

#### DIAGNOSIS OF OPIATE ADDICTION

The diagnosis of addiction is usually made by the patient's statement that he is addicted to and needs drugs. At times, however, addicts attempt to conceal their addiction and the diagnosis may be difficult. There are no pathognomonic physical signs of addiction, but emaciation, needlemarks and abscess scars are suggestive. In some instances, none of these signs may be present. Miosis is not a reliable sign, as partial tolerance to the pupillary constriction caused by morphine develops during addiction. Signs of intoxication, such as ataxia and slurred speech, are seldom present unless the addicts are taking barbiturates or some other sedative drug in addition to morphine. Meperidine hydrochloride addicts are likely to show pronounced dilatation of the pupils and muscular twitching. Laboratory tests for the presence of morphine or other drugs in the urine furnish almost absolute evidence that the patient is receiving drugs, but these tests are difficult to carry out and ordinarily are not available. In questionable cases, the only possible method of diagnosis may be isolation of the patient from the source of drugs and observation for signs of abstinence.

The signs of abstinence have been delineated best by Himmelsbach and his co-workers.<sup>9</sup> One must always distinguish between the true signs of abstinence and signs which are attributable to anxiety reaction or symptoms which are feigned in an effort to obtain drugs. If morphine is abruptly withdrawn from a patient who has been receiving as much as 4 to 6 grains (0.26 to 0.39 Gm.) daily for a period of thirty days or more, few signs are seen in the first eight to sixteen hours of abstinence. The patient is likely to go into a restless tossing sleep which lasts several hours. About fourteen hours after the last dose of the drug, yawning, rhinorrhea, sweating and lachrimation are noticed. These mild signs increase in intensity during the first twenty-four hours of abstinence; thereafter they become constant. At this time, dilatation of the pupils and recurring waves of gooseflesh appear. One must observe patients carefully in order to detect these signs.

About thirty-six hours after the last dose, uncontrollable twitching of the muscles occurs (the origin of the term "kicking the habit"). Severe cramps develop in the legs, abdomen and back; anorexia and insomnia become prominent; vomiting and diarrhea are frequently seen. Rectal temperature rises about 2 degrees (F.); respiratory rate rises to 25 to 30 per minute; systolic blood pressure is usually elevated about 15 mm. of mercury; caloric intake is sharply reduced; weight loss averages 5 or 6 pounds (2.3 or 2.7 Kg.) a day. These acute signs and symptoms reach their height forty-eight hours after the last dose of morphine is taken and remain at a peak until seventy-two hours have passed. They then gradually subside over the course of the next five to ten days. Insomnia and changes in pulse rate, body temperature and the hematocrit reading can be detected for as long as three to four months after withdrawal. A simple clinical method for grading the intensity of abstinence is shown in table 1.

9. (a) Himmelsbach and Small,<sup>4</sup> (b) Kolb, L., and Himmelsbach, C. K.: Clinical Studies of Drug Addiction: III. A Critical Review of the Withdrawal Treatments with Method for Evaluating Abstinence Symptoms, Supplement 128 to the Public Health Reports, United States Treasury Department, Public Health Service, 1938, p. 1. (c) Himmelsbach, C. K.: Studies of Certain Addiction Characteristics of (a) Dihydromorphine ("Paramorphan"), (b) Dihydrodesoxymorphine-D ("Desomorphine"), (c) Dihydrodesoxycodine-D ("Desocodine"), and (d) Methyl-dihydromorphinone ("Metopon"), J. Pharmacol. & Exper. Therap. **67**: 239 (Oct.) 1939.

The intensity of abstinence from morphine is dependent more on the dose the addict has been receiving than on any other single factor.<sup>10</sup> Mild grades of abstinence may be detected in former morphine addicts after the administration of as little as 20 mg. ( $\frac{1}{3}$  grain) of morphine four times daily for thirty days. Grades of abstinence which are as intense as any that can be developed with any drug for any period of time can be produced by the administration of 60 to 90 mg. (1 to  $1\frac{1}{2}$  grains) of morphine four times daily for thirty days.

The picture of abstinence from heroin, dihydromorphinone hydrochloride<sup>11</sup> and metopon<sup>9c</sup> is qualitatively similar to that of morphine, and the intensity is as

TABLE 1.—*Simple Clinical System for Evaluating Intensity of Abstinence Syndrome*

Mild (+)	Moderate (++)
Yawning	Gooseflesh
Lacrimation	Dilated pupils
Rhinorrhoea	Anorexia
Perspiration	Muscle tremor
Pronounced (+++)	Severe (++++)
Insomnia	Emesis
Restlessness	Diarrhea
Hyperpnea	Weight loss
Elevation of blood pressure	(5 pounds [2.3 Kg.] in 24 hours)

great, except in the case of metopon. Abstinence from these drugs comes on more rapidly than does abstinence from morphine and subsides somewhat more quickly. Abstinence from codeine,<sup>12</sup> while very definite, is less intense than abstinence from morphine, comes on more slowly and subsides more slowly. Abstinence from meperidine hydrochloride ("demerol hydrochloride")<sup>13</sup> is also milder, comes on more rapidly and subsides somewhat more rapidly than the illness from withdrawal

10. Andrews, H. L., and Himmelsbach, C. K.: Relation of the Intensity of the Morphine Abstinence Syndrome to Dosage, *J. Pharmacol. & Exper. Therap.* **81**: 288 (July) 1944.

11. King, M. R.; Himmelsbach, C. K., and Sanders, B. S.: Dilaudid (Dihydromorphinone): A Review of the Literature and a Study of Its Addictive Properties, Supplement 113 to the Public Health Reports, United States Treasury Department, Public Health Service, 1935, p. 1.

12. Himmelsbach, C. K.; Andrews, H. L.; Felix, R. H.; Oberst, F. W., and Davenport, L. F.: Studies on Codeine Addiction, Supplement 158 to the Public Health Reports, Federal Security Agency, Public Health Service, 1940, p. 1.

13. Himmelsbach, C. K.: Studies of the Addiction Liability of Demerol (D-140), *J. Pharmacol. & Exper. Therap.* **75**: 64 (May) 1942; Further Studies on the Addiction Liability of Demerol, *ibid.* **79**: 5 (Sept.) 1943.

of morphine. Abstinence from methadon<sup>14</sup> comes on rather slowly, is mild in intensity and subsides slowly. Abstinence from methadon is qualitatively different from abstinence from morphine in that few of the signs of autonomic dysfunction, which are so prominent following withdrawal of morphine, are seen after withdrawal of methadon. The comparative intensity of abstinence following withdrawal of morphine, codeine, meperidine hydrochloride and methadon is shown in figure 1.

Experience is of the utmost importance in diagnosing and treating drug addiction. The factors which have

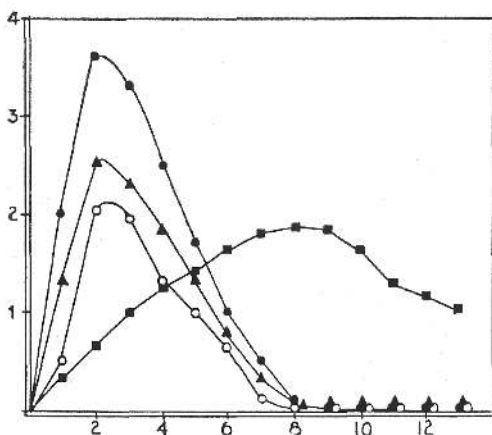


Fig. 1.—Comparative intensity of abstinence from various drugs. The solid circles indicate abstinence from morphine, the open circles abstinence from codeine, the triangles abstinence from meperidine hydrochloride and the squares abstinence from methadon. The vertical line of figure shows the intensity of abstinence (clinical grades), and the horizontal row of figures shows the number of days of abstinence.

operated to induce addiction must be remembered. The problems which have arisen during the course of a person's becoming addicted to the drug, such as the legal and emotional aspects and other psychiatric and social implications, must be developed in the addiction history and evaluated before the individual addict can be fully understood.

14. Isbell, H.; Wikler, A.; Eddy, N. B.; Wilson, J. L., and Moran, C. F.: Tolerance and Addiction Liability of 6-Dimethylamino-4,4-Diphenyl-Heptanone-3 (Methadon), *J. A. M. A.* **135**: 888 (Dec. 6) 1947.

## TREATMENT OF DRUG ADDICTION

Withdrawal of drugs from narcotic addicts on an outpatient or office basis should not be undertaken; it almost surely will fail. Withdrawal in any environment except that of a well managed institution under the control of persons trained in treatment of addiction is difficult to accomplish. In the treatment of addiction, short hospitalization for withdrawal without a prolonged period of institutional rehabilitation is as futile as simple detoxification for chronic alcoholism. Men and women addicted to the drugs controlled by the Harrison Narcotic Act, as amended, are eligible for treatment as federal prisoners, as federal probationers or as voluntary patients at the Lexington and Fort Worth hospitals. Applicants for voluntary treatment should write to the Surgeon General of the United States Public Health Service, Washington, D. C. Voluntary patients are asked to pay \$1 per day toward the cost of their treatment, but this may be waived if the patient is unable to pay. Women are treated only at the Lexington hospital. Since the great majority of addicts are in an impecunious condition, the two Public Health Service hospitals offer the only opportunity of successful treatment for most addicts.

Although withdrawal is the least important part of the treatment of drug addiction, it should be accomplished in the quickest, smoothest and most humane manner possible, so as to establish good rapport between patient and physician on which to base subsequent psychotherapy and rehabilitation.

A large number of methods of withdrawing morphine from addicted patients have been advocated over the years past. Some of these methods of treatment have been illogical, and some have even been more dangerous than abrupt withdrawal of morphine.<sup>15</sup> We are referring to the purgation, the blister, the scopolamine hydrobromide, atropine, insulin and heavy sedation treatments.

Wieder<sup>15</sup> recently conducted carefully controlled experiments on the effect of insulin on the withdrawal syndrome, since favorable reports on this treatment had appeared in the literature. He observed that insulin did not allay the withdrawal picture and, in one or two instances, seemed to make it worse.

15. Wieder, H.: Objective Evaluation of Insulin Therapy of the Morphine Abstinence Syndrome, to be published.

Until the discovery of methadon, rapid reduction of the intake of morphine over a period of about ten days has been the most satisfactory method of treatment in our hands. In recent years, it has rarely been necessary to give more than 30 mg. ( $\frac{1}{2}$  grain) of morphine every six hours to prevent the appearance of signs of abstinence in the first two days of withdrawal; usually 15 mg. ( $\frac{1}{4}$  grain) of morphine every six hours suffices for this purpose. The dosage of morphine is reduced rapidly at the beginning of withdrawal and more slowly near the end of the withdrawal period. It is unnecessary to substitute codeine for morphine.

Since the introduction of methadon and its acceptability as a physiologic and psychologic substitute for morphine, we have used it extensively in withdrawing morphine from addicts by shifting to methadon which is then withdrawn gradually. Ordinarily one can substitute one-fourth the amount of methadon by weight for the dose of morphine the addict has been receiving without signs of abstinence appearing. Since methadon is a slowly acting cumulative drug, it is started in doses of 10 to 20 mg. ( $\frac{1}{6}$  to  $\frac{1}{3}$  grain) three times daily twenty-four hours before morphine is discontinued. The dose of methadon is then reduced rapidly over the course of the next ten days. Signs of abstinence still will be observed but are not as pronounced as the signs seen during gradual reduction of morphine (fig. 2). Since drug addicts do not like to bear even minimal discomfort, they may complain bitterly during methadon reduction and may refuse to continue treatment, as they often do during morphine reduction.

Adjunctive therapy to either the morphine reduction or the substitution and reduction of methadon treatments includes use of small doses of sedative drugs. It is important not to use large doses of sedative drugs in treating physical dependence since excessive sedation seems to accentuate the development of emotional upsets during withdrawal. Furthermore, the use of sedative drugs prolongs emotional dependence on drug therapy. Flow baths are helpful in relieving excessive nervousness. A generous intake of fluids and an abundant diet should be supplied. In cases of addiction which are complicated by serious debilitating organic disease, the withdrawal period should be extended for as much as several months. The chief complication which has to be dealt with in the withdrawal of morphine in

current circumstances is the presence of simultaneous barbiturate addiction. Anxiety and hysterical reactions and attempts at malingering occur frequently during withdrawal and must be handled by appropriate psychotherapeutic technics as they arise. As regards major psychotic reactions, in a series of 400 narcotic addicts observed, only 1 became definitely psychotic during withdrawal.<sup>16</sup>

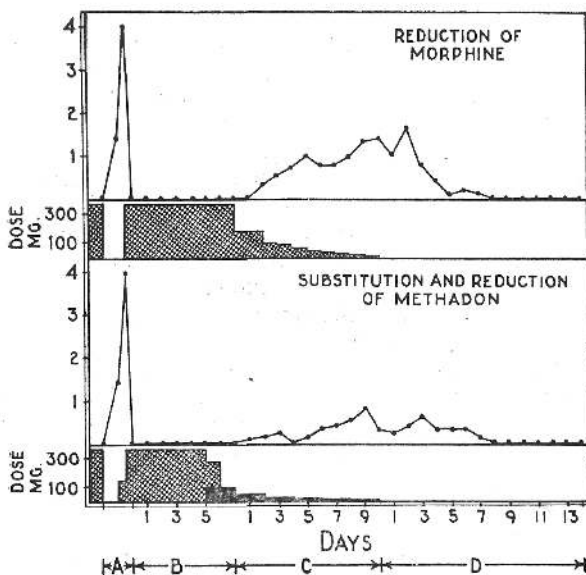


Fig. 2.—Graph of treatment of physical dependence on morphine by substitution and reduction of methadon as compared to reduction of morphine. The points shown represent the average intensity of abstinence (grades 1, 2, 3 and 4 in vertical column at left) in 10 patients who were addicted to 360 mg. (6 grains) of morphine daily. In the first experiment, 5 patients were withdrawn by simple reduction of morphine and 5 patients were withdrawn by substitution of methadon for morphine, followed by reduction of methadon. After fourteen days of total abstinence all 10 subjects were readdicted to morphine and, when withdrawal was again carried out, the 5 men who were originally withdrawn by reduction of morphine were withdrawn by substitution and reduction of methadon, and *vice versa*. Period A: preliminary thirty-six hour withdrawal of morphine for proof and assessment of intensity of physical dependence. Period B: restabilization on morphine. In the methadon graph, substitution of 90 mg. (1½ grains) of methadon for 360 mg. (6 grains) of morphine was effected on the sixth and seventh days. Period C: reduction of morphine or methadon. Period D: total abstinence from drugs.

Prefrontal lobotomy may be useful in the treatment of narcotic addiction so far as it relieves intractable pain.

16. Pfeffer, A. Z.: Psychosis During Withdrawal of Morphine, Arch. Neurol. & Psychiat. 58: 221 (Aug.) 1947.

The patient should remain in an institution for a minimum period of four to six months, so that there will be sufficient time to relieve the patient of any physical ailments and give him an opportunity to develop habits of living, eating, playing and working without drugs. During this period, every effort should be made to help him discover the source of his emotional difficulty and develop some insight into his problems.

Unfortunately, only about 25 per cent of our patients are able to benefit by other than coercive treatment. The remainder are persons whose characters have been so disordered from childhood that they have never been able to grow up and make mature adjustments or establish the proper relationship with other persons. Voluntary patients frequently leave the hospital prematurely and against medical advice, so that, in the present state of our knowledge, we are not able to do much for these persons.

#### PROPER USE OF NARCOTIC DRUGS

*Analgesic Effect.*—Since the presence of severe pain which cannot be relieved by simpler means is the major indication for the administration of any of the potent analgesic drugs, an understanding of the mechanism of relief of pain with these drugs is important in their use. Wolff and his collaborators<sup>17</sup> have developed a theory of analgesia which states that the pain-relieving effects of the opiates, or similar drugs, are due to a combination of three factors: (1) elevation of the threshold for perception of pain, (2) an alteration of the emotional reaction to pain and (3) the production of sedation and sleep. Elevation of the pain threshold and the production of sedation and sleep appear to be less important than alteration of the emotional reaction to pain. If morphine is given after the experimental production of pain in human subjects, the pain threshold is not elevated and yet the pain is relieved.<sup>17</sup> Since most patients who receive morphine have experienced pain prior to administration of the drug, elevation of the pain threshold is probably of minor importance in clinical practice. Relief of pain is not necessarily associated with the production of sedation and sleep. The

17. Wolff, H. G.; Hardy, J. D., and Goodell, H.: Studies on Pain: Measurement of the Effect of Morphine, Codeine and Other Opiates on the Pain Threshold and an Analysis of Their Relation to the Pain Experience, *J. Clin. Investigation* **19**: 659 (July) 1940.



barbiturates, though powerful sedative and hypnotic drugs, are not effective analgesics. Most of the pain-relieving action of the powerful analgesics must, therefore, be ascribed to a rather specific alteration in the emotional reaction to pain. A person with severe pain who receives a dose of morphine, or some other potent analgesic drug, may continue to perceive the pain, but, since the pain seems to have lost its dangerous quality, the patient disregards it and, under the hypnotic influence of the drug, drifts off to sleep. It seems reasonable to assume that the alteration of the emotional reaction to pain by the analgesic drugs may be associated with the euphoria produced by these compounds. The exact

TABLE 2.—*Comparative Efficacy of Single Doses of New Drugs in Altering Various Factors Concerned in Analgesia\**

Drug	Dose (Mg.)	Alteration			Duration of Clinical Relief of Pain—Hours
		Elevation of Pain Threshold	of Reaction to Pain	Sedation	
Morphine.....	10	2	2	1	4
Metopon.....	6	1	1	3	4
Meperidine hydrochloride	100	4	3	2	3
Methadon.....	5-10	3	4	4	4-10
Codeine.....	30	5	5	5	4

\* The figure 1 indicates the most effective of the 4 drugs in producing the effect noted; the figure 4 indicates the least effective of the 4 drugs.

sites and mechanism of action of these drugs within the central nervous system are not yet understood, but the fact that patients who have had prefrontal lobotomy for the relief of pain continue to perceive pain, but are not disturbed by it, suggests that the important effect of altering the reaction to pain may be mediated through an action on the cortex of the frontal lobe.

The comparative efficacy of the three new analgesics, metopon, meperidine hydrochloride and methadon and of morphine in altering the factors concerned in analgesia is shown in table 2.

With the exception of the elevation of the pain threshold, which has been measured, the comparisons represent the personal opinions of the authors, and were assigned on the basis of experience with all the drugs.

*Morphine.*—Morphine is the most familiar drug used for the relief of severe grades of pain. The conditions

which produce pain of such intensity as to require morphine cover the entire field of medical practice, are well known to physicians and need not be recapitulated here. It is more important to remember that the physician must be careful in using morphine, or any equivalent drug, in situations in which the patient's complaints are out of proportion with the cause of the pain. Such patients usually require reassurance and emotional support rather than drug therapy. Morphine is contraindicated in acute abdominal pain until a definite diagnosis has been established and specific treatment begun. It should not be used in the treatment of head injuries or in any condition associated with increased intracranial pressure. Morphine is also used to relieve severe dyspnea due to cardiac disease or pulmonary disease, but the drug is almost always contraindicated in bronchial asthma. Morphine remains the best drug for allaying fear prior to operative procedures. Morphine should never be used primarily for its sedative action, since less dangerous drugs are available for this purpose.

The chief disadvantages of morphine are the production of vomiting, the depression of respiration, the induction of spasm of smooth muscle and the rapid development of addiction under conditions of chronic use. Despite these disadvantages, morphine, because of its cheapness, reliability and rapidity of action, remains the drug of choice for conditions requiring relief of severe pain for periods of less than two weeks. If pain relief is required over a longer period, metopon and methadon are more suitable drugs.

*Codeine.*—Codeine is used for grades of pain which cannot be relieved by antipyretic drugs, but which are not severe enough to require morphine or an equivalent drug. As with morphine, care should be taken not to use codeine for patients who are overreacting emotionally to minor pathologic disturbances. The administration of codeine should be stopped when the need for it has passed, since it possesses definite, though low grade, addiction liability. The second indication for the administration of codeine is the presence of severe cough, but the use of the drug for this purpose should be carefully limited.<sup>18</sup> Coughing serves a useful purpose

18. Hatcher, R. A.: Narcotics in the Treatment of Coughing, J. A. M. A. 96:1383 (April 25) 1931.

and should be interfered with only when the cough is so distressing and so constant that the patient is disturbed and weakened. It should be prescribed only after other measures have failed. One should remember that, in conditions in which cough is due to irritation of the mucous membranes of the pharynx or larger air passages, inhalations of medical steam and the use of lozenges or syrups containing volatile oils with local anesthetic properties are more effective than the use of codeine.

*Metopon*.—Metopon is as effective by mouth as when administered hypodermically. Tolerance develops more slowly to metopon<sup>19</sup> than to morphine, and, when given orally, metopon produces less sedation and less mental confusion and is not as nauseating as morphine.<sup>19</sup> After tolerance is developed to metopon, the full analgesic potency of the drug is restored by a short period of withdrawal.<sup>20</sup> Metopon is regarded as an excellent drug for oral use in the relief of chronic pain. It is difficult to manufacture; it is rather expensive, and the amount available probably will always be limited. Its total addiction liability probably equals that of morphine.

*Meperidine Hydrochloride*.—Meperidine hydrochloride is a synthetic piperidine derivative which has been widely used in medical practice since 1941. It is not as effective an analgesic as are morphine, metopon and methadon, but has the advantage of possessing a spasmolytic action on the smooth muscle of the intestine of human beings<sup>21</sup> and the ureter.<sup>22</sup> However, the drug has recently been shown to increase intrabiliary pressure.<sup>23</sup> The drug is less likely to produce nausea and vomiting than is morphine and is said to produce less respiratory depression. It is particularly useful in the

19. Eddy, N. B.: Metopon, *J. Am. Pharm. A. (Scient. Edition)* **8**: 430 (Sept.) 1947.

20. Lee, L. E.: Studies on Morphine, Codeine and Their Derivatives: XVI. Clinical Studies of Morphine, Methyl dihydromorphinone (Metopon) and Dihydrodesoxymorphinone-D (Desomorphine), *J. Pharmacol. & Exper. Therap.* **75**: 161 (June) 1942.

21. Batterman, R. C.: Clinical Effectiveness and Safety of a New Synthetic Analgesic Drug, Demerol, *Arch. Int. Med.* **71**: 345 (May) 1943. Yonkman, F. F.; Noth, P. H., and Hecht, H. H.: Demerol, a New Synthetic, Analgesic, Spasmolytic and Sedative Agent: II. Clinical Observations, *Ann. Int. Med.* **21**: 17 (July) 1944.

22. Climenko, D. R., and Berg, H.: The Influence of Demerol on the Ureter, *J. Urol.* **49**: 255 (Feb.) 1943.

23. Gaensler, E. A.; McGowan, J. M., and Henderson, F. F.: A Comparative Study of the Action of Demerol and Opium Alkaloids in Relation to Biliary Spasm, *Surgery* **23**: 211 (Feb.) 1948.

relief of pain associated with spasm of smooth muscle (except in biliary colic) and can be used in persons who are intolerant to morphine. The addiction liability of meperidine hydrochloride is rather high—reports in the lay press notwithstanding. Many cases of both “primary” and “secondary” addiction to this drug have been seen.<sup>24</sup>

*Methadon.*—Methadon is a synthetic heptanone derivative which is very morphine-like in its pharmacologic actions. In human beings it has most of the disadvantages of morphine. It produces constipation, nausea, vomiting, itching of the skin and respiratory depression.<sup>24</sup> It is not well tolerated by mouth and causes more local reaction than morphine when injected subcutaneously. Methadon is a slowly acting cumulative drug and may not, in a single dose, provide adequate pain relief. Due to its slowness of action and to the low degree of sedation obtained with single doses, it is not suitable for preoperative medication or for conditions requiring rapid pain relief. In repeated dosage, methadon has a powerful cumulative sedative action, so that patients who are receiving the drug at short intervals must be carefully observed for evidence of excessive drowsiness. It is, however, an excellent drug for the relief of chronic pain, because tolerance develops to its analgesic actions more slowly than does tolerance to the analgesic action of morphine and the degree of physical dependence on methadon is less than that of physical dependence on morphine.

The total addiction liability of methadon is almost equal to that of morphine, although its physical dependence liability is less.<sup>24</sup> The euphoric effect of methadon in the addict (and undoubtedly in the addiction-prone person) is equal to that of morphine, so that its habituation liability is high. The comparative addiction liabilities of the commonly used analgesic drugs are shown in table 3.

#### PREVENTION OF ABUSE OF NARCOTIC DRUGS

In general, there are two approaches to the prevention of drug addiction. The first line of effort is the long range program envisaged under the National

24. Wieder, H.: Addiction to Meperidine Hydrochloride (Demerol Hydrochloride): Report of Three Cases, *J. A. M. A.* **132**:1966 (Dec. 28) 1946. Anslinger, H. J.: Demerol, Correspondence, *ibid.* **132**:43 (Sept. 7) 1946.

Mental Health Act. The basic problem in preventing drug addiction is, of course, the development of a people so emotionally sound and well integrated that they will have no need for chemical aids to adaptive behavior. Such proper personality integrations, which can be achieved only through well adjusted parents, normal environment and proper schooling in social behavior, would do much to prevent drug addiction. The high incidence of emotional instability in our times, as reflected by the large numbers of noncombat psychiatric casualties during the war and the increasing use of alcohol, indicates that we have a long way to go in helping persons to adjust to life in our increasingly complex society.

TABLE 3.—*Comparative Addiction Liability of Analgesic Drugs\**

Drug	Physical Dependence Liability	Habituation Liability	Total
Morphine.....	4	4	8
Dihydromorphinone hydrochloride.....	4	4	8
Metopon.....	3	4	7
Meperidine hydrochloride.....	2	3	5
Methsdon.....	1	4	5
Codeine.....	2	1	3

\* Comparative addiction liability of analgesic drugs. The numeral 4 indicates that the particular drug has the greatest liability of all the drugs with respect to the particular addiction characteristic shown; the numeral 1 indicates the lowest liability; the sum of the two characteristics gives the total addition liability, the highest possible addiction liability score being 8 and the lowest 0.

The second approach to the prevention of drug addiction, and the point of immediate attack, is to separate effectively the addiction-prone person, or the ex-addict, from narcotic drugs. The Harrison Narcotic Act, with its legal prohibitions and penalties, its vigilance in preventing the introduction of contraband narcotics into the market and its careful control over use of narcotics, has had a progressive influence on the reduction and prevention of narcotic addiction. In addition to the Harrison Narcotic Act, the Geneva Convention of the League of Nations has operated to reduce worldwide production and refining of opium.

Although accidental addiction by medical use occurs occasionally, the great majority of patients become addicted under the influence of other addicts, and the efforts of the Public Health Service hospitals for the

treatment of narcotic addicts at Fort Worth, Tex., and Lexington, Ky., prevent addiction so far as they cure persons who would otherwise become foci of "infection." The hospital at Lexington alone has treated slightly more than 11,000 patients since 1935. Follow-up reports indicate that over 16 per cent of these patients have remained abstinent over a seven year period, and probably at least an additional 20 per cent have remained abstinent for extended periods of time.

Physicians should keep the danger of addiction to analgesic drugs in mind and should exercise caution in prescribing them. These drugs should never be used when other drugs or other measures will suffice. The dosage should be held to the minimum compatible with adequate pain relief, and the interval between doses should be as great as possible. The drugs should be discontinued as soon as the need for pain relief has passed. They should never be used primarily for their sedative actions. In chronic cases, they should be administered orally whenever possible. Self medication with a hypodermic should not be allowed. The drugs should not be given intravenously unless the need for rapid pain relief is great, since this method produces maximum euphoria and carries an increased risk of addiction. The drugs should not be administered to persons with known neurotic personalities unless definite indications for the use of a potent analgesic are present. Narcotic drugs should never be used for the relief of symptoms due to alcoholic excess, since alcoholic persons are very addiction-prone. Analgesic drugs should rarely, or never, be used in the treatment of asthma, since asthmatic persons are very susceptible to addiction. It is significant that in many cases of morphine addiction and several of the cases of primary addiction to meperidine hydrochloride observed at Lexington addiction resulted from its use for the relief of asthma.

Suggestions are made from time to time that clinics should be established where known addicts would be given drugs free, or sold drugs at minimum cost, for the continued support of their addiction. The proponents of this plan believe that addiction is incurable or that treatment is inhumane and that if addicts are given the minimum amounts of drugs necessary to

maintain their addiction lawlessness attendant on contraband traffic in narcotic drugs would be eliminated. This reasoning is unrealistic, as has been shown by several attempts in this country and abroad that have failed. Addicts on such "rations" connive to get more than their allotted amount of drugs, so that they can increase their dosage and continue to obtain a euphoric effect. They may sell, or give away, part of the extra supply so obtained to persons who are not addicted. This creates new addicts who are potential customers for the contraband market and thus increases the problem which the ration plan is supposed to abolish. Furthermore, many addicts can be treated and learn to live a useful effective life instead of one of personal neglect, indolence and semisomnolence which is so typical of the addict. Addiction is "infectious," and treatment, rather than support of addiction, is necessary to minimize its spread.

#### SUMMARY

Because of vigorous enforcement of the Harrison Narcotic Act and to treatment of addicts in federal facilities the total number of narcotic drug addicts in the United States has declined from 150,000 to 200,000 in 1914 to approximately 48,000 at the present time.

Drug addiction is a state in which a person has lost the power of self control with reference to a drug and abuses the use of the drug to such an extent that the person or society is harmed. The drugs to which addiction commonly occurs in the United States are opium and the opium alkaloids, the synthetic morphine-like analgesics, the barbiturates, bromides, alcohol, marihuana, cocaine, amphetamine and, rarely, peyote. The characteristics of addiction to these drugs are discussed.

Drug addiction is primarily a psychiatric problem and should be regarded as a symptom of a basic underlying personality maladjustment. The common personality types of drug addicts are described. The diagnosis of narcotic addiction is usually easy, but may be difficult. Isolation of the patient and observation for signs of abstinence is, at times, the only conclusive means of diagnosis.

Withdrawal of drugs is the first and the least important step in the treatment of narcotic addiction. Withdrawal of morphine is best achieved by a ten day

reduction of morphine or by substitution and reduction of methadon. Institutional therapy is necessary for the successful treatment of addiction. A minimum period of treatment of four to six months is essential. The patient's entire personality must be reoriented by appropriate psychotherapeutic technics.

The pharmacologic characteristics, the advantages and disadvantages, and the comparative addiction liabilities of the older and newer analgesic drugs are discussed. The prevention of drug addiction involves the development of an emotionally sound people through the program of the National Mental Health Act, the reduction of the illegitimate use of narcotics by the control measures provided for under the Harrison Narcotic Act, the isolation and treatment of addicts, which prevents them from spreading addiction, and proper cautious use of addicting drugs by physicians.