

ETIOLOGY

A total of 411 drugs have been mentioned as possible etiological agents in the 1,195 cases of blood dyscrasia reported in this country since 1955. Of these cases, 488 have been associated with the administration of a single drug and 707 with the administration of combinations of drugs. It is particularly difficult to pinpoint the responsible agent when a number of drugs have been administered, and it is hard to prove a specific cause-effect relationship even when a single drug has been given. Studies of the cases of agranulocytosis²⁸ and hypoplastic anemia²⁹ have suggested that about 40% are of idiopathic origin; that is, they could not be associated with a specific cause. Furthermore, civilized man is exposed to so many chemicals at work and at home (food additives, detergents, solvents, and "smog") that it is impossible to assert that the single drug he received was the only significant chemical exposure. Consequently, not all of the 109 drugs listed as having been given alone were necessarily of etiological importance.

After a thorough analysis of these cases, as well as a critical review of the pertinent literature, the Study Group has compiled a list of 54 drugs believed to be potentially toxic to the blood cells (see table). This list does not state the degree of toxicity of the individual drugs but merely states that these drugs have been associated with the development of blood dyscrasias under circumstances which have convinced the members of the Study Group that a cause-effect relationship exists. In addition to being a useful compilation of potentially toxic drugs, this list may be used to evaluate cases in which multiple drugs have been administered. These cases can be divided into 2 categories: In the first category are those cases in which one of the drugs administered is known to be potentially toxic and, presumably, is responsible for the detrimental effects. In the second category are those cases in which 2 or more drugs were administered, none of which are known to be toxic. In these latter cases, a greater degree of suspicion of the potential toxicity of the unknown drugs is justifiable.

DRUGS OR CHEMICALS SHOWN BY DIRECT OR CIRCUMSTANTIAL EVIDENCE TO BE
ASSOCIATED WITH BLOOD DYSCRASIAS

Acetanilid ³⁰	Pamaquin ³⁰
Acetazolamide	Phenindione
Acetophenetidin ³⁰	Phenylbutazone
Allylisopropylacetylurea	Phenylhydrazine ³⁰
Aminopyrine	Primaquine ³⁰
Aminosalicylic Acid ³⁰	Primidone
Arsphenamine	Probenecid ³⁰
Benzene	Promazine
Carbutamide	Pyrimethamine
Chloramphenicol	Quinacrine
Chlordane	Quinidine
Chlorothiazide	Quinine
Chlorpromazine	Ristocetin
Chlorpropamide	Stibophen
Colchicine	Streptomycin
Diphenylhydantoin Sodium	Sulfacetamide ³⁰
Dipyrrone	Sulfadiazine
Gamma Benzene Hexachloride	Sulfamethoxypyridazine ³⁰
Gold Salts	Sulfanilamide ³⁰
Imipramine	Sulfisoxazole
Lead	Sulfoxone ³⁰
Mepazine	Thiazolsulfone ³⁰
Meproamate	Thiobarbital
Methimazole	Thiouracils
Methylphenylethyl Hydantoin	Tolbutamide
Naphthalene ³⁰	Trimethadione
Nitrofurantoin ³⁰	Trinitrotoluene

²⁸ McGovern, F. H.: Granulocytopenia Following Ingestion of Causalin *JAMA* 115:1359 (Oct. 19) 1940.

²⁹ Scott, J. L.; Cartwright, G. E.; and Wintrobe, M. M.: Acquired Aplastic Anemia: Analysis of 39 Cases and Review of Pertinent Literature, *Medicine* 38:119-172 (May) 1959.

³⁰ These drugs have been associated with the induction of hemolytic anemia principally in patients with glucose-6-phosphate dehydrogenase-deficient cells.