

# Rachel's Environment & Health News

## #364 - Dioxin And PCBs Linked To Endometriosis

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Endometriosis is a mysterious, painful disease that affects 6 to 9 million American women, according to estimates by the Mayo Clinic.[1] Endometriosis occurs exclusively in species that menstruate (humans and non-human primates). The disease occurs when bits of the endometrium (the tissue that lines the uterus) somehow escape the uterus and become implanted on other pelvic organs. Usually the implants occur on the outside of the ovaries, the fallopian tubes, the uterus or its supporting muscles.

The misplaced cells imitate the menstrual cycle, first thickening and then bleeding as menstruation begins. Because the implants are embedded within other tissues, there is nowhere for the blood to go. Blood blisters form, irritating the surrounding tissue, which may create a cyst (sometimes also called a nodule, tumor, lesion, implant, or growth) to encapsulate the blister. The cyst, in turn, may become a scar or an adhesion (abnormal tissue that binds organs together). Scars or adhesions on the ovaries or fallopian tubes can prevent pregnancy.

Typical symptoms of endometriosis include chronic pain, particularly pelvic pain; severe period pain; pain with sex; infertility; painful bowel movements with the period; painful urination or other urinary problems with the period and at other times; chronic fatigue; chemical sensitivities and/or extensive allergies and other allergic diseases; and, sometimes, autoimmune diseases, including Hashimoto's thyroiditis and lupus.

Endometriosis can run in families; it most commonly strikes women between 25 and 49 but it can begin as early as 11. It generally ends with menopause, though estrogen replacement therapy can reactivate the disease.

Although more than 4500 research papers have been published on endometriosis, the cause of the disease remains a mystery.

Now new thinking about endometriosis has been stimulated by research linking dioxin exposure to the disease in rhesus monkeys. In rhesus monkeys, endometriosis develops spontaneously and resembles the human disease both anatomically and clinically. In the rhesus, disease manifestations include growth of cysts and adhesions involving the ovaries, ureters, colon, and urinary bladder, just as in humans.

The recognition of dioxin as a contributor to the disease in rhesus monkeys is considered an exciting breakthrough by scientists who have been studying the disease for two decades or more, unsuccessfully seeking a cause.

The new research reveals a clear dose-response relationship between low levels of dioxin in the diet and development of endometriosis in rhesus monkeys. The more dioxin, the worse the endometriosis, according to experiments conducted at University of Wisconsin and reported this month by Sherry E. Rier and co-workers in the journal, *FUNDAMENTAL AND APPLIED TOXICOLOGY*. [2]

A colony of 24 wild [feral] female rhesus monkeys 6 to 10 years of age was obtained in 1977. From 1977 to 1983 the animals were housed at the University of Wisconsin's Biotron; from 1983 to the present, the animals have been housed at the Harlow Primate Lab in Madison, Wisc. In 1977, the monkeys were randomly assigned to 3 groups of 8 animals each. Control animals were not exposed to dioxin, animals in the low-dose group were exposed to 5 parts per trillion (ppt) in their diet and monkeys in the high-dose group were exposed to 25 parts per trillion. Dioxin was administered in the animals' feed for 5 years, from 1977 to 1982. The point of the original research was to see if low doses of dioxin in the diet interfered with reproduction in the rhesus colony.

The dioxin connection to endometriosis was discovered almost by accident. As the researchers themselves wrote, "This study was originally undertaken 15 years ago to investigate the long-term reproductive effects of exposure to dioxin in the rhesus monkey.

Twelve years after the initiation of this work, [in 1989], a dioxin-exposed animal died and was noted at autopsy to exhibit widespread endometriosis. In 1990 and 1992, two additional dioxin-treated animals died of severe infiltrating endometriosis. During this time, we became aware that these animals and others in the colony displayed symptoms similar to human disease at the onset of menses, including anorexia [diminished appetite; aversion to food] and behavior consistent with pain. In view of these findings, the present study was performed to document endometriosis in this unique colony of monkeys and to determine whether the severity of the disease was correlated with exposure to dioxin."

This new study describes the 17 live monkeys currently remaining in the colony, plus the 3 monkeys that died of extensive endometriosis and were evaluated at autopsy.

The 17 living monkeys underwent laparoscopy in 1992. Laparoscopy is surgery performed under general anesthesia. A small incision is made in the abdomen, and a thin optical tube is inserted, so that the animal's internal organs can be observed and photographed. In humans, as in monkeys, laparoscopy is the only sure way to diagnose endometriosis because some forms of cancer create the same symptoms.

Among the 20 monkeys, the presence and severity of endometriosis was determined according to human criteria, using the revised American Fertility Society (rAFS) system, which is universally accepted. The rAFS system classifies the severity of endometriosis according to number, size and placement of endometriotic implants and the presence of adhesions. There are 4 stages of the disease: minimal, mild, moderate, and severe.

Among the rhesus monkeys, the incidence of disease directly correlated with dioxin exposure. Endometriosis was present in 71% of the animals treated with 5 ppt dioxin, and in 86% of animals treated with 25 ppt. This compares to 33% of the animals exhibiting disease in the control group.

The severity of the disease was also correlated with the dose of dioxin. According to the severity classification system, control animals not exposed to dioxin exhibited either no disease (4 of 6 animals) or minimal disease (2 of 6 animals). Animals treated with 5 ppt dioxin had no disease (2 of 7 animals), mild disease (1 of 7 animals) or moderate-to-severe disease (3 of 7 animals). Among the animals dosed with 25 ppt, 5 of 7 animals had moderate-to-severe disease and only one was disease-free.

The authors conclude, "The results of these studies demonstrate that chronic exposure to the chemical toxicant dioxin is directly correlated with an increased incidence in the development of endometriosis in rhesus monkeys. As determined by [standardized] scoring systems, stage II [mild], III [moderate], and IV [severe] disease were exclusively found in animals exposed to either 5 or 25 ppt dioxin. Furthermore, the severity of disease, as reflected by the [standardized severity] score, was positively correlated with the daily and cumulative dose of dioxin administered."

The reproductive history of these particular monkeys had previously been reported. Reproductive function of mothers exposed to 5 ppt was not significantly different from the control group. Seven of eight females bred after 7 months of exposure to 5 ppt dioxin were able to conceive; 6 of these females gave birth to viable infants and one gave birth to a stillborn infant. In contrast, among the monkeys dosed with 25 ppt, only 5 could conceive and of these only one gave birth to a viable infant; there were 3 spontaneous abortions and one infant died shortly after birth.

These data suggest that maternal exposure to dioxin before and during pregnancy can result in fetal mortality without overt toxic effects on the mother. Humans in industrial countries now eat an average of 133 picograms [trillionths of a gram] of dioxins each

day, 90 percent of it in fish, meat and dairy products, according to the World Health Organization.[3]

A 1992 study from Germany revealed that endometriosis is correlated with the presence of PCBs in humans,[4] thus confirming findings first reported in 1985 linking PCBs to endometriosis in rhesus monkeys.[5] PCBs and dioxin both interfere with the immune system and with the endocrine system (the body's chemical control system made up of endocrine glands, which produce hormones). Researchers have suspected for some time that endometriosis is somehow caused by malfunction of both the immune and endocrine systems.

Dr. Audrey Cummings with U.S. Environmental Protection Agency is now conducting laboratory research to see if dioxin exposure causes endometriosis-like changes in rats.

Dioxin and PCBs are not the only potential culprits. As Dr. Theo Colborn has recently shown, at least 45 chemicals widely distributed in the environment, including 35 pesticides and 10 industrial chemicals, are now thought to damage or impair the endocrine systems of fish, birds and mammals, including humans.[6]

For further information on endometriosis, contact: The Endometriosis Association, 8585 North 76th Place, Milwaukee, WI 53223. Fax: (414) 355-6065. Families affected by the disease can call the Association's toll free line: 1-800-992-3636 for a free packet of information.

--Peter Montague

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[1] David E. Larson, editor, MAYO CLINIC FAMILY HEALTH BOOK (N.Y.: William Morrow, 1990), pgs. 1101-1102.

[2] Sherry E. Rier and others, "Endometriosis in Rhesus Monkeys (MACACA MULATTA) Following Chronic Exposure to 2,3,7,8-Tetrachlorodibenzo-P- dioxin," FUNDAMENTAL AND APPLIED TOXICOLOGY Vol. 21 (1993), pgs. 433- 441.

[3] World Health Organization, SUMMARY REPORT; CONSULTATION ON TOLERABLE DAILY INTAKE FROM FOOD OF PCDDS AND PCDFS [REPORT NO. EUR/ICP/PCS 030(S) 0369N] (Geneva, Switzerland: World Health Organization, 1990).

[4] I. Gerhard und B. Runnebaum, "Grenzen der Hormonsubstitution bei Schadstoffbelastung und Fertilitatsstorungen," ZENTRALBLATT FUR GYNAKOLOGIE," Vol. 114 (1992), pgs. 593-602.

[5] J.S. Campbell and others, "Is simian endometriosis an effect of immunotoxicity?" Presented at the Ontario Association of Pathologists 48th Annual (1985) Meeting, London, Ontario, cited in Sherry Rier, note 2, above.

[6] Theo Colborn and others, "Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans," ENVIRONMENTAL HEALTH PERSPECTIVES Vol. 101 No. 5 (October 1993), pgs. 378-384.

Descriptor terms: endometriosis; mcs; immune system; endocrine system; allergies; lupus; hashimoto's thyroiditis; rhesus monkeys; studies; laboratory research; university of wisconsin biotron; harlow primate lab; laparoscopy; audrey cummings; epa; theo colborn; pesticides;