schizophrenic men in 35 Veterans Administration Hospitals.[1] A double blind control was employed, using "equivalent" doses of each of the 6 agents in both an initially determined and later flexible dosage schedule. Biasing factors were that the sample was composed of men under the age of 51 years, some of whom had previously received phenothiazine derivatives. Except for their mental illness, the patients were generally in good health.

Methods of study

Four specific types of information were sought: (1) the prevalence of clinical symptoms or signs frequently reported as occurring with phenothiazine derivatives[2,5,7,11]; (2) the prevalence of abnormalities in hematologic measures, especially total leukocyte count, absolute neutrophil count, and eosinophil count; (3) the prevalence of positive hepatic findings; (4) the occurrence of aberrations in body temperature, pulse rate, or blood pressure.

A symptom-sign check list for each of 14 specific items was completed weekly by the attending physician on each patient. Thus information was obtained about the prevalence, the time of onset, and the duration of each of these manifestations.

Total and differential leukocyte counts were obtained on each patient prior to and during each of the 12 weeks of treatment. If other hematologic tests were deemed necessary, these were obtained at the discretion of the attending physician. For purposes of this study leukocytosis was considered to be present if the total leukocyte count exceeded 13,500 per cubic milliliter. No lower limit was imposed on the total leukocyte count for determining the presence of leukopenia; rather this was deemed to be more accurately represented by a calculation of the absolute neutrophil count (total leukocyte count times per cent of neutrophils). An absolute neutrophil count of 3,000 per cubic milliliter was considered as the lower limit of normal. A patient was regarded as leukopenic when the absolute neutrophil count dropped below 1,800. Absolute neutrophil counts of less than 1,500 per cubic milliliter were considered to represent a potentially dangerous situation, but the decision as to whether or not treatment should be continued was left to the attending physician. Eosinophil counts of 7 per cent or more were considered to be elevated. All these data were tabulated on an appropriate form for each of the 12 weeks of treatment.

The study protocol also recommended that each patient have hepatic tests performed prior to and during the first 5 weeks of treatment. Recommended as preferential screening hepatic tests were the alkaline phosphatase determination and the serum glutamic oxalacetic acid transaminase (SGO-T) test. If either of these tests was abnormal (over 8 Bodansky units for the alkaline phosphatase test and over 40 units for the SGO-T test), other hepatic tests were to be performed. These included determinations of the total serum bilirubin, cephalin flocculation, and Bromsulphalein (BSP) retention. The upper limits of normal were set at 1.2 mg. per 100 ml., 3+ at 48 hours, and more than 8 per cent retention, respectively, for each of the tests.

Each participating hospital was requested to make daily measures of patients' temperatures during the entire treatment course and daily measures of blood pressure and resting pulse rates during the first week of treatment. Naturally, great variations occurred in conditions under which these measures were made in various patients.

Results of study

Control values for total neutrophil count, alkaline phosphatase and SGO-T determinations. Data on the total leukocyte count of 475 patients prior to treatment were tabulated. The mean control leukocyte count was 8,200 per cubic milliliter with a standard deviation of 2,750. Ninety-seven patients (more than 20 per cent) had control total leukocyte counts of over 10,000 per cubic milliliter. In 80 of these 97 patients the total leukocyte count