

required that more than one doctor sign the prescription or the order for the drug; is that what you were saying?

Dr. WATKINS. Yes, sir. They put out a bulletin. I have it here, at Johns Hopkins for all interns and residents to read.

Senator NELSON. Do you have a copy of it?

Dr. WATKINS. Yes, sir.

Senator NELSON. What did it say?

Dr. WATKINS. This letter was written to me on September 1, 1952.

Memorandum: Subject: Chloramphenicol.

At the request of Dr. A. McGehee Harvey, the following is submitted for the information of the entire medical staff of the Hospital:

Cases of aplastic anemia attributable to the administration of chloramphenicol are occurring throughout the United States with alarming frequency.

Observations to date suggest that two types of reaction may occur. Occasionally patients receiving this drug develop evidences of bone marrow depression during therapy. This may be manifested by leucopenia, granulocytopenia, thrombocytopenia and anemia. In our experience in this Hospital there is suggestive evidence that this type of bone marrow depression may be treated to the plasma concentration of the drug since most of our patients either had received large doses, or had evidence of renal insufficiency. In these cases the blood has returned to normal after the drug was discontinued.

A much more serious type of reaction concern the production of a real aplastic anemia. In cases of this type the occurrence of a blood disorder has apparently most often been associated with repeated administration of the drug, suggesting that a prior sensitization has occurred. In many of these patients relatively small doses of chloramphenicol have been used, and the blood disorder seems definitely not to be related to plasma concentration.

An outstanding feature of the aplastic anemia associated with the use of chloramphenicol has been the development of profound thrombocytopenia. In all of the fatal cases which have come to my attention, death has resulted from hemorrhage. Leucopenia and neutropenia occur, but present a less serious problem. Anemia in most of the cases apparently has been mild, except for that which can be attributed to hemorrhage. In a number of patients, death has not occurred for many months after the initial bone marrow depression. Efforts to bring about bone marrow regeneration through the use of ACTH, cortisone, and numerous other agents have been extremely disappointing. Observations to the present time suggest that unless recovery occurs soon after the drug has been discontinued, it is not likely to occur.

It seems not unlikely that as more individuals are sensitized by the use of this drug, the incidence of aplastic anemia may increase. For this reason, and because of the serious nature of aplastic anemia, I believe that the drug should be used with very great caution. I recommend that chloramphenicol be used only for the treatment of seriously ill patients suffering from infections not amenable to treatment with other antibiotic or chemotherapeutic agents. When chloramphenicol is used, blood counts should be performed. However, I doubt that the precautions of frequent blood examinations will eliminate the danger of the use of this drug.

That is very important, because they always said that you should get a blood count. But many people didn't show anything wrong with their blood count when they were taking it. This blood disease order came on months later, and a blood count did not help you at all.

"It seems not unlikely that by the time blood changes have occurred, the disorder may be irreversible."

This is by Dr. Edwin L. Crosby. I am sorry. I do not have that one. But Dr. Conley had to OK every bit of Chloromycetin that was used. And I personally talked to Dr. Conley, who was head of the department at that time. I am sorry, I thought I had that letter with me. My recollection is, I was in his study, and he told me he had to OK it every time it was ordered, that he had to pass on it. And they watch those cases very carefully.