

# Treatment of Drug Addiction\*

H. F. FRASER, M.D. and JAMES A. GRIDER, JR., M.D.

*Lexington, Kentucky*

THIS discussion will be limited to the treatment of patients addicted to natural and synthetic narcotics, cocaine, marihuana and barbiturates. Although addiction to alcohol constitutes the greatest single addiction problem in most of the world, it will not be discussed since a separate treatise would be required for alcohol alone. For convenience of presentation treatment of addiction will be discussed under three phases, (1) outpatient or office management, (2) withdrawal of drugs and (3) rehabilitative and psychiatric treatment.

## OUTPATIENT MANAGEMENT

*Office Handling of Narcotic Addicts.* A comprehensive procedure for the physician to follow when an addict appears in his office has been described recently in the Journal of the American Medical Association.<sup>1</sup> First, the physician must be familiar with the Federal Narcotic Laws and Regulations. The addicting drugs which are controlled by the Harrison Narcotic Act include opium, morphine, heroin, dihydromorphinone (dilaudid®), methyl-dihydromorphinone (metopon®), 3-hydroxy-N-methylmorphinan (dromoran®), codeine, dihydrocodeinone (hycodan®), meperidine (demerol®), methadone (dolphine®), and cocaine. Marihuana is controlled separately by the Marihuana Tax Act. The United States Bureau of Narcotics has interpreted the Harrison Narcotic Act, insofar as it affects physicians and pharmacists, in Pamphlet No. 56, "Prescribing and Dispensing of Narcotics under the Harrison Narcotic Law." The most pertinent provision of the narcotic regulations respecting addiction reads in part as follows: "An order purporting to be a prescription issued to an addict or habitual user of narcotics, not in the course of professional treatment, but for the purpose of providing the user with sufficient narcotics to keep him comfortable is not a prescription within the meaning and

intent of the act; and the person filling such an order, as well as the person issuing it, may be charged with violation of the law." In addition to federal laws there are state laws with which the physician must familiarize himself but, in general, the physician will be acting in accordance with the consensus of medical opinion with regard to addiction and will be complying with the letter and spirit of both federal and state laws if he follows two principles set forth by the House of Delegates of the American Medical Association: (1) Ambulatory treatment of narcotic addicts should not be attempted as institutional treatment is always required; (2) narcotic drugs should never be given to an addict for self-administration.

The physician should realize that treatment of drug addiction of any type is primarily a psychiatric problem and favorable results cannot be anticipated unless treatment has been continued for several months. Attempts to carry out such therapy in the home or office fail almost invariably.

When the patient has agreed to go to an institution for treatment and has presented satisfactory evidence that he has taken steps to obtain admission, the physician may then administer narcotics in minimal doses but only for the minimal period of time necessary for the patient to complete arrangements for institutional treatment. Drugs must be administered by the physician or, if the patient is in a hospital, by nurses on proper written orders. Drugs, or prescriptions for drugs, must never be given to the patient for self-administration. It is advisable to limit the initial dose to 16 mg. ( $\frac{1}{4}$  gr.) of morphine or 10 mg. ( $\frac{1}{8}$  gr.) of methadone. It practically never should be necessary to exceed as a single dose 60 mg. (1 gr.) of morphine or 30 mg. ( $\frac{1}{2}$  gr.) of methadone.<sup>1</sup> The type of drug administered and the dose should be unknown to the addict and every precaution should be taken to prevent

\* From the National Institute of Mental Health, Addiction Research Center and the Clinical Division, Public Health Service Hospital, Lexington, Ky.

the addict from obtaining narcotics from other sources.

The narcotic laws do not, of course, prohibit the use of opiates in patients suffering from advanced carcinoma, tuberculosis or other chronic painful diseases. In such cases the physician is concerned primarily with relieving suffering and only secondarily with addiction. Nevertheless, ethical medical practice demands that certain principles be followed: (1) The physician prescribing narcotics for such patients should be personally attending them; (2) the diagnosis of a painful, incurable disease should be confirmed by consultation; (3) all means for relieving pain other than narcotics should be exhausted and (4) narcotics should not be given to the patient for self-medication.

While it is known that it is practically impossible for addicts in advanced states of tolerance to take a lethal dose of narcotics, addicts who have lost their tolerance may take a fatal dose. N-allylnormorphine (nalline<sup>®</sup>), a chemical analogue of morphine, is a specific antidote and in these cases it should be administered intravenously in a dose of 5 to 20 mg.<sup>2,3</sup>

*Office Treatment of Barbiturate Addicts.* The Harrison Narcotic Act does not apply to barbiturates, which are controlled by state laws and by the Federal Food and Drug Law.

When barbiturates are administered in the usual therapeutic doses under supervision of a physician, addiction does not occur even though the drugs may be taken for many months. However, chronic consumption of large amounts of barbiturates results in true addiction.<sup>4</sup> Abrupt withdrawal of barbiturates from persons who have been consuming 0.8 gram or more of these drugs daily may provoke a serious abstinence syndrome characterized by convulsions and delirium.

Institutional treatment of barbiturate addiction is just as necessary as it is in narcotic addiction. The physician should refuse to prescribe barbiturates for a person he believes is addicted to them until the patient agrees to institutional treatment and he should not continue to prescribe these drugs if the patient procrastinates and does not promptly complete arrangements for institutional treatment.

*Selection of an Institution for Treatment.* When the diagnosis of addiction has been made and the patient has agreed to go to an institution for treatment, the next step is the choice of the institution. The selection will depend upon the

type of case, the financial situation of the patient and other factors. Many private sanitoriums make a specialty of treating various kinds of addiction. Advice regarding these private institutions may be obtained from local medical societies or from the American Medical Association. If the addict is unable to pay for treatment, local or state facilities may be available. Advice concerning these can be obtained from City and State Health Departments. If no such facilities are available, the patient may be referred to one of the two Federal Hospitals that treat narcotic addiction, the U. S. Public Health Service Hospitals located in Lexington, Kentucky and Fort Worth, Texas. Communications respecting admission may be directed to the Medical Officer in Charge of either hospital. Patients addicted to opiates, synthetic analgesics, marijuana and cocaine are eligible for admission to these institutions. Patients addicted to alcohol and barbiturates are not eligible for admission to these Federal Hospitals unless they are concurrently addicted to narcotic drugs. If the patient is indigent, there is no charge for treatment; but if the patient has funds, there is a charge of \$5.00 per day. The hospital in Lexington accepts both men and women but in the Fort Worth hospital only males are admitted.

The physician should explain to the patient that withdrawal from drugs is an unpleasant but not a dangerous procedure, and that the patient should cooperate with the institution until the full program of treatment is completed. Although physical dependence on drugs may be relieved in two weeks, psychic dependence and a poor physical condition persist, so patients are requested to remain a minimum of 135 days in these hospitals.

#### WITHDRAWAL OF DRUGS

*Opiates.* Although a great many withdrawal procedures have been published,<sup>5-7</sup> the best method of withdrawing heroin, morphine or similar drugs from addicted patients involves substitution of methadone for whatever opiate or synthetic analgesic the patient has been using, followed by reduction of the dosage of methadone over a period of about ten days. This method of treatment is based on the facts that methadone will prevent the appearance of signs of abstinence from any known analgesic drug and that abstinence from methadone is milder than abstinence from any of the other commonly used analgesics. One milligram of

methadone can be substituted for 4 mg. of morphine, 2 mg. of heroin, 1 mg. of dilaudid, or 20 to 30 mg. of either meperidine (demerol) or codeine.

The speed with which withdrawal is completed is dependent on the physical condition of the patient and the extent to which he is dependent on narcotics. Addicted patients with serious organic disease should not be subjected to the strain of relatively rapid withdrawal. In such cases it is best to treat the organic disease before attempting to treat the addiction. When, in the judgment of the physician, the organic disease has improved to the point where mild abstinence carries no danger, withdrawal is cautiously begun and, depending on the patient's response, withdrawal is completed in fourteen to thirty days. In the experience at the Lexington Hospital less than  $\frac{1}{2}$  of 1 per cent of narcotic addicts require such special treatment.

The first decision which must be reached before withdrawal begins is the degree of dependence on narcotics. The patient's history is of little use in this connection since addicts frequently exaggerate the quantities of drugs taken in the hope of receiving large amounts of narcotics in the first part of withdrawal. Furthermore, illegal drugs, especially heroin, are adulterated and the narcotic concentration may vary enormously. Hence the patient, unless he has had considerable experience with various narcotics, is unable to estimate the quantity of narcotics used.

The degree of dependence is best estimated by the physical examination, which will disclose whether the patient is intoxicated with narcotics or is exhibiting symptoms of abstinence.<sup>7,8</sup> If a patient shows morphine-like intoxication, or if he displays no signs of abstinence, narcotics should not be administered until definite symptoms of abstinence appear. When symptoms of abstinence are present on admission or develop shortly afterward, it is usually possible to estimate the addiction dosage, especially if the physical findings are considered in conjunction with the addiction history. Information regarding the specific drug and the number of hours which have elapsed since the last dose of self-administered narcotics is very helpful in this connection.

During the first two days of hospitalization the dose of methadone should be sufficient to control nearly all symptoms of abstinence. By

this method the patient will be able to eat, become oriented to the hospital regimen and psychiatric rapport may be established with the physician. During this interval routine laboratory work, roentgenograms and physical examination should be completed. Depending on the severity of abstinence, a dose range of 5 to 40 mg. of methadone three times daily is usually sufficient to prevent the appearance of abstinence signs, regardless of the amount or the drugs the patient has been using. Reduction is started after two days by cutting the dosage of methadone by 50 per cent. This level should be maintained for about two days, after which the dose is reduced at approximately two-day intervals to 30, 10 and 5 per cent of the amount of methadone which just prevented the appearance of abstinence in the initial phase of treatment. As the end of withdrawal approaches both the amount and frequency of medication should be reduced. If the degree of physical dependence is not great, withdrawal may be completed in five to seven days and, in some cases, even less time may be required.

While narcotics are being withdrawn all addicts require reassurance; they should be examined daily for withdrawal signs so that appropriate changes in the treatment schedule may be made.

No special dietary measures are necessary during withdrawal unless the presence of an organic disease requires a special diet. Fruit juices and other attractive drinks should be available during the first four or five days. Anorexia is very common during withdrawal but a return of appetite is spontaneous and rapid.

Insomnia is conspicuous during withdrawal. After three to five days it is advisable to give 0.1 to 0.2 gm. of pentobarbital or a similar hypnotic at bedtime, but the use of sedatives should not be continued for more than a few nights.

It is not advisable to permit visitors during this phase of treatment since the addict may be depressed, his craving for narcotics has not diminished and he may attempt to have relatives or friends smuggle drugs to him. Furthermore, addicts receiving narcotic drugs should be segregated from other addicts who are in the rehabilitative phase of treatment. Observing other patients receiving narcotics creates a situation which is favorable for developing an intensified craving for morphine.

*Cocaine and Marihuana.* Since no physical

dependence is produced by cocaine or marijuana, withdrawal should be abrupt and complete and no substitution therapy is necessary. Insomnia and irritability should be treated with sedatives.

*Barbiturates.* Isbell<sup>9</sup> has emphasized that barbiturates should be withdrawn very slowly and cautiously from barbiturate addicts. As in the case of morphine addicts, statements of the barbiturate addict regarding daily intake may be very unreliable. Patients showing barbiturate intoxication<sup>4,10</sup> on admission should not be given additional sedatives until signs of intoxication have become mild. Patients who show signs of mild barbiturate abstinence on admission such as anxiety, weakness, nausea and tremor are in danger of developing convulsions and/or psychosis.<sup>4,10</sup> Such cases should be given 0.2 to 0.5 gm. (3 to 6 gr.) of pentobarbital (nembutal<sup>®</sup>) orally or parentally at once. If symptoms are not relieved after one hour, the dose should be repeated.

After symptoms of intoxication have become mild, or after early withdrawal symptoms have been brought under control, the patient should be given barbiturates orally four times daily. The dosage of barbiturates should be adjusted to that which just maintains a mild degree of intoxication. Ordinarily 0.2 to 0.4 gm. of pentobarbital four times daily will suffice for this purpose.

After the patient has been observed for a day or two, reduction of barbiturates can be started. The dosage should not be reduced more than 0.1 gm. (1½ gr.) daily. If the patient has been taking 1.0 or more gm. daily, the total withdrawal period should extend over a period of three or four weeks.<sup>11</sup> If the patient becomes nervous, apprehensive and weak, or if paroxysmal high voltage spike and dome waves appear in the electroencephalogram, the reduction should be stopped until these signs have cleared.

Patients being withdrawn from barbiturates must be kept under close observation. Their beds should be provided with sideboards or else their bed should be a mattress on the floor so that if convulsions occur they will not fall to the floor. Patients should not attempt to walk, bathe or go to the bathroom unattended. Diet should be light during the first few days but subsequently no restrictions are necessary.

The diagnosis of barbiturate addiction should always be borne in mind in patients who suddenly develop convulsions and/or a toxic

psychosis. If such cases are not recognized and properly treated, a fatal result may ensue.<sup>12,13</sup> If after complete examination of such cases the diagnosis of abstinence from barbiturates seems likely, appropriate treatment consists of rapid re-intoxication with barbiturates which may be given intramuscularly or intravenously if necessary. This program will arrest further convulsions but it may not completely control the toxic psychosis.<sup>13</sup> Prompt administration of *sufficient* barbiturates will control excessive hyperactivity during the delirium and prevent exhaustion.

Delirious patients must be under continuous observation, rectal temperature checked three times daily and adequate fluid and food intake maintained. Fever of more than 104°F. is a serious sign<sup>12,13</sup> and should be combated by measures which favor body heat loss, such as keeping the room cool, the patient uncovered and administration of antipyretics. "Cold packs" should be avoided since these place undue strain on an already impaired circulatory mechanism.<sup>12,13</sup> Once improvement is noted withdrawal is accomplished by gradual reduction of barbiturates as described previously.

It should be remembered that acute barbiturate intoxication may be superimposed on chronic barbiturate intoxication. Patients who are chronically intoxicated with barbiturates may become confused and ingest such large amounts of barbiturates that serious acute poisoning develops. Whenever a patient who has been acutely poisoned with barbiturates recovers from coma, every effort should be made to ascertain if he has been taking large doses of barbiturates daily and, if so, he should be mildly re-intoxicated with barbiturates and then gradual reduction begun as described above.

Combined barbiturate and opiate addiction has become quite common. Withdrawal of both drugs can proceed concurrently with more time usually being required to withdraw barbiturates than opiates.

#### REHABILITATIVE AND PSYCHIATRIC TREATMENT

Following the withdrawal of opiates and/or barbiturates rehabilitative and psychiatric treatments are instituted.

Residual symptoms of abstinence from drugs, such as feelings of weakness, varying degrees of insomnia and anorexia may persist for several weeks but "the physician must adopt a reassur-

ing but uncompromising attitude." Opiates and barbiturates must not be indulged in once the withdrawal period is completed. Intercurrent physical illnesses are handled in the same manner as they would be in a non-addict patient. If surgical procedures are required in an addict who has been withdrawn from drugs, opiates and barbiturates are administered preoperatively and postoperatively in the same dosages as would be given to a non-addict. Once the acute phase of illness has passed, opiates and barbiturates must be rapidly eliminated.

General rehabilitative measures consist of dietary, vocational, recreational and social procedures.

Malnutrition is a common condition of addicted patients. But once drugs have been withdrawn recovery of appetite is spontaneous and a good general diet will rapidly improve the nutritional status. Gastrointestinal complaints often may be ameliorated by ancillary psychiatric measures after ruling out organic diseases. Often, symptoms suggestive of visceral disease are not confirmed and they may subside as the patient's adjustment within the hospital improves.

Vocational therapy plays an important part in the rehabilitation of the addict. A large percentage of addicts have not developed a satisfactory work pattern. Mere assignment of a job to an addict patient carries little hope of permanent occupational adjustment. Nevertheless a job of some kind within the institutional setting is necessary to occupy part of the patient's time. In the younger addicts particularly, a profitable and interesting vocational assignment, leading to some specialized skill, may prove very helpful. A well rounded school program, which functions at all educational levels, is a valuable supplement to vocational treatment. Complete vocational rehabilitation requires that during hospitalization plans should be made for finding the patient a suitable job in the community to which he returns. Such job placement may prove difficult because of social ostracism of former addicts.

The inadequate recreational and social life of many addict patients reflects a further deficiency in their adjustment to our cultural environment; just as the addict frequently has not learned to work, neither has he learned to play. Recreational measures should be more than a matter of physical exercise and should teach socialization and group participation as

well. For these reasons the recreational program should be diversified and include organized sports, motion pictures, shows directed and staged by patients, a library and facilities for playing indoor games, cards, etc.

The above general rehabilitative measures are only supportive. Psychologic treatment directed toward the patient's personality needs is necessary if any permanent success is to be expected. These include participation in "Addict Anonymous" (based on the principles of Alcoholics Anonymous), group psychotherapy and individual psychiatric treatment with a complete follow-up of the patient to his own community. In addition, where specifically indicated, such physical forms of psychiatric treatment as electroshock therapy, insulin shock, lobotomy, etc., may be used provided the severity and specificity of the emotional illness warrants this; but it must be emphasized that these more radical measures are of no value in the treatment of drug addiction *per se*.

Addict Anonymous was first organized by the patients at the Public Health Service Hospital in Lexington, Kentucky. Participation in this program yields a type of mutual support and acceptance that some addicts are able to utilize whereas insight psychotherapy may be unacceptable. It has been the experience of the Lexington Hospital that Addict Anonymous has contributed significantly to better institutional adjustment. Many discharged addicts later identify themselves with their local "chapter" of Alcoholic or Addict Anonymous.

Group therapy has been used in this institution on a trial basis. As with other types of treatment of addiction, the effectiveness of group therapy is difficult to evaluate since follow-up studies to determine the incidence of relapse in any specially treated group as compared to a group given routine treatment are very difficult to carry out. However, mutual discussion of emotional problems and social participation with other patients would seem partially to fulfill some of the obvious needs of the poorly motivated addict.

Individual treatment of the addict is a challenging problem. Many addicts deny any need of psychiatric assistance and many frankly refuse therapy. The drug addict has "found something"—morphine—which allays his vague free-floating anxiety. To demand of him that he relinquish a tested product for the relatively unpredictable success of psychotherapy is to

demand more than many addicts can give. In older addicts frequently patterns of dependence, aggressiveness, passivity and other faulty adjustments have been so firmly established that significant changes in personality structure are not to be expected. However, there are many patients who have sufficient awareness of their anxiety to recognize the need for psychiatric help. As with the alcoholic, psychiatric success is difficult to evaluate and actual cure is regarded by some as unobtainable. Nevertheless, some of these patients are helped. "As with the chronic alcoholics many relapses may be followed by a permanent cure."

If individual psychiatric therapy is to be administered it is necessary to evaluate the therapeutic prognosis of individual patients by medical, psychiatric and psychologic measurements so that patients potentially amenable to psychiatric therapy can be selected. Such measurements would eliminate the aged and chronically ill patients, the physically healthy addicts who have repeatedly resorted to drugs for the solution of their emotional problems, and the severely disturbed neurotics or psychotics who may defy treatment whether or not they are addicts. Experience indicates that psychiatric treatment should be directed toward young patients with relatively well developed ego strengths who express, or are capable of expressing, overt anxiety and whose strivings and goals show good contact with reality and awareness of social and cultural demands. The merits of psychoanalytical or non-analytical treatment will not be argued here. Whatever type of psychotherapy is given should be individualized and administered at regular intervals over a prolonged period. Although continuation of psychotherapy after discharge may be difficult, every effort should be made to provide the patient with psychiatric treatment in the community to which he returns.

*Prognosis.* The use of addicting drugs to the point of physical dependence does not necessarily produce a habitual life-long addict. Social and environmental pressures may lead to a state of addiction but once satisfactory treatment has been carried out the patient may find, either individually or through psychotherapy, ways of handling tensions and anxieties without resorting to drugs. Data are available that indicate that a fair percentage of addicts are able to abstain from the use of drugs for prolonged periods and, in some instances, permanently.

Pescor,<sup>14</sup> in a follow-up study of 4,766 male patients discharged from the Lexington hospital between January 1, 1936, and December 30, 1940, found that the status of 39.6 per cent was unknown, 7 per cent had died, 39.9 per cent were known to have relapsed to the use of drugs while 13.5 per cent were known to have remained abstinent for at least three years. Vogel<sup>15</sup> stated that up to January 1, 1948, 11,041 patients had been admitted to this hospital. Of these 61.4 per cent had been admitted only once, 25.6 per cent twice, 6 per cent three times, 2.9 per cent four times and 3.8 per cent five times or more. His report also showed that 54 per cent of discharged male patients and 61.9 per cent of discharged female patients had not been reported to have been admitted to any correctional institution or held for any law violation. Nemeč<sup>16</sup> currently reports that since the opening of the Public Health Service Hospital in 1935 at Lexington, Kentucky, a total of 18,699 patients had been admitted through June 30, 1952. Of this number 12,005 or 64 per cent were first admissions only; 4,004 or 21 per cent were second admissions; 1,170 or 6 per cent were third admissions, while all other patients with four or more admissions comprised the remaining 9 per cent.

Although there are no statistics available on the prognosis of barbiturate addiction, there is no reason to suppose that the outlook is more favorable than in narcotic addiction or alcoholism.

Even though an addict may return to the use of drugs, hope should not be abandoned. Although the prognosis becomes worse with each relapse, cases are known that have abstained permanently after several relapses. Also, addicts, even though they do relapse, are frequently productive and socially useful during periods of abstinence between addictions. This definitely represents a considerable gain and makes further treatment worth while.

*Prevention of Drug Addiction.* The prevention of addiction would seem to depend on (1) control of the source and supervision of the dispensing of addicting drugs; (2) prompt and satisfactory treatment of addicts and (3) a well directed mental health and education program.

The legal control of all sources of narcotics and barbiturates is one effective prophylactic measure available.<sup>17,18</sup> For example, during the last world war, when smuggling of contraband narcotics was at a minimum, the census at the Lexington hospital was significantly reduced.

In the United States the highest occupational incidence of narcotic addiction is among physicians and nurses, those having the greatest accessibility to narcotics.

Prompt treatment of all addicts is, of course, indispensable since each addict is a potential source for extension of addiction. For example, it is well known that if one spouse is an addict the other spouse is much more apt to become addicted.

In the United States mental health and educational programs are now being employed more extensively and, after several years, we may be able to better evaluate their effectiveness in reducing addiction.

The physician should avoid prescribing barbiturates *continuously* for relief of nervousness and insomnia, especially in neurotic patients or those with a history of alcoholism, because such patients are prone to take drugs in excess and so become addicted. Likewise, caution is in order when administering narcotics to this class of patients.<sup>19</sup>

The physician should also employ the same care in the prescription and administration of any of the new synthetic analgesics that he knows to be applicable to the use of morphine. All of these substances (methadone,<sup>®</sup> dromoran,<sup>®</sup> nisentil,<sup>®</sup> etc.) have morphine-like properties, have proven addiction liability and are subject to the same restrictions as morphine and its derivatives.

#### REFERENCES

1. What to do with a drug addict. Report of the Council on Pharmacy and Chemistry, American Medical Association. *J. A. M. A.*, 149: 1220-1223, 1952.
2. ECKENHOFF, J. E., ELDER, J. D., JR. and KING, B. D. N-allyl-normorphine in the treatment of morphine or demerol narcosis. *Am. J. M. Sc.*, 223: 191-197, 1952.
3. FRASER, H. F., WIKLER, A., EISENMAN, A. J. and ISBELL, H. Use of N-allylnormorphine in treatment of methadone poisoning in man. *J. A. M. A.*, 148: 1205-1207, 1952.
4. ISBELL, H., ALTSCHUL, S., KORNETSKY, C. H., EISENMAN, A. J., FLANARY, H. G. and FRASER, H. F. Chronic barbiturate intoxication. *Arch. Neurol. & Psychiat.*, 64: 1-28, 1950.
5. WOLFF, P. O. The treatment of drug addicts. A critical survey. *Bull. Health Organ., League of Nations*, 12: 455-688, 1945-46.
6. ISBELL, H. and FRASER, H. F. Addiction to analgesics and barbiturates. *J. Pharmacol. & Exper. Therap.*, 99: part 2, no. 4, 1950.
7. 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. *Am. J. Psychiat.*, 94: 759-799, 1938.
8. HIMMELSBACH, C. K. Studies of certain addiction characteristics of (a) dihydromorphine, (b) dihydrodextromorphine-D, (c) dihydrodesoxycodeine-D, (d) methyl dihydromorphinone. *J. Pharmacol. & Exper. Therap.*, 67: 239-249, 1939.
9. ISBELL, H. Addiction to barbiturates and the barbiturate abstinence syndrome. *Ann. Int. Med.*, 33: 108, 1950.
10. ISBELL, H. and WHITE, W. M. Clinical characteristics of drug addiction. *Am. J. Med.*, 14: 558, 1953.
11. ISBELL, H. Treatment of barbiturate addiction. *Postgrad. Med.*, 9: 256-258, 1951.
12. MEYER, H. J. Über chronischen Schlafmittelmissbrauch und Phanodorn Psychosen. *Psychiat.-neurol. Wchnschr.*, 41: 275, 1939.
13. FRASER, H. F., SHAVER, M. R., MAXWELL, E. S. and ISBELL, H. Death due to withdrawal of barbiturates. Report of a case. In press.
14. PESCOR, M. J. A statistical analysis of the clinical records of hospitalized drug addicts. *Pub. Health Rep. Supp.*, 143, 1943.
15. VOGEL, V. H. Treatment of the narcotic addict by the Public Health Service. *Federal Probation*, 12: (2) June, 1948.
16. NEMEC, F. C. Unpublished data.
17. TENNYSON, ALFRED L. The history and mechanism of national and international control of drugs of addiction. *Am. J. Med.*, 14: 578, 1953.
18. ANSLINGER, H. J. Narcotic control by physicians. *J. A. M. A.*, 148: 1275-1277, 1952.
19. VOGEL, V. H. The treatment of narcotic addiction. *Postgrad. Med.*, 12: 201-206, 1952.