



Scientists conclude prenatal chemical exposures may impair breast-feeding and increase breast cancer risk later in life

Chemical safety testing should evaluate risks

Male breast development also affected by low-dose exposures

An article published June 22, 2011, in the peer-reviewed journal *Environmental Health Perspectives* reports the conclusions of an international workshop on the effects of mothers' exposures to chemicals in the environment on their daughters' developing breasts. Exposures to the developing fetus and newborn may program changes that cause problems in breast-feeding, increase the risk of breast cancer, and result in enlarged breasts in boys and men. Current chemical safety testing does not include these effects. Participants included experts in breast biology, cancer biology, epidemiology, and risk assessment along with public health advocates.

Background

The breast develops both before and after birth in girls and women. Exposure to chemicals during critical periods of development – for example, in the womb, during puberty, or during pregnancy – may influence how the breast develops, causing changes in growth that could interfere later in life with a woman's ability to breast-feed or increase her breast cancer risk. Exposures may also cause breast development in boys and men.

Because normal breast tissue cannot be studied in humans, scientists turn to studies of rats and mice to evaluate whether chemicals in common use might cause harmful changes. The stages of breast development in rats and mice are similar to development in humans, although there are some differences. Studies in rodents have the advantage of being relatively fast; cancer in humans develops over decades, too long to wait for information about the safety of chemicals in use today.

By studying how environmental chemicals influence breast development, scientists can help government, manufacturers, and consumers make better decisions about chemicals in consumer products and air and water pollution. This is a new area of science, so methods for conducting studies, interpreting results, and evaluating the relevance to humans are under discussion.

What did this project do?

The Mammary Gland Evaluation and Risk Assessment Workshop was convened in Oakland, CA, in November 2009, to develop standard methods for safety testing to identify effects of chemicals on breast development. Participants included more than 60 biologists, epidemiologists, toxicologists, physicians, public health officials, and breast cancer activists.

Workshop leaders conducted a systematic review of scientific literature. In addition, they interviewed 18 toxicologists and risk assessors to learn how they interpret data from mammary

gland studies. In order to standardize and validate a new method for assessing disruption of breast development, experts from 7 laboratories in Canada, the U.S., and Argentina independently observed and evaluated laboratory slide preparations of mammary gland tissue (whole mounts) to see whether all agreed on the interpretation of study data.

What are the findings from the workshop?

A majority of workshop participants agreed that:

1. Rats and mice are reasonable surrogates for the study of human breast development.
2. For some chemicals, effects on breast development occur at doses lower than the lowest dose that affects other tissues. In the small number of studies that have tested for effects in the breast and other tissues, some studies of atrazine, BPA, DDT, and genistein found the breast is most sensitive.
3. Changes in mammary gland development are a concern, because they may lead to increased susceptibility to tumors and difficulty breast-feeding.

Exposure to chemicals before birth and in infancy can alter the structure of breast tissue and the timing of breast development at puberty. These types of changes have been reported for numerous EDCs, including atrazine, bisphenol A (BPA), dibutylphthalate, dioxin, methoxychlor, nonylphenol, polybrominated diphenyl ethers, and perfluorooctanoic acid (PFOA). Effects also occur from exposure to hormones, such as estrogen, and from plant estrogens, such as genistein from soy. The EDCs that affect breast development include anti-androgens and thyroid disruptors as well as estrogens.

This research shows the importance of studies that evaluate the effects of mothers' exposures during pregnancy on breast development and susceptibility to carcinogens in their daughters. Many of these studies evaluate effects on the structure of the mammary gland, using measurements such as the number of terminal end buds (TEBs). TEBs are tear-drop shaped structures where the milk ducts are growing during puberty, and they later mature into structures that can give rise to breast cancer. Studies of prenatal dioxin exposure, for example, show a longer period when TEBs are present and increased numbers of tumors developing when the daughters are later exposed to a carcinogen.

What are the recommendations from the workshop?

Currently, tests to evaluate the safety of chemicals do not assess effects on breast development. The 7 collaborating laboratories concluded that future testing should incorporate studies with prenatal exposure and assessment of changes to breast development at puberty. Additional research is needed to understand the relationships between changes in breast development and later breast-feeding and breast cancer. Changes in breast development should be a focus of chemical risk assessment.

What are the sources of exposure to the EDCs reported to affect breast development?

The chemicals reported to affect breast development are common environmental contaminants and some are in consumer products. They have been detected in human blood or urine in a representative group of U.S. residents tested in the National Health and Nutrition Examination Survey (NHANES). These chemicals are examples:

- Atrazine is a pesticide widely used in agriculture to control weeds. It is found in food and contaminated drinking water, and agricultural workers are exposed.

- Bisphenol A (BPA) is used to make polycarbonate plastics, epoxy resins, vinyl (PVC) and other common materials. It is used in food can liners, water bottles, and thermal paper for receipts, among other uses.
- Dibutylphthalate is used in some consumer products such as paints, modeling clay, and nail polish.
- Dioxin is an industrial byproduct and is primarily a product of chlorine bleaching of paper pulp and of burning PVC and some other plastics. People are exposed primarily from food and breast milk, because this pollutant bioaccumulates in the food chain.
- Methoxychlor is an organochlorine pesticide that is banned in the U.S. It is commonly detected in house dust in older homes.
- Nonylphenol is a plasticizer and a breakdown product of alkylphenol ethoxylate surfactants used in some laundry and other detergents.
- Polybrominated diphenyl ethers (PBDEs) are flame retardant chemicals used in furniture, electronics, and other products. They have been phased out in the U.S. PBDEs are abundant contaminants in house dust.
- Perfluorooctanoic acid (PFOA) is used in some non-stick and stain-resistant coatings on cookware, clothing, carpets, furniture, and other products. It is also used to coat food-use papers to make them grease resistant.

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Related editorial:

Brody, Julia Green, Rudel, R., Kavanaugh-Lynch, M. 2011. Testing chemicals for effects on breast development, lactation, and cancer. *Environmental Health Perspectives*; <http://dx.doi.org/10.1289/ehp.1104077> [Online 22 June 2011].