

TABLE 2.—REPORTED INCIDENCE OF THROMBOCYTOPENIA ASSOCIATED WITH DRUG ADMINISTRATION (1960)

Drug	Only drug	With other drugs	Total
Total cases.....			44
Chloramphenicol (Chloromycetin).....	3	3	6
Quinidine.....	5	3	8
Sulfamethoxypyridazine (Kynex, Midice).....	3	0	3
Chlorothiazide (Diuril).....	3	1	4
Hydrochlorothiazide (HydroDiuril).....	2	0	2

Leukopenia was reported 93 times. Only 4 drugs appeared more than once as the only drug administered prior to onset. These drugs are listed in Table 3.

TABLE 3.—REPORTED INCIDENCE OF LEUKOPENIA ASSOCIATED WITH DRUG ADMINISTRATION (1960)

Drug	Only drug	With other drugs	Total
Total cases.....			93
Chlorpromazine (Thorazine).....	8	13	21
Imipramine (Tofranil).....	2	6	8
Methimazole (Tapazole).....	2	1	3
Phenylbutazone (Butazolidin).....	4	3	7

Of the entire 448 cases, chloramphenicol had been given alone to 24 patients and together with other drugs to 46 patients, a total of 70 patients. Phenylbutazone was the only drug administered to 8 patients and was received by a total of 17 patients. Both of these drugs were associated with cases of each type of blood dyscrasia under discussion here. As a rule, other drugs tended to be related to only one type of dyscrasia; for example, of the 22 patients who developed a dyscrasia after receiving chlorpromazine, 21 had leukopenia, and all 8 cases associated with quinidine administration were thrombocytopenia.

Members of the Study Group have compiled a list of cases with hypoplastic anemia and agranulocytosis seen in their respective institutions during 1959 and 1960. In each case an opinion was rendered as to whether the dyscrasia probably was or probably was not caused by a specific drug. In this 2-year period, 74 cases of hypoplastic anemia were seen at these 8 institutions and, of these, 33 were thought to be unrelated to drugs. Thirty-three were associated with the administration of chloramphenicol and 8 with other drugs. The idiopathic cases were about equally divided by age and sex, whereas among the cases associated with chloramphenicol administration there were 28 females and only 5 males. Twenty-seven of these 33 patients were in the 1 to 10-year-old age group. This predilection of hypoplastic anemia associated with chloramphenicol for young girls has been noted previously.⁶ Thirty-three of the total 74 patients were already dead, and only 9 had recovered during the short period of follow-up.

The production of a blood dyscrasia by a drug is not usually the result of the pharmacological properties of the drug but more often is the consequence of an idiosyncrasy in the patient which produces a sensitivity to the drug. In some types of drug-related blood dyscrasias, the pathogenetic mechanism is understood and can be demonstrated by laboratory methods. In other types, the mechanism is wholly unknown.

Drug-induced hemolytic anemia is a classic example of the type of blood dyscrasia in which the pathogenetic mechanism has been demonstrated. In the red blood cells of the susceptible person there is a deficiency of an enzyme, glucose-6-phosphate dehydrogenase (G-6-PD), which is important in the metabolism of glucose. A side effect of the action of the enzyme is the maintenance of a supply of reduced glutathione (GSH). Deficiency of this enzyme in erythrocytes is a newly recognized heritable disorder and can be demonstrated by incuba-

⁶ Welch, H.; Lewis, C. N.; and Kerlan, L.: Blood Dyscrasias: Nationwide Survey, *Antibiot Chemother* 4: 607-625 (June) 1954.