In-utero exposures

What are in-utero exposures?

Although the womb is traditionally exemplified as safe and protected, just as with alcohol consumption and smoking, there is growing concern that exposures to harmful chemicals may have adverse effects on a developing child in the womb (in-utero).

The growth of a baby inside the womb and after birth is mediated by hormones, such as oestrogens, progesterone, androgens, insulin and thyroid hormone, which are released from endocrine glands (including the placenta) into the bloodstream and transported to different tissues and organs. For normal growth and development to occur, tissues require specific concentrations of particular hormones at particular times (1). This is why early development is especially susceptible to those chemicals that disrupt the hormone (endocrine) system (so called endocrine disrupting chemicals or EDCs).

Why should we be concerned?

Studies show that EDCs are commonly found in human and animal tissues, including the placenta and amniotic fluid (2). For example, BPA is routinely found in blood, amniotic fluid, breast milk and the placenta (3). Phthalates, parabens, synthetic musks (fragrances), pesticides and UV filters (4) have been shown to be present in breast milk, and polychlorinated biphenyls, dioxins and methylmercury in placenta (5).

Studies also show that EDCs can affect the reproductive system of both sexes by interfering with hormones such as testosterone and oestrogens. Studies on wildlife and in the laboratory suggest that foetal exposure to EDCs may result in problems such as deformed reproductive organs and decreased fertility in adult life (6, 7, 8). In human studies, EDCs have been associated with an increase in incidence of endometriosis, infertility and reproductive cancers (9).

Some changes induced by exposure to EDCs during early development may cause permanent alterations that can be passed on to future generations. Such changes may affect "epigenetic" control mechanisms, a means by which cells switch genes on or off, without altering the primary DNA sequence of a gene (10). Diethylstillbestrol (DES), used in the U.S. until the 1970s (and Europe until the 1980s) to help prevent miscarriage, is an example of an oestrogenic EDC which induces epigenetic changes in breast cells (11). In the U.S., daughters of exposed mothers have an increased risk of breast (12) and uterine cancer (13). Similarly, DDT, an insecticide once used widely in the U.S. until its ban in 1972, has been identified as an oestrogenic EDC (14). A recent U.S. study found that women whose mothers had been exposed to significant levels of DDT during pregnancy were four times as likely to have had breast cancer by the age of 52, as woman whose mothers were exposed to small quantities (15).

How are in-utero exposures linked to breast cancer?

There is increasing evidence that in utero exposure to certain EDCs may increase the risk of developing breast cancer later in life. EDCs may delay or inhibit post-natal breast development and cause a lack of response to hormones (16). They may also cause an increase in breast tissue

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density, a known risk factor in breast cancer, or increase sensitivity of the breast to carcinogens, thereby increasing breast cancer risk following carcinogen exposure (17). Some EDCs bind to oestrogen receptors and mimic the action of natural oestrogens (18). Binding of oestrogens to their receptors results in increased breast cell division which is thought to explain why lifelong exposure to elevated levels of oestrogens is a known breast cancer risk (19). Furthermore, oestrogen metabolites (break-down products) may increase mutations and promote cancer (20).

Prenatal exposure to EDCs no longer in use, such as DES (21) and DDT (22), is associated with increased breast cancer risk. Exposure to elevated levels of certain polychlorinated biphenyls (PCBs), may also be linked to increased breast cancer risk, specifically in young women (23). PCBs were once used widely in electrical insulating fluids and as plasticisers, and, like DDT and its metabolites, are common contaminants of soil and water. Exposure occurs following consumption of contaminated food and water.

Associations between currently used EDCs and an increased breast cancer risk are generally based on extrapolations from animal and cell culture studies. For example, studies in rodents suggest in utero exposure to BPA increases the risk of mammary gland tumours (24); enhances sensitivity of mammary glands to carcinogen-induced tumours (25); could cause epigenetic changes thought to contribute to the development of pre-cancerous and cancerous lesions (26); and may also induce mammary carcinogenesis by binding to oestrogen receptors present in foetal breast tissue (27). Other EDCs linked to breast cancer risk in animal and cell culture studies include benzyl butyl phthalate, (commonly used as a plasticiser in PVC plastics) (28), vinclozolin (a pesticide) (29) and methoxychlor (a banned insecticide) (30,31). Exposure to mixtures of common oestrogenic EDCs may also affect mammary gland development (32).

Breast Cancer UK position:

- Breast Cancer UK is calling for the Government and NHS advice services to publish a comprehensive guide for pregnant woman which explains the potential risk of in utero environmental exposures and their possible effects on the unborn child,
- Breast Cancer UK believes greater investment should be directed towards research which helps us to understand the environmental causes of breast cancer in order that we can prevent the disease before it starts.

Find out how to Reduce your Risk

For a list of references cited please see <u>here</u>. For further information download our full background briefing <u>here</u>.

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