

[Dioxin-I] Effects of Polychlorinated Biphenyls on the Uterus

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SBRP "Research Brief" - Number 62

Title: Understanding the Effects of Polychlorinated Biphenyls on the Uterus

Regulation of uterine contractility is vital to successful reproduction. During a full-term pregnancy, the uterus remains relatively inactive from conception until the initiation of labor -- a period of about 280 days for humans. As the time of delivery approaches, the uterus becomes highly active with muscular contractions that increase in frequency and intensity until the fetus is forced out of the womb. =

Fine-tuned control of uterine contractions is imperative not only for an effective labor at the end of pregnancy, but also for preventing premature labor. However, for reasons that are poorly understood, the regulation of uterine contractions appears to be susceptible to interference by certain environmental contaminants. =

Some studies suggest that polychlorinated biphenyls (PCBs), a group of widespread, persistent environmental contaminants, may disrupt the natural termination of pregnancy by stimulating premature uterine contractions. Both PCB mixtures and individual congeners can stimulate contractions in isolated segments of uterus. Yet the cellular and molecular events underlying this

form of reproductive toxicity are relatively unknown. =

Researchers at the University of Michigan -- a partner in the Michigan State

University Superfund Basic Research Program -- recently elucidated a possible mechanism for PCB-induced uterine contractions. In a series of experiments they discovered that the PCB mixture Aroclor 1242 can affect several cellular events known to be involved in the development of contractions in uterine muscle cells. =

In one set of studies, Aroclor 1242 increased levels of the cellular messenger arachidonic acid in cultured uterine muscle cells. Enzyme inhibition experiments revealed that this activity was mediated by an enzyme known as phospholipase A2. Thus, the Aroclor 1242-induced release of arachidonic acid likely occurred through activation of phospholipid cell signaling pathways. Other experiments showed that Aroclor 1242 both increased the influx of intracellular calcium and activated voltage-operated calcium channels in uterine muscle cells, a significant finding because calcium is an essential stimulus for initiating uterine muscular contractions. Based on these findings, the scientists report "it is possible that arachidonic acid liberated by Aroclor 1242 activates voltage-operated calcium channels of [uterine muscle cells] and thus stimulates uterine muscle contraction." =

PCBs have been associated with spontaneous abortion and shortened gestation length in women, wildlife and laboratory animals exposed to these industrial chemicals. Because premature birth is a considerable health problem in this country -- it accounts for 75% of newborn deaths not related to malformations -- it is important to determine how and to what extent PCBs may disrupt normal uterine functioning. The mechanistic understanding acquired in these studies is providing much needed insight into reproductive risks that may arise from PCB exposures. =

For more information please contact: =

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To learn more about this research please refer to the following sources: =

Bae, J., M. Peters-Golden, and R. Loch-Caruso. 1999. Stimulation of pregnant rat uterine contraction by the polychlorinated biphenyl (PCB) mixture Aroclor 1242 may be mediated by arachidonic acid release through activation of phospholipase A2 enzymes. *J Pharmacol Exp Ther* 289: 1112-1120.

Bae, J., E.L. Stuenkel, R. Loch-Caruso. 1999. Stimulation of oscillatory uterine contraction by the PCB mixture aroclor 1242 may involve increased $[Ca^{2+}]_i$ through voltage-operated calcium channels. *Toxicol Appl Pharm* 155: (3) 261-272.

As always, your feedback is welcomed.

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