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Drug Therapy in Schizophrenia

A Controlled Study of the Relative Effectiveness of Chlorpromazine, Promazine, Phenobarbital, and Placebo

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Despite the vast number of clinical investigations of tranquilizing agents which

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followed their introduction, relatively few studies have used adequate controls. Such controlled studies as were done often were based on small numbers of patients, involved differing control techniques, or led to contradictory conclusions.¹⁻⁶

Because of the difficulty in obtaining controlled drug studies of sufficient scope to be clinically meaningful, a cooperative study was planned to include psychiatric hospitals in the Veterans Administration nation-wide system. Such a study had the advantage of including a large and well-defined sample of patients treated in multiple hospital settings. Difficulties, anticipated in establishing a commonly understood research protocol and obtaining evaluations of treatment sufficiently similar to permit pooling of the data, did not prove to be insurmountable.

At the time this study was planned, two trends were already evident in regard to tranquilizing drugs.⁷ One was that reserpine and Rauwolfia alkaloids were diminishing in popularity for psychiatric use. The other was that interest in the phenothiazine derivatives, based on the successes with chlorpromazine, was mounting. Although preliminary clinical studies had indicated effectiveness of a dechlorinated analogue, promazine, this drug had not been tested under conditions of a "double-blind" control. Thus, these two phenothiazine derivatives, chlorpromazine and promazine, were selected for study. For comparison, an active agent, phenobarbital, and an inert placebo (lactose) were chosen. The purpose of the study was to determine whether these treatments differed in efficacy for specified