

dealing with physicians and to discuss the untoward affects only if the physician raised the question. The fact that a causal relationship between the use of Chloromycetin and the development of aplastic anemia had not been scientifically proven was emphasized. This latter argument was set forth despite the summary of the FDA report of 1952 which stated that—

From the data available from case records secured in this survey, it appears beyond a reasonable doubt that chloramphenicol, in certain susceptible individuals, causes blood dyscrasias, including aplastic anemia, thrombocytopenic purpura, granulocytopenia, and pancytopenia.

All of which are conditions of severe bone-marrow depression.

Similarly, in April of 1960 a report by the Subcommittee on Blood Dyscrasias of the Committee on Research of the American Medical Association published a cautionary reminder to the medical professions in the AMA Journal on the potential ill-effects of Chloromycetin on the blood-forming system. The report decried any possibility of a mere "chance association" in the case reports of aplastic anemia allegedly caused by Chloromycetin and concluded that there was no longer even a reasonable doubt that the drug could cause aplastic anemia. Making note of the widespread, indiscriminate use of Chloromycetin, the report called for judicious use of the antibiotic and stated that it should not be used prophylactically, in trivial infections, or in infections in which other, less dangerous antibiotics might be used effectively. This was the same year that Dr. Dameshek pleaded similarly to the profession in an AMA Journal editorial in which he reported four new cases of aplastic anemia (which he saw in 1 month, incidentally), as a result of Chloromycetin therapy for minor respiratory infections. It was also the same year, 1966, that enough Chloromycetin was sold and prescribed to treat nearly 4 million patients.

Such case reports and the inevitable conclusions therefrom must have, or should have, been known to Parke, Davis & Co. and to the medical profession in general. Yet, the Chloromycetin advertising was not altered until the second FDA warning became required in 1961. This warning was more specific, more forceful, and more detailed in its wording; and it was to be boxed and placed in a prominent position in the advertising. However, the tenor of the advertising and detailing did not change; emphasis was still placed on the broad-spectrum-type effectiveness of the drug, although its toxicity was documented in more detail. Obviously, as the huge sales of Chloromycetin since 1961 indicate, this change in the written advertising has not been an adequate deterrent to the indiscriminate use of this antibiotic. The small number of cases where Chloromycetin is specifically indicated can justify only a fraction of the doses prescribed. Undoubtedly, the fact that this unfortunate pattern for the clinical use of Chloromycetin has already become established plays a role in its continued administration (which serves to emphasize the importance of proper education of physicians in the initial period of a drug's availability); but more important, I believe, are the factors of drug detailing and physicians' inertia.

Mr. GORDON. When you talk about educating a doctor in the initial period of a drug's availability, have you any idea how this should be done and who should do it?

Dr. HEWSON. Well, certainly it is a crucial period because many of the side effects such as bone marrow aplasia do not show up for several