

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-