therapy. The failure to encounter any instance of frank jaundice or agranulocytosis in 530 patients treated with phenothiazine derivatives suggests that these complications may have been more feared in the past than was warranted. In view of the frequent abnormalities associated with phenobarbital therapy, especially those not commonly attributed to this drug before, one must be cautious in ascribing all that happens during drug therapy to the drugs being used. The original intent to discover some index between therapeutic effectiveness of the drugs and side reactions or laboratory abnormalities was not feasible with so little difference between the agents in either regard.

Although this study offers considerable information regarding the clinical effectiveness, side effects, and toxicity of 5 phenothiazines used under the described conditions, the data necessary to guide drug therapy of individual schizophrenic patients are not provided. With the data from this and other studies and his personal experience with drugs as background material, the physician must still select a specific drug for an individual patient, taking into consideration such factors as speed of action; dosage schedules; treatment goals; combinations, potentiation, and sequences of drugs; duration of effects; calculated risks and safety; convenience; cost; subjective patient response; compatability with other treatments; and any special features or unique advantages of a given drug.

Summary

Six hundred forty newly-admitted schizophrenic men in 35 VA hospitals were randomly assigned to chlorpromazine, trifluprom azine, mepazine, prochlorperazine, perphenazine and phenobarbital groups. Treatment followed a double blind procedure for 12 weeks. Patients were started on low "equivalent" doses of each drug which were gradually increased in a predetermined manner during the first 4 weeks. During the final 8 weeks, each prescribing physician adjusted the dose for each of his patients in order to evoke an optimal therapeutic response.

Average daily doses during the flexible period were: chlorpromazine, 635 mg.; trifluprom azine, 175 mg.; mepazine, 190 mg.; prochlorperazine, 90 mg.; and perphenazine, 50 mg. Clinical evaluations using two rating scales provided 24 criteria of change. For each criterion, the mean of each of the 6 treatment groups adjusted for the net effect of 12 control variables was compared by analysis of multiple covariance with the mean of every other treatment group at each of three evaluation periods; first month, the following 2 months, and over the entire 3 months. Side effects, hematologic and hepatic function data were also recorded during the course of treatment. One hundred sixty-eight patients failed to complete the study.

In general, the results indicated that all 5 phenothiazine derivatives were therapeutically more effective than phenobarbital. Mepazine was less effective than the other 4 drugs at the doses employed. No significant differences in therapeutic efficacy were noted between chlorpromazine, trifluprom azine, prochlorperazine, and perphenazine. Criterion measures showing change toward improvement after treatment with phenothiazine derivatives included resistiveness, belligerence, thinking disturbance, and degree of illness. Other criteria affected favorably, especially by the 4 more potent phenothiazines, were motor disturbance, paranoid projection, perceptual distortion and withdrawal.

Only 21 patients (3%) were discontinued from treatment because of side reactions or deviant laboratory tests. Most side reactions, especially the extrapyramidal syndromes, were produced by perphenazine and prochlorperazine. Phenobarbital was associated with a number of side reactions ("turbulence," autonomic symptoms) commonly attributed only to the phenothiazine derivatives. Abnormal hematologic tests including eosinophilia, leucocytosis and leucopenia were neither frequent nor severe. The distribution of the 36 patients with leucopenia was not significantly different among the treatment groups. Continued treatment with the drugs in 31 leucopenic patients produced no case of agranulocytosis. Although abnormal hepatic tests occurred in 88 patients, these were sporadic. No clear-cut case of jaundice or hepatic dysfunction was encountered during treatment.