experience and advice of drug manufacturers, with possible unknown bias in favor of one treatment over another. The relatively brief duration of treatment may have tended to minimize changes.

Despite these handicaps, the results obtained were consonant with most clinical experience. When chlorpromazine was used, either preceding or following another treatment, the effect of the drug was clearly superior to that of the others. As chlorpromazine is generally considered to be the "standard" against which all other tranquilizers should be measured, the results obtained here bear out this high opinion of the drug. Promazine, while showing definite therapeutic effects, produced changes of less degree and in fewer instances. Here, too, clinical opinion is that this drug is less effective than chlorpromazine at the same dose levels, especially in chronic schizophrenics.[22] Had a higher or a flexible dose of this drug been used, differences between promazine and chlorpromazine might have been less striking, and the superiority of the former drug over phenobarbital and placebo more evident.

The fact that placebo and phenobarbital produced little therapeutic benefit in chronic schizophrenics came as no surprise to clinicians with extensive experience in treating such patients. The placebo effect is contingent upon a high degree of spontaneous remission and a high level of suggestibility of the patient, neither situation obtaining in chronic schizophrenics. On the other hand, the retention of therapeutic gains from tranquilizers for as long as three months following the cross-over to placebos or phenobarbital was surprising. Although it is a common clinical experience that some patients may stay in remission for a long time after discontinuation of medication, it is equally common for patients to relapse within days or weeks. The process of group averaging of morbidity might tend to mask a frequency of relapse that would be intolerable clinically, but relapse of individual patients in this study could not have been very frequent, else the changes in averages would have been greater. Another controlled study has indicated that carry-over effect from chlorpromazine may last as long as three months after patients have been switched to placebos.[23] While tending to support this idea, the present study does not constitute definitive proof because of the comparatively small sample (39 to 42 patients) in each of these treatment groups.

Another interesting aspect of the use of placebos in this study was the apparent amelioration of a symptom of mental depression (self-depreciation) by placebo when given continually for 24 weeks, as compared with the other three agents given in the same fashion. Here the effect may be negative rather than positive; the drugs may have aggravated this particular symptom. Clinical evidence suggests that, at least with the phenothiazine derivatives, some patients may have depressive symptoms aggravated.

Summary

A large cooperative study involving 692 men with schizophrenic reactions hospitalized in 37 Veterans Administration neuropsychiatric hospitals was undertaken to determine the relative effectiveness of chlorpromazine, promazine, phenobarbital, and placebo. Controls included random assignment of treatments, use of the double-blind technique for drug administration, and provision for similar conditions of treatment. Chlorpromazine and promazine were administered in daily doses of 400 mg., and phenobarbital, in doses of 200 mg. After 12 weeks of treatment, some patients continued for 12 more weeks on the drug initially assigned, and some were switched to control medications following the tranquilizing drugs, or vice versa.

Chlorpromazine was found to be significantly better in reducing total morbidity of patient groups treated with this drug over a 12-week period than were any of the other three agents. Over the 24-week period chlorpromazine was significantly more effective than either control medication. Promazine was significantly more effective than either control medication over the 12-week period,