

In accordance with these recommendations, the labeling of chloramphenicol was revised in February of 1961 to include a prominent "warning box" containing the following information:

Warning—Serious and even fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, granulocytopenia) are known to occur after the administration of chloramphenicol. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. Bearing in mind the possibility that such reaction may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used when other less potentially dangerous agents will be effective. It must not be used in the treatment of trivial infections such as colds, influenza, or infections of the throat; or as a prophylactic agent to prevent bacterial infections. Precautions: It is essential that adequate blood studies be made during treatment with the drug. While blood studies may detect early peripheral blood changes such as leukopenia or granulocytopenia, before they become irreversible, such studies cannot be relied on to detect bone marrow depression prior to development of aplastic anemia.

Mr. GORDON. Dr. Goddard, what is meant by "adequate"? Is this a scientifically fixed and precise term, or does it lend itself to individual interpretation?

Dr. GODDARD. In the phraseology used in 1961, adequate blood studies to be made during treatment, was subject to judgment on the part of the physician. We subsequently have changed this phraseology. Mr. Goodrich points out that this is why we pointed out specifically early peripheral blood changes, in that same context.

Senator NELSON. Is the warning used in 1961 still the warning that is used?

Dr. GODDARD. No, sir. It was subsequently revised, I believe—minor revisions were made in 1966, as I recall.

Dr. LEY. Change from "should" to "must" not be used.

Senator NELSON. One word.

Dr. LEY. Yes, sir.

Dr. GODDARD. "Chloramphenicol must not be used when other less potentially dangerous agents would be effective." That was the change.

Senator NELSON. I would like to read to you a section of the warning statement:

Bearing in mind the possibility that such reactions may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effect.

I suppose if you read that sentence to even a layman, he would say, "Of course it should be used only against organisms which are susceptible"; the sentence means nothing. And then the advertising continues to talk about its value as a broad-spectrum antibiotic. The PMA ad in Reader's Digest says it is useful against dozens of diseases. It seems to me that the sentence is at best useless, and may be harmful.

Dr. GODDARD. Of course, Senator, this refers to the use of sensitive testing—using the organisms obtained from the patient, cultured by disk, and then the antibiotics that are under consideration being used. That is what this particular sentence refers to.

Senator NELSON. You mean the sentence is saying that a culture should always be taken, and then a test of its effect on the organism made prior to administration?

Dr. GODDARD. That is what lies behind that sentence, Senator. Dr. Ley, do you wish to comment on this?

Dr. LEY. Yes. This is a point which we discussed at great length with our advisory committee this past Monday.