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## Women's Exposure to Chemicals May Explain Unexpected Breast Cancer

Vials of blood from the 1960s may help resolve why women without a family history still developed breast cancer

By Lindsey Konkell and Environmental Health News | Monday, February 25, 2013

Deep in a laboratory freezer, 100,000 vials of blood have been frozen for the better part of five decades.

For scientist Barbara Cohn, it's a treasure trove. Collected from more than 15,000 San Francisco Bay Area women after they gave birth in the 1960s, each vial of blood holds a woman's lifetime of secrets.

Scientists say these vials could help them unravel one of the most enduring medical mysteries: Why do some women, with no family history, develop breast cancer?

The blood bears the chemical signature of environmental pollutants, some long banned, that the women were exposed to decades ago. Cohn, who directs the research in Berkeley, Calif., believes these early-life exposures may hold the key to understanding a woman's risk of breast cancer today.

The women's blood is being tested for traces of dozens of pollutants – used by industry and found in many consumer products – that can impersonate estrogen and other hormones. The theory is that early exposure to these chemicals, even before birth, inside the mother's womb, may fundamentally alter the way that breast tissues grow, triggering cancer decades later.

Cancer patients and their doctors have long puzzled over what factors in a woman's environment may raise her risk of breast cancer. One of every eight women in the United States is diagnosed with breast cancer during her lifetime, with more than 232,000 new cases diagnosed yearly, according to the American Cancer Society. Only five to 10 percent can be accounted for by genetics; other known risk factors include age, obesity and low physical activity.

Earlier this month, a science advisory panel urged the federal government to fund more projects aimed at uncovering the environmental causes of breast cancer because eliminating these factors may provide the greatest opportunity to prevent it.

It's particularly vexing for scientists because it's difficult to unlock a woman's exposures during her most critical times for breast development: in the womb and during puberty and pregnancy.

“As researchers looking at adult outcomes of disease processes such as breast cancer, one of the biggest challenges we face is trying to



Women attend a fundraiser for breast cancer in San Francisco. Image: Flickr/cpurl

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get a handle on prenatal exposures and what is going on in the prenatal environment,” said Shanna Swan, an environmental health scientist at Mount Sinai School of Medicine in New York.

Many scientists have been looking for connections between various environmental exposures and the disease – with mixed results. Some findings suggest links to a few chemicals, including the banned pesticide DDT. But others have found no link.

For example, experts from the American Cancer Society, reviewing previous studies, in 2002 found no association between breast cancer and chlorinated chemicals including DDT.

And in 2011, an institute of the National Academies of Sciences reported “a possible link” between breast cancer and some common ingredients of vehicle exhaust, benzene and 1,3-butadiene. But the report said the jury is still out for most other widespread chemicals, such as pesticides, ingredients of cosmetics and bisphenol A (BPA).

Nevertheless, absence of evidence isn't evidence of absence, said Elizabeth Ward, National Vice President of Intramural Research at the American Cancer Society. Many of the biggest risk factors remain unknown, she said.

The problem with most studies is that they measured levels of chemicals in women later in life, after they were diagnosed with cancer, not during periods when the breast is most susceptible, said Suzanne Fenton, a reproductive toxicologist at the National Institute of Environmental Health Sciences in North Carolina.

“The research doesn't prove that the link doesn't exist or that these chemicals are safe for the breast,” Fenton said. “It shows that we may not have been asking the right question.”

The strongest evidence for this link emerged decades ago. Researchers first suspected that hormone-mimicking chemicals may play a role in breast cancer when they discovered that women who took the anti-miscarriage drug diethylstilbestrol (DES) – a potent form of estrogen prescribed for pregnant women from 1938 until 1971 – had about a one-in-six lifetime risk of developing breast cancer. The risk is one in eight for all women. In addition, their daughters, who were exposed to DES in the womb, developed breast cancer at about two times the rate of unexposed women.

Some scientists say timing of exposure may be the single most important factor when evaluating how chemicals may contribute to breast cancer risk.

The breast is a complex tissue that undergoes several important periods of development and remodeling over the course of a woman's life. During these periods – before birth when the bud of the mammary gland forms, at puberty when breast cells are rapidly growing and dividing and during pregnancy as the mammary gland transitions to lactation – the breast may be especially susceptible to outside chemicals.

When breasts are exposed to hormone-like substances during those sensitive times, it could “influence susceptibility of the tissue to carcinogens or other hormonal stimuli that could increase cancer risk later on,” said Ruthann Rudel, a researcher at the Silent Spring Institute, a nonprofit research group in Massachusetts, and lead author of a 2011 review.

Cohn and colleagues at the Public Health Institute are using the blood samples of more than 100 women who enrolled in the Child Health and Development Studies in the 1960s to investigate exposures during two of these critical periods, pregnancy and postpartum. The women were members of the Kaiser Permanente Health Plan in the Oakland, Calif., area who gave birth between 1959 and 1967.

The scientists recently reported that women who had high levels of a certain PCBs in their blood shortly after giving birth were three times more likely to develop breast cancer later in life than women with lower levels. Because PCBs break down very slowly in the body, a woman's blood levels postpartum may also predict the PCB levels in her blood during earlier periods of her life, such as puberty, Cohn

said.

Banned in the United States 35 years ago, the industrial chemicals persist in the environment and accumulate in food webs. Nearly every U.S. resident still has detectable levels in his or her blood.

In a previous study, Cohn and her colleagues demonstrated that age at time of exposure matters for other chemicals, too. In the same group of women, they found that those with high blood levels of the banned pesticide DDT shortly after giving birth were five times more likely to develop breast cancer before age 50 than the women with the lowest blood levels. Other studies measuring DDT exposure later in life found no link.

Cohn can't say for sure that the associations they observed between breast cancer and PCBs or DDT were not due to some other factor. "No human study can be definitive," said Cohn, an epidemiologist who has been involved with the study group for 17 years. "It's impossible to measure every single exposure pertinent to breast cancer."

Laboratory research may bear out a definitive link. In lab animals, scientists can test the effects of various levels and mixtures of chemicals, which would be unethical in humans. "The work we do in humans helps frame the type of questions to be answered by animal studies," Cohn said. Such collaboration, she said, "is critical to advancing our knowledge."

These questions involve knowing more about how hormonally active chemicals interact with developing breast tissue.

"A chemical that has weak effects later in life may have very different effects during earlier periods of development when the mammary gland is most sensitive," said Dr. Hugh Taylor, professor of obstetrics and gynecology at the Yale School of Medicine.

Taylor and his colleagues found that in mice, BPA, an estrogen-like chemical, can have the same effect in a developing fetus as the drug DES, a more potent estrogen. Both "turned up" the expression of genes in the developing mammary gland that are known to play a role in tumor formation. "You are essentially changing the software so that things are programmed to read differently," Taylor said.

Most cancers aren't one single piece of damage, but a collection of injuries to a cell or a tissue over a lifetime, making it hard to pin a cause on any one agent, Taylor said. Yet, if endocrine disruptors give you a predisposition for tumor growth, "you're starting life with one strike against you," he said.

BPA, used to make hard plastics, liners of food cans and some paper receipts, is found in most human bodies.

Studies in mice and rats suggest that exposure to BPA and other endocrine disruptors in the womb not only alters the structure of the breast, but the way that the tissues communicate with one another and receive hormonal signals from other parts of the body.

"BPA sets the thermostat in a more sensitive way so the mammary gland has more sensitivity to estrogen, and the breast tissue now exhibits an exaggerated response to the hormone. It sees a little bit of estrogen and now thinks it is a lot," said Dr. Ana Soto, a cancer researcher at Tufts University School of Medicine in Massachusetts. And the body can't tell the difference between synthetic estrogen mimics and natural estrogens.

BPA and other chemicals also may play a role in breast density – a known risk factor for breast cancer. A preliminary study by University of Wisconsin researchers found that women with higher blood levels of BPA had denser breast tissue than women with low levels.

With so much uncertainty about environmental risk factors, these issues remain largely absent from major breast cancer awareness campaigns.

“Despite billions spent in the name of breast cancer, we still don’t know enough about the causes,” said Karuna Jaggar, executive director of Breast Cancer Action, a San Francisco-based advocacy organization that itself is the watchdog of the breast cancer movement.

While decades of research have failed to turn up strong, environmental risk factors, Cohn is optimistic that scientists are now on the right track. “The science is playing catch up. We have learned from what we didn’t learn,” she said.


Nevertheless, federal funding is in short supply, and there is always the risk it will run out for the Oakland group. Research now is turning to the second and third generations -- the daughters and granddaughters of the original study members. Just like she did with their mothers and grandmothers, Cohn will look for patterns of exposure and disease as they age.

Like a treasure trove about to be unlocked, Cohn said these generations of women “hold the key to understanding” breast cancer.

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