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CHLORAMPHENICOL—A NEW WARNING

In one month recently, I saw 4 new cases of aplastic anemia. Although they ranged in age from 3 to 63, and came from different sections of the country, they had one common denominator: chloramphenicol had been used in the recent past for minor respiratory infections. There was no history of the use of other antibiotics or potentially toxic drugs and since the anemia and the other manifestions appeared a few months after the last administration of chloramphenicol, it seemed clear that this drug was responsible for the marrow aplasia.

In our recently studied series of aplastic anemia (seen within the past 3 years) 8 of 30 had received significant amounts of chloromycetin, almost invariably for minor infections. Of the most recent 10 cases of aplastic anemia, 5 had followed therapy with chloramphenicol. The tragic thing about all these seriously ill cases, most of whom died, is that the drug need never have been given.

It is becoming increasingly clear that chloramphenicol, an excellent broad-spectrum antibiotic, has antimetabolic effects as well—that is, it may injure the intrinsic "machinery" of certain rapidly proliferating cells, notably of the bone marrow. Thus, Rubin and associates, using radioactive techniques, demonstrated a depressant effect of chloramphenicol on erythropoiesis; this occurred in 5 of 15 subjects receiving ordinary doses and in all of 4 cases with cancer who were given unusually large doses of the drug.[1] In another study by Saidi and Wallerstein[2] 10 of 22 cases treated with chloramphenicol for various infections developed striking vacuolization of nucleated red cells in the bone marrow, associated with a maturation arrest phenomenon and marked reduction in blood reticulocytes. The possibility is present that these temporary changes could go on to complete or partially complete destruction of the bone marrow providing (a) that sufficient drug was used or (b) the patient became sensitized in some manner and was given a second course of drug therapy at another time. It is thus conceivable that both an immediate or direct effect as well as an indirect or hypersensitivity mechanism may be responsible for the marrow reactions seen.

Following the introduction of chloramphenicol in 1948 and the reports of the first cases of aplastic anemia between 1950 and 1952, many editorials and reports of special *ad hoc* meetings appeared. Evidently the medical profession was profoundly influenced; in any event, the sales of chloromycetin declined sharply, reaching their lowest level in 1954. This lull was short-lived. By 1958,

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