

Dr. WEHRLE. Yes, sir. I will have to mail you one. I seem to have forgotten my copies. The references are attached to the last page of my bibliography. We have also included the Houston studies, reference No. 6, by Barrett, Eardley, Yow, and Leverett; and the studies from our institution are items Nos. 3, 4, 5, 7, and 8.¹

The first two references pertain to Drs. Burns, Hodgman, and Cass, and Drs. Hodgman and Burns concerning the problem with the gray baby syndrome in young infants who receive this drug in what we now consider excessive dosage. Those are also from the Los Angeles group.

In addition to the laboratory studies that I just mentioned where the extreme diffusibility of this drug is clearly evident, item 4 points out—

Senator NELSON. May I interrupt for 1 second. I have a question.

Dr. WEHRLE. Yes.

Senator NELSON. You say, "whereas another antibiotic with smaller zones of activity may be equally effective clinically," are you referring to the situation whereas chloramphenicol may be very effective, an invitro study may indicate that another antibiotic with a smaller zone of activity, as you put it, may be just as effective? Is that what you are referring to?

Dr. WEHRLE. Yes, sir. This is exactly what I mean. In other words, chloramphenicol is a drug that does diffuse very beautifully through tissues, into the eye, for example, into joints, areas such as this. It also diffuses very well through culture media used to test for antibiotic susceptibility. Consequently, two drugs that may have the same activity in tube dilutions where you have the drug already diluted may be different on an agar plate where diffusion plays a part in determining the disk or zone size.

So consequently, chloramphenicol, a drug that diffuses very beautifully, gives very impressive rings where the bacteria don't grow around the disk containing this particular antibiotic, whereas one that diffuses very poorly, like polymyxin, for example, may have the same tube activity, yet the zone is very difficult to see. It is a very small zone.

Now, this can mislead the hospital bacteriologist on occasion unless experienced in this problem, and can certainly mislead the physician if the physician stops and looks at the plates from the laboratory on his way to the patient's bedside.

Senator NELSON. Haven't clinical studies indicated over the past few years those instances where, say, Ampicillin would be as effective as chloramphenicol though less toxic?

Dr. WEHRLE. I personally feel so; yes sir.

4. A continuing aggressive advertising and detailing program, suggesting that the physician can "trust" this drug. This has continued to perpetuate the habit, established in earlier years, of prescribing this drug for both major as well as minor problems.

5. The availability of both oral and parenteral dosage forms which are comparatively free from minor gastrointestinal and local reaction.

I think it is apparent that a physician is interested in the welfare of his patient. This drug is so well tolerated by the intravenous route as well as by the oral route that in fact, I think, has often influenced the physician's judgment in prescribing it.

¹ See apps. IV-XI, pp. 4799-4857, *infra*.