The registry is an iceberg peak of unknown proportion. We do not know what percentage of all cases occurring are represented. All we can say is that these are the cases that were reported to the registry. Undoubtedly, there are biases involved in this process. Some physicians have not known about the registry; others perhaps might feel that one reaction is too mild to bother reporting or that another reaction to a particular drug is so well known that it does not need further documentation. I am sure all sorts of biasing considerations like this go into it. Although we would like to draw inferences from this data, there is always a question as to just how much the trends we see in the registry reflect what the across-the-board experience is.

Senator NELSON. So this was a total of 408 cases. What period of time does this cover?

Dr. BEST. 1953 through 1964.

Senator NELSON. These were cases voluntarily submitted?

Dr. BEST. Actually, there are two sources of cases. One which accounted for the vast majority, something like 75 or 80 percent, were voluntarily submitted. Some of the people on the AMA staff also screened literature that came in through their library and whenever they found a report in the literature that would bear on this, they would add that to the registry, too. Some of these are culled from the literature, about 20 percent; about 80 percent were voluntary reports submitted by the physicians.

Senator NELSON. Those 80 percent, were they submitted by the original prescribing physician or a mix of the original prescribing physician and the specialist at the end of the line?

Dr. BEST. I would say the latter is the case most often, although I do not think we actually have figures on this. The impression I have is that a majority are physicians who took care of the patient after this complication developed. Probably in most cases this was a different physician than the one who had prescribed the drug originally.

Senator NELSON. So, we have no notion as to how many other cases there are?

Dr. BEST. No. The registry itself gives us no way of estimating that.

Senator NELSON. May I ask one more questions? Of the specialists who would be called upon to diagnose or treat a patient subsequent to the onset of the problem, do you have any notion of what percentage of those in the United States have cooperated in sending in cases?

Dr. BEST. I do not think I have any way to say. I do not know.

To continue with my prepared statement—it is in relation to the details of chloramphenicol-associated bone marrow depression that I should be considered most expert. The statements I would make in terms of the use, indications for use, other side effects and impressions with regard to promotional activity would reflect more my knowledge and judgment as a board-certified internist with a particular interest in these topics.

In making these statements I wish to make it clear that I am speaking on the basis of my independent judgment and not as a spokesman for the Veterans' Administration, for the University of Illinois College of Medicine or for the American Medical Association.

When should chloramphenicol be prescribed? A universal rule for making therapeutic decisions is to balance the likelihood of benefit