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 two weeks we encountered two more such cases of transposotion 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.

We reported the results of the animal studies in mouse first,[2] and in mouse, chick and drosophila later.[3] Amphetamine produced malformations in all three models. But this doesn't mean it produces malformations in humans. The fact that three phyla were affected, and that two strains of one species were also affected was suggestive of the teratogenic potential of the drug. An unexpected finding that greatly influenced our thinking about the etiology of congenital heart diseases in general was that in one species of mouse we caused ventricular septal defect and in another species we caused atrial septal defect.[4] We were unable to produce transposition. It appeared that amphetamines brought out the malformation to which the strain was predisposed. And it was this observation that led us