Biology of breast cancer

Cancer is a complex disease involving many stages of development, often over long periods of time. The “causes” of breast cancer are numerous and not always known. However, a closer look at the biology of breast cancer can help us to understand why exposure to harmful chemicals such as EDCs matter and why they are of potential significance to breast cancer risk.

The role of DNA in cancer

DNA plays a central role in cancer development. Cell growth is regulated by DNA, which sends instructions to our cells. Each time a new cell is formed by division, the instructions (or DNA) are copied. Ideally they should be copied exactly each time, but sometimes they are not.

DNA contains repair genes which are able to self-correct mistakes in the structure of the DNA as they occur. However, some mistakes - known as mutations - do not get corrected; instead the error is reproduced and passed on. Over time, mutations accumulate and their combined effects can lead to cancers.

The more often a cell divides, the greater the risk of mutations occurring and accumulating. Anything that accelerates the rate of cell division also increases the likelihood of mutations occurring. Oestrogens (female sex hormones), for example, can stimulate cell division. Other agents such as X-rays, ultraviolet light and some chemicals can also increase mutation rates, by damaging DNA directly.

The role of oestrogen in breast cancer

Breast cancer occurs when abnormal cells in the breast grow in an uncontrolled manner. It occurs in both men and woman, but women are at greater risk due to their breast development and lifelong exposure to oestrogens.

Oestrogens are present in relatively high concentrations in the breast and play a central role in many breast cancers (1). Oestrogens exert their effects on cells at very low concentrations. They act by entering cells and binding to specific proteins called oestrogen receptors. These can then bind to specific DNA sequences in the cell’s nucleus resulting in rapid cell multiplication and differentiation (2). Rapid cell multiplication means there is less time for DNA repair, leading to DNA damage and mutations (3). Oestrogen break-down products also contribute to risk; they can bind to DNA and generate mutations in critical genes that initiate breast cancer (4).

Causes and risk factors for breast cancer

Biological risk factors

- Oestrogens: Naturally occurring oestrogens increase the risk of developing breast cancer, mainly because of their ability to increase rates of cell division and their ability to promote the growth of oestrogen-responsive tumours (5).

- Gender: Females have a higher lifetime exposure to oestrogens. After menopause, fat tissue becomes the main source of oestrogens for women (6) and is the main source for men (7).

- Pregnancy and breast feeding: Women who have children at a younger age and women that breast feed have a reduced risk of developing breast cancer (8,9). However, pregnant women have a higher risk of breast cancer due to this increase in reproductive hormones.

- Age: As time passes and our cells undergo more divisions, DNA mutations accumulate and there is a higher chance that mutations associated with cancer will occur (10). As a woman ages, the levels of androgens (male sex hormones) and progesterone that normally exert inhibitory effects on the growth of breast tumours reduce, thereby increasing breast cancer risk (11).

- Family history and genetics: Our genetic makeup is associated with our breast cancer risk and is thought to account for approximately 20-30% of all breast cancer cases (12).

- Benign breast disease: Benign (non-cancerous) breast lumps are common in women. Those with certain types have an increased risk of developing breast cancer (13).

- High breast density: Mammographically dense breast tissue is associated with epithelial cell proliferation which is also associated with breast cancer (14).

Lifestyle risk factors

As well as biological factors, breast cancer risk is affected by lifestyle choices.

- Weight: Being overweight is associated with an increased risk of breast cancer. Obesity is associated with higher levels of circulating oestrogens in the body which in turn increases breast cell division and the rate of growth of oestrogen-responsive tumours (15). Lack of physical activity (16) and a diet low in fruit and vegetables is thought to contribute to increased risk (17).

- Alcohol consumption: Alcohol metabolism produces chemically reactive molecules containing oxygen which may increase cell proliferation and cause mutations that can contribute to breast cancer. Additionally, alcohol metabolism involves the conversion of alcohol to acetaldehyde. Acetaldehyde can induce DNA damage associated with cancers (18). Alcohol intake is also associated with increased concentrations of circulating oestrogens in the body (19).

- Ionizing radiation exposure, especially during adolescence, is known to be associated with an increased risk of breast cancer (20). Radiation can damage DNA and generate mutations.

- Other carcinogens: Dioxins, polychlorinated hydrocarbons (21) and tobacco smoke (22), have all been linked to breast cancer, mainly when exposure occurs between menarche and first pregnancy. Air pollution, especially nitrogen oxides originating from car exhaust fumes, may also increase premenopausal breast cancer risk (23).

- Shift work is associated with increased breast cancer risk (24), possibly due to a decreased production of melatonin, a hormone thought to have cancer protective properties.

Endocrine Disrupting Chemicals

There is growing scientific evidence that routine exposures to substances known as endocrine disrupting chemicals (EDCs) can lead to cell changes that may increase the risk of developing breast cancer (25).

EDCs are chemicals that interfere with the normal hormonal regimes within the body. Some EDCs mimic and enhance the effects of the body's normal oestrogen production. Others interfere with the natural binding of hormones to cell receptors, and others may cause epigenetic changes which switch genes on or off within certain cells (26). In a healthy body there is a finely regulated control of hormonal levels and actions. EDCs present in the external environment can interfere with this balance, in potentially harmful ways.

Some of these EDCs have a medical or clinical purpose. For example, Diethylstilboestrol (DES), once used as a drug treatment to reduce the risk of miscarriage, was found to increase breast cancer risk (by 40%) in those who used it (27). It also increased breast cancer risk in daughters of women who used this drug (28). Hormone Replacement Therapy (HRT) and the oral contraceptive pill are also both thought to increase risk during the period in which women use the drugs (although increased risk is no longer evidence within five and ten years of stopping treatment (29)).

Other endocrine disrupting chemicals: The above are examples of a medical or voluntary exposure to a risk; matters of individual need or choice. A more contentious debate surrounds other endocrine disrupting chemicals which we are usually involuntarily exposed to, such as bisphenol A (BPA), a synthetic oestrogen used in plastics, parabens used as preservatives in food and cosmetics and phthalates, used in plastics and fragrances. All are weakly oestrogenic in tissue culture, and some have been found to act additively with natural oestrogens and other compounds (30,31) to adversely impact the breast, in a way which could increase its vulnerability to breast cancer. Although most EDCs do not directly cause genetic mutations, several that are associated with increased breast cancer risk, including BPA, have been shown to cause epigenetic changes that may be associated with breast cancer (32). These are examples of risks that may be pervasive and unrecognised and to which we are unknowingly or involuntarily exposing ourselves. For more on EDCs see here.

Breast Cancer UK position

- Breast Cancer UK is calling for increased research investment into all of the risk factors associated with breast cancer
- An improved cancer strategy based on a better understanding of the causes of cancer and an acknowledgement of the environmental causes of the disease.
- Greater investment and efforts towards primary prevention
- Improved chemicals regulation of harmful chemicals including EDCs – and their phase out from products such as food and drinks packaging, cosmetics and toys.

Please see here for a list of references cited and for more information download our Background briefing on Breast Biology

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