

## Disturbed Steroid Hormonal Milieu is a Potential Cause of Cancer

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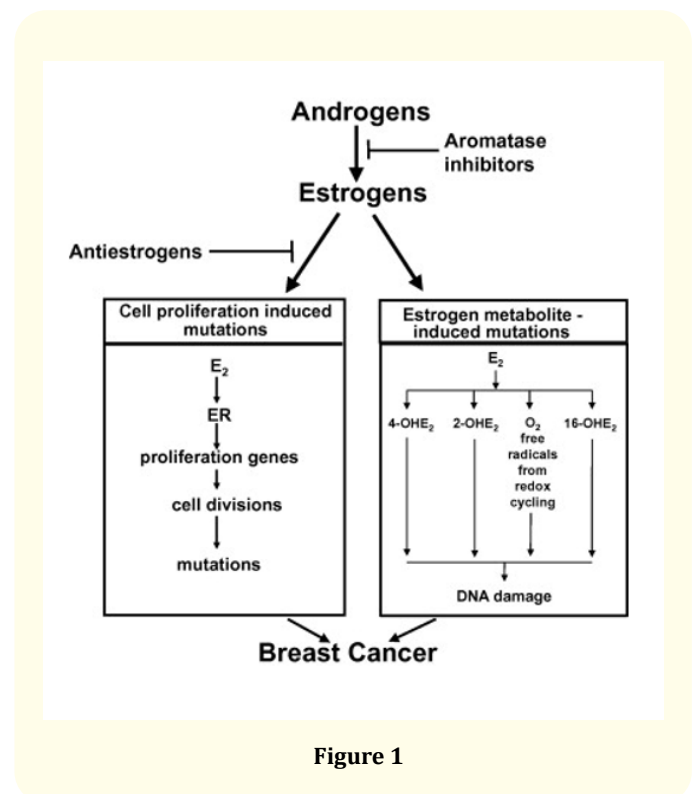
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Environment and diet regulate menstrual cycle in human females. The length of the period between menarche (activation of ovarian hormones) and menopause (inactivation of ovarian hormones) depends on 4 hormones, estrogens, progesterone, follicular stimulating hormone and luteinizing hormone [1]. In our epidemiological survey we found now menarcheal age is decreasing.

During pregnancy the remodelling of the different systems follows including mental faculty. These changes are necessary to assist foetal development and prepare the body for labour. A study suggested that the absence of pubertal development by age 14 is associated with a high probability of conditions with impaired reproductive potential. In precocious puberty before the full development of different systems, reproductive maturity is attained such as full breast development is not over before pregnancy for further remodelling to suckle the baby soon after delivery.

As a hormonally driven disease, its incidence and mortality rates within different populations are modified by the myriad of environmental, reproductive, hereditary, and dietary influences that affect estrogen metabolism [2]. Some breast cancer cells need estrogen to grow whereas others can grow even in the absence of this hormone (Figure 1).

The concept that hormones can cause cancer, i.e., increase the incidence of, neoplasia was first developed by Bittner et al. [3], based on experimental studies of estrogens and mammary cancer in mice. We have refined that concept into a hypothesis for a major role of estrogen and other hormones in the etiology of several human cancers [4]. A key element of this hypothesis is that neo-



**Figure 1**

plasia is the consequence of excessive hormonal stimulation of a particular target organ, the normal growth and function of which are under hormonal control. On binding of estrogen to its receptors, the cancer cells with these receptors grow. Estrogen receptor-positive breast cancers have many cells with hormone receptors and can be treated with hormone therapy whereas hormone inde-

pendent cancers continue to grow. High estrogen levels in the body are believed to dramatically increase the risk of breast cancer. For example, elevated estrogen levels are a risk factor for breast, ovarian and endometrial cancer. The response of this end organ (e.g., endometrium, and breast) to the proliferative effects of the hormone is a progression from normal growth to hyperplasia to neoplasia.

Estrogens, the class of female steroid hormone are responsible for making a woman a woman. Women are characterised by their menstrual cycle which in turn is regulated by ovarian hormones, estradiol and progesterone. However, if a female is exposed with xenohormones which are omnipresent in air, water, and soil (food) now a days, her reproductive cycle is disturbed and she suffers with many disorders in reproductive system. If this hormone is for a longer period in her system, she may suffer with hormone dependent diseases such as early maturity, teen pregnancy and hormone dependent cancers. Xenohormones or xenoestrogens are endocrine disruptors because of their ability to interfere with the body's natural hormone regulation. In adolescents, experts say, this may mean advanced reproductive maturing - defined by signs of puberty, namely menstruation, in girls as young as 8 to 11. The effects these chemicals have on female reproductive hormones aren't limited to the direct user, but in fact, harm infant girls whose mothers used these products while pregnant. This is important, because we know that the age at which puberty starts in girls has been getting earlier in the last few decades; one hypothesis is that chemicals in the environment might be playing a role [5,6].

There have been increasing indications that exogenous factors may influence the endogenous hormone balance. Caution should be taken to avoid unnecessary exposure of foetuses and children to exogenous sex steroids and endocrine disruptors, even at very low levels. Of greatest concern is that parabens are known to disrupt hormone function, an effect that is linked to increased risk of breast cancer and reproductive toxicity, "Parabens mimic estrogen by binding to estrogen receptors on cells [7]. Hormone-related cancers like testicular [8], breast [9] and prostate cancer [10,11].

### Exposure to chemicals in cosmetics

some of the chemicals in modern day cosmetics may contribute to the development of cancer. These chemicals are grouped as "hormone disruptors", such as Parabens (the most common are methylparaben, propylparaben, ethylparaben, and butylparaben) and Phthalates. Parabens are used as preservatives. They prevent

bacteria from growing in things like face moisturizer, which repeatedly comes into contact with germs from your hands as you scoop it out to apply it to your face. The American Chemical Society estimates that parabens are in about 85% of personal care products -- everything from shampoo to shaving cream. Researchers believe most of us get our greatest exposure from these products as they're absorbed through the skin.

### Parabens

Parabens can also be found in foods like baked goods, beverages, syrups, jellies, jams and preserves, in the packaging that keeps food fresh, and in drugs, according to the CDC's National Biomonitoring Program. The most commonly used parabens are methylparaben, propylparaben, and butylparaben, according to the FDA [12,13].

Parabens disrupt the normal function of hormone systems affecting male and female reproductive system functioning, reproductive development, fertility and birth outcomes. Parabens can also interfere with the production of hormone. Both children and adults show the presence of parabens in their urine samples, however, adults tended to have more of these chemicals in their urine than children, probably because they used about twice the number of personal care products. The more personal care products a person used, the higher their paraben levels. Women tend to have higher levels than men, probably because they use more. These chemicals are cleared from the body pretty quickly, says Claire Philippat, who studies paraben exposure. Nevertheless, they're so widely used; we always have some in our bodies. "Even if you eliminate them quickly, you're continually exposed to them", Philippat says [14].

### Phthalates

In the past few years, researchers have linked phthalates to asthma, attention-deficit hyperactivity disorder, breast cancer, obesity and type II diabetes, low IQ, neurodevelopmental issues, behavioral issues, autism spectrum disorders, altered reproductive development and male fertility issues.

Phthalate exposures in humans have been linked to changes in sex hormone levels, altered development of genitals, and low sperm count and quality. Benzyl butyl phthalate (BBP) and dibutyl phthalate (DBP) have been shown to be weakly estrogenic, cause estrogen-triggered cell responses, and act in conjunction with the body's own estrogens.

### Parabens, phthalates and breast cancer

Parabens have a chemical structure that's similar to estrogen, which means they can mimic the effects of that hormone in the body. Parabens can spur the growth of certain types of breast cancer cells. And they appear to be able to do this even in tiny amounts. Parabens are used in many food and personal care products. But they seem to do this weakly, and on the scale of chemical threats, researchers thought parabens were pretty low on the list of things to worry about. New research suggests, though, that they may be more harmful than previously thought.

For the study, scientists grew breast cancer cells in a lab. They treated the cancer cells with low doses of parabens along with heparin, a growth-promoting substance that's normally found in breast tissue. The two chemicals are known to have a more powerful effect when combined.

When the two chemicals were combined, the dose of parabens needed to stimulate growth was 100 times lower. That suggests parabens may be exerting effects at levels people are being exposed to in real life, according to study author Ruthann Rudel [15]. The scientists tested breast cancer cells that were known to be sensitive to (or fuelled by) hormones. "Those cells aren't the same as normal human cells," Rudel says. "We'd love to know how sensitive normal cells are. That's something we're working on".

But she says "you can imagine that if you have some abnormal cancer cells growing in breast tissue, a chemical mix including parabens might act like fertilizer, further encouraging their growth".

And she admits that these are cells growing in a petri dish in a lab. It's a very precise but simple way to test exposure, but it's not necessarily representative of what's going on inside the body, which is a much more complex system.

There have only been a few studies that have ever tried to measure the chemical in blood or tissues. The question remains as to whether any of the parabens can accumulate intact in the body from the long-term, low-dose levels to which humans are exposed. These studies demonstrate that parabens can be found intact in the human breast and this should open the way technically for more detailed information to be obtained on body burdens of parabens and in particular whether body burdens are different in cancer from those in normal tissues [16]. Two studies have found parabens in human breast tumors. But those studies have been ques-

tioned, because researchers can't rule out that the samples may have been contaminated with parabens as they were being prepared for analysis [14].

A large, ongoing study by the CDC is tracking Americans' exposure to many chemicals, including parabens. Based on data collected for that study [16,17], Rudel says "people who get exposed to the highest levels in the U.S. have paraben concentrations in their bodies that are about at the levels used in the new study".

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