by reducing the dosage—this is the gray baby syndrome—no method of predicting or preventing bone marrow depression has yet been found. The California Medical Association study, published more than 2 years ago, indicated a fatal outcome attributed to this drug in one of each approximately 20,000 patients treated with chloramphenicol. The continued pattern of frequent usage, despite the availability of other drugs of equal or greater effectiveness, appears to be due to at least five factors.

Senator NELSON. May I interrupt for a moment. I have been curious about the statistics in the California study in that we have had witnesses, doctors, testify that in a case where the doctor discovers that it was administered for a nonindicated case he obviously isn't going to report it because he's subject to a lawsuit. I don't know how they extrapolated or how they got this figure, one in 20,000, from the study. How accurate an estimate do you think this record represents?

Dr. WEHRLE. I think this is certainly subject to error in each direction. I think this is the best estimate that anyone has come up with to date, but it should be regarded as an estimate and one that may be inaccurate and presents only part of the picture in each direction. I simply don't know whether this is in the center or whether this is to one extreme, the high extreme or the low extreme. I simply don't know.

Senator NELSON. Are there any other blood dyscrasias that result as a result of administration of chloramphenicol?

Dr. WEHRLE. I think it should be recognized that this is based on fatal episodes, and this is a death certificate type of reporting. I would not—let me back up one moment. There are other kinds of problems that do occur. For example, in patients treated in the controlled evaluation when we were comparing chloramphenicol and Ampicillin in the treatment of meningitis, about 10 percent of the patients who received chloramphenicol had some evidence of marrow depression in terms of development of anemia or some lowering of the white count.

One of these patients developed a severe granulocytopenia; in other words, a very marked depression of the bacteria-fighting cells of the blood. He developed a staphlocci pneumonia, presumably as a consequence, which was an extremely serious infection. This was fortunately controlled by the use of the Methicillin.

Now, I have no idea in these one of 20,000 patients whether there are additional patients who may have died of asepsis secondary to marrow depression with the use of this particular drug. On the other hand, there is no way of knowing how many of these patients may have had a suppression of the marrow for presently unknown and unrelated reasons.

Senator NELSON. Is it possible that they may have had some bone marrow depression which they lived with a good many years without dying, of course, and not being reported in the statistics?

Dr. WEHRLE. I think this quite possible; yes.

Senator NELSON. Did I understand you to say that the one in 20,000 figure was based on death certificate——

Dr. WEHRLE. This was a survey of deaths or fatalities, and I am not certain whether this was from the vital statistics approach or a survey approach.

Senator NELSON. Well, obviously then, if these statistics were based on deaths as a consequence of aplastic anemia, they certainly don't