

# Amphetamines: A Dangerous Illusion

GEORGE R. EDISON, M.D., Salt Lake City, Utah

**Amphetamines are among the most dangerous of currently abused psychoactive drugs. They cause dependence, behavioral toxicity, and physical damage. Despite their extensive medical use, the evidence suggests they are ineffective or minimally effective in most of the conditions for which they are prescribed. Their widespread use in medical practice is more likely the result of the euphoria and the dependence they induce than of any significant clinical results. This paradox, presented by the legality of amphetamine use, compounds the difficulty of treating youthful drug abusers and educating potential abusers. The following recommendations are urged: prescription of these drugs should, with few exceptions, cease; and production should be sharply curtailed and probably be limited to one or two pharmaceutical companies.**

THE rapidly increasing abuse of amphetamines among the young makes it important to reevaluate the status of this group of agents in medical practice. Are they valuable drugs, and in what conditions? What results can be expected from their use? What is their mode of action? To what extent are they indispensable? What are their hazards? How often do these hazards occur? Does their medical use have any influence on their illegal use? This article briefly reviews evidence suggesting that the amphetamines are both ineffective and unsafe, offers speculations about why we continue to use them, and recommends changes in the way we use them.

## History

Amphetamine, a close relative of epinephrine,

From the Student Health Service and the Department of Community and Family Medicine, University of Utah, and the Community Drug Center, Salt Lake City, Utah

Annals of Internal Medicine 74:605-610, 1971

ephedrine, and other sympathomimetic amines, was synthesized in 1927. Shortly thereafter, descriptions of its effects on blood pressure and nasal congestion began to appear. Within 5 years it was found to act as a bronchodilator and a respiratory stimulant and also to have remarkable effects on the central nervous system, specifically cerebral stimulation and reduction in appetite. Because of these central effects, several authors warned of the possibility of dependence and tolerance as early as 1937. These warnings are well reviewed by Connell (1).

Despite the warnings, the amphetamines and their uses have proliferated to an amazing degree. The list of "accepted" medical indications for their use now includes obesity, mild depressive reactions, epilepsy, parkinsonism, central nervous system depression caused by barbiturates and other sedative-hypnotics, narcolepsy, and hyperkinetic reactions of children. They have also been used widely to maintain alertness and to increase physical performance.

The 1970 edition of the Physicians' Desk Reference (2) lists 65 amphetamine and amphetamine-like preparations produced by 40 companies. These are available either as single-drug preparations or in combination with salicylates, barbiturates, tranquilizers, and other substances. One can obtain a choice of vitamins or hormones along with an amphetamine in 15 preparations from 14 companies. This listing does not, of course, exhaust the preparations available from pharmaceutical companies.

In four cases companies describe in the Physicians' Desk Reference the amphetamine they produce and only one other product. In four other cases the amphetamine is the company's sole listed product.

What amount of amphetamines is legally manufactured? No one knows exactly. Estimates range from 5 billion to 8 billion doses a year. The Food and

Drug Administration estimated, for example, that over 100,000 lb were available in the United States in 1962—enough to supply each man, woman and child with 250 mg (3). About one half of this supply is thought to be diverted into illegal channels (4).

### Effectiveness of Amphetamines

While production has flourished, the list of indications has gradually withered, for three reasons: [1] For such conditions as parkinsonism, epilepsy, and depressive reactions newer kinds of treatment have simply proved more effective; [2] for severe central nervous system depression from drug intoxication it is now accepted that no drug is as effective as other treatment such as artificial ventilation, support of the circulation, and hemodialysis (5); [3] for obesity control, now the commonest reason for use, it has slowly become obvious that although appetite-suppressants may have some temporary utility, they are ineffective in long-term treatment.

Narcolepsy and hyperkinetic reactions of children remain the two conditions for which amphetamines are still said to have effect. For narcolepsy, however, methylphenidate is "the present drug of first choice," according to the Cecil-Loeb Textbook of Medicine (6); for hyperkinetic reactions preliminary evidence suggests that if any drug is indicated, imipramine may be more effective than amphetamines (7), so that even here good alternatives may be available.

The two commonest reasons for prescribing amphetamines are depression and obesity, and it is for these conditions that we must examine most carefully the evidence for amphetamine effectiveness.

#### NONEFFECTIVENESS IN MILD DEPRESSIVE REACTIONS

Depressive reactions include a variety of syndromes with a wide range of severity and a strong natural tendency toward spontaneous remission. Their very diversity makes evaluation of any treatment extraordinarily difficult. Yet, common to many depressed persons are conflicts around oral-dependent needs, which suggests that drugs such as alcohol, barbiturates, and amphetamines be used with caution because of their ability to produce dependence. Indeed, depression is the underlying mood in many, if not most, high-dose amphetamine abusers or "speed freaks" (8).

But many doctors ask if amphetamines, although theoretically dangerous, are nonetheless a useful and practical measure for treating mild depressions. Tradition grants them a position of sorts in the treatment of mild cases, although recommendations for their use are becoming increasingly rare (for example, the

1968 edition of Noyes' Modern Clinical Psychiatry ignores them). Occasionally one finds a favorable mention, as in Mendelson's article (9) in Freedman and Kaplan's textbook of psychiatry:

The amphetamines are often useful and sometimes gratifyingly efficacious in lifting the spirits in a mild depression. When antidepressive medication is resorted to, the amphetamines should probably be tried before prescribing the newer antidepressive drugs.

Virtually no authority, however, supports their use for more than an immediate euphoriant lift, and most believe that they have no place at all in the treatment of depression. According to Jarvik, in Goodman and Gilman's text, (10), no well-controlled long-term study has been able to demonstrate their effectiveness.

The sympathomimetic amines, such as amphetamine and phenmetrazine, and similarly acting central nervous system stimulants, such as methylphenidate and pipradrol, were tried in the treatment of depression and found wanting except in certain mild cases in which a drug-induced acute euphoric state would suffice....

The report of an AMA committee states (3):

Published studies have indicated that, in general, dextroamphetamine is only slightly more effective than a placebo in ameliorating depressive symptoms.

Cole and Davis (11), also writing in Freedman and Kaplan's textbook, review the evidence thus:

Amphetamine was found to be less effective than placebo in the treatment of depressed outpatients by British general practitioners. ... In still another British study, amphetamine also proved less effective than phenelzine, and no better than placebo, in the treatment of depression. In a Veterans Administration study, dextroamphetamine was no more effective than placebo in treating hospitalized depressed patients.

In a recent review of the pharmacologic treatment of depressions Schildkraut (12) states:

The psychomotor stimulants (for example, amphetamine, methamphetamine and methylphenidate) cause mood elevation, increased alertness and enhanced performance in normal subjects. These drugs may alleviate some of the symptoms of depression in certain depressed patients, but such beneficial effects are often transient and may be accompanied by a number of unwanted side-effects. ... It is fairly generally agreed that the psychomotor stimulants have relatively little to offer in the treatment of major depressive disorders.

#### NONEFFECTIVENESS IN CONTROLLING OBESITY

Obesity is usually regarded as a complex, long-



term problem with major social and psychological determinants. Frequently recognized psychological factors are chronic tension and depression, unusually strong oral dependent needs, inability to tolerate frustration, and substitution of food for other forms of gratification. These psychological characteristics may lead to dependence on many kinds of drugs as well as on food. As in the case of depressive reactions, it may be illogical to include in the treatment of such a condition drugs that have a strong potential for causing dependence. "In fact, the use of amphetamine-type drugs is contraindicated for alcoholic persons and other dependence-prone persons" (3).

**Short-Term Effect:** It is granted by most that amphetamines can induce a period of appetite suppression and increased weight loss for a few weeks. Whether this is of lasting value is questionable, however, since in most cases obesity continues to be a problem over a period of years. Very few short-term gains in treatment of obesity have been translated into long-term successes. More importantly, it is likely that short-term effectiveness is caused more by a stimulant effect than by any direct effect on the appetite control center of the brain. Thom and Bondy (13), in their textbook article, state:

As a result of stimulation, or a "lift," the patient's drive toward overeating may be significantly modified and as far as he is concerned, the over-all effect of the drug is "appetite-depressing." Obviously, drugs which create such a state of euphoria may lead to habituation in certain individuals.

Modell (14) pointed out in his 1960 report:

Central stimulation, not a specific central depressant effect on appetite, is then the common mechanism through which these drugs act; it is clear, therefore, why undesirable central stimulant effects, which have constituted their chief clinical limitation, have thus far appeared to be indivisible from anorexic action.

In other words, obese patients may use the drugs in the same way the "speed freak" does—to obtain a "high."

There is also some doubt whether amphetamines are effective in the short term. Again from Modell's report (14):

The amphetamines present special problems in the evaluation of their effectiveness. Patients often promptly recognize the drug by one or another of the central stimulant effects (usually the "lift"). Thus, they can distinguish between drug and placebo when these are used in what theoretically appears to be a well-designed clinical evaluation with a double-blind control. In patients with emotional disturbances particularly, who include most compulsive overeaters, the ability to distin-

guish medication from placebo by any effect other than the one under examination (in this case weight loss) makes it exceedingly difficult to prevent bias and psychological factors from shaping the apparent effects of the drug.

**Long-Term Effect:** Thom and Bondy (13) evaluate pharmacological treatment of obesity as follows:

Depression of appetite by a pharmacologic agent can facilitate weight loss, although it is apparent that as soon as the pharmacologic effect wears off, or the medication is discontinued, appetite will return and weight gain will recur unless the patient's inherent capacity to control his food intake has been altered fundamentally. That the pharmacologic agent used for these purposes be devoid of serious toxic side effects is axiomatic [emphasis added].

Unfortunately there is no pharmacologic agent available at this time which acts primarily by depressing the "appetite center."

In her textbook article Albrink (15) devotes 3,600 words to the treatment of obesity. This is her discussion of amphetamines:

Drugs. Appetite-suppressant drugs of the amphetamine group are effective for only a few weeks. Dependence on their stimulatory effect occasionally makes withdrawal a problem. Such drugs have no demonstrated role in the long-term management of obesity.

Reinforcing this opinion is the report of the AMA Committee on Alcoholism and Addiction and Council on Mental Health (3):

In long-term (more than a few weeks) programs of weight reduction, the superiority of these substances to placebo has not been demonstrated.

In 1959 Stunkard and McLaren-Hume (16) reviewed the literature on the treatment of obesity. Their summary states:

A review of the literature on outpatient treatment for obesity reveals that the ambiguity of reported results has obscured the relative ineffectiveness of such treatment. When the per cent of patients losing 20 and 40 pounds is used as a criterion of success, the reports of the last thirty years show remarkably similar results. Although the subjects of these reports are grossly overweight persons, only 25% were able to lose as much as 20 pounds and only 5% lost 40 pounds.

In 1966 Glennon (17) reported a follow-up:

Review of the literature since 1958 did not reveal a successful long-term study using a diet regimen by itself or in combination with drugs, psychological treatment, or an exercise program.

Astwood (18) is even more negative in his evaluation of all methods of treatment, including the pharmacologic,

AU of us know that we can't get fat people to become slim by suggesting a diet, so we conclude, for the time being at least, that obesity is incurable.

Modell (14) reemphasizes the point in the summary of his report:

New and logical pharmacotherapy for persons who overeat will more likely come with understanding of the processes involved than through the current practice of developing more variations on old themes which have already been well exploited and have not satisfied the need. There is really nothing new on the scene. There are no "anorexiant" to fit specific disturbances in eating patterns, and there are no useful depressants of the appetite center, wherever it may be. . . . Current pharmacotherapy for persons who overeat has limited use. Insofar as drugs are concerned, at the very best, their potential is secondary to the elimination of the cause of the hyperphagia. Drugs which give assistance along the lines now available provide short-lived symptomatic relief only.

Despite 30 years of extensive use, then, the place of amphetamines in clinical practice is far from established. They represent the treatment of choice for only a small number of those patients for whom they are prescribed. Their effectiveness in treating obesity and depressive reactions is minimal and controversial.

Interestingly, the pharmaceutical industry tells us indirectly that the amphetamines and related drugs offer only a low order of effectiveness by constantly introducing new congeners and combinations. For example, in the 1970 Physicians' Desk Reference eight companies have listed nine "new" amphetamine products not listed in the 1968 edition. The industry sends the same message in another more encouraging way; within the last 2 years four companies have voluntarily discontinued their production of amphetamines (Methedrine®, Burroughs Wellcome; Phetobese®, Cole; T.V.D. Formula®, Lambda; Ad-Nil®, Medics).

### Hazards of Amphetamines

The irony of the amphetamine situation is that whereas we have been slow to admit the negligible utility of these agents, we have also been slow to recognize their dangers. Their illegal and casual use as stimulants of the central nervous system has grown tremendously. They have become perhaps the most serious drug of abuse in the United States (as in several other countries), except in the large cities, where heroin addiction is widespread. Most physicians are not yet sufficiently familiar with these hazards, which are well documented elsewhere (1, 3, 8, 19-22). Briefly, they fall into all three major areas of concern in psychoactive drugs.

1. Amphetamines are associated with tolerance

and with an intense psychological dependence, which makes it difficult to withdraw from the drug without help. High-dose use may begin in a pattern of illegal experimentation, but it may also begin with a physician's well-intended prescription. The nature of the drug's effects leads easily to progressively increasing dosage in susceptible persons. Prediction of "susceptibles" cannot be made with confidence, but patients for whom amphetamines are prescribed are probably, by the very nature of their illnesses, among those most likely to increase the dose and become dependent. Then begins a prolonged struggle to discontinue drug use, an effort usually attended by intense lethargy and depressive symptoms. The period of depression during the withdrawal (or "crash") is frequently associated with suicidal feelings and actions. The absence of physical dependence in amphetamine abuse may give the impression that it is easier to withdraw from than heroin. This has not generally been the case; in fact, the reverse may be true, although data on this point are lacking.

2. The behavioral toxicity of high doses is usually such that the user cannot maintain work, school, or family relationships. With high doses a typical psychosis often develops, characterized by hyperactivity, distortions of reality, impaired judgment, paranoid ideation, and hallucinations. Despite this disturbance, the sensorium is clear, and the individual may appear superficially normal (19).

3. The physical toxic effects on the autonomic nervous system and cardiovascular system include sympathetic gastrointestinal and urinary symptoms, occasional systolic and diastolic hypertension, sometimes cardiac arrhythmias (8, 21), and possible necrotizing angitis (22). In addition, malnutrition, hepatitis, and other serious infections are associated with the intravenous use of these drugs.

These are the major toxic manifestations of illegal, high-dose amphetamine use. But damage also results from the less spectacular adverse reactions to small, legally prescribed amounts and may cause disability for greater numbers of people. These case examples are familiar to most practicing physicians:

Case 1: A 23-year-old male first-year medical student asked his physician for stimulants to help him overcome classroom drowsiness, difficulty in studying, and mild depression. He did not have narcolepsy. Dextroamphetamine, 5 mg daily, was prescribed. He was asked to return but did not. When next seen, he had flunked out of school. Although not the sole factor in this patient's failure, the amphetamine obviously did not help his studying and may have been a critical determinant in his avoiding early, appropriate counseling.

Case 2: To control her appetite a 47-year-old woman had used various amphetamines almost daily for 10



years. Despite this, she was grossly obese. She realized that she had continued to take the medication largely to avoid lethargy and to get through each day. She was now attempting to withdraw but was finding herself depressed, gaining weight, unable to mobilize enough energy to keep her house clean, fighting with her husband, and blaming herself for all her children's personal problems because she had worked while they were growing up. Her use of amphetamines had allowed her to manage her personal and family problems in ways she no longer considered appropriate and had provided a comfortable alternative to counseling (which she had tried unsuccessfully). With the children grown, menopause reached, and husband alienated, she was now decompensating without the drug.

Case 3: A 20-year-old female student was well-adjusted but occasionally depressed in the face of religious conflicts between strict parents and a more relaxed 6anc6. With marriage and a job 6 months away, she felt the need to lose some weight even though she was not obese. She approached her physician for diet pills. He reluctantly prescribed 30 Desbutal Gradumet® tablets, each containing 10 mg of methamphetamine hydrochloride and 60 mg sodium pentobarbital. She lost 7 lb in the next 30 days. She also engaged in her first coitus during this period, experiencing deep guilt. After finishing the prescribed amount she felt lethargic and depressed. Four days after taking the last tablet she had fights with her fiancé and her sister, became very upset and depressed, and impulsively ingested 30 tablets of a sedative-analgesic (Fiorinal®), each containing 50 mg of an intermediate-acting barbiturate (butalbital). She was hospitalized moderately intoxicated, and recovered. For this girl the combination of major emotional conflicts and the depression caused by amphetamine withdrawal led to a suicide attempt.

It is important to recognize that these patients were giving their physicians a common message: they needed help with an emotional problem. The physician's response to the overt request for a pill prevented him from providing help for the real problem.

### Why Are Amphetamines Still Being Prescribed?

Why are drugs of such dangerous potential and so little objective advantage still in wide use? Amphetamines are, after all, not life-saving agents. Several explanations are possible:

1. Most physicians have not had an opportunity to observe a seriously affected high-dose amphetamine abuser or "speed freak."

2. Most physicians feel a need to offer something to the patient trying to lose weight, both physician and patient often sensing, but not verbalizing, that they are dealing with a problem nearly untreatable in traditional terms.

3. The economic value of amphetamine sales is substantial, judging from the industry's enthusiastic promotion of these agents despite the serious questions about their utility.

4. Tens of thousands of respectable adults are to some extent dependent on them and exert suasion on their physicians to continue prescribing them.

5. Physicians themselves use and abuse psychoactive drugs more often than the general population (23). This suggests that sometimes they may also have difficulty objectively evaluating the use of these drugs for their patients.

6. It is possible that amphetamine popularity reflects American culture. As Fiddle (24) has observed, the amphetamine user is a caricature of many widely admired American traits: intense activity, efficiency, persistence and drive, and the desire to excel, to break records, and to move with ever greater speed. These are admirable behavior patterns that are not easily relinquished, even when a drug may be required to achieve them.

The result is the perpetuation of the legal use of dangerous agents of little therapeutic advantage. This is not the first description of the hazards or of the minimal effectiveness of these drugs, nor is it the first effort to suggest that their medical use be curtailed (25-27). But the problem grows.

To some extent the current drug-abuse epidemic may relate to the way we as physicians have handled the amphetamine problem. Our use of the drug may be providing a poor model for children and adolescents to emulate. By treating with drugs a condition such as obesity, which probably most often has its roots in social custom and psychological conflict, are we giving license by example to youngsters who would treat their own social and psychological discomforts pharmacologically?

The time to face the unpleasant facts is long overdue. Amphetamines are fascinating substances with a wide range of effects—some good, some bad. Their use represents a sincere effort to treat major causes of human suffering. At present, however, we are not in a position to handle them safely. The situation raises uncomfortable questions: If amphetamine use of all types—legal and illegal—were to cease completely tomorrow, would we be better or worse off with regard to health than we are today? Do we really need these drugs?

We must begin taking steps now to end the epidemic overuse and misuse of amphetamines. Few of us would welcome more restrictive legislation in the drug field or more extensive activity by the Food and Drug Administration. Yet this is the prospect if we avoid taking immediate remedial action.

This action should begin with the physician's voluntary cessation or sharp reduction of prescriptions for amphetamines and their congeners. Exception might be granted in individual cases for the treatment

of narcolepsy and hyperkinetic reactions of children but rarely in other conditions. It is difficult, if not impossible, to justify their continued use in obesity and depression. Physicians may need a buffer against pressures for continued prescriptions from some patients. If so, a medical committee or board could be established to authorize these exceptions, as in Sweden (28). To circumvent the weariness most of us feel toward more committee work and the suspicion that an endless list of drugs may later come under such scrutiny, let me suggest that it is no more than we would do if heroin were made legal. Amphetamines are no less a menace.

Severe curtailment of production is essential. Less than 1 % of the current volume would probably be an adequate supply for the exceptional case. No more than two pharmaceutical houses are needed to provide this amount. The industry's voluntary action toward this goal would provide refreshing evidence that it puts the public welfare first and that legislation is not required on every urgent health matter. Finally, advertising of these products in medical journals is inappropriate.

We need not delude ourselves that these measures will end amphetamine abuse: they will not. It is not certain they will even reduce it measurably for several years. Black-market production will doubtlessly expand. The diagnosis of narcolepsy may suddenly become more popular. These measures are, however, a step in the direction of removing one major inconsistency in our approach to drugs and of establishing a climate that does not so vigorously promote drug abuse.

**ACKNOWLEDGMENTS:** Received 18 November 1970; revision accepted 12 January 1971.

Requests for reprints should be addressed to George R. Edison, M.D., Student Health Service, University of Utah, Salt Lake City, Utah 84112.

## References

1. Connell PH: Clinical aspects of amphetamine dependence, in *77re Pharmacological and Epidemiological Aspects of Adolescent Drug Dependence*, edited by Wilson CWM. Oxford: Pergamon Press, 1968, pp. 41-53
2. Physicians' Desk Reference to Pharmaceutical Specialties and Biologkals, 24th cd. Oradell, NJ., Medical Economics, Inc., 1970
3. American Medical Association Committee on Alcoholism and Addiction and Council on Mental Health: Dependence on amphetamines and other stimulant drugs. *JAMA* 197:1023-1027, 1966

4. National Institute of Mental Health, U.S. Department of Health, Education, and Welfare: *The Up and Down Drugs*. PHS Publication No. 1830. Washington D.C., U.S. Government Printing Office, 1969
5. Hadden J, Johnson K, Smith S. et al: Acute barbiturate intoxication. *JAMA* 209:893-900, 1969
6. Plum F: Sleep and its disorders, in *Cecil-Loeb Textbook of Medicine*. 12th ed., edited by Beeson PB, McDermott W. Philadelphia, W.B. Saunders Co., 1967, p. 1432
7. Graded imipramine regimen favored in hyperkinetic children (medical news), *JAMA* 208:1613-1614, 1969
8. Smith DE: Speed freaks vs. acid heads. *Clin Pediat (Philo)* 8:185-188, 1969
9. Mendelson M: Neurotic depressive reaction, in *Comprehensive Textbook of Psychiatry*, edited by Freedman AM, Kaplan HI. Baltimore, The Williams & Wilkins Co., 1967, p. 936
10. Jarvix ME: Drugs used in the treatment of psychiatric disorders, in *The Pharmacological Basis of Therapeutics*, 3rd cd., edited by Goodman LS, Gilman A. New York. The Macmillan Co., 1965, p. 198
11. Cole JO, Davis JM: Antidepressant drugs, in *Comprehensive Textbook of Psychiatry*, edited by Freedman AM, Kaplan HI. Baltimore, The Williams & Wilkins Co., 1967, p. 1272
12. Schildkraut J: Neuropsychopharmacology and the affective disorders (first of three parts). *New Eng J Med* 281:197-201, 1969
13. Thorn GW, Bondy PK: Obesity, in *Principles of Internal Medicine*, 5th ed., edited by Harrison TR, Adams RD, Bennett IL, et al. New York, McGraw-Hill Book Co., 1966, p. 398
14. Modell W: Status and prospect of drugs for overeating (Report to AMA Council on Drugs). *JAMA* 173:1131-1136, 1960
15. Albrinx MJ: Obesity, in *Cecil-Loeb Textbook of Medicine*, 12th cd., edited by Beeson PB, McDermott W. Philadelphia, W.B. Saunders Co., 1967, p. 170
16. Stunkard A, McLaren-Hume M: The results of treatment for obesity. *Arch Intern Med (Chicago)* 103:79-85, 1959
17. Glennon JA: Weight reduction—an enigma. *Arch Intern Med (Chicago)* 118:1-2, 1966
18. Astwood EB: The heritage of corpulence. *Endocrinology* 71:337-341, 1962
19. Connell PH: Amphetamine Psychosis. Maudsley Monograph No 5. London, Oxford University Press, 1958
20. Kramer JC, Fisciiman VS, Littlefield DC: Amphetamine abuse. *JAMA* 201:305-309, 1967
21. Louria DB: Medical complications of pleasure-giving drugs. *Arch Intern Med (Chicago)* 123:82-87, 1969
22. Citron BP, Halpern M, McCarron M, et al: Necrotizing angitis associated with drug abuse. *New Eng J Med* 283: 1003-1011, 1970
23. Vaillant GE, Brighton JR, McArthur C: Physicians' use of mood-altering diugs. *New Eng J Med* 282:365-370, 1970
24. Fiddle S: Circles beyond the circumference: some hunches about amphetamine abuse, in *Amphetamine Abuse*, edited by Russo JR. Springfield. 111.. Charles C Thomas, Publisher, 1965, pp. 80-85
25. Kiloh LG, Brandon S: Habituation and addiction to amphetamines. *Brit Med J* 2:40-43, 1962
26. Wilson CWM (editor): *The Pharmacological and Epidemiological Aspects of Adolescent Drug Dependence*. Oxford, Pergamon Press, 1968, pp. 256-257
27. Edison GR: Abuse of amphetamines (letter). *JAMA* 205: 882-883, 1968
28. Perman ES: Speed in Sweden (editorial). *New Eng J Med* 283:760-761, 1970