

which it is being prescribed, and the reason this happens is clearly that the vast majority is being used in such things as the respiratory diseases, in which the condition is self-limited, or being used in the prophylactic situations which I have outlined, where the results cannot be evaluated.

In our University Research Hospital I happened to have had the opportunity to study the use of antibiotics of all kinds, several years ago. At that time, well over 50 percent of all patients receiving chloramphenicol, received 1 gram a day. One gram a day in adults should not be able to treat anything either by pharmacologic principles nor in any well substantiated study.

Now, you say, why it is used in this dosage? It is used in this dosage, I believe, because—and I agree with Dr. Best—the message has gotten across in the university hospitals that it is a dangerous drug. For some reason the message hasn't gotten across that it doesn't do any good to give a dangerous drug in small doses if it doesn't do any good for the patient.

Mr. GORDON. Dr. Dameshek, although I don't recall in what connection, talked about 6 grams. Now, is that an average daily dosage?

Dr. LEPPER. Six grams a day is the initial starting dose recommended for the treatment of typhoid fever. In other words, a concept of a loading dose followed by 3 to 4 grams a day, depending on the patient's size.

The dose of 100 milligrams per kilo recommended in hemophilis meningitis translated to an adult is about 7 grams a day. The child is getting a standard dose equivalent to 7 grams a day, and because he is getting it intravenously, there is less wastage as oral drug has wastage.

Consequently, he is getting a full 7 grams a day at the recommended dose and, as a matter of fact, if you use much less than this in hemophilis meningitis, you begin to lose effectiveness. So I think it is clear from the California study, that the vast majority of the patients are getting a drug at a level you can't expect to work and in spite of that you are still getting aplastic anemia.

Senator NELSON. Even at that low a level, it does expose the patient to the risk of aplastic anemia?

Dr. LEPPER. Yes. At a rate of 1 in 20,000 to 1 in 40,000 as specified from the quote.

In fact, the most definitive evidence from the treatment of typhoid fever and hemophilis meningitis is that the dose cannot be compromised. Yet it is.

Now, there are several other blood dyscrasias that I have mentioned which are less serious, but at times fatal, and many more reversible such as agranulocytosis, thrombocytopenia, and so forth, which also occur.

Other reactions which are more related to prolonged use include neuritides causing disability such as blindness, but fortunately usually reversible. Morbidity, such as gastrointestinal upset is more common than any of these, of course.

One other serious, often fatal, reaction that is dose related is "gray sickness." This occurs only with an overdose in adults and children, but in young infants, particularly those born prematurely, in whom there is an underdeveloped detoxifying mechanism, it can occur with a standard dose. Hence, the dose must be reduced in such instances.