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Environmental Chemicals and Breast Cancer Risk: Why is There Concern?

Healthy Ecosystem

Breast cancer rates are the highest in North America, Northern Europe and Australia. Breast cancer rates are much lower in Japan, China, Africa and India.

There has been a growing interest in whether environmental factors, including whether exposures to certain chemicals or changes in lifestyle, may increase the risk of breast cancer. Risk factors consistently associated with a higher breast cancer risk are called "established" risk factors. Established risk factors include getting older, having regular menstrual periods earlier, going through menopause later in life, having your first child late in life, not having any children, having a mother or sister with breast cancer, past exposure of breasts to ionizing radiation, or having certain types of benign breast disease. But these factors only account for about 25 to 50% of breast cancer cases.

Geography, Migration and Rates of Breast Cancer

Breast cancer rates vary widely in different parts of the world. Rates are the highest in North America, Northern Europe and Australia. Breast cancer rates are much lower in Japan, China, Africa and India. It is not clear why there are geographical differences in breast cancer rates. Differences in age of childbearing, diet, lifestyle and exposure to environmental chemicals have been offered as possible explanations. Within one or two generations, the breast cancer rates of Japanese women migrating to the US increase, and become similar to the higher breast cancer rates of western women. Results of studies on twins in Scandinavia also suggest that a woman's environment plays a significant role in determining her breast cancer risk.

Exposure to Environmental Chemicals

We are exposed to thousands of naturally occurring and synthetic chemicals over a lifetime. Many chemicals are essential for life and are beneficial, while exposures to other chemicals can be harmful and affect our health. There are many ways we can be exposed to chemicals. This includes exposure in the air we breathe, in the food and beverages we eat, and by contact with our skin. The fetus can be exposed to chemicals that cross the placenta during pregnancy. Some environmental contaminants can pass from a mother's body to an infant through breast milk. Certain chemicals can be stored in fish or animal fat, can pass up and concentrate through the food chain, and be stored in our bodies for long periods of time. Other chemicals may be broken down and quickly eliminated from the body. Some chemicals first need to be "activated" by enzymes in the body to become cancer-causing chemicals (carcinogens). Other chemicals pose no cancer risk, while others may act as beneficial "anti-cancer" agents. It is impossible to make generalizations about environmental chemicals. Each

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chemical has a unique pattern in the way it is handled by the body, and a different potential for whether or not it can contribute to breast cancer risk.

Chemicals in the Home & Workplace

We can be exposed to a variety of synthetic chemicals in many different settings, including in our homes and workplaces. There are some chemical exposures in the workplace that have been associated with a higher risk of breast cancer. More research is needed to help identify the chemicals of concern for different professions and workplace situations. There are relatively few studies of women in the workplace (most occupational studies of cancer risk have been done on men). There is a need for better quality studies to give us better answers. Many of the studies done so far had very limited data on exposure to specific chemicals, and usually only small groups of women were followed for a limited time period. Several groups that need further evaluation because of potential exposures to known or potential carcinogens include those employed in the chemical and pharmaceutical industries, laboratory and biomedical workers, cosmetologists and hair dressers, workers in printing and textile dyeing industries, airline personnel, health care workers, and metal plate workers. Of recent interest is whether breast cancer risk may be indirectly affected in night-shift workers exposed to "light at night" which may affect melatonin synthesis. Scientists are exploring whether changes in melatonin levels may affect levels of estrogen and breast cancer risk.

Researchers are also interested in measuring chemicals women may be exposed to every day in our homes. Researchers on Long Island, New York and on Cape Cod, Massachusetts are measuring levels of environmental chemicals in the homes of women with and without breast cancer. Such studies may help identify the types of chemicals in the home that may be linked to a higher risk of breast cancer.

Breast Cancer Risk?

There has been concern about exposure to pesticides because of their widespread use in agriculture for crop and livestock protection, for public health in controlling disease-bearing insects, for pest control in homes, schools, workplaces, gardens, and recreational areas such as parks and athletic fields. Currently, there are about 865 pesticide active ingredients registered with the Environmental Protection Agency (EPA), and thousands of products containing these chemicals alone or in combination.

Much of the concern about whether pesticides affect breast cancer risk stems from observations of higher rates of cancer in male workers with high exposures to pesticides. There are higher rates of some cancers in male farm workers, including lip and skin cancer, non-Hodgkin's lymphoma, and cancer of the stomach, brain and prostate. Some of these cancers are due to excessive exposure to UV radiation from the sun (lip and skin cancer). There are many types of exposures on the farm that may affect cancer risk, including exposures to pesticides, solvents, fuel exhaust, and toxins (called mycotoxins) from molds in stored crops. While some scientists have found higher cancer rates in farmers exposed to certain pesticides, other studies have not supported an association. An ongoing, large-scale study that will help provide better answers to whether specific chemicals used in agriculture affect cancer risk is the "Agricultural Health Study" (for more information go to http://www.aghealth.org/index.html).

There are very few studies that have evaluated whether farm women have a higher risk of breast cancer. In a study of North Carolina farm women, overall breast cancer rates were lower in women who lived or worked on a farm compared to women who did not work or live on a farm. These farm women tended to have healthy life-styles that could have reduced their risk of breast cancer. However, in this study, one group of farm women who did not wear protective clothing when applying pesticides had a two-fold higher risk of breast cancer compared to women who did take proper precautions. The results of this small study suggest that breast cancer risk may be increased in some farm women with high exposures to pesticides, and illustrate the importance of reducing exposures to pesticides in workplace situations.

Organochlorine Chemicals

Organochlorine pesticides were used extensively during and after WWII because of their long-lasting effects in controlling insects. Most

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were banned during the 1970s and '80s in the US, Canada and Europe because of human health and ecological concerns. Some examples of organochlorine pesticides include: DDT (used in mosquito control and agriculture), dieldrin (used to control termites and other soil insects), chlordane and heptachlor (used to control termites and fire ants), lindane (currently used in agriculture and anti-lice shampoos), and hexachlorobenzene (fungicide with past use to prevent mold on crops). These long-lasting chemicals can concentrate up the food chain and are stored in body fat of animals, fish and humans. Some are endocrine disrupters that affect reproduction in wildlife, especially birds and reptiles. While there are links to some types of cancers (for instance, several organochlorines induce liver or thyroid tumors in laboratory animals), effects on breast cancer risk in humans have been studied only recently.

The organochlorine pesticide that has been studied the most extensively has been the insecticide DDT. Over time, DDT breaks down in the environment to a very long-lasting chemical called DDE. Early reports suggested that women with high levels of DDE in their blood or fat had a higher risk of breast cancer. However, the majority of the more recent, well-controlled studies have not been able to confirm these findings. Most of these studies have looked at breast cancer risk in white women living in North America and Europe. These studies of western women have not shown a higher risk of breast cancer in those with higher levels of DDT or DDE. Other populations, including different ethnic groups, have not been studied as well. The results from several studies suggest that breast cancer risk may be higher in African American women who have higher body levels of DDE. More studies are need to confirm these findings, and to see if breast cancer risk is higher for women who live in less industrialized tropical countries that still use DDT against mosquitoes for malaria control. For many of the other organochlorines, we have very limited data from human studies. Breast cancer risk was higher in Danish women with high blood levels of dieldrin, but the few studies done on American women have not confirmed this finding. For dieldrin, and other organochlorine pesticides, there are too few studies in women to make a conclusion of whether or not body levels can predict breast cancer risk.

Early Chemical Exposures

In utero exposures to estrogenic chemicals may increase breast cancer risk. A drug that acts like estrogen, called diethylstibestrol (DES), was prescribed to pregnant women form the mid-1940s to '70s, to prevent abortions. Daughters of women that were treated with DES have a moderately higher breast cancer risk. DES can also cause mammary (breast) tumors in mice. This is one of the reasons researchers are interested in whether early exposures to chemicals in the womb, or during childhood and adolescence when the breast is developing, affects breast cancer risk later in life (See BCERF Fact Sheet no. 9 on *Childhood Life Events and the Risk of Breast Cancer*). Results from animal studies have shown that early exposures to some chemicals can have permanent effects on the way the breast develops and its susceptibility to carcinogens. The developing mammary gland (breast tissue) of young rats and mice have bud-like structures composed of rapidly dividing cells. These dividing immature breast cells are more susceptible to the damaging effects of cancer-causing chemicals.

Early exposure to certain environmental chemicals may keep the mammary gland in an immature state for longer periods of time, increasing its susceptibility to carcinogens. So, many chemicals may not cause a tumor to develop directly, but they may work in subtle ways to increase breast cancer risk. For instance, in one study female rats were exposed pre-natally to an environmental contaminant, a dioxin called TCDD. When these dioxin-exposed rats were older, they were also exposed to a known breast carcinogen called dimethylbenz [*a*]anthracene (DMBA). The female rats pre-treated with dioxin developed more breast tumors than the rats not pre-treated with this dioxin. The researchers suggested that dioxin treatment prenatally changed how the breast tissue developed, keeping the breast in an immature state with a greater number of dividing bud structures for a longer period of time. Similarly, results of preliminary studies conducted by EPA researchers have suggested that prenatal treatments with the herbicide atrazine can also help keep rat breast tissue in an immature state for prolonged periods of time. While the implications for human cancer risk are not yet known, it is important that researchers fully explore the many ways chemicals may affect breast cancer risk.

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For example, women with high body levels of environmental chemicals called polychlorinated biphenyls (PCBs) usually do not have a higher risk of breast cancer. However, in one study breast cancer risk was higher in a group of women who had both a high level of PCBs and a variation in an activation gene called CYP1A1. This is an example of a "gene-environment interaction."

Gene-Environment Interactions?

Many chemicals have to become "activated" in the body to become carcinogens. Some people have differences (called also variations or polymorphisms) in certain genes that control these activation pathways. If a person has a variation in such gene, this may result in more activation and a higher level of the active form of the carcinogen. This may put the person at greater risk for developing certain cancers, including breast cancer. For example, women with high body levels of environmental chemicals called polychlorinated biphenyls (PCBs) usually do not have a higher risk of breast cancer. However, in one study breast cancer risk was higher in a group of women who had both a high level of PCBs and a variation in an activation gene called CYP1A1. This is an example of a "gene-environment interaction." More research is being done to identify important gene-environment interactions. This will help identify groups of women who may have a higher breast cancer risk if they are exposed to certain chemicals.

New Avenues for Research

We can expect to see more studies explore breast cancer. For instance, there is interest in whether certain antihistamines and anti-depressants affect breast cancer risk. There also is interest in whether environmental chemicals, such as certain phthalates used in plastics, play a role in premature breast development and later risk of breast cancer. New powerful molecular techniques have been developed that may help to identify "molecular" footprints, including chemicals that activate specific cancer genes or that turn off genes that can suppress cancer. Studies are ongoing to screen for and identify breast carcinogens in animal cancer bioassays. New screening techniques are being developed that will allow for more rapid screening of a larger number of chemicals. Researchers will continue to identify gene-environmental interactions that may help identify groups of women who may be at higher risk when exposed to certain chemicals, and identify endocrine disrupting chemicals which can support the growth of breast tumors. More research is needed not only to define the types of exposures encountered in the workplace and the home, but also to evaluate how exposure during critical periods of breast development may affect cancer risk later in life. A combination of human, animal, and molecular-based studies are needed to address how environmental chemicals may affect the risk of breast and other cancers.

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