For many years, both the VA and NIMH have been supporting research on the clinical efficacy of the major tranquilizers and antidepressants. The first multi-hospital collaborative study of drug treatment with schizophrenics was conducted by the VA in 1957. This study compared the clinical efficacy of compazine, chlorpromazine and a placebo on 640 schizophrenic patients and definitively established the superiority of chlorpromazine over a placebo in the treatment of schizophrenia. Both the VA and NIMH have also conducted multi-hospital trials of drug efficacy in chronic schizophrenia and in depression. A recent report on the NIMH chronic schizophrenia study indicated that high doses of chlorpromazine were especially efficacious for younger patients, i.e., those under 40, with at least five years of continuous hospitalization. These large collaborative studies have been of particular value in delineating the subgroups of schizophrenic and depressed patients who are likely to be helped most by certain of the tranquilizers and antidepressants. For example, Dr. Colomon Goldberg of the Psychopharmacology Research Branch of NIMH has developed equations, based on pretreatment symptom profiles, that predict the response of schizophrenics to a variety of tranquilizers including chlorpromazine and thioridazine. Drs. Hollister and Overall of the VA have also reported that thioridazine, a tranquilizer, was particularly efficacious in a subgroup of anxious depressions whereas imipramine, an antidepressant, was especially efficacious for an additional subgroup of withdrawn-retarded depressions. Similarly, a recent NIMH supported collaborative study of drug treatment in depression revealed that imipramine was efficacious for psychotic depressions, but of little value for neurotic depressions.

The collaborative VA and NIMH studies have also made major contributions with regard to the methodology of evaluative drug trials. Symptom rating scales for evaluating patient change were developed which are now widely used and accepted by investigators at individual hospitals. Statistical techniques for discerning drug effects were also developed.

The VA and NIMH have also been very active in establishing centers for early clinical trials with new agents for the treatment of mental disorders. Dr. Hollister of the VA has established a drug screening center at the Palo Alto VA Hospital. The Psychopharmacology Research Branch has an Early Clinical Drug Evaluation Unit which includes investigators from approximately 15 psychiatric hospitals. Standard rating forms are used by these investigators to facilitate comparisons of drug effects across hospitals.

Finally, as you know, the VA and NIMH have recently undertaken a joint effort to evaluate the effects of lithium carbonate in both manic and depressed patients. As you are also aware, Dr. Cole, who was formerly Chief of the Psychopharmacology Research Branch, was instrumental a number of years ago in making this compound available to investigators in this country for early clinical trials.

If I can be of further assistance, please let me know.

Sincerely yours,

STANLEY F. YOLLES, M.D.,
Director.

Senator NELSON. Please go ahead.

Dr. AYD. All right. It came from France, but its value was demonstrated in the United States. We both agree. All right, sir.

Within 3 years after chlorpromazine and reserpine were made available, American psychiatric hospitals were reporting a decrease in the use of physical restraints, seclusion rooms, hydrotherapy, shock therapies, and other somatic methods of treatment; a reduction in destructiveness, combativeness, and assaultiveness; a greater number of ground privileges; and, above all, an increase in the discharge rate, especially of chronic patients who previously had been considered hopeless cases, and by some as "the living dead." Private practicing psychiatrists claimed that, properly used, these drugs increased the number of patients who could be treated in the office, facilitated psychotherapy, and made hospitalization unnecessary in many cases, thereby decreasing the number of admissions to overcrowded public mental hospitals and reducing the cost of psychiatric care.