tion with acetylphenylhydrazine, which results in a fall in the erythrocyte content of GSH. The depletion of GSH is somehow related to the susceptibility of the erythrocyte to destruction. It is possible by testing for G–6–P dehydrogenase activity or for glutathione instability in the erythrocytes to determine the susceptibility of a given person to drug-induced hemolytic anemia. Among the drugs which can produce acute hemolytic anemia in susceptible persons are the 8-aminoquinoline antimalarials, such as primaquine, certain sulfonamides, acetanilid, acetophenetidin, nitrofurantoin (Furadantin), and many others. Favism is associated with the same or a closely related heritable deficiency. The subject has been reviewed by Beutler.[6]

Hemolytic anemia can also be produced through an immune mechanism in which antibodies are formed against a combination of the drug and the erythrocyte and may lead to agglutination of and damage to the erythrocyte only in the presence of the drug. Such a mechanism has been demonstrated in hemolytic anemias produced by stibophen (Fuadin)[7] and quinidine.[8] This is very rare.

Thrombocytopenia has been produced through a similar immune mechanism by drugs such as allylisopropylacetylurea (Sedormid),[9] quinidine, and quinine. This mechanism, however, has not been demonstrable in all cases of thrombocytopenia attributed to drugs.

In some cases of agranulocytosis due to drugs, an immunologic mechanism has been demonstrated, for example, in agranulocytosis produced by aminopyrine.[10] In other cases such a mechanism could not be shown. Aminopyrine and dinitrophenol, the drugs first shown to produce agranulocytosis, are now seldom the cause of granulocytopenia because they are seldom used. The antithyroid drugs, propylthiouracil, methylthiouracil, and methimazole (Tapazole) and the phenothiozine derivatives, notably promazine (Sparine) and chlorpromazine (Thorazine) are the more common causes of agranulocytosis today.

Aplastic anemia remains the most difficult problem among drug-induced blood dyscrasias because it has such a serious prognosis and because it takes so long to recognize the casual relationship to a drug. The mechanism of production is unknown. Only a very small proportion of the patients who receive a drug capable of producing aplastic anemia will be sensitive to it. Pancytopenia may appear only after prolonged administration or repeated courses of the drug. Most patients with aplastic anemia have received several drugs. Furthermore, aplastic anemia may occur in patients who have had no known exposure to drugs or toxic chemicals. These factors may be responsible for the late recognition of the relationship of a drug to aplastic anemia. Nevertheless, some drugs have been so often associated with aplastic anemia as to leave no doubt that they can produce it. In recent years the most common agent associated with aplastic anemia has been chloramphenicol (chloromycetin).

Because chloramphenicol is associated with such a large proportion of the cases of pancytopenia reported in recent years, it is appropriate to consider in more detail the hemopoietic effects of this drug. Chloramphenicol has been observed to cause a general inhibition of protein synthesis by bacteria[11] and has been shown to block the synthesis of many enzymes.[12] Two types of hematological toxicity have been observed: (1) a temporary erythroid hypoplasia, associated with anemia and occasionally with thrombocytopenia and leukopenia, and (2) a severe, often fatal, pencytopenia.

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