teria with respect to which chlorpromazine, trifluprómazine, prochlorperazine, and perphenazine were better than mepazine. There were no instances in which any of these phenothiazines was reliably worse than mepazine.

3. *The remaining four phenothiazine derivatives were not differentiated from one another in therapeutic effectiveness.* Over the entire 3-month period there were no significant differences among these 4 treatment groups on any of the 24 criteria.

SIDE EFFECTS AND LABORATORY FINDINGS

Only 21 patients (3%) were discontinued from treatment because of side reactions or deviant laboratory tests, this number being fairly evenly distributed among the 6 treatment groups. Five patients were dropped because of leucopenia. Four had deviant hepatic tests. Other reasons for termination included: 3 cases of Parkinsonism, 1 epigastric pain, 1 photophobia, 1 dermatitis, 2 deviant temperature or blood pressure, and 4 patients who became pale, nauseated, weak or hypotensive.

A detailed report of the abnormal symptoms, signs and laboratory tests has been published elsewhere(19). The piperazinyl-phenothiazines, perphenazine and prochlorperazine, produced most of the side effects followed by the aliphatic phenothiazines, chlorpromazine and trifluprómazine. Mepazine and phenobarbital produced the fewest side effects. Although the extrapyramidal syndrome was unique for the phenothiazines (and most pronounced with the piperazinyl derivatives), most of the other side effects measured, including adverse behavioral reactions and autonomic nervous system effects, were also reported in some measure for phenobarbital. Hematologic changes (leucopenia, eosinophilia, and leucocytosis) were encountered with all drugs without significant differences in frequency. The same was true of abnormal hepatic tests, none of the patients having a definite clinical picture of jaundice.

DISCUSSION

Since this study was designed as a comparative evaluation of 4 newer phenothiazines with chlorpromazine serving as a standard or reference treatment, emphasis was placed upon the *relative* effectiveness and toxicity of these 5 agents rather than the evaluation of any one considered independently. Phenobarbital, mimicking some of the properties of the phenothiazines, was included as an active placebo. To be considered an effective agent, any phenothiazine derivative should be superior, at least, to a conventional sedative.

The fact that all the phenothiazines studied were effective in reducing some aspects of psychopathology is evident from their comparison with phenobarbital and is consistent with most published reports. Of greater interest are the symptoms affected. After one month of treatment with these drugs, patients were less resistive, belligerent, and disturbed in their thinking than patients receiving phenobarbital. These changes were accompanied by a decrease in the amount of physical nursing care required. Further gains were made during the last two months of the study. Psychiatric judgments indicated that patients receiving the phenothiazine derivatives had better prospects for early discharge and were more likely to be independent and self-supporting after discharge than patients receiving phenobarbital.

In short, any of the 5 phenothiazine derivatives produced clinical effects superior to phenobarbital. It is inferred that these 5 agents would be superior to an inert placebo group or to a group that had received no capsules at all. The reduction in morbidity of the phenobarbital group during treatment was slight and did not reach significance. A previous VA cooperative study based on a large sample of chronic schizophrenic patients demonstrated that neither a placebo nor phenobarbital had therapeutic value nor was either more effective than the other(1).

Although all the phenothiazines were more effective than phenobarbital, mepazine was less effective than the other four. This finding may be related to differences in chemical structure as discussed by Himwich(20). One explanation of mepazine's apparent inferiority might be that it had been used at too low a dose. During most of the first month of treatment, mepazine patients received 150 mgs./day, the lower limit of the range of maximal therapeutic