

clusive effects that are, on the positive side: (1) the ability to prevent death; (2) the ability to maintain the permanent integrity of tissue, that is, the arrest of the process before irreversible and, therefore, crippling conditions have occurred, and this has to do with empiric use of drugs; and (3) the ability to shorten the duration of essentially reversible processes and limit morbidity.

Similarly, there are several endpoints for toxicity in their order of importance; (1) fatalities and the available countermeasures for their prevention; (2) permanent damage from the drug; and, (3) production of reversible disability and morbidity.

Now, obviously, in making these ratios, one tends to equate the categories and it is hard to equate a lethal toxicity with prevention of morbidity, for instance. It is a different order of magnitude in the equation.

Chloramphenicol is one of the early antibiotic discoveries, hence much information has accumulated for it. I think this is quite clear in the testimony and much of what we are talking about is the way the drug was developed, and in talking about relative indications, the way they came about, and whether they are still current.

Most of the information that reaches the profession really is about new agents. Once they are established, the amount of knowledge disseminated is relatively small. Hence, much of what is said about chloramphenicol indications come from the early years and are not well stated in terms of competitive new drugs.

Senator NELSON. I didn't understand that last statement.

Dr. LEPPER. Changes in indications have not been well emphasized in terms of competitive new drugs as we shall see later on when we come to the staphylococci. This was a lifesaving drug in the late fifties. It is no longer indicated as such, so that when you look at indications, you have to realize that this is a constantly changing field and the physician doesn't really get a reevaluation of old drugs and their relative role nearly as thoroughly as he gets an evaluation of the new drugs and their potential toxicities in relative roles.

Chloramphenicol has wide antibacterial activities and, therefore, may be considered for use in many infections. This has already been indicated. As a matter of fact, from the package insert, one can pick out 17 groups of infections which are mentioned or listed, and some of these groups, such as salmonellosis, which includes typhoid fever, have hundreds of organisms of different species involved. Most of the indications have more than one species of organism involved. Hence, the range of potential specific indications is quite great.

Second, because of this, the empirical use has often been ordered without prior diagnosis, either because of urgency, which may be considered an indication or a feeling that the condition is not serious enough to warrant the expense of the work-up. In this situation they are used because potentially you can treat a lot of things, hence you do not need do a work-up. This is not a valid indication for chloramphenicol, although it is one that undoubtedly is the heart of the use in minor respiratory illnesses which is still going on.

Moreover, we have to consider the prophylactic use because this is one of the big uses of antibiotics.

Senator NELSON. In what kind of situation is a prophylactic use of chloramphenicol indicated?