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To the Editor:

The conclusions drawn in the paper, "Imipramine and Thioridazine in Depressed and Schizophrenic Patients" (JAMA 189:605, August, 1964) were recently criticized by one of your readers. It may be helpful to indicate that in another study now in press in Psychopharmacologia, the clinical efficacy of chlorpromazine in combination with an anticholinergic agent, procyclidine, is described in the treatment of depressive states. In that report, 35 consecutive voluntary hospitalized depressed psychiatric patients referred for drug therapy were randomly assigned to one of three treatment regimens. On clinical behavioral ratings, both the chlorpromazine-procycyclidine combination and imipramine had significantly better therapeutic results than placebo. The two therapeutic groups did not differ from each other except that manic reactions were seen only with imipramine.

It was our conclusion that both drugs are effective in retarded depressive syndromes, including apathy and anorexia. We suggested that chlorpromazine-procycyclidine may be more immediately effective in agitated depressive states, while imipramine was seen to be advantageous in depressive patients with phobic anxiety features.

The evidence in the literature regarding the initiation of depressive states by chlorpromazine is exceedingly sparse, and we have suggested that the early strikingly favorable results in the treatment of depressive states by chlorpromazine was obscured by its inaccurate equation with reserpine. It is with regard to the latter drug that many reports are available indicating that de-

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pressive states, including those of suicidal intensity, have been associated with treatment.

These studies indicate that a systematic reevaluation of the applicability of phenothiazines, especially phenothiazines combined with anticholinergic agents, in the treatment of depressive states is necessary. We concur with Drs. Hollister and Overall that anecdotal evidence is not sufficient in the determination of the clinical efficacy of agents in the treatment of the mentally ill.

Sincerely yours,

Max Fink, M.D.
Director

mf/lc
c.c.: Leo Hollister, M.D.
enclosure