

ganisms get resistant—they have standard genes and extra parts of genetic material which are easily transmitted between organisms that allow the build-up of these populations of resistant organisms. These studies show that chloramphenicol resistance is commonly mediated by this mechanism. And this means, of course, chloramphenicol resistance is potentially a serious problem, and indeed has been so documented recently.

In short, it is likely that this is one of the most overused and poorly used drugs in the antibacterial armamentarium, in spite of the warnings by the AMA council and the package insert.

My reaction, then, is that if you ask whether warnings have been adequate, I would say they, by all criteria, looking at what has happened, have not been adequate.

Senator NELSON. Both Dr. Best and Dr. Dameshek made what they said was a guess about the percentage of patients who receive chloramphenicol in cases in which it was clearly indicated out of the total number of patients who are given the drug? Do you have a guess of your own about that?

Dr. LEPPER. Yes. My guess, of course, gets back to this idea of absolute indications and relative indications. I would think if we stuck to the absolute indications, if we take the AMA council's absolute indications, salmonella infections that are serious enough to treat, which is mainly typhoid fever, acute typhoid fever, even if we throw in hemophilus meningitis because this is so controversial and we can call it a definite area, and then we put in septic shock, which, for instance—there were perhaps 100 in a city like Chicago in the last 5 years—and we put in some of the urinary tract infections, perhaps 1 to 5 percent, you cannot come up with a figure that is much greater than 10,000 to 50,000 people.

Senator NELSON. You come up with a figure of what?

Dr. LEPPER. Between 10,000 and 50,000 people, and this is a relatively generous estimate in my opinion. I think if you ask me if I were doing all of the ordering, how many would you use it in, I would probably use it in less than 10,000 people a year.

Now, I will grant that statements such as using evidence of failure of other drugs, less toxic drugs, and you get into the problem of kanamycin toxicity versus chloramphenicol toxicity, you could increase this, but I don't believe you would get it over 100,000, no matter how you tried to increase it.

Senator NELSON. Well, if the figure is even roughly correct that the drug is being prescribed for somewhere around 3½ million people, this is certainly a fantastic overprescription of chloromycetin, isn't it?

Dr. LEPPER. I think—I certainly concur in this. This has been a great source of concern to some of us, at least. One must realize, however, that we may be talking about two kinds of overuse. It is quite likely that the antibiotic overuse is greater than 50 percent for all antibiotics. In fact, because of the respiratory problem and the relatively few indications in the respiratory diseases, it is quite likely that we are talking about a four- or five-fold overuse for the entire antibiotic field, and then you talk about misuse within that remaining, you obviously have a very big overuse factor.