

I also turned to the 1960 Physicians' Desk Reference, a yearly compilation of pharmaceuticals which the various drug companies wish to bring to the attention of physicians. The writeups for particular drugs are usually abbreviated versions of the product package inserts. I chose 1960 as a year during which the possibility of toxic marrow depression was well known but which was prior to the recent tightening of controls by the Food and Drug Administration. The writeup says: "Chloromycetin is a potent therapeutic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy." Though not as detailed as the precautions mentioned in recent advertising, this description did point to the danger of marrow depression.

So far, the only adverse effects to Chloromycetin which I have mentioned are those related to bone marrow depression. This is because it is the area with which I am most familiar and because it is the type of reaction most frequently associated with a fatal outcome. As an aside, I might mention that in the Registry on Blood Dyscrasias, chloramphenicol has been associated with a plastic anemia more commonly than has any other group of drugs. Nonetheless, there are a variety of other types of reactions which can occur to this antibiotic. These include, in addition to minor symptoms such as fever, diarrhea, or minimal skin reactions, the following:

- (1) Anaphylactic reactions.
- (2) The "gray syndrome" in newborn infants. This is characterized by a distended abdomen, shock, and a bluish-white skin color. It can be fatal.
- (3) Severe skin reactions.
- (4) Optic neuritis with loss of vision, usually reversible.
- (5) Overgrowth of nonsusceptible bacteria or fungi.

Most such complications are readily reversible on stopping the drug. Some can be fatal or permanently disabling. None occur very often.

It should be pointed out that no antibiotic is 100 percent safe. All have potential side effects, some fatal. Penicillin and its variants probably constitute the most widely used group of antibiotics. Fatal anaphylactic reactions to the penicillins have undoubtedly been more numerous than have deaths from aplastic anemia following chloramphenicol. Unfortunately, we do not have adequate information to precisely evaluate the relative risks of such reactions under standard regimens of therapy. In regard to penicillin, I might say that one estimate has been that there are somewhere from 100 to 300 fatalities a year due to anaphylactic reactions to penicillin. I am sure this far exceeds the number of fatalities due to chloramphenicol. Of course, penicillin is much more widely used than chloramphenicol. A recent study in Boston hospitals showed the order of use of some of the more common antimicrobial agents. Penicillin and its analogs were far and away the No. 1 drug. The sulfa drugs occurred next in line among the drugs to be mentioned. The sulfa drugs can also cause severe and even fatal side reactions. Chloramphenicol was the third in this group, and the tetracyclines were No. 4. Tetracyclines have