schizophrenic patients under controlled conditions.

Procedure *

Population.—The study population was made up of men under 51 years of age who were hospitalized for schizophrenic reactions. Patients with organic brain disease, previous leukotomy, or active systemic disease were specifically excluded.

Sampling. — Thirty-seven hospitals contributed 805 patients to the study. Patients were selected from four main categories: acute disturbed, acute nondisturbed, chronic disturbed, and chronic nondisturbed. Chronic patients greatly outnumbered the acute (81% to 19%); the number of nondisturbed patients was greater than the number of disturbed patients (73% to 27%). Chronic nondisturbed patients made up about two-thirds of the sample because a sufficient number of acute disturbed patients was not available.

Patients selected within each of the four categories of chronicity and disturbance were randomly distributed among four treatment groups. The number of patients dropped during the course of the study because of serious side-reactions, inadequate evaluation, or other reasons was distributed evenly among the categories. The final sample available for analysis consisted of 692 patients.

Treatment.—"Double-blind" controls were used in applying the four treatments: chlorpromazine, promazine, phenobarbital, and placebo. Patients nominated for the study were assigned medication in random order. Neither the patients nor their physicians knew which of the four agents was assigned. As a safeguard, the manager of the hospital was provided with this information for release only if the welfare of the patients so dictated. As pharmacologic and side-effects might impair "double-blind" conditions, using two tranquilizers reduced the chances of identifying the drugs. The commonest side-effect, drowsiness, was duplicated by phenobarbital.

Decisions regarding dosage and duration of treatment were made only after considerable discussion. The issue of flexible doses as opposed to fixed doses was decided in favor of the latter, it being recognized that an arbitrarily selected dose of a drug might not be optimal for all patients. A daily dose of 400 mg. of chlorpromazine was considered enough to demonstrate any therapeutic effect of this agent. An equal dose of promazine was recommended by the manufacturer. The dose of phenobarbital was 200 mg. daily. All medications were packaged in capsules containing one-fourth the total daily dose of drug, that is, 100 mg. of chlorpromazine or promazine or 50 mg. of phenobarbital in each capsule. Each patient's supply of medication was labeled only with his name and the code number. All medications were odorless and identical in appearance and taste. No previous tranquilizing medication had been given for at least two months prior to the study to chronic patients and one month to acute patients. Initiation of medication was gradual, beginning with 1 capsule on the first day of the study, 2 on the second, 3 on the third, and the full dose, of 4 capsules, daily thereafter. All medication was given orally, divided into 2 or 3 daily doses given at least eight hours apart.

The duration of treatment was arbitrarily determined at 12 weeks, a period of sufficient length to demonstrate therapeutic effects. At the end of this time, a "blind cross-over" was effected for another 12 weeks, as diagramed in Figure 1. Thus some patients were allowed to continue on the same treatment for 24 weeks; others had a control medication replaced by a tranquilizer or vice versa. Of the 692 patients completing the first 12 weeks of treatment, 489 (from 26 hospitals) completed the second 12-week treatment period.

The only treatment activities restricted were individual and group psychotherapy, shock therapy, and interward transfer. All other treatment activities available in the hospital were continued during the study. Supplemental conventional hypnotics, not barbiturates, were permitted when deemed essential.

Method of Evaluation of Treatment.—Clinical changes in patients were measured by three rating devices: (1) The Multi-Dimensional Scale for Rating Psychiatric Patients (MSRPP),[11] (2) a Clinical Estimate of Psychiatric Status,[12] and (3) the Manifest Anxiety Scale.[13]

The MSRPP consists of 62 items, 40 of which require a clinical psychiatric interview for rating. The deviations of a patient's item scores from the norm yield a "total morbidity score." Subgroupings of items also provide scores for 11 factors of psychopathology: activity level, withdrawal, conceptual disorganization, perceptual distortion, mannerisms, paranoid projection, retarded depression, melancholy agitation, self-depreciation, resistiveness, and belligerence. In this study, a team of observers at each hospital gave a consensus rating for each patient with this scale. Data for this

* Detailed statements about the population, the sampling procedure (randomization procedure, homogeneity of groups, etc.), treatment procedure (precautions, laboratory methods, etc.), and method of evaluation (training of raters, arriving at team consensus rating, recording observations, nature of scales, etc.) are available elsewhere.[8-10] Detailed statistical tables of the complete data may be obtained from the Central Neuropsychiatric Research Laboratory, Veterans Administration, Perry Point, Md.