for carefully in all cases of hemolytic anemia, whether exposure to drugs has occurred or not. A hypersensitive person may respond to minimal concentrations of a chemical; for example, children have developed hemolytic anemia after exposure to aniline laundry marks[17] or to naphthalene in moth-protected clothing.[18] Drugs marked by an asterisk in the table have been associated with the production of oxidative hemolytic anemia.[15]

Other biochemical abnormalities of blood cells, which render them hypersensitive to specific drugs and chemicals, will undoubtedly be found. Since these abnormalities would be primarily genetic, it is important to obtain a complete family history and to inquire about consanguinity, which often may be the first clue to a genetic mechanism.[19] Because of this interest, the report form distributed by the Study Group on Blood Dyscrasias contains a space for checking the presence or absence of consanguinity.

A quantitative difference in the response to a drug may also be of pathogenetic importance in the development of many blood dyscrasias. In a number of drugs, the difference between therapeutic and toxic levels is quite small, and severe cellular suppression or destruction may be caused by a minor metabolic deviation from the normal. In order to relate the development of a blood dyscrasia to this mechanism, excessive doses of a drug given to normal individuals should cause the same type of toxic reaction which is observed when regular doses are given to hypersensitive individuals.

Results of recent studies strongly suggest that chloramphenicol-induced bone marrow suppression represents an accentuated normal response to the drug. Toxicity studies in animals, with the possible exception of monkeys,[20] have failed to reveal that chloramphenicol has marrow-suppressive properties. However, studies in man have shown that large doses given for prolonged periods of time will cause bone marrow suppression and maturation arrest. Krakoff and co-workers[21] and Ozer and co-workers[22] gave large doses of chloramphenicol to 5 people, and all 5 developed pancytopenia and bone marrow suppression. In addition, studies by Saidi and co-workers[23] and by Rubin and co-workers[24] have shown that mild reversible bone marrow suppression is a common complication of chloramphenicol therapy. Results of in vitro studies of normal bone marrow have shown also that chloramphenicol in high concentrations inhibits desoxyribose nucleic acid (DNA)[25] and heme synthesis[26] in a manner which could explain the lack of cellular proliferation and the impairment of iron utilization observed in vivo. The metabolic handling of chloramphenicol has been studied in a few patients after they had recovered from chloramphenicol-induced pancytopenia, and, in these patients, the drug was found to be detoxified and excreted in a perfectly normal manner.[27] Consequently, it appears that the pancytopenia which occassionally is found in patients treated with chloramphenicol may represent an exaggerated response to the suppressive action of chloramphenicol on bone marrow. A few cases have been reported in which the action of chloramphenicol on the blood cells has been suggestive of an antigen-antibody reaction,[6] but, in the great majority of cases, there is no evidence that this is caused by an immunologic mechanism or by a genetic abnormality in the handling of or in the response of this drug.

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