Rachel's Environment & Health News
#290 - Young Male Rats Are 'Demasculinized' And 'Feminized' By Low Doses Of Dioxin
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Three new studies by researchers at University of Wisconsin reveal that very low doses of dioxin alter the sexual development of young male rats, causing demasculinization and feminization.[1,2,3]

Dr. Linda S. Birnbaum, a scientist with U.S. EPA [Environmental Protection Agency] calls the new studies "highly significant."[4] Birnbaum is one of the chief scientists conducting the EPA's formal reassessment of the toxicity of dioxin (see RHWN #269, #270, #275). As we reported earlier (RHWN #279), many scientists, including Birnbaum, now consider dioxin an "environmental hormone." The new Wisconsin studies support that view.

The Wisconsin researchers, led by Dr. Richard E. Peterson, showed that dioxin interferes with the sexual development of male rats exposed to dioxin before, and shortly after, birth. Pregnant female rats were given a single oral dose of dioxin on the 15th day of pregnancy; their male offspring showed reduced levels of male hormones in their blood and a variety of sexual aberrations that stayed with them as they matured. The young males are demasculinized and feminized by doses of dioxin too low to cause any measurable toxicity in the mother rat. The sexual changes in the young males are both physiological and behavioral, and last into adulthood.

Dioxin passes through the placenta and enters the fetus, so the rat fetuses received part of the mother's dose almost immediately. After birth, the baby rats continued to receive a small dose of dioxin through their mother's milk. Peterson says the baby rats received the bulk of their dose through milk. In rats and humans both, females rid their bodies of dioxin chiefly by excreting it in their milk. Dioxin is soluble in fats and oils, and milk is high in fat.

Dioxin is the common name for a family of 75 toxins, the most potent of which is TCDD [2,3,7,8-tetrachlorodibenzo-P-dioxin]. The Wisconsin researchers used TCDD in their experiments.

Dioxin is not made intentionally for any industrial purpose, but is produced as a byproduct of the combustion of chlorine-containing wastes, the bleaching of paper, and the manufacture of some pesticides. The burning of municipal solid waste, and of many hazardous wastes, releases dioxin into the environment, as does paper manufacture. Government officials responsible for the quality of the environment in the Great Lakes have called for a phase-out of chlorine, to reduce dioxin levels in wildlife and humans around the Lakes. (See RHWN #284.)

In the Wisconsin experiments, young males whose mothers were given as little as 0.064 micrograms of dioxin per kilogram of body weight showed consistently reduced levels of male hormones, plus a variety of physical and behavioral changes, including:

--reduced testosterone levels and probably a reduced response to testosterone. Testosterone is a powerful hormone controlling various aspects of sexual development in males.

--smaller accessory sex organs, including smaller testicles;

--slower sexual maturation;

--distinctly feminine-style regulation of one hormone related to testosterone production;

--greater willingness to assume a receptive-female posture when approached by a sexually stimulated male.

These effects "strongly suggest, though do not conclusively prove, that TCDD impairs sexual differentiation in the CNS [central nervous system]," according to Peterson and co-workers. They go on to say that, "The present study provides the first evidence that TCDD impairs sexual differentiation of the CNS." Sexual differentiation--the full development of a female instead of a male, or vice versa--is affected by hormones circulating in the blood before and after birth.

Furthermore, these studies "strongly suggest" that "the demasculinization and feminization caused by IN UTERO and lactational TCDD exposure are irreversible," the Wisconsin researchers say. IN UTERO means "in the womb" and lactational means "from milk."

Other effects revealed by these studies include:

--Even the lowest dose tested (0.064 micrograms of dioxin per kilogram of the mother's body weight), yielded consistent reductions in a male offspring's daily sperm production.

--The developing male reproductive system is more sensitive to the effects of this hormone-like toxicant [dioxin] that any other organ or organ-system studied.

--the unborn or newborn is about 100 times more sensitive to dioxin than the sexually mature animal.

What do these studies mean for humans?

The Wisconsin researchers speculate, "Thus the findings from this study raise the possibility that TCDD could potentially affect sexually dimorphic behavior in man if exposure were to occur during fetal development." "Sexually dimorphic behavior" refers to the bodily and behavioral differences between men and women.

Peterson and co-workers point out that male rats typically inseminate a female rat with up to 10 times as many sperm as are typically needed to ensure impregnation. Humans, by contrast, typically release only about as many sperm as would be required for fertilization. "As a result," Peterson and his co-workers write, human reductions in sperm production "similar in magnitude to that in rats would be expected to reduce fertility in man." In other words, rats can continue to reproduce despite a reduction in sperm count because they produce an excess of sperm, but humans do not produce excess sperm so a reduction in human sperm count would likely reduce humans' ability to reproduce.[5]

"The real question is how general these effects are," Birnbaum says. Her EPA lab will repeat the Peterson studies with another strain of rats and eventually other species. And if these effects occur in another species? "I would get very concerned [about the potential human- health implications]," Birnbaum told SCIENCE NEWS reporter Janet Raloff.

At a public hearing on EPA's dioxin reassessment at EPA headquarters in Washington April 28, a representative of the American Paper Institute argued that only the study of humans can reveal anything meaningful about humans. Birnbaum responded somewhat testily, spelling out a dozen ways in which studies of rats and mice reveal useful information about dioxin's potential effects on humans.

June 10 at a Congressional hearing on dioxin in Washington, Assistant U.S. Surgeon General Barry L. Johnson, announced that a new study by the National Institute for Occupational Safety and Health (NIOSH) has found that workers exposed to high levels of dioxin have abnormally low levels of testosterone (male hormone) in their blood streams.[6] This finding is consistent with the rat studies of Peterson and co-workers. We have learned that this new NIOSH study was presented at a scientific meeting on June 10, but NIOSH sources have so far not released details of the new study to the general public.

At the Congressional hearing June 10, under questioning from Representative Ted Weiss (D-NY), Barry Johnson said that if it were faced with the Times Beach, Missouri, situation today, the U.S. Public Health Service would do exactly what it did 10 years ago, which is to evacuate people from their homes. He said the

Times Beach evacuation was the appropriate response and would be repeated under similar circumstances today. Another official of U.S. Public Health Service, Vernon L. Houk, made headlines 14 months ago saying if he had the decision to make over again, he would not evacuate people from Times Beach. Times Beach is a town near St. Louis where an unscrupulous waste hauler spread dioxin-contaminated oil around as a dust suppressant in the 1970s. Horses and other animals became sick and died, and the Public Health Service evacuated the town in the early 1980s.

During the Congressional hearing Dr. Houk's views were further contradicted by the testimony of Dr. Marilyn Fingerhut of NIOSH, who studied the health of 5172 workers exposed to dioxin on the job. (See RHWN #219.) Dr. Houk made headlines a year ago when he said that, if dioxin causes cancer in humans at all, it is only "a weak carcinogen." (See RHWN #249.) Dr. Fingerhut contradicted this view, reporting that, among workers who had been exposed to dioxin for at least a year at least 20 years ago, there was 46% more cancer than among average U.S. males. During the hearing, Representative Weiss characterized Dr. Houk's views on dioxin as "quirky" and "cockamamie."

--Peter Montague

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[1] Thomas A. Mably and others, "IN UTERO and Lactational Exposure of Male Rats to 2,3,7,8-Tetrachlorodibenzo-P-dioxin. 1. Effects on Androgenic Status." TOXICOLOGY AND APPLIED PHARMACOLOGY Vol. 114 (May, 1992), pgs. 97-107.

[2] Thomas A. Mably and others, "IN UTERO and Lactational Exposure of Male Rats to 2,3,7,8-Tetrachlorodibenzo-P-dioxin. 2. Effects on Sexual Behavior and the Regulation of Luteinizing Hormone Secretion in Adulthood." TOXICOLOGY AND APPLIED PHARMACOLOGY Vol. 114 (May, 1992), pgs. 108-117.

[3] Thomas A. Mably and others, "IN UTERO and Lactational Exposure of Male Rats to 2,3,7,8-Tetrachlorodibenzo-P-dioxin. 3. Effects on Spermatogenesis and Reproductive Capability." TOXICOLOGY AND APPLIED PHARMACOLOGY Vol. 114 (May, 1992), pgs. [118-126.]118-126.

[4] J. Raloff, "Perinatal dioxin feminizes male rats," SCIENCE NEWS Vol. 141 (May 30, 1992), pg. 359.

[5] In unrelated studies, Congress's Office of Technology Assessment (OTA) reported several years ago that Americans in their prime reproductive years (ages 20 to 24) have experienced an increase in infertility in recent years. See "Reproductive Dysfunction in the Population," in U.S. Congress, Office of Technology Assessment, REPRODUCTIVE HEALTH HAZARDS IN THE WORKPLACE [OTA-BA-266] (Washington, DC: U.S. Government Printing Office, 1985), pgs. 341-364. At the time of this 1985 OTA report, low doses of dioxin were not known to interfere with reproductive systems of rats or humans.

[6] Barry L. Johnson, "Testimony... Before the Subcommittee on Human Resources and Intergovernmental Relations, Committee on Government Operations, House of Representatives, June 10, [1992,"] pg. 8. Johnson is Assistant U.S. Surgeon General with the U.S. Public Health Service.

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