

against the likelihood of harm, in terms of both frequency and degree, for all reasonable courses of action or inaction. That course which seems to offer the best balance should then be implemented. The physician must then periodically evaluate the apparent effect of his therapy on the course of the disease, making a new decision as to mode of treatment if the initially chosen method seems to be ineffective or detrimental. While this general principle is quite clear, details of implementation may be muddy. Exact figures often are not known regarding the likelihood of benefit or harm; optimal methods of balancing potential good against potential harm have usually not been spelled out.

The type of balance which has appeared to make most sense to those concerned about bone marrow depression following chloramphenicol is based on the following observations:

(1) Rare individuals, probably somewhere between 1 in 20,000 to 1 in 100,000, who receive courses of chloramphenicol will develop significant bone marrow depression. This is a rather broad range of estimates. Dr. Dameshek, if I remember, threw in a figure of maybe 1 in 10,000. It is a reflection of our ignorance that we do not really know what the exact figure is. There have been a couple of attempts made to outline just how frequently this occurs and the truth appears to be somewhere in this general range. It is not an extremely frequent thing, but it does happen.

(2) There is no known way of determining beforehand whether or not a given individual is likely to develop this complication from chloramphenicol.

(3) When bone marrow depression does occur, it is serious, carrying a mortality rate of about 50 percent. There is no really good method of treating this complication. Some who do not die of it suffer prolonged disability. Dr. Dameshek mentioned 50- to 75-percent mortality and I think that 75 percent would probably come closer for the severe cases. The so recent figure is based on an across-the-board estimate, including some mild as well as severe cases.

(4) Careful attempts to detect the early stages of marrow depression with the idea of stopping the drug and preventing death are doomed to failure in many cases. The first evidence of marrow depression has most often appeared after the drug was stopped, and in many cases has been seen weeks or months later. In a minority of cases periodic blood counts during therapy may permit a more favorable outcome through early detection.

(5) Thus, under our present knowledge, there is no way to prevent fatalities due to this complication in rare cases if the drug is to be used at all.

(6) However, chloramphenicol can be a very effective drug in combating a variety of infections. In some life-threatening infections it will be clearly superior to all other available agents.

Based on these propositions, the following conclusions appear warranted:

(a) When the greatest likelihood for control of a serious infection appears to be through use of chloramphenicol, it should be used. More lives will be saved through superior therapy than will be lost through adverse reactions to the drug.