

3. Direct toxicity varies with age. In the adult, anemia is the most common manifestation. Prolonged, high dosage use of chloramphenicol can halt maturation of red blood cells in the bone marrow; anemia results. Rarely, there may be inflammation of the optic nerve, causing blurring of vision or perverted sensation—of a tingling, crawling feeling—in the skin.

Premature and newborn infants are especially vulnerable to direct toxicity because the capacity to eliminate chloramphenicol in the urine, and to inactivate this antibiotic by chemical change in the liver, is not fully developed until the human is more than a month old.

4. Hypersensitivity to chloramphenicol is quite uncommon. Skin rashes, fever, inflammation of the tongue are annoying when they occur but are not life-threatening.

Pancytopenia, a marked reduction in the numbers of all of the formed elements of the blood—the red and white blood cells, blood platelets—results when hypersensitivity to chloramphenicol brings about failure of production of these elements in the bone marrow. When such failure is complete, termed aplasia of the marrow, death is usually the outcome. Reactions of this severity are rare occurrences. Precise determination of incidence is not possible since:

- (a) The size of the population at risk is not known.
- (b) All cases of drug-associated marrow aplasia are not reported.
- (c) The incidence of bone-marrow failure without exposure to any cause is not known.¹

As a footnote to this statement (c), I put in the reference to the report from the California report which has been cited previously, wherein a figure is given of one in 524,600 persons not exposed to chloramphenicol will develop fatal aplastic anemia, fatal bone-marrow aplasia. In the portion of the report which I had access to, I did not find any basis for this particular calculation and this is why I say I have no feeling for how reliable it is or how it was arrived at. It is one of the few figures that are put down on paper, however, as the natural, normal incidence, if you will, of bone-marrow aplasia.

There is a certain risk, apparently, in just being alive to having bone marrow fail, and that is the problem of (c); I do not know what that risk is.

However, several estimates of the risk of induction of pancytopenia from use of chloramphenicol have been made, and these are tabulated. I must apologize here, Senator Nelson. The first reference is in error, so I discovered after the copies of this statement were made.

The first figure should actually be one in 80,000 and the reference is the Scottish Medical Journal, volume 7, page 96, 1962, and the reference as given, the first one, one in 800,000, that is incorrect and should not be in the table.

The second one is one in 10,000 to one in 100,000, which appeared in the British Medical Bulletin in 1960. The third one, one in 156,000 to one in 227,000, reference as given, and finally, the reference in the California State report.

¹ According to the report to the California State Assembly and senate, made by the California Medical Association and State department of public health, dated Jan. 1, 1967, one in 524,600 persons in California, not exposed to chloramphenicol, will develop fatal aplastic anemia.