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## Organic Solvents and Pregnancy

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Exposures to organic solvents may occur in a variety of settings, including occupational exposure in the workplace, non-occupational or incidental exposure in the home, or exposure as the result of solvent abuse.

There are numerous organic solvents, therefore, this issue of RISK||NEWSLETTER will focus on those organic solvents commonly found in the workplace or home, or are frequently abused.

### OCCUPATIONAL EXPOSURES

Occupational exposure is defined as chronic exposure in amounts less than the threshold limit value causing maternal symptoms. As with many teratogens, critical parameters, which determine the level of the exposure, include duration of exposure, route of exposure, and dosage of exposure. Occupational exposures may involve exposure by inhalation or by skin contact. The dosage of the solvent exposure, measured by airborne concentration or blood level, is often difficult to assess accurately. Therefore, precautions such as wearing protective clothing and gloves and working in an adequately ventilated environment are strongly recommended.

### TOLUENE

Toluene, also called methylbenzene, is the most commonly used organic solvent. It is a volatile, aromatic hydrocarbon metabolized differently in the adult than in the fetus or neonate. In the adult, half of inhaled toluene is converted to hippuric acid, while the other half is excreted as toluene in the urine. The fetus or newborn does not make the conversion of toluene to hippuric acid (Goodwin, 1988).

Occupational exposure to toluene occurs in many industrial settings, including shoe manufacturers, painting, printing and adhesive industries, as well as laboratory exposure. The threshold limit value for toluene is 50 to 100 ppm.

In a retrospective study of 535 laboratory workers exposed to toluene, Taskinen et. al. (1994) found a significant association with spontaneous abortion. A study, which monitored worker's biologic levels of six solvents by the same investigators found the highest risk for spontaneous abortion in printing workers, exposed to toluene and other organic solvents. This study also found an increased frequency of spontaneous abortion in toluene-exposed shoe workers (Lindbohm, 1990). One hundred sixty-eight women working with varnishes containing toluene at a level of 55 ppm were reported to have children with a higher incidence of fetal asphyxia and low birth weight (Syrovadko, 1977).

### BENZENE

Benzene is an aromatic hydrocarbon whose composition differs from toluene by the absence of a

methyl group attached to the benzene ring. This industrial organic solvent has an occupational exposure limit of 0.1 ppm. Chronic exposure to benzene has been found to cause chromosomal abnormalities in white blood cells, bone marrow hypoplasia, and aplastic anemia (National Academy of Sciences, 1976). However, this finding does not appear to be relevant to the risk of teratogenicity in typical industrial level exposures. A cohort study of 41 pregnant laboratory workers exposed in the first trimester did not find an increased rate of miscarriage (Axelsson et. al., 1984). In another study, 150 women with occupational exposure to benzene had a slightly increased risk of stillbirth but no increased association was found for premature delivery, low birth weight or length (Savitz et. al., 1989).

In a study of eight hundred and twenty-three men occupationally exposed to approximately 5 ppm of benzene, the risk of spontaneous abortion was not increased in 1739 pregnancies (Strucker et. al., 1994).

## XYLENE

Xylene, also called dimethylbenzene or xylol, is an aromatic hydrocarbon solvent commonly found in paints, lacquers and adhesives and also in laboratories. After toluene, it is the most common solvent encountered in the workplace (Brown-Woodman, 1991). A study of women working in pathology or histology laboratories showed an association of xylene exposure with an increased risk of spontaneous abortion (Taskinen et. al., 1994). No association with congenital malformation was found, however. Other studies report that unless there are signs of maternal toxicity, e.g., irritation of the skin, mucous membrane, or respiratory tract, xylene is not embryotoxic (Von Burg, 1982). The threshold limit value for Xylene is 100 ppm.

## HOUSEHOLD EXPOSURE

Under normal circumstances, household use of solvent-containing products does not exceed the threshold limit value applied to occupational exposures. Most exposures to organic solvents in the home are typically episodic and at low airborne levels, rather than chronic or at high concentrations. Therefore, household use of organic solvents is usually not associated with spontaneous abortion and this type of exposure does not confound data on occupational exposure. However, because measurements of airborne levels of solvents are difficult to interpret, precautions to reduce household exposure to solvents are advisable.

## SOLVENT ABUSE

Abuse of solvents refers to intentional sniffing of vapors of solvents in order to obtain a feeling of euphoria, light-headedness or dizziness. As with other chemical abuses, it is difficult to determine the exact level or pattern of exposure. The air concentration of the solvent is very likely to be greater with abuse than with an occupational or accidental exposure, otherwise the desired euphoric effect in the mother would not be sought after. Due to higher concentrations with abuse, teratogenic effects may be more likely.

## TOLUENE

Since toluene is the main component found in spray paints, glues and lacquers, the typical method of abuse is spraying a material with the aerosol, placing the material over the nose and mouth, and then inhaling. A phenotype of toluene embryopathy had been described in pregnancies in which women reported chronic toluene abuse. This toluene embryopathy includes a spectrum of features similar to those present in the fetal alcohol syndrome. Pearson et. al. (1994) proposed a common mechanism for the craniofacial features: a deficiency of craniofacial neuroepithelium and mesodermal components due to increased embryonic cell death. these facial characteristics include a narrow bifrontal diameter, short palpebral fissures, hypoplastic midface, and wide nasal bridge (Wilkins-Haug et. al., 1994). Other

features include premature delivery, low birth weight, microcephaly, growth retardation, development delay, abnormal palmar creases, blunt fingertips, small fingernails, deep-set eyes, micrognathia, and abnormal auricles (Pearson et. al., 1994; Arnold et. al., 1994). Pearson et. al. (1994) examined eighteen pregnancies in which there was known maternal toluene abuse and did follow-up evaluations of 9 of these infants 3 to 36 months after an initial neonatal examination. Thirty-nine percent of the infants were born premature and 9% of the pregnancies experienced perinatal death. Eighty-three percent of the newborns displayed the craniofacial features similar to those seen in fetal alcohol syndrome and of these patients, 89% had other minor anomalies. Fifty-four percent were small for gestational age and 52% displayed continued growth retardation. Developmental delay was the most common finding, occurring in 80% of the pregnancies.

Lindemann (1991) reported two cases of solvent abuse in which mothers had been sniffing paint thinner containing toluene, ethanol and butylacetate. The infants were premature and displayed dysmorphic features similar to the toluene embryopathy phenotype. In addition, they exhibited transient hyperchloraemic acidosis and aminoaciduria, suggesting renal tubular dysfunction. The proposed mechanism is that sniffing toluene during pregnancy may change membrane permeability in the tubules of the kidney and enhance liver enzyme activity (Lindemann, 1991).

#### FETAL SOLVENT SYNDROME

Other forms of solvent abuse include sniffing paints, lacquers, glues and gasoline to achieve a “high”. These solvents are known to contain variable proportions of many solvents, the most common components being toluene, benzene and xylene. Gasoline also contains methanol and petroleum ether. Case reports of mothers who sniffed these substances described a syndrome of birth defects analogous to the fetal alcohol syndrome. This fetal solvent syndrome or fetal gasoline syndrome has also been associated with hypotonia, mental retardation, and poor postnatal head growth. In these instances, it is difficult to determine whether there is a primary solvent responsible for the effects or if a combination of solvents were the cause for the embryopathy.

#### SUMMARY

There are a number of recommendations common to many solvents, which, if followed, are likely to reduce the level of risk associated with prenatal exposure. Duration, route, and dosage of exposure are characteristic elements, which define the nature of any exposure. In general, an exposure that is sporadic or short in duration and without maternal effects typically does not cause fetal anomalies or pregnancy complications. An exposure that is lower than the threshold limit value is also unlikely to be teratogenic. However, because many solvent exposures occur by inhalation, it is difficult to assess the exact concentration of an airborne solvent. Women are often advised to take added precautions if an exposure is unavoidable. Wearing gloves, masks and protective clothing is advisable. Reducing the airborne concentration of a solvent by providing good ventilation is also recommended. The Occupational Safety and Health Association (OSHA) can be useful by evaluating questionable workplace exposures. In Chicago, OSHA can be reached at (312) 353-2220. The telephone number of the National Office of OSHA, Section of Risk Standards, is (202) 219-7157.