

(The table referred to follows:)

Source	Incidence
Am. J. Med. 19:274, 1955-----	1 in 800,000
Brit. Med. Bull. 16:67, 1960-----	1 in 10,000 to 100,000
Clin. Proc. Children's Hosp. Wash. D.C. 17: 171, 1961-----	1 in 156,000 to 227,000
Report to California State Assembly and Senate, California Medical Assoc. and the State Dept. of Pub. Health, 1 Jan., 1967-----	1 in 24,200 to 40,500

Dr. HOEPRICH. I would like to say with reference to this last estimate, one in 24,200 to one in 40,500, that the variation here was correlated with the assumed dose of chloramphenicol given to the patient. I think in the circumstance of bone-marrow aplasia where, so far as we understand it at present, hypersensitivity is the important mechanism, that the dose given to a particular individual probably is not the essential and entirely the critical factor. I would prefer, myself, in calculating this incidence, to regard any exposure to chloramphenicol as being significant; if this is done, then the incidence in the California report becomes one in 73,333 exposures to the drug, an incidence more nearly in keeping with other estimates.

You may or may not agree that this is a justified interpretation, but it is mine.

Mr. GORDON. Doctor, what is the importance of blood levels in treatment and in the production of side effects?

Dr. HOEPRICH. In treatment, I would say the importance of blood levels lies in the need to get enough antimicrobial to the site of infection to inhibit the growth of bacteria.

Ideally, we would like to measure, then, the concentration of the drug where the infection is. But suppose the infection is in the covering membranes of the brain, in a meningitis. It is very difficult to get a piece of this to make analysis for the content of the drug. Therefore, we do the next best thing, we get at the thing which we can get at, namely, the blood, and by correlating clinical experience and the susceptibility of micro-organisms to a particular antimicrobial, which can be determined very accurately in the test tube, we can arrive at some estimation of how much a person has to have aboard in his blood for there to be enough in the site of infection, where we cannot measure the drug, to bring about cure of an infection.

Mr. GORDON. Has it ever been determined how high a blood level you would need?

Dr. HOEPRICH. In a particular infection?

Mr. GORDON. Yes.

Dr. HOEPRICH. If you are treating, as an example, an infection caused by a pneumococcus—pneumococci are exquisitely susceptible to chloramphenicol, as well as to other agents. You would not need very much. I would say something like one or two micrograms per milliliter of blood.

On the other hand, if your problem was an infection caused by *Klebsiella*, a gram negative bacillus which is notably resistant to antimicrobial agents, you might well have to have 15, 20, 30 micrograms per milliliter of blood, and again if your infection is in an enclosed space, where we know penetration may be problem, or where there may be pus formation, or the infection may be walled off by an actual mechanical membranous structure that is not very well supplied with