

Other patients with diseases which damage these mechanisms, such as liver disease, also may be easily overdosed. The symptoms are those of abdominal distention, cyanosis collapse and often death in a few hours.

This has an interesting history. Its use stemmed from the broad spectrum concept and in the midfifties because of the staphylococcal outbreaks in newborn nurseries and because of the frequency of the gram negative rod gastrointestinal organisms. Mother frequently infected the infant with such organisms in different ways, like premature rupture of the membranes. Thus, many infants had infections caused by organisms which are susceptible to chloramphenicol as a general rule, and for this reason many nurseries began using chloramphenicol prophylactically in the newborn nurseries. It was finally discovered in some controlled studies, one in Los Angeles County Hospital, that there were more deaths in the chloramphenicol group than there were in the control group, and out of this, gray sickness was discovered. Thus, in fact, we were poisoning the infants in the newborn nurseries all over the country at that time with an otherwise unrecognized syndrome.

This use grew out of the concept of the broad spectrum and its prophylactic potential.

For this reason chloramphenicol by and large is not used in the newborn. Almost all the recent papers on the treatment of newborn infections with gastrointestinal organisms transmitted from the mother to the child, emphasize Kanamycin as the choice. This is a direct outgrowth of this unfavorable experience in the late fifties.

This is a drug that has great therapeutic potential, but several serious toxicities which can and continue to give much difficulty. Essentially it has an unfavorable clinical therapeutic index.

On the toxicity side, the fact that the aplastic anemia can start even after the drug has been stopped and is almost completely nonpredictable and irreversible, makes the therapeutic ratio based on death, one much less favorable than with several competitive agents, even including Kanamycin, which is a relatively toxic drug.

For example, we have summarized for teaching purposes the 25 major diseases which antibiotics have helped control in the United States, and while chloramphenicol is potentially useful in at least half of these, we listed it as the drug of choice in only three—typhoid fever, other salmonellosis, certain gram negative rod infections in well-studied situations.

This is best summarized, perhaps, by the 1966 edition of "New Drugs Evaluated by the Council on Drugs or the AMA" which says:

This drug should be used only for the treatment of typhoid fever, other salmonellosis, and infections that do not respond to less potentially dangerous agents.

That implies a trial of less potentially dangerous agents or a considerable knowledge of the ability to predict where a bacteria sensitive to chloramphenicol only is going to occur. The package insert itself has a strong similar warning, as has just been mentioned.

I might point out one thing about typhoid fever. Interestingly enough, while chloramphenicol works very well in acute typhoid fever in shortening the duration and preventing gastrointestinal hemor-