



Polychlorinated Biphenyl Exposure, Reproductive and Genital Abnormalities: Still a Problem for the World and Wildlife

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Introduction

United States Environmental Protection Agency (EPA) defined an endocrine-disrupting chemical (EDC) as “an exogenous agent that interferes with synthesis, secretion, transport, metabolism, binding action, or elimination of natural blood-borne hormones that are present in the body and are responsible for homeostasis, reproduction, and developmental process” [1]. These chemicals were originally thought to exert actions primarily through different hormone receptors, including estrogen receptors (ERs) and androgen receptors (ARs) [1]. However, basic scientific research shows that the mechanisms are much broader than originally defined.

The group of molecules identified as EDCs belongs to various chemical groups and have very different chemical structures. They can be both synthetic and natural. The synthetic chemicals include several industrial solvents/lubricants and their byproducts [polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins], plastics [bisphenol A (BPA), phthalates], pesticides [methoxychlor, chlorpyrifos, dichlorodiphenyltrichloroethane (DDT)], fungicides (vinclozolin), and pharmaceutical agents [diethylstilbestrol (DES)] [1,2].

Discussion

Polychlorinated biphenyls (PCBs) are a class of synthetic chlorinated aromatic compounds, used in cutting oils, lubricants, and as electrical insulators. They were widely used in industrial and consumer products for decades. Their production started in 1929 and was banned in the late 1970s [3]. The general population is exposed primarily through the consumption of contaminated foods like fish, meat, and dairy products and they can bio-accumulate up the food chain. As they are lipophilic, they are biologically concentrated and stored in human and animal adipose tissues. As a result of their persistence and ubiquity, measurable levels of serum PCBs are found in the majority of the general population [4].

The effects of PCBs on reproduction and hypothalamus-pituitary-gonadal (HPG) axis are shown in many rodent studies. In male rodents, phthalates and to a lesser extent PCBs are shown to induce

testicular dysgenesis syndrome (TDS) entirely or partly. Among wildlife, polar bears (*Ursusmaritimus*) showed waned testosterone production in males, elevated progesterone in females, altered behavior and thyroid hormone levels [5,6]. In humans, many PCBs have estrogenic or anti-androgenic activity. Although estrogenic activity of these compounds is a suspected mode of action, there is also evidence that PCBs inhibit estrogen sulfotransferase activity in the liver and effectively increase bioavailable estrogen in the body [7]. PCBs are also shown to be related to reproductive dysfunction (decreased sperm motility, decrease in fecundity, earlier menarche, altered sex ratio, and altered gonadal hormones in newborns) [8-11]. Several epidemiological studies suggest an inverse association between PCB concentrations in biological fluids and semen quality. High PCB levels in humans are specifically suggested to cause reduced sperm motility. These results were constantly reported from different parts of the world including the United States, The Netherlands, Taiwan, Sweden, and India [12-14]. Studies suggest that consumption of contaminated fish or exposure to contaminated rice oil could cause high PCB concentrations in humans [15,16]. However, there is limited epidemiological evidence that reveal the association between maternal serum concentrations of PCBs and cryptorchidism or hypospadias in the offspring [17-22]. Prenatally exposed infants to PCBs showed lower birth weight, smaller head circumference and alterations in the thyroid hormone homeostasis [23], while exposed children showed altered neural development, cognitive, motor and learning abilities [24,25].

PCBs were also shown to cause perturbations in the prostate gland. A recent study was conducted on Swedish men who did and did not have prostate cancer revealed that their PCB concentrations (specifically in the higher PCB level quadrants) of adipose tissue showed a significant correlation with prostate cancer odds ratio, with the most marked associations for PCB 153 and transchlordan [26]. The results of another important epidemiological study conducted on capacitor manufacturing plant workers exposed to high levels of PCBs also indicated a strong exposure-response correlation for prostate cancer mortality [27]. These results support previous findings of correlations between PCB 153 and PCB 180 and prostate cancer risk in electric utility workers [28,29].

Different PCB congeners have been banned more than 35 years ago; however they are still present in the environment and biological fluids. This phenomenon indicates their persistence in the environment as well as illegal usage. Although there is enough evidence that these compounds cause reproductive, genital and neurobehavioral anomalies in rodents, wildlife and humans, there are still gaps in knowledge for their mode/mechanism of action/s.

Conclusion

Further investigation using *in vitro* and *in vivo* models should be conducted to reveal the mechanism underlying their reproductive and developmental toxicity. Scientific societies should work together to increase the awareness to the hazard of EDCs, particularly PCBs. As toxicologists and pharmacists, we suggest that regulatory authorities take strict measures to decrease human exposure to different PCB congeners.

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