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Effects of Chronic Oral Exposure to PCBs on Estrus Cyclicity.

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Polychlorinated biphenyls (PCBs) reduce brain levels of dopamine (DA) in the striatum and the number of tyrosine hydroxylase positive neurons in the substantia nigra of exposed animals. These studies however have all been conducted in male animals, and hence information on the neurotoxic effects of PCBs in females is lacking. Recent epidemiological data suggest that women may be more susceptible to PCB-induced DA dysfunction in the basal ganglia than men. Indeed an ongoing epidemiology study of PCB-exposed workers shows that the density of dopamine terminals is reduced in women only. Additionally, in another study the risk of mortality from Parkinson's disease was increased only in women PCB-exposed workers. These findings were obtained in post-menopausal women, suggesting that reductions in ovarian hormones may contribute to these gender differences. Alternatively, PCBs may directly alter ovarian hormone function. Indeed preliminary data from our laboratory suggest that oral exposure to 500 ppm PCBs alters estrus cyclicity. Sixty-six percent of exposed female rats enter into a state of persistent estrus (PE) and 17% enter into persistent diestrus (PD) after 39 days of exposure. These changes in cyclicity are associated with alterations in circulating ovarian hormones. Estrogen levels are high in PE whereas both estrogen and progesterone levels are low in PD. Both estrogen and progesterone are neuroprotective and estrogen has been shown to attenuate the effects of neurotoxicants that target dopamine neurons in the basal ganglia. Our long-term goal is to better understand the role of ovarian hormones in influencing PCB-induced neurotoxicity in the human.