DOCUMENT RESUME

ED 099 708 CG 009 214

TITLE	Amphetamine. Report Series 28, No. 1.
INSTITUTION	National Inst. on Drug Abuse (DHEW/PHS), Rockville, Md. National Clearinghouse for Drug Abuse Information.
REPORT NO	DHEW-ADM-74-52
PUB DATE	Feb 74
NOTE	17p.; Prepared jointly by the Clearinghouse and Donald R. Wesson Associates, San Francisco, California
AVAILABLE FROM	National Clearinghouse for Drug Abuse Information, P.O. Box 1908, Rockville, Maryland 20850
EDRS PRICE	MF-$0.75 HC-$1.50 PLUS POSTAGE
DESCRIPTORS	*Drug Abuse; *Drug Education; *Information Dissemination; *Physical Health; *Psychological Needs; State of the Art Reviews

ABSTRACT

This report, prepared by the National Clearinghouse for Drug Abuse Information, presents substantial information on the use and abuse of the drug "family" known as amphetamines. A brief history of the drug is given, along with its basic pharmacology. The current medical uses for amphetamines include: (1) short-term treatment of obesity, (2) treatment of the hyperkinetic syndrome, (3) treatment of narcolepsy, and (4) treatment of mild depression. The many nonmedical uses of these drugs are listed, along with the treatment process for overdoses and the amphetamine withdrawal syndrome. The legal status of those caught illicity using or selling these drugs is reviewed, along with other important issues and opinions on the topic. (Author/PC)

report series

NATIONAL CLEARINGHOUSE FOR DRUG ABUSE INFORMATION

SERIES 28, NO. 1 FEBRUARY 1974

The National Clearinghouse for Drug Abuse Information recognizes the need for clarifying some of the more complex issues in drug abuse by gathering the significant research findings on each subject and developing fact sheets on the problem. These fact sheets, which are part of the Clearinghouse Report Series, present information about treatment modalities, the pharmacology and chemistry of various drugs of abuse, and opinions and practices of recognized authorities in the field. This publication was prepared by the Clearinghouse and Donald R. Wesson Associates, 527 Irving Street, San Francisco, California 94122, under Contract No. HSM 42-72-99.

AMPHETAMINE

Amphetamine is part of a chemical "family" which includes methamphetamine, dextroamphetamine, and other drugs. Its best known major effects include the dilation of the bronchial passages, appetite depression, the relief of fatigue, and the stimulation of the central nervous system (CNS). Some of the undesirable side effects at high dose levels include insomnia, stomach disorders, cardiac arrhythmia, and, more rarely, paranoid psychosis.

The beneficial properties have led to extensive medical use, both by prescription and over the counter. However, recreational use of amphetamine has created problems in Japan and Sweden as well as in the United States, and although amphetamine problems have partly abated in this country, they still exist.

Brief History

Amphetamine was first synthesized in 1887; the first significant investigation into its pharmacology, or therapeutic possibilities, was performed in 1927. At that time, Gordon Alles, a California pharmacologist, prepared a number of phenylalkylamine compounds in an effort to find a synthetic substitute for ephedrine, a drug derived from various plants and used for treating asthma. Alles' research led to his receipt of the patent for the drug in 1932. In exchange for royalties on sales, he assigned the patent to Smith, Kline, and French Laboratories which used the drug in the Benzedrine® inhaler to aid in dilating the bronchial passages.

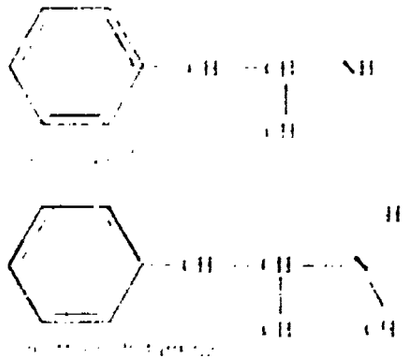
Most of the other major effects of the drug were discovered during the 1930's. In 1937, amphetamine became available as a prescription tablet. It was used to treat narcolepsy - a disease producing an uncontrollable urge to sleep - and, paradoxically, to alleviate the hyperactive syndrome of children. As clinical use continued, amphetamine's effects as an appetite suppressant and a stimulant became known.

During World War II in Japan, amphetamine was extensively used both by Japanese civilians and the military to counteract battle fatigue, to maintain alertness, and to achieve high production quotas imposed by the war. After the war, large stocks of the drug became available without prescription, and the number of heavy users of amphetamine increased so rapidly that medical problems from its use developed. From 1948 to 1955, legal controls were steadily developed and tightened, along with expansion of treatment facilities and strengthening of penal provisions. These measures were complemented by a massive public education campaign, with the result of greatly reducing the amphetamine abuse problem in later years.

Sweden also had a problem with amphetamine and stimulant abuse. Since the early 1960's, increased legal and medical restrictions on the distribution and use of amphetamines have generally acted to halt the illegal misuse of the drugs. Legally, stimulants are restricted to very selected medical cases by special license.

In the United States the recent phase of abuse - intravenous injection of methamphetamine - spread throughout the country from its beginnings in the San Francisco Bay area in the late 1950's and early 1960's. Prescription of injectable amphetamine as an alternative to opiate addiction, and unethical distribution of the drug by a few physicians, made the drug easily available to potential abusers as a liquid in ampules. Although closer legal controls then were placed on prescriptions, a black market developed. In 1970 and 1971, the amphetamines and methamphetamine were placed under strict Federal controls. Continued Federal concern about the drugs was reflected in Senate hearings in 1971 and 1972, which focused on high-dose intravenous use, misuse of prescribed amphetamines, and diversion of legally-produced amphetamine into illegal channels.

The class of drugs designated amphetamines comprises three chemically related compounds. The term "amphetamine" is derived from the chemical designation of the compound: alpha-methyl-phenethyl-amine. Two of the three compounds are optical isomers--different compounds with the same chemical formula, with the atoms arranged in a "mirror image" of each other, and the third is a methylated form of either or both of the isomers. Chemical formulae for the compounds are shown below:



They are chemically similar to epinephrine (adrenaline), a hormone secreted by the adrenal gland which acts as a central nervous system (CNS) stimulant.

The amphetamines, one of the most powerful of the CNS stimulants, may be injected, taken orally, or absorbed through the nasal mucous membranes. Once in the body they are poorly metabolized, taking 2 to 3 days to eliminate 10 to 20 milligrams (mg.) of the drug. The amphetamines are excreted primarily by the kidneys without metabolic alteration of the chemical structure. Excretion is more rapid when the urine is acidic.

Amphetamine is rapidly absorbed when taken orally, and with the usual therapeutic dose of 10 mg. peak effects are found 2 to 3 hours after ingestion. Tolerance to the appetite-depressant effects of amphetamine occurs within 4 weeks. Tolerance to the cardiovascular effects, increased heart rate, and elevated blood pressure, develops much more rapidly than tolerance to the central nervous system effects of arousal and euphoria.

The amphetamines' major effects are thought to take place in two brain systems that seem particularly relevant to their clinical use as well as their misuse. One system is the reticular activating system, which is responsible for controlling the level of activation of the brain and which is itself regulated by inputs from many areas of the brain as well as by stimuli from the senses. The reticular system in turn arouses the brain to prepare it to receive and process these sensory inputs. The degree of arousal is thus related to the degree of stimulus input and its meaning.

Amphetamine is thought to cause a biochemical arousal of the reticular activating system in the absence of sensory input. The activation is transmitted to all parts of

the brain: the individual is aroused, alert, and hypersensitive. This activation in itself may be pleasant, though there is some evidence that a continual high level of activation by itself may induce anxiety.

The other system believed to be strongly acted on by amphetamines is the medial forebrain bundle, the reward system. Increased activity in this system is experienced as a feeling of pleasure. This is doubtless the basis for the euphoria experienced even when amphetamines are taken in low doses. The "flash" or sudden feeling of intense pleasure experienced from an intravenous dose probably results in part from the delivery of a very high blood concentration of the drug to the reward area of the brain.

Current Medical Uses

Until mid 1970, amphetamines had been prescribed for a large number of conditions including depression, fatigue, and long-term weight reduction. In 1970, the Food and Drug Administration restricted the legal use of the amphetamines to three types of conditions: narcolepsy, hyperkinetic behavior, and short-term weight reduction programs.

Short term treatment of obesity

Amphetamine, as well as a host of similar compounds, is prescribed for appetite control because it decreases hunger. The drug does this by a variety of mechanisms not clearly understood at this time. One theory is that amphetamine acts to suppress the appetite center in the hypothalamus. Its action of decreasing food intake without affecting blood sugar levels is the basis for the Food and Drug Administration's approval of amphetamine for use in some weight-loss programs.

In spite of this advantage, two factors argue against the widespread, prolonged use of amphetamine for weight control. One is that tolerance develops rapidly to the appetite depressant characteristics of the drug. Even with moderate dosage increases, 4 to 6 weeks seems to be the limit before tolerance develops to the anorectic effect of amphetamine.

The second reason is that overeating seems to be controlled primarily by psychological and behavioral factors, not by the physiology of the body. Overeating is regarded by many authorities as a habit, which must be changed if the individual is to lose weight after developing tolerance to the anorectic effect of the amphetamine drugs.

Marked differences in opinion occur between physicians involved in the treatment of obesity and those treating drug abuse. Signor B. Penick has stated (1969):

Psychiatrists see the complications of amphetamine usage: they see [illegible] psychosis, psychological habituation, etc. But those of us who use these drugs to treat obesity have many patients who have tolerated them well over a period of years without ever using them or becoming habituated. There is no question that overuse and habituation are problems. However, there is no way of accurately estimating the statistical risk involved in prescribing an amphetamine for an obese patient.

John Griffith et al. (1972) present this example of the "drug abuse" orientation:

> Studies show that these drugs will suppress appetite and that subjects will lose an average of 6.75 pounds more during an 8 to 12 week period than will matched subjects on placebos. At the end of this time, the patient becomes resistant to the anorexic (appetite reducing) effect of the amphetamine and derives little or no further benefit. The cosmetic and health advantages derived from a 6.75 pound weight loss are quite minor. For this reason, responsible physicians are of the opinion that amphetamines should not be prescribed for appetite suppression.

Hyperkinetic syndrome of childhood (minimal brain damage)

This disorder is manifested by impulsive, hyperactive behavior. The child has an unusually short attention span, and in spite of normal or superior intelligence is frequently an underachiever in school. Amphetamines have the paradoxical effect in such children of acting as a tranquilizer, increasing attention span, and decreasing hyperactive behavior. Considerable professional controversy and widespread public attention have recently been focused on drug treatment for the hyperkinetic syndrome. However, the main issue relates more to the prevalence of the syndrome and reliable diagnostic criteria than to the efficacy of amphetamine in its treatment. Caffeine has been reported in recent studies to be as effective as amphetamine in treating hyperkinesis with less undesirable side effects.

Narcolepsy

This is a very rare disorder in which the individual experiences frequent episodes of sudden, uncontrollable desire for sleep, sometimes as many as a hundred times a day. Amphetamine was first used to treat narcolepsy in 1955, with the discovery three years later that acute paranoid psychosis was a side effect to be guarded against.

Mild depression

Stimulants - excluding amphetamines - are still prescribed for the treatment of

depression. However, their use is limited because a "let-down" period usually follows the euphoria produced by the stimulant, tending to increase the existing depressed mood rather than alleviating it. Usually, agitated depressions are aggravated by amphetamines rather than relieved: their use would thus be counter-productive.

Other uses

Occasionally patients with epilepsy or parkinsonism - a syndrome including muscular rigidity, immobility of the face, and tremor - have benefited from amphetamine treatment when other drugs failed. However, other drugs are considered the drugs of choice for treatment of these disorders.

Non-Medical Use of Amphetamines

Most medical authorities believe that amphetamines have a substantial potential for abuse. The definition of "abuse", in relation to amphetamines, however, is not completely agreed upon. While most authorities would agree that high-dose intravenous methamphetamine use constitutes abuse, there is slight disagreement on how to label intermittent recreational use of amphetamine; use of the drug by a patient in greater quantities than prescribed; or unprescribed self-medication for such purposes as staying awake or alleviating boredom while working.

The classification of levels of amphetamine use presented below - a synthesis of descriptions by several authorities - avoids the term "abuse" altogether, and covers most situations in which amphetamines are used beyond initial experimentation.

1) Intermittent low dose use

Many individuals occasionally take 5 to 20 mg. of amphetamines orally to allay fatigue, elevate mood while doing an unpleasant task, produce prolonged wakefulness, help recover from a hangover, or to "get high." Often the pills are obtained from friends, who more than likely obtained them by prescription for weight reduction. Only rarely are they purchased on the black market. Individuals may be any age and usually have little interest in amphetamine use as a "life style."

2) Sustained low-dose use

In this pattern, the individual obtains amphetamine pills from his doctor for weight control, but takes the pills 3 to 4 times a day for the stimulation and euphoria produced by the drug. He may develop a strong psychological dependence on the pills and feel that he cannot get along

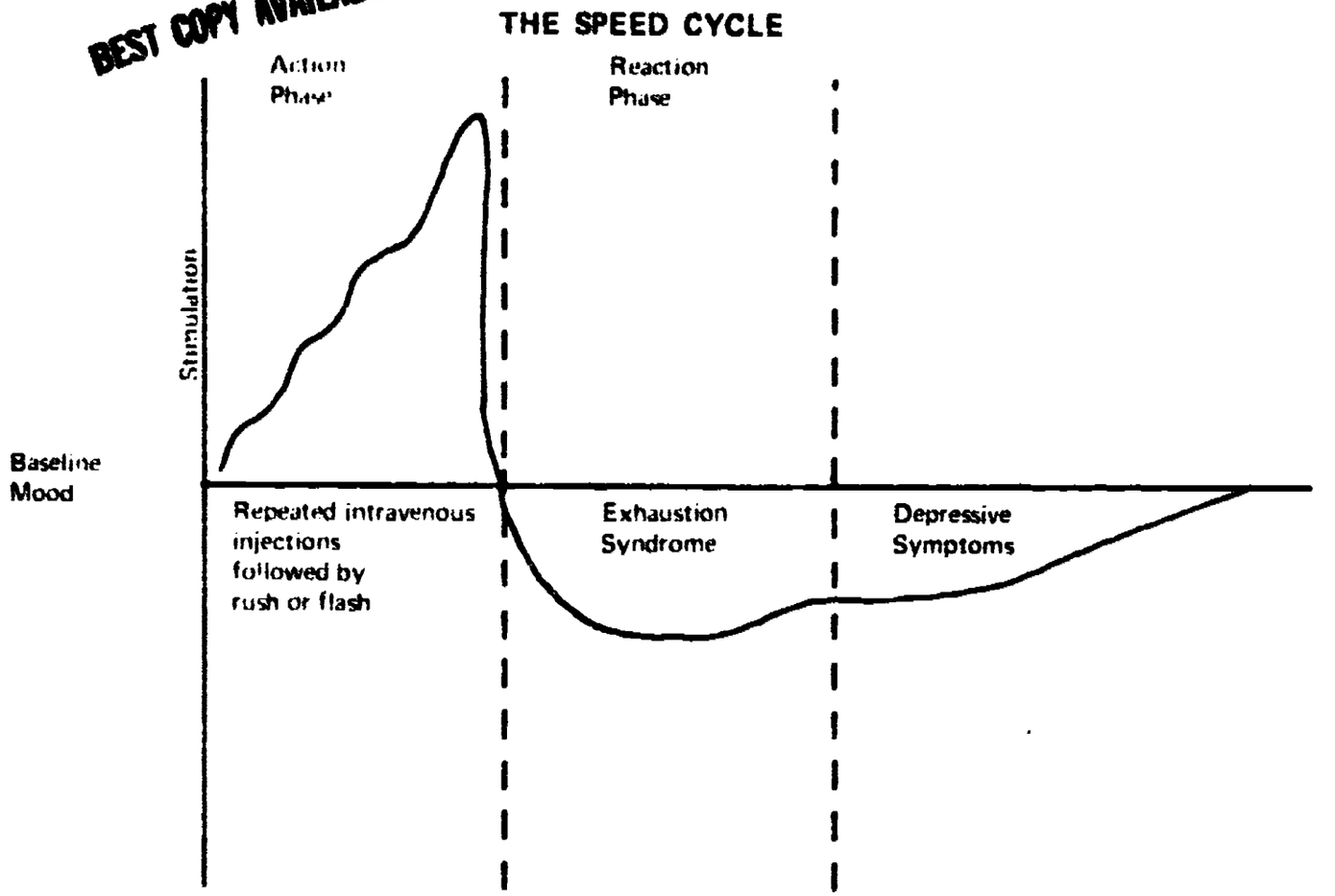
without them. If he stops taking daily amphetamines, withdrawal depression occurs. Since the depression can be easily and temporarily "cured" by renewed dosage of pills, the dependence becomes difficult to break. Some individuals gradually increase their daily intake of amphetamines and begin taking sleeping pills or alcohol to relieve the insomnia which usually develops. The development of this "upper-downer" cycle is especially dangerous because it increases the probability of overdose.

3. High-dose intravenous methamphetamine use

This is the widely publicized pattern of "street" amphetamine abuse. Although the pattern involves fewer individuals than does oral amphetamine use, the bizarre behavior and dress of the intravenous "speed freak," the high incidence of violent behavior and the resultant medical complications have focused disproportionate public and professional attention on this pattern. A major motivation is the "flash" or "rush," an intense feeling of pleasure immediately following the injection. During a speed binge, an individual may inject between 500 and 1,000 mg. of methamphetamine every 2 or 3 hours; by contrast, the usual prescribed dose ranges between 2.5 and 15 mg. per day. The substance, called "crank" or "crystal," may consist of illegally produced methamphetamine or dissolved prescription tablets.

David E. Smith (1969) described the "speed cycle" in terms of an "action-reaction" phenomenon, illustrated in the accompanying diagram. With the onset of the drug effect, one sees the "action phase" or "high." During the action phase the individual is hyperactive and may continue to shoot methamphetamine many times a day, in order to perpetuate his "high" when it begins to wear off. Because of the marked stimulation the individual is unable to sleep, and because of the anorexic effect may not eat. As the individual accumulates progressively larger amounts of methamphetamine within his body, he frequently develops extreme suspiciousness which merges into an overt paranoid psychosis. The high energy level associated with paranoia results in unpredictable behavior and, sometimes, violent behavior.

For a variety of reasons - fatigue, paranoia, or simply the lack of the drug - the individual eventually stops injecting methamphetamine and the "reaction phase" begins. As the effects of the amphetamine wear off, the individual lapses into a period of exhaustion and may sleep continuously for 1 or 2 days. Following this exhaustion phase, the individual often has a prolonged and severe depression which may last days to weeks.



Acute and Chronic Toxicity

Low-dose amphetamine

The acute toxic effects of amphetamines include restlessness, tremor, talkativeness, irritability, insomnia, anorexia, assaultiveness, anxiety, delirium, hallucination, panic states, paranoid ideation, palpitation, cardiac arrhythmias, hypertension or hypotension, circulatory collapse, dry mouth, nausea, vomiting, labile affect (mood swings), abdominal cramps, convulsions and coma. The toxic dose varies widely and may occur as an idiosyncrasy after as little as 2 mg. but more usually in excess of 30 to 60 mg.

Anecdotal reports indicate that chronic amphetamine use may predispose certain individuals to violent behavior. George Bach-Y-Rita (1971), in a study of 130 violent patients manifesting "episodic dyscontrol" with violent behavior, noted that chronic amphetamine use played a role in 12 of his 130 patients. Hemmi (1969),

reporting on the Japanese amphetamine experience, noted that prisoners who had used amphetamines had a considerably higher proportion of violent offenses, such as assaults, than non-users. Family members of chronic amphetamine users notice personality changes and increased irritability which may not be apparent to the user. With increasing doses, irritability, insomnia, and paranoid thought may cause the user to seek medical or psychiatric treatment.

High-dose intravenous methamphetamine

In an analysis of 310 cases of high-dose methamphetamine abuse, David Smith (1970) divided psychological adverse reactions into five categories:

1) Anxiety reactions, in which the individual becomes fearful and tremulous, with concerns about his physical well-being.

2) Amphetamine psychosis, in which the individual misinterprets the actions of others, hallucinates, and becomes unrealistically suspicious.

3) Exhaustion syndrome, an intense feeling of fatigue and need to sleep following the stimulation phase.

4) Prolonged depression.

5) Prolonged hallucinosis, in which the individual continues to hallucinate after the drug has been metabolized.

Secondary effects of the use of the drug include skin lesions, abscesses, respiratory problems, acute gastrointestinal distress, and abdominal cramps resulting from factors in the user's environment. High-dose users usually sustain a marked weight loss, multiple vitamin deficiencies and dental caries (decay).

The possibility of brain damage has been suggested, since coma and its resultant brain damage can occur from amphetamine overdose. Cerebral vascular changes with resulting brain damage have been documented in monkeys.

In addition to direct high-dose amphetamine toxicity, the intravenous amphetamine user is exposed to a number of medical complications resulting from injection of drug contaminants, undissolved particles, or non-sterile injection techniques. He may also contract serum hepatitis.

He may inject live fungus or bacteria into the bloodstream, resulting in tetanus, syphilis, malaria, septic pulmonary emboli, endocarditis (an infection of heart valves), or peripheral obstruction of arteries. Septic pulmonary emboli (infected blood clots which lodge in the lungs) may originate from infected heart valves or septic thrombophlebitis (an infection of the veins at an injection site). Peripheral

obstruction of arteries may be due to injection of small particles of undissolved material, or formation of a blood clot within the artery, usually associated with infection.

The Amphetamine Withdrawal Syndrome

For many years the medical consensus was that amphetamines were not addicting because of the supposed absence of a withdrawal syndrome. Part of the difficulty lay in disagreement over the definition of addiction, but a greater part was the failure to recognize the withdrawal syndrome because of its qualitative difference from the narcotic or general depressant withdrawal syndrome. The amphetamine withdrawal syndrome is characterized by apathy, decreased activity, and sleep disturbances which can last for weeks or months. Another withdrawal sign was noted by Oswald and Thacore (1963). Following abrupt withdrawal of large doses of amphetamines, an increase in the percent of rapid eye-movement sleep (REM) occurred. REM returned to normal when amphetamine was given, but increased again when amphetamine was withheld. This phenomenon provides additional evidence for the existence of physical dependence. Since suicides have occurred during amphetamine withdrawal, doctors have been advised to bring about withdrawal slowly, in a controlled environment.

Treatment for Overdose

Clinical Management of Drug Abuse Crises (1973) recommends certain procedures for doctors in dealing with overdoses of stimulants, including amphetamines. The following description, of course, is not a substitute for consultation by a physician who would vary treatment in accordance with clinical judgment in a real overdose crisis.

A patient enters the physician's office showing the symptoms of very high dosage of amphetamine. After examining the patient and taking his medical history, the physician must resolve conflicts between the patient's statements and his clinical condition using his own clinical judgment. If during the consultation the patient expresses suspicion or feels that he is being threatened, the physician must reassure him that he is safe and that treatment, not punishment, is being given. The physician's overall attitude should be one of calm acceptance. He can administer diazepam (a sedative) to reduce severe anxiety, and in the case of amphetamine poisoning, he can give ammonium chloride to acidify the urine, thus allowing the amphetamine to be more readily excreted.

If a patient is withdrawing from an acute toxic episode, the physician should take general supportive measures and show calm reassurance. Continued observation and supervision are required for several days, in part because of possible suicidal tendencies on the part of the patient.

Legal Status

Since its emergence in an over the counter inhaler in the 1930's, amphetamine has been placed under closely defined controls. The Comprehensive Drug Abuse Prevention and Control Act of 1970 established five schedules, or lists, of controlled substances, ranging downward in their potential for abuse. Amphetamines were first placed in Schedule III, but on July 7, 1971, were moved to Schedule II. According to the Act, this schedule is designed for drugs which have a high potential for abuse; which have a currently accepted medical use in treatment in the United States, or a currently accepted medical use with severe restrictions; or which may lead to severe psychological or physical dependence. Other drugs in Schedule II include certain opiates, methadone, methamphetamine, and cocaine.

The Act also gives the Attorney General authority to regulate "the registration and control of the manufacture, distribution, and dispensing of controlled substances." Specifically, every manufacturer, distributor, or dispenser of amphetamines must register annually with the Attorney General. "Dispensers" include scientists who are conducting research, as well as doctors and pharmacists. In addition, certain requirements for labelling and packaging amphetamines - such as securely sealing their containers - are in effect.

A third significant control is that the Attorney General determines annual production quotas for certain controlled substances. It had been estimated that before quotas, some 8 billion doses of amphetamines had been manufactured annually in the United States. During 1972, production quotas were established, reducing production approximately 80 percent below 1971 levels.

The Canadian government established new controls on amphetamine use as of January 1, 1973. The drug is restricted to the treatment of narcolepsy, hyperkinetic disorders in children, mental retardation (minimal brain dysfunction), epilepsy, parkinsonism, and hypotensive states associated with anesthesia. In short-term therapy, the doctor must report all prescriptions to the government. In long-term therapy (over 30 days), the diagnosis must be confirmed by another physician and his name and address reported. Amphetamines may also be used for certain research projects with government permission.

Comments

After several decades of widespread popularity among the medical profession and the general public, amphetamine has come under severe scrutiny. The reasons for this decline in popularity include questions as to its effectiveness in some medical treatment, and observation of its toxicity and potential for physical dependence.

There is general agreement among psychiatrists that psychomotor stimulants such as amphetamines, dextroamphetamine, methylphenidate deanol and pipradrol have little value in the treatment of severe depression. . . A series of studies showed amphetamines to be less effective than placebo with depressed outpatients.

--Donald F. Klein and John M. Davies (1969)

A problem now being considered in most of the capitals of the free world is whether the benefits derived from amphetamines outweigh their toxicity. It is the consensus of the world scientific literature that the amphetamines are of very little benefit to mankind. They are, however, quite toxic.

--John D. Griffith (1972)

The question of whether or not amphetamines are addictive or habituating is a matter of semantics. Habitual users develop a marked psychological dependence on the drug and evidence definite withdrawal symptoms, including tenseness, anxiety, tremor and nervousness, which may be of such degree as to incapacitate the user during his period of withdrawal.

--Edward R. Bloomquist (1970)

It is generally felt that the behavior of heavy amphetamine users is consistent with the stereotype of the "dope fiend." From all evidence, amphetamines tend to set up conditions in which violent behavior is more likely to occur than would be the case had an individual not used it. Suspiciousness and hyperactivity may combine to induce precipitous and unwarranted assaultive behavior.

--John C. Kramer (1967)

References and Suggested Additional Reading

Alles, Gordon A. The comparative physiological actions of dl-B-phenylisopropylamines: I. Pressor effects and toxicity. Journal of Pharmaceutical and Experimental Therapeutics, 47(3): 339-354, 1933.

Alles, Gordon A., and Prinzmetal, Myron. The comparative physiological actions of dl-B-phenylisopropylamines: II. Bronchial effect. Journal of Pharmaceutical and Experimental Therapeutics, 48(1):161-174, 1933.

Bach-Y-Rita, George; Lion, John R.; Climent, Carlos C.; and Ervin, Frank R. Episodic dyscontrol: a study of 130 violent patients. American Journal of Psychiatry, 127(11): 49-53, May 1971.

Bloomquist, Edward R. The use and abuse of stimulants. In: Clark, William G.T., and del Giudice, Joseph, eds. Principles of Psychopharmacology, New York: Academic Press, 1970. pp. 477-489.

Brecher, Edward M., and the Editors of Consumer Reports. Licit and Illicit Drugs. Boston: Little, Brown & Co., 1972.

Brietner, Carl. The hazard of amphetamine medication. Psychosomatics, 6:217-219, 1965.

Clyde, J.H. The use of amphetamines. South African Medical Journal, 46(13): 380, 1972.

Connell, Phillip H. II. Clinical aspects of amphetamine dependence. In: Wilson, C.W.M., ed. The Pharmacological and Epidemiological Aspects of Adolescent Drug Dependence. New York: Pergamon Press, 1968. pp. 41-53.

Connell, Phillip H. Clinical manifestations and treatment of amphetamine type of dependence. Journal of the American Medical Association, 196(8): 718-723, May 23, 1966.

Costa, E., and Garaffini, S., eds. International Symposium on Amphetamines and Related Compounds. New York: Raven Press, 1970. 962 pp.

Edison, George R. Amphetamines: a dangerous illusion. Annals of Internal Medicine, 74: 605-610, 1971.

Ellinwood, Everett H., Jr. Amphetamine psychosis: II. Theoretical implications. Journal of Psychedelic Drugs, 2(2):121-140, 1969.

Ellinwood, Everett H., Jr., and Cohen, Sidney, eds. Current Concepts on Amphetamine Abuse. Washington, D.C.: U.S. Government Printing Office, 1972. 238 pp.

Geekie, D.A. How the Federal Government's amphetamine controls will work. Canadian Medical Association Journal, 108(1): 83-84, January 6, 1973.

Goodman, Louis S., and Gilman, Alfred, eds. Pharmacological Basis of Therapeutics. 4th ed. New York: Macmillan, 1970. 1,794 pp.

Griffith, John D.; Cavanaugh, John; Heis, Joan; and Oates, John A. Dextroamphetamine - evaluation of psychomimetic properties in man. Archives of General Psychiatry. 26: 97-100, February 1972.

Grindley-Ferris, Margaret. The use of amphetamines. South African Medical Journal, 46(15): 451, April 8, 1972.

Grinspoon, Lester, and Hedblom, Peter. Amphetamines reconsidered. Saturday Review, 55(28): 33-46, July 8, 1972.

Hemmi, T. How we have handled the problem of drug abuse in Japan. In: Sjoquist, F., and Tottie, M., eds. Abuse of Central Stimulants. New York: Raven Press, 1969.

Journal of Psychedelic Drugs. Glossary of drug related terms. Journal of Psychedelic Drugs, 4(2): 205-210, Winter, 1971.

Klein, Donald F., and Davies, John M. Diagnosis and Drug Treatment of Psychiatric Disorders. Baltimore: Williams & Wilkins, 1969. 480 pp.

Kramer, John C.; Fischman, Vitezslav S.; and Littlefield, Don C. Amphetamine abuse - pattern and effects of high doses taken intravenously. Journal of the American Medical Association, 201(5): 89-93, July 31, 1967.

Kramer, John C. Introduction to amphetamine abuse. Journal of Psychedelic Drugs, 2: 8-13, 1969.

Leake, Chauncey D. The Amphetamines. Springfield, Ill.: Charles C. Thomas, 1958.

New Zealand Medical Journal. Amphetamines. New Zealand Medical Journal (Dunedin), 75(748): 160, March 1972.

Oss, James N. (editorial coordinator), et al. Clinical Management of Drug Abuse Crises. Nutley, N.J.: Hoffman-LaRoche, 1973. 32 pp.

Oswald, Ian, and Thacore, V.R. Amphetamine and phenmetrazine addiction - physiological abnormalities in the abstinence syndrome. British Medical Journal, (5354): 427-431, August 17, 1963.

Penick, Signor B., M.D. Amphetamines in obesity. Seminars in Psychiatry, 1(2): 144-162, May 1969.

Ray, Oakley S. Drugs, Society, and Human Behavior. St. Louis: The C.V. Mosby Co., 1972. 299 pp.

Rumbaugh, Calvin L.; Bergeron, Thomas; Scalan, Robert L.; Teal, James S.; Segall, Harvey D.; Fang, Harry C.H.; and McCormick, Ruth. Cerebral vascular changes secondary to amphetamine abuse in the experimental animal. Radiology, 101(2): 345-351, November 1971.

Smith, David E., and Fisher, Charles M. An analysis of 310 cases of acute high dose methamphetamine toxicity in Haight-Ashbury. Clinical Toxicology, 3(1): 117-124, March 1970.

Smith, David E. The characteristics of dependence in high-dose methamphetamine abuse. International Journal of the Addictions, 4(3): 453-459, September 1969.

U.S. 91st Congress, H.R. 18583. Comprehensive Drug Abuse Prevention and Control Act of 1970. Public Law 91-513. Washington, D.C.: U.S. Government Printing Office, October 27, 1970.

U.S. 92nd Congress, Hearings before the Subcommittee on Alcoholism and Narcotics of the Committee on Labor and Public Welfare. Amphetamine Abuse Among Truck Drivers. Washington, D.C.: U.S. Government Printing Office, October 1, 1971. 459 pp.

U.S. 92nd Congress, 1st Session, Hearings before the Select Committee on Crime. Crime in America - Why Eight Billion Amphetamines? Washington, D.C.: U.S. Government Printing Office, 1970.

U.S. 92nd Congress, Hearings before the Subcommittee to Investigate Juvenile Delinquency. Amphetamine Legislation, 1971. Washington, D.C.: U.S. Government Printing Office, 1971. 1,039 pp.