Despite the unpleasant side-effects noted, subjects also evidenced "liking" scores which equalled those produced by 30 mg of morphine (Fig. 9). One interpretation of these "liking" scores is that butorphanol is more reliably euphorogenic than agents such as nalorphine or cyclazocine and suggests that there may be a difference in the profiles of subjective effects produced by agents such as pentazocine, cyclazocine and butorphanol.

An additional study was conducted to compare the subjective effects of pentazocine, butorphanol, cyclazocine and morphine. The same experimental procedures and methods were utilized as described above except that the last observation time was omitted. Nine subjects participated. Each received in random order at weekly intervals the following medication: placebo (normal saline); cyclazocine (base), 0.5 and 1.0 mg; pentazocine (base), 40 and 80 mg; butorphanol (salt), 2 and 4 mg; and morphine sulfate (salt), 10 and 20 mg. One subject did not complete the 1 mg cyclazocine treatment because he found this dose to be extremely disturbing. Consequently, the responses to cyclazocine, 1 mg, are based on 8 subjects.

The effects of butorphanol, cyclazocine and pentazocine could be differentiated from morphine by elevated PCAG and LSD Scale scores; greater responses on the symptoms and signs categories, "sleepy," "drunken," "nervous"; and a tendency to identify these effects as barbiturate-like (Fig. 10; Tables 8, 9). Relative potencies (Table 10) were similar to those obtained previously for butorphanol (Fig. 9), pentazocine,[13] and cyclazocine[22] relative to morphine. A second set of relative potencies calculated for comparison of cyclazocine with pentazocine and butorphanol with pentazocine (Table 10) indicate that butorphanol is approximately 15 to 25 times more potent than pentazocine and that cyclazocine is approximately 25 to 100 times more potent than pentazocine. Of interest was the observation that statistically valid relative potencies were not obtained with all measures for these comparisons with pentazocine because of significant "F" ratios for non-parallelism and preparation mean squares in the analysis of variance suggesting differences in the profile of subjective effects among these agents.

Precipitation Studies

The first studies conducted in 5 subjects dependent upon 60 mg of morphine per day (15 mg q.i.d. subcutaneously) involved precipitation tests using our standard procedure[22] in which each subject received placebo; 1.5 and 3 mg of nalorphine; and 4, 6 and 8 mg of butorphanol. Butorphanol, 4 mg, precipitated mild abstinence with abstinence scores equivalent to that produced by nalorphine 1.5 mg (Table 11). However, increased doses, 6 and 8 mg, did not increase abstinence scores. The precipitated abstinence scores for butorphanol were not significantly different from those produced by placebo. Larger doses of butorphanol were not given because the 8 mg of butorphanol produced nervousness, apprehension, and irritability, along with a mild degree of abstinence as would be expected from the single dose studies.