

June 17, 1964

Dr. William C. Janssen
Lakeside Laboratories
Milwaukee, Wisconsin

Dear Dr. Janssen:

Your recent inquiry regarding the potential value of a combination of desipramine and chloral hydrate was discussed with my associates, Drs. Gershon and Itil.

It was my impression that the excitement seen with imipramine was seen in a group of schizophrenic patients treated with this compound, and that chlorpromazine or similar phenothiazine drugs would be a logical and satisfactory blocking agent. With imipramine, when a patient has become excited, the effect of barbiturates has been less valuable than a phenothiazine. However, this experience was in patients with larger doses of imipramine, averaging 225 mg. per day.

It was Dr. Itil's opinion that psychoactive drugs which had a beneficial effect in the treatment of depression seemed to have both stimulatory and depressing qualities. This seems to be true not only for imipramine and amitriptyline, but for those phenothiazines used successfully in the treatment of depression.

There appears to be no a priori reason why the combination of desipramine and a sedating agent like chloral hydrate would not be a satisfactory combination. Indeed, if the proper dose relationships were established, one would expect the drug combination to be beneficial in proportion to the sensitivity of the subject to the imipramine portion of the combination with the potential salutary affect of the chloral hydrate. However, it was our impression that the dose relationships would be critical and we wondered what dose pattern you were going to try.

Finally, we did consider other drugs which might be effective in conjunction with desipramine and wonder if chlordiazepoxide might not be a better sedating drug in combination with desipramine.

Thank you very much for you inquiry. I trust these comments will be of some help.

Sincerely yours,

Max Fink, M. D.
Director

MF/jb