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Program on
Breast Cancer and Environmental Risk Factors

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Breast Cancer and The Estrogen Connection

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The Estrogen Connection: Estrogen, a hormone made by a woman's ovaries, has a role both in the normal development of breast tissue and in the development of breast cancer. Lifelong exposure to estrogen has been tied to an increased risk of breast cancer, and the body of evidence shows that estrogen exposure has a important role in determining breast cancer risk (Yager and Davidson, *New England Journal of Medicine*, 354(3):270-282, 2006).

Women with higher levels of estrogen in their blood have an increased risk of breast cancer (*J. National Cancer Institute*, 94(8):606-616, 2002; Missmer et al., *J. National Cancer Institute*, 96(24):156-1865, 2004). Most breast tumors depend on estrogen for growth. There is also evidence that many risk factors for post-menopausal breast cancer are associated with increased exposure to estrogen (e.g. obesity, alcohol use, hormone therapies). Current use of oral contraceptive agents, and in utero exposure to a synthetic estrogen called diethylstilbestrol, have also been found to moderately increase breast cancer risk (Shantakumar et al., *American Journal of Epidemiology*, 165(10):1187-1198, 2007; Troisi et al., *International Journal of Cancer*, 121(2):356-60, 2007). Hence many breast cancer risk factors are linked to estrogen exposure. This is why there is concern that environmental chemicals that can mimic estrogen may also influence the risk of breast cancer.

The Biology: One of estrogen's many roles is to signal cells to grow and divide (Yager and Davidson, *New England Journal of Medicine*, 354(3):270-282, 2006). This is important both in the normal development of the breast, but this also influences breast tumor development and the growth of most breast tumors. This process involves estrogen interacting with a receptor. Estrogen receptor-alpha provides a gateway for estrogen's entry into the cell and for interaction with key genes involved in cell division. Estrogen-stimulated cell division may lead to increased mutations in DNA. Mutations in key genes that control a cell's ability to grow, divide and die can lead to an increased cancer risk.

These changes take many years to occur. During this process, breast cells start to divide more and form hyperplasias. These hyperplastic cells acquire more estrogen receptors (Lee et al., *Breast Cancer Research*, 8(1):R6, 2005). Certain breast hyperplasias are thought to be precancerous. Estrogen can drive these precancerous breast cells to divide further and acquire additional mutations. Some hyperplasias progress to invasive breast tumors. Since over 75% of breast tumors have estrogen receptors (Li et al., *J. Clinical Oncology*, 21(1):28-34, 2003), estrogens can continue to be a signal for breast tumors to continue to grow. Therapeutic strategies to treat estrogen-dependent breast cancer have focused on preventing estrogen from interacting with its receptor (Yager and Davidson, *New England Journal of Medicine*, 354(3):270-282, 2006).

Environmental Estrogens: Researchers have identified chemicals in the environment that can mimic the effect of estrogen. These are called environmental estrogens (sometimes called xenoestrogens). While environmental estrogens are weaker (less potent) than the estrogen our own bodies make, we are exposed to many environmental estrogens in everyday life. The Centers for Disease Control and Prevention (CDC) researchers have found evidence of widespread, low-level exposure to a variety of environmental estrogens, including bisphenol A, nonylphenol, UV-screens (benzophenones), and metalloestrogens, such as cadmium and lead.

Scientists are concerned that even at low levels the environmental estrogens we are exposed to can add up, and may work together with the body's own estrogen to increase the risk of breast cancer (Rajapakse et al., *Environmental Health Perspectives*, 110(9):917-921, 2002; Silva et al., *Environmental Science and Technology*, 36(8):1751-1756, 2002). European researchers have developed models to predict how exposure to mixtures of low levels of

environmental estrogens may influence the risk of breast cancer and other health effects, and are urging limiting exposure to these chemicals (Monograph on Endocrine Disruptors-Exposure Assessment, Novel End Points, and Low-Dose and Mixture Effects, Environmental Health Perspectives, Vol. 115, Suppl. 1, December 2007; Monograph based on a 2006 conference in Prague, see statement at <http://www.ehponline.org/docs/2007/10517/suppl.pdf>).

Scientists suggest that we need better models to assess the health impacts of environmental estrogen, because current methods that assess the risk of single chemicals do not take into account that we are exposed to a mixture of many environmental estrogens that have a common mechanism of action (Kortenkamp, International Journal of Andrology 31(2):233-240, 2008).

Conclusions: Because the strength of the scientific evidence indicates that exposure to estrogen increases the risk of breast cancer, monitoring studies suggest wide spread exposure to a variety of environmental estrogens, and modeling studies suggest that low level exposures to environmental estrogens can add up and work with the body's estrogen, we conclude that this evidence suggests reducing exposure to environmental estrogens is warranted. Therefore, BCERF is providing information on everyday exposures to environmental estrogens, ways to identify products with environmental estrogens, ways to avoid environmental estrogens exposure, as well as ways to keep environmental estrogens out of the environment, as strategies to reduce exposure to environmental estrogens and hence reduce the risk of breast cancer risk.

Please view our videos on environmental estrogens in everyday products. You will find ways to reduce your exposure and ways to prevent these chemicals from entering the environment.

The Estrogen Connection: [Cosmetics and More](#)

The Estrogen Connection: [Plastics](#)

The Estrogen Connection: [In the Dump and Down the Drain](#)

More on Estrogen Connections: BCERF reviews the current research and provides fact sheets on the breast cancer risk of other factors associated with estrogen exposure, including alcohol use, obesity and hormonal treatments.

FS No. 13 Alcohol: Breast Cancer Risk [Text](#) | [PDF](#) | [Bibliography](#)

FS No. 56 Obesity and Breast Cancer [Text](#) | [PDF](#)

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