prompt detection of the teratogen, thalidomide was on the market for over two years before the first suspicions about its safety were voiced. How much more difficult is it to implicate a "low risk agent" that causes maldevelopment in only 1% of exposures? Yet. if the exposures are frequent, say, in 10% of pregnancies then 3000 malformed infants would be delivered in the United States each year as a result of taking such a "low risk agent."

The pitfalls in conducting epidemiologic studies that will yield a confident answer as to whether or not an agent is teratogenic are many. In brief, precise verification is essential in both retrospective and prospective studies. But, even with careful verification, the possibilities for systematic bias and the limitation in the type of data obtained (no population frequency rates) make retrospective studies less conclusive than prospective ones. The published studies of the potential teratogenicity of amphetamines are retrospective. Prospective studies, in which one could be more confident, have not been done. The reason is simply this: prospective studies require many more patients and no one to date has accumulated a large enough series to address this question prospectively.

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.[1] 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.