

Sins of the Father Parental Smoking and Childhood Cancer

Exposure to passive (or environmental) tobacco smoke has been implicated in numerous childhood ailments ranging from low birth weight to middle ear disease. Passive smoke has also been suspected, but not proven, to increase the risk of childhood cancer. Clarifying this issue is crucial not only for the protection of children's health but also for the fashioning of policy concerning smoking in public and private facilities. In this month's issue, Paolo Boffetta and colleagues present their meta-analysis of the results of more than 30 studies on the association between exposure to tobacco smoke from parental smoking during pregnancy and cancer in childhood [*EHP* 108:73–82].

The biological plausibility of the association between passive tobacco smoke and childhood cancer is based on studies that show that children do take in tobacco components—including carcinogens and mutagens—when exposed to tobacco smoke during both gestation and childhood. Activation of procarcinogens in human fetal and placental tissues has been demonstrated, as has smoke-induced damage to DNA in human placenta.

In conducting their meta-analysis, the authors searched the medical literature for epidemiological studies on childhood cancer where

smoking by one or both parents was recorded. The authors extracted from these studies characteristics of study design and results on risk from exposure to maternal or paternal smoking during pregnancy. They also extracted quantitative results, expressed as numbers of cigarettes per day smoked by the parents, where those data were available. For neoplasms for which risk estimates were available from at least three different studies, the authors combined the relative risk (RR) for any exposure to tobacco smoke into a meta-analysis based on a random effects model.

The results of the meta-analysis suggest an increased risk following exposure to maternal tobacco smoke on the order of 10% (RR = 1.10). The authors state that this increased risk is small and is not clearly concentrated in any specific neoplasm. The only neoplasm for which a significant association was found was leukemia, but the authors say that increase could be explained by information bias (inaccurate recall) and confounding factors such as drug and chemical exposures, parental occupational exposures, diet, and socioeconomic status.

Fewer studies addressed exposure to tobacco smoke from the father. Using those that were available, the authors found a RR of 2.08 for non-Hodgkin lymphoma, 1.17 for acute lymphocytic leukemia, and 1.22 for central nervous system tumors or brain cancer.

The authors report that the overall interpretation of the studies reviewed was hampered by the crude exposure assessment used. Most of the studies did not include quantitative exposure variables, and those that had that information did not provide evidence of a dose–response relationship. They conclude that further studies are needed to overcome the practical difficulties of identifying adequate numbers of cases of childhood cancer and the possible limitations of the available epidemiological investigations.

—John S. Manuel



A meta-analysis of studies, though limited, indicates increased risk of cancer in children exposed to tobacco smoke from parental smoking.

Catch the Drift Assessing Risk from Pesticide Spraying

Farm workers are regularly exposed to pesticides in the course of their labors, and the effects on their health have long been a source of concern. Less well understood and more difficult to study is the risk to residents in nearby communities who are exposed to pesticides that drift when crops are sprayed from airplanes or trucks. In this month's issue, Mary Ward and colleagues have determined that one viable approach to identifying people potentially exposed to agricultural pesticides is to combine analysis of historical records with the technologies of remote sensing and geographic information systems (GIS) [*EHP* 108:5–12].

Many rural residents live within a few hundred yards of fields where pesticides are sprayed. In the past, studies primarily focused on pesticide applicators and exposure was estimated by using questionnaires or biological monitoring. Questionnaires have limitations in that respondents may be unaware of the types of agricultural pesticides in use near their homes. Biological monitoring is useful in estimating past exposure to pesticides with long half-lives but not exposure to the active ingredients and by-products of many pesticides that have short half-lives. Another method—measuring pesticide concentrations in household dust—may provide a useful approach for determining historical exposure, but interpreting the data requires knowledge about the proximity of residences to crop fields and pesticide levels in homes that has not been well defined. Providing some of this information is where sensing and mapping technologies may help.

Using Landsat satellite images of vegetation, the researchers were able to classify the different types of crops that had been planted in a three-county area of south central Nebraska. A Landsat satellite sensor detects reflected energy in infrared, red, and green wavelengths. The relative reflected intensity of these wavelengths can be used to identify different types of vegetation. Checking the resulting patterns against historical crop maps that have been maintained by the Nebraska Farm Service Agency allowed the researchers to classify and validate the farm field cover as either corn, sorghum, soybeans, alfalfa, rangeland, or bare soil. In turn, this information, along with data about the type, timing, and quantity of pesticide most likely to have been applied to a particular crop and the proximity of residences to crop fields, was integrated by GIS software to create maps revealing probable exposure to agricultural pesticide spray over time.

The study showed that approximately 22% of the residents in this extensively farmed part of Nebraska lived within 500 meters of farm fields and may have been indirectly exposed to crop pesticides. In the study, 15% of residents of towns lived within 500 meters of the crop fields and so may have been exposed. This research should aid in the design of future health studies by identifying populations with potential exposures to agricultural pesticides. It should also be useful for studying factors affecting pesticide concentrations in house dust.

—W. Conard Holton

Malformed Frogs Making the Leap to Humans

Since the mid-1990s, large numbers of frogs with missing and extra limbs and craniofacial malformations have been found in ponds in Minnesota, Wisconsin, Vermont, and Canada. Scientists speculate that the malformations are being caused by some environmental agent or agents. There is some concern that this agent might also have an effect on human health. State and federal agencies, including the NIEHS, have been conducting research to characterize the malformations and determine their source. In December 1997, the NIEHS sponsored a workshop to present these findings and provide insight into problems and strategies applicable to continuing investigations. The findings are reviewed by James G. Burkhardt and colleagues in this month's issue [*EHP* 108:83–90].

While a definite source for the malformations has yet to be identified, research has confirmed the existence of the problem and narrowed the field of likely candidates. Information gathered by the Minnesota Pollution

Control Agency indicates that malformations among wild amphibians have increased dramatically at some locations over the last 3–5



A new study combines historical records with remote sensing and GIS technologies to estimate the risk to surrounding communities from crop spraying with pesticides.

degradation products, suggested as possible causes, have been found at any sites in biologically relevant concentrations. However, teratogenic fractions have been identified in water sampled from the affected sites, and limb malformations have been induced in *Xenopus* using pond water from these sites.

Particular interest is being focused on the role of retinoids, which can induce all limb phenotypes observed in the malformed frogs in the field.

Researchers suspect that one or more agents in the environment are in some way targeting a developmental signaling pathway that is retinoid-responsive.

However, efforts using different cloned retinoid receptor binding assays have failed to show any direct correlation between a positive receptor assay and malformation of wild and/or laboratory frogs. Further research on the mechanisms controlling growth and pattern formation in limbs is needed to identify any agents and mechanisms involved.

The authors indicate that a thorough understanding of the environmental chemistry and hydrogeology of the affected sites will be necessary to pinpoint a source of the malformations. They point out that environmental degradation of man-made compounds can lead to products with different, and often more toxic, characteristics than the parent compound. They suggest that researchers need to consider how the effects of man-made agents vary depending on the water matrix (alkalinity, hardness, pH, etc.) and on the naturally bioactive components found in the environment.

It remains unknown whether the malformations are in any way relevant to human health. To date, researchers have not found sufficient evidence to warrant an epidemiological study of human birth defects in the affected areas. Solving the complex mystery will require cooperation between state and federal agencies and collaboration among chemists, toxicologists, field and research biologists, and hydrogeologists. —John S. Manuel

years. Neither larval flukes nor bacteria appear to be responsible for the malformations. Data from wild frogs and from laboratory studies using the South African clawed frog, *Xenopus laevis*, indicate the involvement of waterborne agents.

No striking patterns of metal or chemical contamination have been found in water from affected sites sampled by the agency. Neither the insecticide methoprene nor its more toxic

