Changes in total morbidity which occurred in the smaller groups of patients treated for 24 weeks with a single treatment are shown in Figure 3. Chlorpromazine produced striking improvement in being greatest in the initial 12-week period. Over 24 weeks, improvement from chlorpromazine was not significantly greater than that from promazine but greater than from the control drugs. Improvement from promazine was significantly more than from phenobarbital but not from placebo. The difference between placebo and phenobarbital was not significant.

The first 12-week treatment period was considered to be most important for assessing changes in specific symptoms as the patients were newly treated. After the cross-over of treatments occurred, the situation became more complex, with the possibility of some carry-over effects from the earlier treatment. Table 1 describes the relationships of the various treatments to one another in regard to reduction of symptoms during this initial period of treatment. Chlorpromazine was superior to any of the other three treatment drugs in reduction of certain symptoms. Promazine surpassed phenobarbital and placebo in a more limited range of symptomatic improvement. The differences between phenobarbital and placebo were slight.

TABLE 1.—*Differences in Reduction of Symptoms Between Drug-Treated Groups During Initial Twelve-Week Treatment Period* *

Cl surpassed Pr in reducing symptoms of total morbidity, severity of illness, unimproving mental condition, risk of leaving hospital without permission, withdrawal, conceptual disorganization, perceptual distortion, mannerisms, self-depreciation, resistiveness, belligerence, risk of violence to others.
Cl surpassed Ph in the same respects plus participation in activities and self-care.
Cl surpassed Pl in the same respects with the exception of risk of leaving the hospital without permission and participation in activities and self-care.
Pr surpassed Ph in reducing symptoms of total morbidity, conceptual disorganization, perceptual distortion, mannerisms, resistiveness, and belligerence.
Pr surpassed Pl in reducing symptoms of total morbidity, conceptual disorganization, and perceptual distortion.
Ph surpassed Pl in reducing symptoms of retarded depression.
Pl surpassed Ph in reducing symptoms of belligerence.

* Cl, chlorpromazine; Pr, promazine; Ph, phenobarbital; Pl, placebo.
All differences are beyond the 5% level of statistical significance; only comparisons showing such differences are noted

TABLE 2.—*Differences in Reduction of Symptoms Between Drug-Treated Groups over Twenty-Four-Week Period: Same Drug Used Continually* *

ClCl surpassed PrPr in reducing symptoms of withdrawal, conceptual disorganization, mannerisms, and belligerence; surpassed PhPh in reducing the same symptoms plus total morbidity, unimproving mental condition, and resistiveness; surpassed PlPl in reducing symptoms of total morbidity, conceptual disorganization, paranoid projection, and belligerence.
PrPr surpassed PhPh in reducing symptoms of total morbidity and resistiveness; reduced no symptoms significantly more than ClCl or PlPl.
PhPh reduced no symptoms significantly more than ClCl, PrPr, or PlPl.
PlPl surpassed ClCl, PrPr, and PhPh in reducing the symptom of self-depreciation; surpassed PhPh in reducing the symptom of resistiveness.

*ClCl, PrPr, PhPh, and PlPl indicate successive 12-week courses of each agent.
All differences beyond the 5% level of statistical significance; only comparisons showing such differences are noted.

Comparisons between the smaller groups treated for 24 weeks consecutively with a single treatment yielded essentially similar results (Table 2). Continued treatment with chlorpromazine produced more symptomatic improvement than continued treatment with the other three agents. Twenty-four weeks of promazine therapy reduced total morbidity and resistiveness more than phenobarbital only. Phenobarbital produced no significant symptom reduction as compared with the other three agents. Placebo for 24 weeks reduced the symptom of self-depreciation significantly more than any one of the other agents.

The cross-over design permitted various sequence of drugs (chlorpromazine and promazine) and control medications (phenobarbital and placebo) to be evaluated. Figure 4 shows the changes in total morbidity which occurred when the drugs were preceded by placebo or followed by it. When placebo was administered during the initial 12-week period, slight changes toward improvement were seen. The addition of chlorpromazine for the second 12-week period produced strikingly more reduction in morbidity. The effect of promazine in this regard was slight. When the drugs were