

Dr. NORA. Yes; and I will discuss this in detail a little later, but the proper study of mankind is man and what one finds in an animal may not really relate too well.

Senator NELSON. It is difficult to conduct such studies on humans, but in the case of animals, is it not possible to get relevant data?

Dr. NORA. The traditional animal models do not always yield the data one desires. Thalidomide did not yield the patterns that were found, and in some species it was not teratogenic at all in these traditional models, and yet it turned out to be disastrous in humans, so you can get some peripheral evidence, and I will discuss this in a little bit.

Senator NELSON. It may not be relevant, and it may be a long time ago, but I recall in one of the cases where it was indicated there was very serious side effects of thalidomide, and they dropped these investigators and got some others, and I do not recall what the investigators found that aroused their suspicions to warn the company, but I do recall it was those investigators.

Dr. NORA. The investigators getting positive results probably were using an animal model appropriate to the study, and the best animal model is a primate of some sort which is more closely related to a human.

Mr. GORDON. Is it not also correct that the results of animal studies resulted in the FDA's withholding marketing approval for thalidomide?

Dr. NORA. That could be one of the influences. I am not privy to what went on at that time.

We have considered that amphetamine provides a good model to illustrate the obstacles in the way of reaching confident conclusions about the presence or absence of teratogenic effect of a given agent.

Our own experience with this drug may be summarized briefly. In 1962, the mother of an infant born with transposition of the great vessels—a complex and frequently fatal congenital malformation of the heart—expressed more than the usual concern about the cause of the heart defect in her infant son.

She volunteered that she had taken amphetamine diet pills during her pregnancy and asked directly if the amphetamine could have caused the problem.

We were unable to find any evidence in the literature of such an association and so reassured the mother.

But within 2 weeks we encountered two more such cases of transposition and first trimester exposure to amphetamines.

These three cases represented a very provocative epidemiologic cluster.

At this point we began three studies:

1. A retrospective study to compare histories of maternal exposures to amphetamines in congenital heart patients and in normal children;

2. An animal homology study to see if we could produce transposition of the great vessels giving amphetamines to mice and chicks; and

3. A prospective study, starting with mothers prior to delivery who had documented amphetamine exposure in the first trimester and were awaiting the outcome of their pregnancies.