blood vessels, then we would have to insist that there be more in the blood to soak into the site of infection.

Mr. GORDON. How about the relationship between aplastic anemia and blood levels?

Dr. HOEPRICH. I do not know that that has been demonstrated. In terms of a direct toxic effect, suppression of maturation, particularly of red cells in the bone marrow, this is definitely correlated with the quantity of chloramphenicol present in the individual. With bone marrow aplasia which is generally regarded as a form of hypersensitivity, I do not think the blood level is critical. A little bit has been enough to trigger bone marrow aplasia.

Mr. GORDON. But, the higher the blood levels, the greater chance you have of halting the maturation of the cell?

Dr. HOEPRICH. Yes. With the direct toxic effects, there is no question that the more you have the more successful you are going to be in blocking maturation, or injuring the retina, the optic nerve, or any of the direct, irritative effects of nausea, vomiting, diarrhea.

Rather than total failure of bone-marrow function, there may be selective depression yielding, by itself, anemia, or deficiency of white blood cells, or marked lack of blood platelets. Reactions of this kind are also not dependent on the dose of chloramphenicol but do occur most often in persons who have taken the drug on more than one occasion. There is some indication that complete aplasia will not result if chloramphenicol is discontinued as soon as adverse effect on the bone marrow is detected; for example, increase in serum iron concentration, fall in the number of white blood cells in the circulating blood. I mention these things because people do feel that there is a correlation here, that if you stop the drug, then nothing further ill will happen in terms of bone marrow aplasia. You have to add to that, of course, that you do not know that an aplasia would have resulted had you kept on with the drug. So, it is one of those situations in which the physician's judgment plays a very major part.

IMPACT OF ADVERTISING ON USE

This is most difficult to judge. Perhaps some indication could be gleaned from comparing dollar volume of sales of chloramphenicol with advertising outlay for identical periods of time. Such data are not readily available.

However, advertisements for chloramphenicol, as they appear in medical journals, quite clearly suggest wider use than the limited indications previously described in this statement. Always this is done with written, covering insertions such as, "* * * may be indicated * * *," "* * * in certain severe infections * * *," along with reference, in recent advertisements, to a, "* * * warning box." In the latter, the hazard of aplastic anemia is fairly and adequately described.

The device of display—an instrument, a patient, a physician—is freely used in this effort at subtle, implied, indirect recommendation to prescribe chloramphenicol. For example, the display of a bronchoscope in an ad for chloramphenicol vaguely, indirectly, subliminally suggests that in serious, occult bronchopulmonary disease—it must be serious, why else the instrument; it must be occult, why else