Comparisons of symptom reduction when drugs followed control medications or vice versa are shown in Table 3. In general, the presence of a tranquilizing agent in the sequence increased symptomatic relief, as compared with the control agents. Furthermore, chlorpromazine was generally better than promazine. Phenobarbital was never superior to the tranquilizing drugs in improving any specific symptom. Placebo excelled each of the other three agents in reducing self-depreciation.

Comment

Sampling and Statistical Considerations. The intent of this study was to determine the relative effectiveness of these drugs with schizophrenic patients classified as acute, disturbed and nondisturbed, and as chronic, disturbed and nondisturbed. However, the available sample proved to be composed mainly of chronic nondisturbed patients. Accordingly, the results of this study are most applicable to such patients. One should expect that therapeutic effects of the tranquilizing agents might have been more easily demonstrable in the other three groups of schizophrenics. In the cross-over study, the preponderance of chronic nondisturbed patients was even greater. In addition, the fragmentation of the original sample produced rather small samples for each treatment sequence. Both these factors might be expected to increase the difficulty in demonstrating clear-cut therapeutic differences.

Every effort was made to assure that differences among patient groups following treatment were in fact due to the treatment.

In the statistical analysis, it was assumed that the samples had been randomly selected, that each treatment group resembled the other in most pertinent characteristics, and that the design of the experiment eliminated other biasing factors. As far as could be determined, all these assumptions were tenable in this study.

Tools for Evaluation of Patient Change. The two rating devices utilized consisted of one which was extensively tested and one completely new. The MSRPP has been well validated and very widely used.[11,19,20] As no scale is more accurate than the raters, it is important to note that this scale was used in this study by a team, consisting in all cases of a pyschiatrist and a psychologist, which made a consensus rating. Later evaluation of this technique suggested that it has a high degree of interrater reliability.[21] Each team was specially trained in the use of the scale prior to the initiation of the study. Consequently, it was felt that the results of these ratings were acceptably reliable.

Although the Clinical Estimate of Psychiatric Status required only "global" intuitive judgments, it was felt that such material might prove to be useful. Without previous trial, one could not be sure of the degree of the relevance or interrater consistency of the scale. In most cases significant improvement of patient groups in regard to "severity of illness" measured by this device was consistent with similar improvement in the total morbidity score of the MSRPP. However, what some of the measures in this scale were relevant to had not been established and could not be clearly interpreted.

Drop-Outs and Side-Effects.—The number of drop-outs and side-effects was comparatively small. However, these findings could not be generalized beyond the present sample, since 65% of patients had received tranquilizing drugs before. Presumably, such patients may have had an opportunity before the study to become "desensitized" to some of the side-effects of these agents.

Clinical Findings.—A number of factors in this study tended to introduce a "negative bias." The chronicity of the patients and their previous refractoriness to tranquilizing drugs did not afford the most sensitive group for demonstrating therapeutic effects of these agents. The use of a single fixed dose, while considered necessary in the experimental design, may have limited the effects of treatment. Equivalence of dosage between drugs was determined from clinical