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## **Insecticides**

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The arrival of summer is heralded by a dramatic increase in inquiries from pregnant women and their physicians to the Illinois Teratogen Information Services program at Northwestern concerning the effects of prenatal exposure to insecticides. In this first issue of the RISK||NEWSLETTER, The focus will be on the possible effects of prenatal exposure to the more commonly encountered insecticides.

### **INSECTICIDES IN GENERAL**

An accurate estimation of the risks following prenatal pesticide exposure is difficult for several reasons. First, it is hard to control for the varying degrees of exposure encountered in home and office extermination. Second, commercial preparations may consist of a mixture of several active ingredients or more than one chemical may be applied in a particular setting. Lastly, the vehicles used to enhance application of many insecticides are organic solvents. In a few retrospective studies of chronic exposure to organic solvents in early pregnancy, a slight increased risk for spina bifida and limb defects has been suggested. The majority of studies found no increased risk following chronic organic solvent exposure.

Modern pesticide development began in W.W.II. Pesticides can be classified as follows: insecticides, which are chemicals which have a direct toxic effect on insects; and herbicides and fungicides, which are chemicals which eradicate unwanted plants and fungi, respectively. As insecticides are the most commonly encountered pesticides in the home, these chemicals will be highlighted in this issue.

Insecticides are divided on the basis of their chemical structures:

Organochlorines  
Organophosphates  
Carbamates  
Pyrethroids, and  
Inert growth regulators

Organochlorines are restricted in their applications and are unlikely to be used in home pest controls; they will not be described in this issue of RISK||NEWSLETTER.

### **ORGANOPHOSPHATES**

Organophosphate insecticides are derived from phosphoric and phosphonic acid and because this group is readily hydrolyzed in water, they do not persist for prolonged periods in the environment. Three organophosphates will be described: Malathion, Diazinon and Dursban.

### **MALATHION**

Malathion is one of the most commonly used insecticides in the world for the control of fruit flies, beetles and aphids. Malathion is considered the least toxic of the organophosphates and therefore it is frequently applied to fruit and vegetables and ornamental plants.

The majority of studies in mammalian animal models have found no increase in the rate of birth defects following ingestion of large amounts of malathion by the pregnant animal. A single case report from Holland identified prenatal malathion exposure as the possible cause of an amyoplasia-like condition in a newborn (1). The infant had multiple congenital contractures and virtually all of the skeletal muscle was replaced by fatty tissue.

The condition most likely arose from an innervation defect shortly after the fetal joints were formed. The infant's mother has repeatedly washed her hair with a shampoo containing 0.5% malathion between 13 and 14 weeks gestation; she had no symptoms from her exposure. However, a single case report is unable to show a cause-and-effect relationship, and the congenital malformation present in the infant has occurred in the absence of malathion exposure. Therefore, no conclusions can be drawn as to whether significant malathion exposure at a critical time in pregnancy may pose an increased risk for similar anomalies.

Data analyzed from hospital newborn discharge reports for 22,465 births in 1982 for which the mothers were potentially exposed to aerial malathion spraying early in gestation indicated no difference in the risk for birth defects or low birth weight, when comparisons were made between the exposed and nonexposed infants. This study suggests that aerial malathion spraying is not likely to pose a significant risk to a developing fetus.

#### DURSBAN

Dursban (chlorpyrifos) is commonly used in the extermination of ants, cockroaches, fleas and termites. Solutions containing more than 15% Dursban are only sold to professional exterminators; liquids used in homes and on lawns are usually diluted to contain only 1% Dursban or less. Dursban has a low vapor pressure and therefore it is unlikely that accurately toxic levels of the vapor would accumulate at room temperature. According to the manufacturer (Dow Chemical), this chemical is poorly absorbed through the skin of human volunteers and is rapidly metabolized with a half-life of 27 hours. No increased risk of birth defects among exposed rat offspring was found; in mice, an increase in the rate of skeletal variants was seen only at the maximum dose. Skeletal defects in animal studies are thought to be indicators that the dosage used was toxic to the fetus. Since no other birth defects were increased at this or lower exposure levels, Dursban is not considered teratogenic in mice. No studies have been conducted which examine the possible reproductive effects of prenatal Dursban exposure in humans. However, given the negative findings in animal studies, Dursban exposure at levels with no evidence of maternal toxicity are unlikely to pose a significant risk to a developing fetus.

#### DIAZINON

Diazinon is a broad-spectrum insecticide, with particular usefulness in the eradication of cockroaches resistant to the organochlorine insecticides. Diazinon was not found to be teratogenic in most animal species when administered orally to the pregnant animal during organogenesis. Diazinon produced an increased incidence of limb abnormalities following injection in chick embryos but, since the chemical was directly injected into the embryo, this finding is unlikely to have significance for human pregnancies. No studies have examined prenatal diazinon exposure in humans. However, since the majority of animal studies found no increased risk at exposure levels far in excess of the doses humans are likely to encounter, the available data suggest that diazinon is not a significant cause of birth defects.

#### CARBAMATES

The carbamate class of insecticides are only slightly soluble in water, however, they do not persist long in the environment as they are readily oxidized by light, heat and air. In hot, humid weather, dermal absorption of these chemicals is increased.

#### FICAM

Ficam (bendiocarb) is a carbamate insecticide frequently used for home pest control. There are no studies conducted in humans to systemically examine prenatal Ficam exposure. However, given Ficam's large margin of safety, exposure to this insecticide is not likely to increase the risk to a developing fetus at the exposure levels used in home and office extermination.

#### PYRETHROIDS

The pyrethroids are synthetic insecticides chemically related to pyrethrins, natural insecticides derived from chrysanthemum flowers, and highly effective against lice and insects. The compounds are poorly absorbed through the skin and are rapidly inactivated.

#### PERMETHRIN

Permethrin is present in Nix crème rinse in a 1% concentration to treat head lice. No human studies have been reported which examine permethrin exposure in pregnancy. Given their low potential for toxicity in humans, they are unlikely to pose a significant risk to a developing fetus. If a pregnant woman requires treatment of lice, the pyrethroids are generally considered the safest treatment in pregnancy.

#### CYPERMETHRIN

Cypermethrin is marketed under the brand name Demon. Despite the lack of teratology studies in humans, prenatal cypermethrin exposure probably does not significantly increase a pregnant woman's risk for birth defects given the low toxicity of this group of insecticides.

#### INERT GROWTH REGULATORS

Inert growth regulators affect the processes necessary for normal insect development and reproduction. They are usually not toxic to the target but act at a particular life stage of the insect. Inert growth regulators do not bioaccumulate and do not persist for prolonged periods in the environment.

#### METHOPRENE

Methoprene (Altosid) is used for mosquito control, particularly for cattle. Whereas studies in mice and rats found an increased incidence of birth defects, no human studies or case reports have been published which examine prenatal methoprene exposure. Therefore, because positive findings in animal studies are not always predictive of human response, it is not presently possible to determine whether methoprene exposure in pregnancy poses an increased risk.

#### INSECT REPELLENTS – DEET

DEET is the most effective topical insect repellent in use today, being effective against mosquitoes, ticks, sandflies and deerflies. In humans, DEET is partially absorbed through the skin, with an estimate of 16.7% of the applied dose penetrating the skin. DEET has been demonstrated to cross the placenta in rats whose mothers had been orally dosed with large amounts of DEET in pregnancy. Three separate studies in rats, however, found no evidence of teratogenicity following oral administration.

In 1975, Hall et al. reported on two maternal first cousins born within two weeks of each other with congenital heart defects, including coarctation of the aorta. The only exposure their mothers, who are sisters, had in common was the use of large amounts of several insect repellents, including one containing DEET, while on a camping trip together at eight weeks gestation. Although this case does

not prove a causal relationship, it does prompt concern over excessive DEET exposure in early pregnancy. Given this case report, it is wise for a pregnant woman to use DEET-containing insect repellents sparingly and use those formulations which contain a low concentration of DEET. DEET should be used in early pregnancy only when necessary.

## RECOMMENDATIONS

### General Insecticides

- Have pesticide sprayed in the pregnant woman's absence

- The pregnant woman should remain outside of the sprayed area for eight hours

- The area should be adequately ventilated before the pregnant woman returns.

### Insect Repellents

- Avoid products with high concentrations of DEET

- Use in moderate amounts

- Do not use for a prolonged period

### Lice Treatment

- Products containing a pyrethrin or pyrethroid as the active ingredient are the safest in pregnancy

- Kwell is contraindicated in pregnancy, as it has been associated with CNS toxicity in treated individuals

## SUMMARY

The majority of teratology studies on the effects of insecticides during pregnancy are based on animal experimental systems which use large doses of insecticides. Little data is available from case control studies in humans. Therefore, a slight human reproductive risk from insecticide exposure cannot be ruled out but is unlikely based on the available animal data. Adverse effects will most likely be demonstrated at exposure levels far in excess of likely human exposures such as extermination of a home, as the evidence suggests that symptoms of severe poisoning of the mother must occur before such adverse effects on the pregnancy are demonstrated.