Effect of TCDD on the human reproductive system: 30 years after "Seveso"

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Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated biphenyls (PCBs) and polychlorinated dibenzofurans (PCDFs) are products and byproducts of industrial or combustion processes. These compounds have been identified in almost all animal species, including humans. Some of these chemicals can disrupt multiple endocrine pathways and induce a large spectrum of toxic responses depending on target organs, sex, age, and species. We have studied possible effects of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) or dioxin on females and males of different ages. The residential exposure took place in and around Seveso, Italy on July 10, 1976, as a result of an explosion at a plant manufacturing the herbicide 2,4,5-trichlorophenol (TCP). We have measured the serum TCDD levels out of 2200 of the about 35000 samples drawn in 1976 and 1977 and stored at –20°C. No liver toxicity has been observed. Studies on about 900 females have shown doubled non significant risk for endometriosis among women with serum TCDD levels of 100 ppt or higher. Premenarcheal TCDD exposure was associated with a lengthening of the menstrual cycle of 0.93 days. A reduction of risk of leiomyoma, consistent with TCDD as anti estrogen, has been observed. No consistent effect has been seen on the risk of onset of menarche, but a non monotonic dose-related association with increasing risk of earlier menopause up to 100 ppt has been observed. Studies of about 450 families of exposed and unexposed partners have shown a lowered male/female sex ratio in their offspring, which may persist for years after exposure. This is due only to TCDD father exposure even if in infancy. The median concentration of dioxin in fathers is about 20 times the estimated average concentration of TCDD currently found in human beings in industrialized countries. Very recently we demonstrated in 135 males exposed to TCDD that exposure in infancy reduces sperm concentration and motility, and an opposite effect is seen with exposure during puberty. Exposure in either period leads to permanent reduction of estradiol and increases of FSH. These effects are permanent and occur at TCDD concentrations < 68 ppt, which is within only one order of magnitude of those seen in the industrialized world in the 1970s and 1980s and may be responsible at least in part for the reported decrease in sperm quality, especially in younger men. Taken together these results document an effect of dioxin on human reproductive system and could have important public-health implications.