METHOD*

Six medications were randomly assigned to 640 schizophrenic males as they were successively admitted over a six month period to 35 cooperating hospitals. The drugs used were chlorpromazine,† mepazine,‡ perphenazine,§ prochlorperazine,† and trifluprom azine.|| Phenobarbital was used as an active control substance. Treatment was carried out under double-blind conditions, and dosage followed a fixed-flexible schedule. Dosage was progressively increased at a specified rate during the first four weeks until it reached the following levels: prochlorperazine, 75 mg.; mepazine and trifluprom azine, 150 mg.; phenobarbital, 96 mg.; chlorpromazine, 600 mg.; and perphenazine, 48 mg. A flexible dosage schedule was used during the remaining 12 weeks of the study, during which period the physician adjusted the dosage, within limits, to meet the optimal chemotherapeutic needs of his individual patients. The daily dosage in mg. during the flexible period was as follows: prochlorperazine, 25 to 150; mepazine and trifluprom azine, 50 to 300; phenobarbital, 32 to 192; chlorpromazine, 200 to 1200; and perphenazine, 16 to 96.

At the beginning of the study, the average patient was 34 years old and had first been treated for mental illness about 7 years prior to current hospitalization. Eighteen per cent had never been hospitalized previously, and one third had been hospitalized more than three times. Fifty-six per cent had received some variety of ataractic drug previously.

Clinical changes in patients were measured by two rating scales: the Multidimensional Scale for Rating Psychiatric Patients[9] (M.S.R.P.P.), and the Clinical Estimate of Psychiatric Status Scale (C.E.P.S.S.). The M.S.R.P.P. yields scores for 11 factors or symptom clusters as well as an over-all score called Total Morbidity. The C.E.P.S.S. required judgments from psychiatrists on 12 items referring to psychopathology and prognosis. Patients were evaluated by both rating devices before treatment and after 4 and 12 weeks of treatment. Detailed laboratory studies were also conducted.

The statistical model used to evaluate the relative therapeutic effectiveness of the drugs studied was analysis of multiple covariance (simple randomized design). Each of the 24 criterion measures (12 from the M.S.R.P.P. and the 12 C.E.P.S.S. items) was analyzed for relative changes in clinical status during the first month, the second two months, and over the entire three month study period. Final criterion mean scores in each analysis were

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* A more complete description of project III has been prepared for separate publication. The study protocol, reproduced in its entirety in the *Transactions of the Third Annual Research Conference on Chemotherapy in Psychiatry*, edited by Clyde J. Lindley and published by the Veterans Administration Department of Medicine and Surgery, April, 1959, contains considerable detail concerning selection of patients, the randomization procedures, precautions, restrictions, laboratory controls, and forms. A statistical appendix in the *Transactions of the Fourth Annual Conference on Chemotherapy in Psychiatry*, edited by Clyde J. Lindley and published by the Veterans Administration Department of Medicine and Surgery, May, 1960, presents the results, as well as other data, in great detail.

† The trade name of Smith, Kline & French Laboratories for chlorpromazine is Thorazine, and for prochlorperazine is Compazine.

‡ The trade name of Warner-Chilcott Laboratories for mepazine is Pacatal.

§ The trade name of Schering Corporation for perphenazine is Trilafon.

|| The trade name of E. R. Squibb & Sons for trifluprom azine is Vesprin.