

large. Although their molecular structures differ slightly and they produce different side effects, all appear to be the same with respect to their main therapeutic action, which is reduction of schizophrenic symptoms. This has been shown in a number of studies. John Davis, in a review,¹ summarizes this research saying: "Numerous studies showed the other phenothiazines to be approximately equal to chlorpromazine in their therapeutic effect . . . For example, a multiple variance analysis in the VA Cooperative Study showed no difference between perphenazine (Trilafon), trifluoperazine (Vesprin), prochlorperazine (Compazine), and chlorpromazine (Thorazine). The same results were found with a state hospital population, in the carefully done studies of Kurland *et al.* . . . Again we selected the studies which were methodologically best. They indicated that chlorpromazine, perphenazine, trifluoperazine, fluphenazine (Prolixin), trifluoperazine (Stelazine), prochlorperazine and thioridazine (Mellaril) were about equally effective . . ." The overall therapeutic equivalence of these phenothiazines is a generally accepted fact.²

It is also true however that patients will vary somewhat in their response to these drugs; at times a patient who is doing poorly on one will seem to improve on another. If this sort of differential response could be predicted it would be good to know because each patient could be assigned the drug most effective against his particular symptoms. Can we identify different constellations of symptoms or subtypes of schizophrenia each of which is most appropriately treated by a different phenothiazine? Galbrecht and Klett³ addressed themselves to this question by studying 310 schizophrenics randomly given one of three different phenothiazines. They used a method of computerized data analysis which would discover whether different types of patients were responding systematically to one drug or another. They conclude: "results from the present study failed to support the hypothesis that those patients who received their drug of choice [a computer's choice—not the patient's] would respond more favorably than those randomly assigned to the other drug . . . *in no case was evidence of differential drug action obtained.*" (my italics) This is an impressive statement since Galbrecht and Klett are experienced researchers using the newest methods of data collection and analysis. Hollister, in a recent review of psychotropic drug treatment⁴ cites no research which contradicts Galbrecht and Klett's conclusion.

Evidence such as this, which never finds its way into pharmaceutical advertising, suggests that there is no way at present to predict the best drug for a given patient. It suggests that the most rational way to begin therapy is with the least expensive drug, switching to something else only if the least expensive drug doesn't work or if idiosyncratic side effects should be encountered. I feel diffident to suggest such a simple approach to anti-psychotic therapy in view of the enormous promotion which different companies have given to the nuances of their competing products and of the clinical lore which has grown up in the wake of this promotion, but, at the present time, evidence for predictable differences in therapeutic effect does not exist.

Exhibit #1 is a good example of the current promotional effort. This advertisement (American Journal of Psychiatry, June 1969)⁵ recommends the combination of two phenothiazines, chlorpromazine and trifluoperazine. It says: "Often extends control when single agents prove less than satisfactory. When the schizophrenic patient's progress is hampered by persistence of certain symptoms, consider switching to Combined Stelazine-Thorazine Therapy."

Casey *et al.*⁶ tested precisely this claim. They studied 520 schizophrenic patients who had not responded satisfactorily to chlorpromazine alone. These patients were given different combinations of drugs including the Stelazine-Thorazine combination recommended in the ad. The authors conclude: "None of the drug combinations was superior to chlorpromazine and placebo." Again, this was highly competent research, a phase of the VA Cooperative Studies of Chemotherapy in Psychiatry. It was published eight years ago, long before the Stelazine-Thorazine campaign was started and nothing has been discovered since then to cause Casey's conclusion to be revised.

¹ "Archives of General Psychiatry," vol. 13, pp. 552-572, 1965.

² Mepazine and promazine may be exceptions but are hardly ever used in schizophrenia.

³ *Journal of Nervous and Mental Disease*, vol. 147, pp. 173-183, 1968.

⁴ *Clinical Pharmacology and Therapeutics*, vol. 10, pp. 170-198, 1969.

⁵ Specific citations are given for each advertisement. However they all appeared in a number of journals, often over a period of months.

⁶ "American Journal of Psychiatry," vol. 117, pp. 997-1003, 1961.