

POLLUTANTS, SEDENTARISM, CIRCADIAN RHYTHM

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Pollutants have been a major concern to environmentalists, public health departments, government agencies and medical societies over the years. Commercial pesticide formulations of which there are more than 50,000 provide the major contaminants to the environment. Of these contaminants the "so-called" endocrine disrupting compounds (EDCs) represent a group of chemicals of particular interest because they mimic endogenous hormones, act as hormone antagonists, modulate hormone receptor activity or alter steroidogenic pathways leading to adverse developmental and reproductive effects [1]. These effects depend on the timing and duration of exposure as well as the dose. Recent evidence suggest that these chemical contaminants may be contributing to adverse reproductive outcomes such as infertility, spontaneous abortion, preterm labour, polycystic ovary syndrome, endometriosis, and intrauterine growth retardation in the general population [2,3]. Consideration will be given to a few of these contaminants – p,p' dichlorodiphenylchloroethylene (DDE), phthalates, bisphenol-A and polybrominated diphenyl ethers (PBDE, flame retardants).

DDE is a persistent metabolite of DDT an insecticide widely known for its efficacy in eradicating mosquitoes the carriers of malaria. Although banned it is still used in underdeveloped countries. DDE has been implicated in spontaneous abortions, decreased cycle length, intrauterine growth retardation, preterm birth, sexual precocity and early menopause in women and sperm abnormality in men [reviewed in 1]. DDE has been shown to have a non-genomic effect on human granulosa-lutein cells suggesting that this could be a mechanism of its action [4].

Phthalates are used to make plastics softer and more flexible. Products that contain phthalates include food packaging, cosmetics, fragrances, hairspray, nail polish, pharmaceuticals, building materials, paints, automobiles, children's toys, modeling clay, cleaning products and insecticides. Exposure can occur through direct contact with products containing phthalates, through leaching of phthalates into other products, or through general environmental contamination. Recent studies have confirmed that exposure to phthalates can lead to decreased ano-genital distance in newborn males, a sign of anti-androgenic action [5] as well as hypospadias [6]. In females phthalates may be involved in early breast development [7].

Bisphenol A (BPA) was synthesized in 1891 and first recognized as a synthetic estrogen in the 1930s. Individual monomers of BPA could be combined to make two kinds of plastics: polycarbonate and epoxy resins. BPA-based polycarbonates are used in products such as baby bottles, water bottles, eyeglass lenses, medical equipment, toys, CDs/DVDs, cell phones, consumer electronics, household appliances, sports safety equipment, airplanes, and automobiles. Epoxy resins containing BPA are used as liners for most food and beverage cans, adhesives, industrial protective coatings, and automotive primers. BPA is also used to make dental sealants and flame retardants, and is an additive in many other widely used consumer products. It is one of the highest volume chemicals produced worldwide with a global production capacity exceeding 6 billion pounds per year. BPA has been linked to many health problems including prostate cancer, diabetes, obesity, cardiovascular disease and reproductive problems such as altered mammary gland development, breast cancer, longer cycles, accelerated puberty and recurrent miscarriage [8]. Canada is the first country to ban BPA in baby bottles.

PBDEs comprise a possible number of 209 congeners and are used as flame retardants. They are persistent, bioaccumulative and ubiquitous. Because of these properties they are being found in rapidly increasing levels in tissues of humans. Concern is being raised as a result of the doubling of PBDE levels every five years in mother's milk in the United States, Japan, Sweden and the Netherlands. Reports that PBDEs can have adverse developmental and reproductive effects underscore this concern [reviewed in 1]. However, there has not been any human data to date to suggest that PBDEs have adverse effects on reproductive processes but the possibility remains since dust seems to be the major route of intake into the body [9].

With regard to a sedentary life style it is often associated with an increase in body weight. Body mass index (BMI) or waist-hip ratio is used to describe body habitus but BMI is more common. Obesity and overweight have consequences on reproductive health. Obese women are generally infertile, are anovulatory and have menstrual irregularities, reduced conception rate and a reduced response to fertility treatment. Miscarriages and maternal and perinatal complications often occur in obese women [10]. Ghrelin and leptin may be involved in obesity [11,12]. Thus it is important to reduce weight by changes in life style habits or in extreme cases, surgery, in order to reverse these adverse reproductive endpoints.

Circadian rhythms occur in many organ systems. Light is the primary regulator which acts via a retinal ganglion cell photoreceptor in the mammalian eye. In many mammalian species the circadian clock functions through the rhythmic transcription and translation of several genes, forming an oscillatory feedback loop [13]. The circadian clockwork genes are expressed in all female and male reproductive tissues studied to date and even in the conceptus. Environmental influences can affect the function of these genes. Although the evidence for the existence of clock genes in small animals is clear the presence of similar genes in man remains to be determined. Human studies are limited to disruptions in light dark cycles. With the advent of electricity the constant exposure to light has been considered as pollution [14]. Epidemiological evidence points to an association between artificial light and cancers such as breast and prostate. Women shift workers may have menstrual irregularities, miscarriages and reduced fecundability.

In conclusion, the evidence for adverse effects of environmental pollutants on human reproduction while limited in extent, favours the adoption of the precautionary principle on the basis of animal studies. Sedentary life style and its consequent overweight condition need to be addressed to achieve successful fertility. Circadian rhythm genes and human reproduction remain an area for fruitful and worthwhile investigations.

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