

14698 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

any drug to the mother during pregnancy should be greatly justified and, at least, an agonizing decision made in each case. The physician is confronted with two medical imperatives: alleviating suffering and doing no harm. I think that it is time in considering pregnant women that the balance be shifted to doing no harm. It is here that I feel that I am an advocate of the unborn child when I say that the use of drugs should be extremely limited during pregnancy, and then only when the medical indication is compelling. There should be a clear advantage of benefit over risk in each case.

The first principle that applies to human fetal malformation which I would like to mention is that the kind of fetal effect an agent produces is dependent upon the time of its action during development. Fertilization of the egg by the father's sperm occurs within 24 to 36 hours after ovulation. Implantation of the early embryo in the uterus occurs in the human around the 9th day of pregnancy. The differentiation of the embryo proceeds in this site until the 8th or 9th week of pregnancy at which time almost all organs are fully formed. From the end of the 3rd month when differentiation is virtually complete, the embryo becomes a fetus whose main function thereafter is growth. The critical period for malformations then is during the first 3 months of pregnancy. Thus, the most severe damage caused by a drug in the embryo can occur before the woman in many cases is even aware that she is pregnant.

The drugs known to cause human malformation fall into four main categories: The first group of drugs consists of the anticancer agents consisting primarily of folic acid antagonists and antimitotics. These drugs are highly toxic to the embryo and produce malfor-