

Blood picture.—In 21 cases the peripheral blood showed a severe pancytopenia (anaemia, leucopenia, and thrombocytopenia). Twelve cases showed selective aplasia with either leucopenia or thrombocytopenia. No case showed selective red-cell aplasia. In seven cases specific data relating to the peripheral blood picture were not given.

Clinical presentation.—The commonest presenting symptom was spontaneous bleeding—for example, epistaxis, purpura, menorrhagia. In one case jaundice was the earliest sign of complication.

Prognosis.—The details of the marrow changes were available in only 25 reports. All 12 patients with aplastic marrows died. In eight the marrow was classified as hypoplastic, but they too died. The marrow derived from five of the nine patients who recovered was hypoplastic. Therefore recovery may take place if the marrow is not completely aplastic. Complete marrow aplasia would appear to carry a hopeless prognosis.

DISCUSSION

Chloramphenicol is an efficient antibiotic, but its use is justified only in the treatment of life-endangering infections when no other effective antibiotic is available—for example, typhoid fever.

Yet this series has shown that fatalities apparently due to chloramphenicol therapy have occurred in numbers sufficient to cause concern. Further, it would seem that this drug has been used indiscriminately in the treatment of a wide variety of mild infections and that extravagant doses of the drug have been administered.

Hutchison and Pinkerton (1962) have suggested that the incidence of blood dyscrasias due to chloramphenicol might be 1 in 80,000 patients treated, in which case it might be argued that this risk justifies the use of this antibiotic in even trivial infections. However, these authors based their imputation on the number of deaths reported to the Registrar-General, and incidence based on the Registrar-General's report can be misleading; it is likely that more cases do exist than are officially recorded.

Dameshek (1960) has stated that in the majority of fatal cases the patient would not have died if he had not received this drug. There would appear to be no justification for using chloramphenicol to treat nonspecific pyrexial illnesses or nasopharyngeal infections in childhood, or recurrent bronchitis, asthma, chronic or post-prostatectomy urinary infection, recurrent boils, or superficial skin infections unless it has been shown by careful bacteriological sensitivity tests that the offending organism is sensitive to no other antibiotic.

This present series shows that, while a high dose and repeated courses appear to be more likely to cause trouble, single courses of less than 10 g. can cause fatal aplasia.

The wide distribution of the time of onset of symptoms attributable to the toxic effect of the drug suggests that two possible mechanisms exist: (1) a hypersensitivity reaction—immediately dangerous but probably reversible; this is often accompanied by immediate systemic symptoms; (2) a slow direct poisoning of marrow "stem" cells due to the accumulation and retention of the drug or its breakdown products in the blood or tissues and so to the delayed effect. The variation of the toxic dose suggests that an individual idiosyncrasy to this drug may exist.

A retrospective survey such as that presented here can never be satisfactory, as significant data are not collected and not all cases are reported. Thus no statistical analysis of dose, time relationships, or incidence rates can be calculated. Only by insisting that chloramphenicol and other drug-induced dyscrasias are notified to some responsible authority as they occur can the case be made whether the popularity or efficiency of this drug as an antibiotic outweighs its established toxic effect.

The purpose of this paper has been to stress once more the dangers of using this antibiotic and to appeal for the compulsory notification of this and other drug-induced blood dyscrasias to a responsible central body in order that a true assessment of the relative risks can be made. This appeal is especially pertinent to the present concern of the medical profession and lay public regarding the dangers of modern drug therapy.

In the meantime this Committee would be grateful if any doctor encountering a case where it is suspected that chloramphenicol might have produced damage to the bone-marrow would send the relevant data to the secretary of this Committee.