

is as simple as all that because the indications for which the physician prescribed the drug were acne, upper respiratory infections, and the like, in which he could either have used no drug or have used a drug that does not cause these severe reactions.

The side effects of the drug depend upon the fact that it is an anti-metabolite or cell poison. Evidences of injury to red cell growth, white cell growth, platelet growth, and lymphocyte growth have been demonstrated from a variety of careful studies. Now, the lymphocyte is not a bone marrow cell in the accepted sense. The lymphocyte is at the center of a special grouping of cells which is concerned with immunity or helping the body either to prevent an infection or to prevent an infection from getting ahead.

Now, it has been demonstrated from a number of studies that this drug also affects these cells concerned with immunity, that is, the lymphocytes.

In general, the drug has demonstrated effects on the production of cell proteins, disturbance in transfer of the synthetic "message" from RNA to ribosome, that is, where proteins are produced within the cells. So that one can say in simple words that an actual "monkey wrench" has been thrown into the machinery of cell growth.

Thus, with lymphocytes, antibody formation is greatly reduced; with red cells, hemoglobin synthesis is delayed and cell maturity greatly slowed down. Similar disturbances occur with white cells of the marrow and with the megakaryocyte platelets. Those are the big cells in the marrow that produce platelets. Sorry about these big terms.

In most instances the entire marrow shows reactions and thus, all the elements of the blood are affected leading to the very serious condition of aplastic anemia, which is frequently fatal.

Senator NELSON. Would you describe aplastic anemia for the record?

Dr. DAMESHEK. Yes. Aplastic anemia is fundamentally a disturbance of bone marrow growth in which the growth of cells normally in the marrow is greatly reduced so that the bone marrow is finally producing something like 1 percent, 2 percent, 10 percent, possibly 25 percent of the normal number of cells produced. This leads, therefore, to a reduced number of red cells, a reduced number of white cells, a reduced number of platelets in the blood. The individual may be perfectly healthy in every respect but if his marrow is not working, he has very little blood. So that this becomes, then, a very important thing because without blood there can be no life. In some ways the blood is the central feature of life.

Senator NELSON. What does the term aplastic mean?

Dr. DAMESHEK. Lack of growth. Aplastic—plastic has to do with growth and "a" means lack of growth.

Senator NELSON. And in what percentage of cases is the disease aplastic anemia fatal?

Dr. DAMESHEK. Well, that is a difficult question to define because it is hard to define what is meant by aplastic anemia. If you say that aplastic anemia is a condition in which 75 percent of the bone marrow has been "knocked out," then I would say that the mortality rate for aplastic anemia varies between 50 to 75 percent, maybe more.

Senator NELSON. In the cases that you have seen where aplastic