

rhage and perforation, which are the two complications besides toxicity that kill, it does nothing to prevent the carrier state. The chronic typhoid carrier, which is the public health menace, is not benefited by the use of chloramphenicol. One of the big errors in the use of chloramphenicol in typhoid fever is to begin to treat a patient because he is a carrier after he has recovered from the acute illness. This will not work.

Ampicillin, probably does not work as well, as Dr. Dameshek pointed out, in acute typhoid fever works better for the carrier state, so that here we have a crossover of the drugs. So we are talking about a highly specific indication even in the typhoid area.

Senator NELSON. Do I understand you to be saying that chloramphenicol is not indicated in the carrier?

Dr. LEPPER. That is correct.

Senator NELSON. But is prescribed.

Dr. LEPPER. It is often prescribed.

Mr. GORDON. Wouldn't that qualification make Ampicillin really a drug of choice for typhoid fever?

Dr. LEPPER. I think it is quite likely that Ampicillin will be the drug of choice for the milder cases of typhoid fever. I think there is the problem. We do not understand why chloramphenicol works as well in typhoid as it does because—and we make a clear differential here—the tetracyclines are equally active in the laboratory, but they do not work as well.

This has been known, essentially, since 1949. We have never had a good explanation, as a matter of fact, still don't, because the mechanisms of action are similar and their body distributions are similar.

Mr. GORDON. In typhoid.

Dr. LEPPER. In typhoid fever. Streptomycin was very active against typhoid organisms in the laboratory. It never worked well at all. Even penicillin itself, in large doses, did not work as well as one would think from the laboratory data. There is some problem in typhoid about the intracellular parasitism of the organism that apparently chloramphenicol overcomes better than the other agents.

In a highly toxic, severely ill typhoid, it is quite likely that one would still use chloramphenicol.

Its use in the other Salmonellosis is not as well proven. It has been used as Dr. Best pointed out—when he said paratyphoid fever, he was talking about some of the other salmonellosis. In the other Salmonella, the actual documentation of chloramphenicol effectiveness is not clear because without drugs the diseases are so variable and infrequent. There are no good studies documenting the dose-effect curve similar to those that we have for typhoid fever.

There is only one condition in which its activity seems sufficiently unrivaled to use without extensive prior laboratory study. That is typhoid fever. Here even the new and less toxic penicillin derivations do not seem as effective. Hemophilus influenza meningitis is another disease for which some will make a case, and this is particularly true of the pediatricians, and stems from the fact that at the time chloramphenicol was introduced it was studied mainly in pediatric clinics and tetracyclines were being studied concurrently in adult clinics.

However, Ampicillin has come on the scene and this is as effective in the hands, at least, of the group working in the Los Angeles County