



Scientists Identify Highest Priority Toxic Chemicals to Target for Breast Cancer Prevention

Study Fact Sheet: Exposure Biomarkers for Suspected Breast Carcinogens

Rudel RA, Ackerman JM, Attfield KR, Brody JG. 2014. **New Exposure Biomarkers as Tools for Breast Cancer Epidemiology, Biomonitoring, and Prevention: A Systematic Approach Based on Animal Evidence.** *Environmental Health Perspectives.*

This study provides a road map for breast cancer prevention by identifying high-priority chemicals and evaluating tools to measure exposure. This is the first study to comprehensively evaluate methods for measuring exposures to suspected breast carcinogens in women's bodies.

These measurement methods in blood, urine, and other tissues are called exposure biomarkers. Biomarkers can be used to study breast cancer risk and to track the success of public health efforts to reduce exposure.

This study helps fill a crucial knowledge gap identified in the Institute of Medicine 2011 report on breast cancer and the environment: "Breast cancer and exposure assessment researchers... should pursue research to improve methodologies for measuring, across the life course, personal exposure to and biologically effective dose of environmental factors that may alter risk for or susceptibility to breast cancer." (p 17)

Background

Only 5-10 percent of breast cancers are due to high-risk inherited genes, and 80 percent of women diagnosed are the first in their family to get it. These statistics are just part of the abundant evidence that breast cancer is not written into inherited genes, so finding additional causes can lead to prevention.

Research has already established links between breast cancer and exposure to certain chemicals, for example, combination hormone replacement therapy (HRT), alcohol, and tobacco smoke. But many chemicals that are similar to these risk factors have never been studied, in part because researchers lacked reliable methods to measure exposures. Exposure measurements are also needed to learn where exposures come from and track the success of exposure reduction efforts. Priorities for exposure tracking include chemicals that are similar to HRT, alcohol, and tobacco smoke, and additional chemicals that cause mammary gland tumors in laboratory animals.

Chemicals that cause mammary tumors in animals include chemicals in gasoline, diesel exhaust, other vehicle exhaust, flame retardants, stain-resistant textiles, paint removers, and drinking water disinfection byproducts.

What was the purpose of this study?

Only a small fraction of chemicals that cause mammary gland tumors in laboratory animals has ever been included in a human [breast cancer study](#). The goal of this study was to greatly expand research about chemical exposures and breast cancer by identifying high priority chemicals for study, evaluating the best methods to measure these chemicals in women's bodies, and identifying health studies in which the exposure biomarkers could be applied.

What was the methodology?

- We started with a list of 216 chemicals that Silent Spring Institute found cause mammary tumors in rodents. Then, we identified which ones were most likely to have common exposures.
- For each of these chemicals, we searched the scientific literature for studies in which researchers had measured either the chemical itself or breakdown products (metabolites) in blood, urine, or other samples from people. We consolidated information about the best measurement methods as a reference for researchers.
- We compared the results from human breast cancer studies and rodent studies to see if their results were consistent to demonstrate that rodent studies can predict results in people.
- We searched for ongoing health studies of large numbers of women in which the exposure biomarkers we identified could be used to evaluate links to breast cancer.

What are the mammary carcinogens you investigated?

We evaluated 102 common chemicals that cause mammary tumors in laboratory studies of rodents.

Gasoline and chemicals formed by combustion are among the largest sources of mammary carcinogens in the environment. These exposures include exhaust from both diesel and gasoline engines, tobacco smoke, and fumes from cooking stoves. Some of these same chemicals can also be found in food, especially if it is charred or burned. Chemicals in this group include benzene and butadiene, which were identified by the Institute of Medicine as high priorities for breast cancer. Polycyclic aromatic hydrocarbons (PAHs), nitroPAHs, acrylamide, and styrene are in this group.

Other mammary carcinogens include solvents, such as methylene chloride and other halogenated organic solvents; pharmaceutical hormones; certain flame retardants; a chemical used in stain-resistant textiles and nonstick coatings; and styrene, which is found in cigarette smoke and is used to make styrofoam. Drinking water can contain mammary carcinogens, such as byproducts of disinfection or solvents that are common well water contaminants.

What did the study find?

- **We identified 102 high-priority chemicals that are linked to breast cancer and that women are commonly exposed to.**
- We found biomarkers that researchers can use to measure women's exposure to 62 of the 102 high-priority mammary carcinogens in blood, urine, or other biological samples. For another 11 chemicals,

we found methods that have been used in animals and could be tested for use in humans. We found no biomarkers for 23 of the mammary carcinogens, although some of these chemicals could be studied using methods very similar to some we did find.

- We consolidated the mammary carcinogens into [17 groups of chemicals](#) that are likely to be common exposures for women. By using measurement methods for these groups, researchers can efficiently evaluate exposures to multiple chemicals simultaneously. For example, several mammary carcinogens used as flame retardants can be measured together. Mammary carcinogen exposures can come from many sources, including tobacco smoke, gasoline, diesel exhaust, air pollution, polyurethane foam, flame retardants, drinking water, and pharmaceuticals, among other sources.
- The US Centers for Disease Control (CDC) regularly measures [23 of the mammary carcinogens](#) as part of the National Exposure Report to track exposure patterns. Some of the biomarkers have been measured in other populations and in workers.
- When a chemical has been included in both human and animal studies, the [results for breast cancer risk generally agree](#). The evidence is consistent in animal and human studies of hormonal pharmaceuticals, ionizing radiation, irregular sleep, alcoholic beverages, ethylene oxide, heterocyclic amines/grilled meat, PAHs/tobacco smoke, and common industrial solvents. However, few chemicals have been studied in humans.
- We found many ongoing studies that could use the biomarkers to greatly expand knowledge about chemical links to breast cancer. We identified 44 cohort studies (studies that follow women long-term) that have collected biological samples in which the biomarkers could be measured to evaluate potential links to breast cancer. More than 3.5 million women are enrolled in these studies. We identified additional studies of girls that could evaluate effects of endocrine disrupting compounds on development and puberty.
- Biomarkers of exposure to mammary carcinogens include measurements of a chemical itself or its metabolites in blood and urine, as well as other kinds of samples (e.g. breast milk, saliva, hair). Generally speaking, measurements in blood and other tissues are more representative of breast tissue exposure than measurements in urine. Measurements of adducts (molecules formed when chemicals or their metabolites bind to DNA or proteins) can in some cases give a better picture of exposure over a long period because they stay in the body longer. Researchers can study exposure to multiple chemicals at once by measuring similar chemicals in one sample, or by measuring metabolites that are shared between multiple carcinogens.

Why do you think that chemicals that cause mammary tumors in animals are relevant to breast cancer in humans?

Animal studies have historically done a good job of predicting human carcinogens; every known human carcinogen that has been extensively tested is also carcinogenic in animals. Most of the rodent mammary carcinogens damage DNA, further strengthening the evidence that they might cause cancer in humans.

Additionally, when the same chemical is studied in relation to both human breast cancer and rat mammary tumors, the results almost always agree.

What are the major limitations of this study?

Most tumor studies in rodents only expose the animals to the chemical when they are adults, so the studies can't tell us about the effects of hormonally active chemicals that might increase breast cancer risk by altering mammary gland development. A limitation of our study is that we don't know which chemicals affect breast cancer risk by altering mammary gland development, so they are not included. In addition, not all rodent mammary carcinogens are equally carcinogenic. The chemicals vary in the strength of evidence that they are likely to be human carcinogens, so each must be evaluated for potency. Information about the strength of evidence is found in the [Mammary Carcinogens Database](#).

What are the implications for researchers?

Breast cancer researchers can apply the biomarkers identified in this study in stored biological samples to accurately measure the exposure of study participants to chemicals of concern long before their diagnoses. Because breast cancer can take so long to develop, and because exposures during early life can influence a woman's risk later on, the most important chemical exposures are often those that happened decades earlier.

One of the most promising opportunities for finding associations is to study exposures to DNA-damaging carcinogens in younger women with high exposures in their workplace or elsewhere, in studies that continue collecting data on participants for at least 10-20 years. As an example, researchers could use new biomarker methods for measuring exposure to chemicals such as butadiene, PAHs, and nitroPAHs to investigate the possible relationship between diesel and other vehicle exhaust and breast cancer.

Additional research is needed to develop biomarkers for the 29 mammary carcinogens for which we did not find existing methods, including products of drinking water treatment that damage DNA and cause mammary gland tumors.

What are the implications for public health?

The biomarkers we identified can be used now to track exposures and evaluate the best strategies to reduce them. The International Agency for Research on Cancer, Institute of Medicine committee on breast cancer and the environment, and other authoritative reviews state that animal carcinogens are reasonably expected to be human carcinogens, so exposure reduction is a sensible public health goal. The CDC is currently tracking 23 of the mammary carcinogens and methods are ready to use for adding many more chemicals with important public health implications. Health and environmental officials can use these measurements to plan and evaluate strategies to reduce exposure. Biomonitoring can also identify highly exposed populations.

Breast cancer is the leading cause of death for American women between the ages of 30 and 50. Because breast cancer is so common, with more than 200,000 women diagnosed in the US each year, and exposure to mammary carcinogens is widespread, finding and eliminating the risks would save many lives.

What can I do to reduce my exposures?

While scientists continue to learn more about how these chemicals affect humans, there is enough information to begin reducing our exposures. Here are some effective ways to reduce exposures.

- Avoid fuel and exhaust:
 - ✓ Turn the engine off instead of idling.
 - ✓ Use electric or hand-powered lawn mowers and leaf blowers, limit use of snow-blowers.
 - ✓ Support strong emission standards and anti-idling rules.
 - ✓ Buy a fuel efficient vehicle and walk or take public transit when you can.
 - ✓ Don't store gasoline in your home, basement, or attached garage.
- Avoid second-hand tobacco smoke (or try to quit!)
- Use ventilation fans when cooking.
- Limit consumption of charred foods.
- Find a dry-cleaner who doesn't use PERC or other solvents; ask for "wet cleaning."
- Avoid stain-resistant rugs, furniture, and fabrics.
- Ask for furniture that doesn't contain flame retardants, including in the foam. If flame retardant free foam isn't available, choose furniture made from naturally flame-resistant fabrics and padding such as wool, hemp, polyester, latex, down, or leather.
- Choose rug pads made from felt, jute, or rubber rather than foam.
- Store solvents and gasoline properly (tightly sealed, away from children) and use only in well-ventilated areas.
- In your workplace, seek to reduce exposure by switching to less toxic materials, increasing ventilation, and using personal protective equipment.
- Use and maintain a solid carbon block drinking water filter.
- Reduce exposure to chemicals in house dust by removing shoes at the door, using a vacuum with a HEPA filter, and cleaning with wet rags and mops.

Who funded this study?

The study was funded by Avon Foundation for Women.

How can I get more information?

Visit the Silent Spring Institute website at www.silentspring.org.

CONTACT: Amelia Jarvinen jarvinen@silentspring.org, 617-332-4288 x226