Endocrine disrupting chemicals and cancer risk  
(testis and breast)

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**Abstract**

There has been much concern whether Endocrine Disrupting Chemicals (EDCs) play a role in the recent increase in the incidence of certain hormone sensitive cancer forms. There is at present, however, no proven causal link between exposure to EDCs and human cancer in any of the organs supposed to be at highest risk, i.e., the testis, breast, prostate, and endometrium. This may be due to a real absence of effects, or difficulties in obtaining such data.

**Introduction**

Surveys show that the public suspects synthetic EDCs to cause diseases in humans, including cancer. This is, however, a contentious area with polarised opinions, and few scientifically documented reports support this view. In the following, a brief review is given on the current status regarding EDCs and cancer risk in humans. Testicular cancer and breast cancer are used as examples, since both have increased in incidence during the past decades and are hormone sensitive.

**The diethylstilboestrol ‘experiment’**

A natural ‘experiment’ was undertaken in the US between 1948 and 1971, when a couple of million pregnant women were prescribed high doses of diethylstilboestrol (DES) to prevent spontaneous abortion. Reproductive organ abnormalities were observed in their offspring (reviewed in 1). Among their female offspring, there was an increased risk of clearcell adenocarcinoma of the vagina after puberty. Due to the young age of the cohort, breast cancer risk has not yet been studied in full, but preliminary data indicate that their relative risk is increased (2). It has been a matter of debate whether the male offspring experienced an increased risk of testicular cancer, but according to a recent comprehensive study, their relative risk is about 3.0 (3). Although this increase did not achieve statistical significance, the point estimate was regarded as sufficiently large to support the notion of an association. The overall lesson from the DES
‘experiment’ was that hormonal action in utero may lead to cancer in the offspring. Furthermore, it has served as a premise for hypotheses which were later to emerge based on increasing concern related to EDCs.

**Testicular cancer**

The incidence of testicular cancer has increased three-fold over the past decades in Norway as well as in other western countries (4), but the reasons for this increase are not known. The origin of testicular cancer is believed to be carcinoma in situ cells, whose malignant transformation is initiated during the early development from primordial germ cells or gonocytes that fail to end proliferation or undergo proper differentiation (5). There are genetic as well as environmental risk factors. A positive family history is a strong risk factor, and a cancer susceptibility gene for testicular cancer has been identified (Xq27) (6). Genetic alterations, however, are not able to explain the great increase in incidence. One relevant risk factor in this regard is an adversely altered balance between oestrogens and androgens in foetal life (5), possibly due to interaction between EDCs and endogenous hormone levels (7).

Few studies have been undertaken to assess a possible association between EDCs exposure and testicular cancer. In 2003, Hardell and coworkers published a case-control study whose aim was to investigate persistent organic pollutants (POPs) in blood from testicular cancer patients versus controls, and in case mothers versus control mothers (8). There was an increased concentration of some POPs among case mothers, which was interpreted as an indication of higher exposure during the fetal and postnatal period for cases than for controls. However, this study has been criticized for several reasons (9). First, there was a considerable time lag, since the mothers provided blood samples some 30 years after the foetal period; second, it was a small study, comprising only 44 case mothers; third, there was only one control per case; and fourth, a multiple comparison problem may pertain since many chemicals were analysed. Finally, there was a potential selection bias due to non-sequential recruitment of cases from hospitals and population-based controls.

The levels of POPs have decreased in human breast milk over the past 20-30 years, which argues against an etiologic role in the increasing trend of testicular cancer (10,11).

**Mycotoxins**

The risk of testicular cancer started to rise for those who were born as early as in the 1920s, i.e., decades before the manmade, potentially harmful chemicals had made their way into the environment. This suggests that natural rather than manmade causes ought to be considered, such as naturally occurring contaminants produced by mould fungi on grain during storage. One candidate has been the mycotoxin zearalenone, produced by specific Fusarium strains. Zearalenone binds to estrogen receptor and has been shown to cause reproductive problems.
in animals. Their occurrence and possibly harmful effects are not negligible (reviewed in 12). Studies have shown that zearalenone induces tumorigenic embryonic germ cells in mice during foetal life, and its proliferative action is mediated by the tumour suppressor Akt/PTEN (13). Zearalenone gives rise to colonies of embryonic germ cells which are tumorigenic (teratocarcinomas) in mice when injected. Other mycotoxins, like ochratoxin A, has also been considered as a potential risk factor for development of testicular cancer (14). As of today, however, there are no epidemiologic data to support the notion of an association between exposure to mycotoxins and the risk of testicular cancer.

**Breast cancer**

The incidence of breast cancer has increased about two-fold over the past decades, but the reasons are not clear. This increase, combined with the recognition that oestrogen exposure is a major risk factor for breast cancer, have been the rationale for investigating whether there is an association between exposure to EDCs and the risk of this cancer form. Many studies have been carried out, and the majority of the studies indicate no association (15). There are, however, some inconsistent results between case-control and prospective studies, and some even show an inverse association (16).

One overlooked route of human exposure to common EDCs might be skin exposure, and a recently raised issue is whether body care cosmetics might impose a risk for breast cancer (17). Some of the cosmetics ingredients are oestrogenic, e.g., parabens, which have even been detected in breast cancer tissue. As yet, however, no convincing data have been published to support the notion of an association between cosmetics and breast cancer risk, but there is clearly a need for further research in this area. Sharpe and Irvine state that women seeking to become pregnant are recommended to reduce use of cosmetics and body creams (18).

**Conclusion**

Although there are indications, there is at present no proven causal link between EDCs exposure and human cancer in any of the organs supposed to be at highest risk, i.e., the testis, breast, prostate, and endometrium. This may be due to difficulties in obtaining such data or a real absence of effects.

**References**


