

Substitution Studies

Following precipitation tests, subjects also participated in 24 hour substitution tests¹⁴ to determine if butorphanol could substitute for morphine and suppress abstinence. On separate weeks, subjects were given, in lieu of regular doses of morphine, three consecutive doses of each of the following: saline placebo; morphine 3 and 6 mg; and butorphanol, 0.6 and 1.2 mg. Abstinence scores were assessed hourly from the 14th through the 24th hour of substitution. At these same times the degree of sickness was assessed as 0 = not sick; 1+ = slightly sick; 2+ = mildly sick; and 3+ = very sick. Partial maintenance doses of morphine suppressed both the symptoms and signs of abstinence (Table 12). Butorphanol, 0.6 and 1.2 mg, both suppressed the abstinence but this effect was slight and no significant dose relationship was found.

On the basis of preliminary studies it appears the pharmacologic profile produced by butorphanol is not morphine-like but more closely resembles that produced by agents such as nalorphine, cyclazocine and pentazocine. Morphine antagonist activity was not clearly demonstrated.

SECTION II: AMPHETAMINE-LIKE DRUGS

Side-Chain Modified Amphetamine Congeners

In 1971, Martin *et al.*²³ reported on the subjective and physiological effects of *d*-amphetamine and several related congeners (Fig. 11, #1-5). While these agents differed in terms of mg potencies, none seemed to have a selective effect on euphoria, blood pressure or appetite (Table 13). Martin²³ proposed that this profile of subjective and physiologic effects be used to classify agents as amphetamine-like in man for the purpose of assessing abuse potential. Since then, several more drugs have been assessed by these same methods. This program is directed by Dr. John Griffith.

The 5 agents originally studied by Martin *et al.*²³ were various side chain modified amphetamine congeners (Fig. 11). Two further examples of this class have been since studied, diethylpropion and benzphetamine (Fig. 11, #6, 7). Diethylpropion was reported last year as being "amphetamine-like." It is a relatively weak compound, however, as indicated by the potency estimates in Table 13.

Benzphetamine

This compound, also a side-chain modified derivative, was assessed more recently. Its profile of subjective and physical effects resembles that of amphetamine but its oral potency is of the same order as diethylpropion or subcutaneously administered α -ephedrine (Table 13).