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CHLORAMPHENICOL BONE MARROW TOXICITY

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The capacity of chloramphenicol to suppress bone marrow activity has recently been reemphasized.¹ Although the incidence of irreversible or slowly reversible blood dyscrasia caused by chloramphenicol is not great, the serious nature of these effects is sufficient reason to restrict its use to situations in which an equally effective and less toxic antibiotic is not available. The purpose of this report is to present studies in 15 patients in whom early toxicity was recognized by morphologic studies available to the clinician, and the drug was discontinued before irreversible damage occurred.

Recent studies^{2, 3, 3a} have suggested that the occurrence of marrow toxicity due to chloramphenicol is more frequent than is indicated by sporadic reports of aplastic anemia which continue to appear in the literature. Using sensitive radioiron techniques, Rubin et al. found evidence for suppression of red blood cell production in 5 of 15 patients tested.² Saidi and associates reported morphologic changes in the primitive red cells of the marrow in each of 10 patients who received 40-85 mg/kg. of chloramphenicol per day, whereas 12 subjects who received 11-45 mg/kg. per day had no such changes.^{3, 3a} When Krakoff et al. gave 6 or more grams of chloramphenicol daily to 4 patients with carcinoma, toxic depression of the hemoglobin and reticulocyte count was found in each.⁴ The latter 2 reports suggest that the occurrence of toxicity is partially dose-dependent, an effect which previously has not been emphasized.

Eleven patients were seen in consultation because of anemia or bleeding during chloramphenicol therapy. Four others were being treated with chloramphenicol without the physician in charge being aware of the subtle hematologic changes that were under way. Depression of erythropoiesis, manifested in a drop in reticulocyte count, was the first and most frequent warning of trouble; it was followed in order by suppression of thrombopoiesis and leukopoiesis. The reversible stage is unpredictable and sometimes quite short. In each of these cases the bone marrow recovered after chloramphenicol administration was stopped. Chloramphenicol should not be given for trivial infections. When it must be used, serial reticulocyte counts should be done, and a sudden or severe drop calls for study of the bone marrow.

MATERIAL AND METHODS

Intensive hematologic investigations on 15 instances of bone marrow depression believed to have been produced by chloramphenicol form the clinical material for this report. Eleven patients (cases 1-9, 14, and 15) were seen in consultation because of an anemia or because of bleeding and thrombocytopenia. Four patients (cases 10-13) were being treated with chloramphenicol, but the physicians in charge were not aware of the subtle hematologic changes which were under way. In 12 of the 15 patients bone marrow punctures and cell studies were done during the period of toxicity. The slides of all these were available for retrospective interpretation of morphologic changes. In two instances the marrow was examined early during recovery, and in the final case the marrow was not examined. In 4 patients, serial bone marrow aspirates were examined before, during, and after recovery from the suppressive effects of chloramphenicol.

REPORT OF CASES

Case 1.—A 64-year-old Negro male was admitted to the hospital because of mental deterioration and heart disease and was treated for pneumonia with 2 gm. (28 mg/kg.) chloramphenicol daily for 24 days. The hematocrit reading fell from 40 vol.% prior to therapy to 21 vol.%. Reticulocyte count was 0.4%, platelet

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NOTE.—Numbered footnotes at end of article, p. 2742.