

## DRUGS IN PREGNANCY

### *Background*

Although most physicians are extremely cautious with medication use in their pregnant patients, it is estimated that at least 10% of birth defects can be attributed to maternal drug exposures. In order to provide guidance to health care professionals, the FDA has developed a categorization system for medications based on their potential for fetal risk (See Table 1).

Medications with recognized harmful effects to a developing fetus are in the categories “D” and “X”. Category “D” medications may provide benefit to the mother in certain medical conditions; however, the benefit must outweigh the risk to the fetus in order for such drugs to be used. Examples of category “D” drugs include ACE inhibitors, lithium, and certain anticonvulsants such as phenytoin and carbamazepine. Category “X” medications are absolutely contraindicated in pregnancy as they are associated with more harm to the fetus than any possible benefit that could be obtained. Examples of category “X” medications are HMG Co-A reductase inhibitors (statins), warfarin, vitamin A derivatives, and many benzodiazepines.

**Table 1: US FDA Pregnancy Category Definitions**

CATEGORY	DESCRIPTION
A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester, and the possibility of fetal harm appears remote.
B	Animal studies do not indicate a risk to the fetus and there are no controlled human studies, or animal studies do show an adverse effect on the fetus but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
C	Studies have shown that the drug exerts animal teratogenic or embryocidal effects, but there are no controlled studies in women, or no studies are available in either animals or women.
D	Positive evidence of human fetal risk exists, <u>but benefits in certain situations</u> (eg, life-threatening situations or serious diseases for which safer drugs cannot be used or are ineffective) <u>may make use of the drug acceptable despite its risks.</u>
X	Studies in animals or humans have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the <u>risk clearly outweighs any possible benefit.</u>

### *Limitations to the FDA Pregnancy Categories*

The FDA pregnancy categories were established in 1979. Since then, several limitations have been observed when this system is applied to practical medicine. First of all, the data upon which these categories are based is varied, incomplete, and often not uniformly applied. There is excessive emphasis placed on animal data and while this in many cases is the best information available, over-reliance on such data has proven detrimental in cases such as the thalidomide tragedy. Because drug effects in animals are not always predictive of their effects in humans, such information must be viewed with great caution. Another shortcoming of the current system is that only 40% of drugs in the Physician’s Drug Reference<sup>®</sup> (PDR) have their pregnancy category listed. For those medications that are listed, greater

than 60% are category “C”. This category is ambiguous at best and fails to provide any guidance in making an informed decision. And finally, the current system often does not address differing dosages or gestational age in their recommendations, further limiting an informed provider decision.

Because of these limitations, the FDA is discussing a new category system. The new system will improve the data collection process to address the safety of medications in the pregnant population. Furthermore, the new labeling system will be separated into three separate sections: fertility, pregnancy, and lactation. More specific recommendations will be made and risk vs. benefit information about each section will be provided. There will also be a brief summary of underlying data used to develop the risk assessment.

#### *Strategies to Avoid Certain Medications in Pregnancy*

While great care is exercised in the management of pregnant patients in the majority of cases, there are certain strategies that a health care provider can apply to help avoid category “D” and “X” medications:

- Perform a pregnancy test in child-bearing aged women before the initiation of a category “D” or “X” medication.
- Use references which provide information from available data and an explanation of possible risks. (i.e., *Drugs in Pregnancy and Lactation* by GG Briggs)
- Find alternative regimens that carry a lesser risk to the fetus than a category “D” drug.
- Encourage patients to stop category “D” or “X” medication if pregnancy is suspected and test immediately.
- Ask about prescription and OTC drug use and herbal products at each visit.
- Write the diagnosis of pregnancy on prescriptions to inform the filling pharmacist, allowing another check for potential adverse effects.
- Contact the Idaho Drug Information Center with questions (1-800-334-7139)

#### *Summary*

Most physicians are very cautious with drug use in pregnancy. To help providers with drug selection in this population, the FDA has provided a category system. Category “D” and “X” medications pose the most risk to the developing fetus. Several limitations have been detected with the current system, thus requiring the FDA to look for an alternative categorization. Despite limitations with the current drug labeling system, health care providers can employ a variety of strategies to help in the avoidance of potentially harmful medications in pregnancy.

#### *References*

1. Cooper WO, et al: Prescriptions for contraindicated category X drugs in pregnancy among women enrolled in TennCare. *Paediatr Perinat Epidemiol* 2004; 18: 106-111.
2. Boothby LA, Doering PL: FDA labeling system for drugs in pregnancy 2001 November; 35: 1485-1489.
3. Doering PL, et al: Review for pregnancy labeling of prescription drugs: Is the current system adequate to inform of risks? *Am J Obstet Gynecol*, 2002 August; 187: 333-339.