below 1,800 per cubic milliliter) had absolute neutrophil counts of less than 3,000 per cubic milliliter during the week preceding treatment. This suggests that patients beginning with low neutrophil counts are more prone to further depression during treatment. On the other hand, leukopenia from phenothiazine derivatives was not significantly more frequent than that from phenobarbital. Still more remarkable was the return to normal levels of considerably depressed absolute neutrophil counts despite uninterrupted treatment. Continuation of treatment did not produce agranulocytosis, but was succeeded eventually by normal counts. Obviously, the decision to continue or abandon treatment in the face of leukopenia must be made on more factors than a declining leukocyte count. In view of the occurrence of leukopenia with phenobarbital, it may be assumed that some patients may have spontaneously occurring cyclic leukopenia unrelated to drugs.

Abnormal hepatic tests were common in all treatment groups. More than one-third of patients with abnormal tests had them during the control period. More significant was the fact that no patient developed a clinical or laboratory picture compatible with jaundice as usually encountered with phenothiazine derivatives. The relatively few equivocal abnormal hepatic tests were probably not related to drug treatment, as these were sporadic, isolated, or not corroborated by other tests. Clinically important hepatic dysfunction from phenothiazine derivatives is usually associated with recognizable jaundice preceded by fever and prodromal symptoms, and easily corroborated by appropriate laboratory or histologic tests.[6,9] What is important is that abnormal hepatic tests occurring during drug therapy should not always be attributed to subclinical manifestations of drug-induced hepatic dysfunction, as has been done.[4,10]

The interpretation of the changes in temperature, pulse rate, and blood pressure was quite difficult. The infrequency of such changes, despite careful efforts to detect them, was surprising. Some patients had lower than usual body temperatures which varied from occasional to sustained low readings. These low body temperatures may have represented a normal variant for some schizophrenic patients rather than drug-induced hypothermia. Changes in pulse rate were few. None of the recorded blood pressures were below normal physiologic limits, the most frequent change occurring when the initial readings were somewhat higher than usual.

The untoward effects recorded in this controlled study were relatively uncommon and appeared in many instances to be manifestations of spontaneous variations in schizophrenic patients or not due to specific actions of the phenothiazine derivatives. Despite rather careful scrutiny for detecting these abnormalities, their occurrence in the various drug treatment groups was neither frequent nor troublesome. Only 21 of 599 patients were dropped from treatment because of side effects or abnormal laboratory tests, none of which were serious in degree.

References

1. Casey, J. F., Lasky, J. J., Klett, C. J., and Hollister, L. E.: Treatment of Schizophrenic Reactions With Phenothiazine Derivations. A Comparative Study of Chlorpromazine, Triflupromazine, Mepazine, Prochlorperazine, Perphenazine, and Phenobarbital. Proceedings of the Fourth Annual Research Conference, Veterans Administration Cooperative Studies on Chemotherapy in Psychiatry, Memphis, Tenn., May 13, 1959. In press.
2. Cohen, I. M.: Complications of Chlorpromazine Therapy, Am. J. Psychiat. **113**:115-121, 1956.
3. Council on Pharmacy and Chemistry: Blood Dyscrasias Associated With Chlorpromazine Therapy, J.A.M.A. **160**:287, 1956.
4. Dickes, R., Schenker, V., and Deutsch, L.: Serial Liver-Function and Blood Studies in Patients Receiving Chlorpromazine, New England J. Med. **256**:1-7, 1957.
5. Fernandes, B., and Leitao, G.: Incidents and Accidents in Chlorpromazine Therapy, J. Clin. & Exper. Psychopath. **17**:70-76, 1956.
6. Gebhart, W. F., Van Ommen, R. A., McCormack, L. J., and Brown, C. H.: Chlorproma-