The temporary erythroid hypoplasia has been observed mainly in patients given large doses of chloramphenical, 4 to 12 gm. daily for 10 to 35 days.[13–16] A retriculocytopenia,[13, 15–17] a rise in serum iron, a reduced rate of clearance of plasma Fe-59, and blockade of the uptake of Fe-59 by erythrocytes[14] have been the first changes noted. These changes are followed by anemia. Some patients have developed thrombocytopenia[13, 15] and some have had leukopenia.[15, 16] Marrow studies have revealed erythroid hypoplasia[15] with abnormal vacuolization of the cytoplasm of erythroblasts[16, 17] and sometimes of cells of the myeloid series.[13] When chloramphenicol is discontinued, all of these abnormalities are reversed. Reticulocytosis develops within 5 to 7 days, with peaks as high as 17.6%,[16] and the hemoglobin level returns to normal. Following recovery from erythroid hypoplasia, one of the above patients was given 2 gm. of chloramphenicol per day for 7 days without recurrence of toxicity, but when the dose was raised to 12 gm. per day the anemia reappeared.[13] Patients with infection or anemia seem to be more susceptible to this effect of chloramphenicol than are normal people.[17] The administration of chloramphenicol to patients with pernicious anemia blocks the reticulocyte response to vitamin B_{12} and, in patients with iron deficiency anemia, it blocks the response to intramuscular administration of iron.[17] Reticulocytosis occurs in these patients several days after chloramphenicol is discontinued.

The other hematologic response to chloramphenicol is a severe pancytopenia. All of the marrow cell types are affected, and the marrow is hypoplastic. The process is progressive over a long period of time, and recovery, if it occurs, is slow. This complication has been observed in patients treated with conventional doses, and appears to be more common in children, especially young girls.[6] Test doses of chloramphenicol have seldom been given to patients who have recovered from pancytopenia. One unpublished case has been reported; the patient received a second course of chloramphenicol following recovery from marrow toxicity thought to be due to previous chloramphenicol administration.[18] This patient, a 15-month-old male infant, received 125 mg. of chloramphenicol every 6 hours for 8 doses before the initial dyscrasia was reported. The total leukocyte count fell from 9,800 per cubic millimeter on the day therapy was started to 3,800 on the second day, 1,900 on the fourth day and then gradually returned to normal. This dose of chloramphenicol is tolerated without demonstrable blood changes by the vast majority of patients who receive it and, thus, this reaction is suggestive of a drug idiosyncrasy. The mechanism by which chloramphenicol produces aplastic anemia appears to be different from that which leads to the acute changes in erythropoiesis. The difference may be only quantitative, however.

SUMMARY

It is incumbent upon the physician to maintain a lively awarness of the risk of blood dyscrasia associated with the use of certain drugs and to use such drugs only when the potential benefits of administration considerably outweigh the relatively small risk of developing a blood dyscrasia. When it is necessary to use such drugs, it is important that appropriate hematological studies be made at intervals and that the patient be warned to report immediately the development of fever, sore throat, weakness and pallor, or a bleeding tendency. Conversely, it is also important that the physician be aware that in the event of development of infection or easy bruising in a patient who has been taking such drugs, blood cell counts must be made immediately. If agranulocytosis, thrombocytopenia, or pancytopenia is present, further administration of the drug must be stopped. Needless to say, this is the most important therapeutic measure.

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