a single subcutaneous injection. For 2 weeks this injection was saline. Then buprenorphine, 0.5 mg, was substituted for the saline injection. The dose of buprenorphine was progressively doubled until the 15th day when a dose of buprenorphine, 8.0 mg, was administered. This dose, which would be equivalent to approximately 240 mg of morphine, was then administered once daily through the remainder of the study. During the period of chronic administration, 2 sets of experiments were performed. Single doses of morphine and placebo were administered under double blind conditions and their effects compared with the effects of single doses of placebo; morphine, 15 mg; and morphine, 30 mg, administered during the control phase when subjects were receiving saline. These experiments were to determine if buprenorphine exerted a significant blocking action. The second set of experiments during chronic administration consisted of the administration of naloxone to precipitate morphine-like abstinence.

During chronic administration of buprenorphine, analysis of responses on the chronic questionnaire administered once daily indicated that subjects identified the drug predominantly as an opiate (dope) and liked the effects of buprenorphine (Fig. 15). The pattern of symptoms from the chronic opiate questionnaire were similar to those observed with morphine in other studies. During chronic administration, pupils constricted and diastolic blood pressure decreased slightly (Table 9). There were no changes in pulse rate, systolic blood pressure, respiratory rate, body weight or significant decrease in caloric intake. Between the 18th through the 25th day of chronic administration of buprenorphine, each subject received single test doses of placebo; morphine, 15 mg, and morphine, 30 mg, subcutaneously. To correct for the effects of buprenorphine, the response to morphine, 15 and 30 mg, was corrected by subtracting out the responses for placebo. Comparison of the placebo-drug differences for morphine, 15 and 30 mg, during chronic buprenorphine administration with effects of morphine, 15 and 30 mg, administered to the same subjects during the control period indicates that these effects were significantly decreased (Fig. 16). Subsequently, single doses of morphine to 120 mg were administered without any significant effects (Fig. 16). In an additional experiment, a placebo was substituted for the 8:30 a.m. buprenorphine injection under double blind conditions and a test dose of morphine, 30 mg, administered at 10 a.m. The morphine effects were blocked to the same degree as they were in the condition when buprenorphine had been administered 1 1/2 hours before morphine administration (Fig. 16) indicating that the blocking effects of buprenorphine persist undiminished for at least 25 to 30 hours after drug administration.