DDT as an Endocrine Disruptor in Human and Nonhuman Test Cases

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"Aware of the health concerns, especially in developing countries, resulting from local exposure to persistent organic pollutants, in particular impacts upon women and, through them, upon future generations."

-Stockholm Convention on Persistent Organic Pollutants, 2001

Since Rachel Carson's *Silent Spring*, the fear that bioaccumulating substances might cause genetic mutations or cancer has resonated with the international developed community. Despite evidence that DDT does not cause permanent genetic mutations [1, 2], International treaties as recent at the Stockholm Convention on Persistent Organic Pollutants effective in 2004 [3] reference multigenerational consequences as a major selling point. If not specifically genetic, what could these health concerns be? One hypothesis is that DDT is an endocrine disruptor, possibly resulting in preterm birth, early weaning, feminization and reduced fertility of male children, and sexual abnormalities of female children [1]. All of these could significantly affect future generations of a species, human or non-human, by increasing infant mortality, and hindering the next generation's ability to reproduce. Rogen and Chen [1] argue that these negative effects might even be large enough to offset the benefits of DDT used for malaria control in a pure human life comparison.

Convincing evidence has been presented for the endocrine disrupting properties of DDT in non-human species, but evidence of the effects in humans is less clear. The number of international conferences on endocrine disruption indicates a commitment of health officials to clarify this problem [4].

Endocrine Disrupting Effects in non-humans

Infant mortality and gender related birth defects related to DDT (and its metabolites) exposure have been studied for a variety of nonhuman species ranging from gulls to monkeys. Studies about DDT's endocrine disrupting effects emerged well before the ban in 1972. In 1968 Bitman et. al. compared the effects of treatment with DDT and estrogen on rats. They showed that treatment with o,p'-DDT resulted in the same effects as estrogen on immature rat uteruses after 24 hours [6]. The dosage used however, 4mg of o,p'-DDT per mouse, is significantly in excess of a normal exposure level. So although this preliminary study indicated the estrogenic effect of o,p'-DDT on rats, it certainly does not have a direct application to environmental concerns.

Of more relevance to natural endocrine disruption was a study conducted on gull embryos in Southern California. Fry and Toone [7] demonstrated that when o.p'-DDT levels as low as 2ppm were injected into fertilized eggs, it resulted in feminization of 7 out of 8 male hatchlings and abnormalities in 7 out of 9 female hatchlings (the control had 0 out of 10 feminized males and 1 out of 21 abnormal females). The level of feminization increased with the dose, strongly indicating a connection between o,p'-DDT and endocrine disruption in male gulls. The number of eggs sampled (264, 108 reaching pipping; 46 for the control, and 14-27 eggs for each of 6 compounds tested) is small for statistical significance, but presents an impressive picture.

In a study on an Alligator population in a DDT contaminated lake in Florida, Guillette et. al. demonstrated that both exposed males and females showed gonad abnormalities that greatly diminished their ability to reproduce [8]. This often sited paper

is probably the most dramatic example of environmentally occurring levels of DDT resulting in an endocrine disrupting manner.

These papers are representative of the hundreds of in depth studies published recording the endocrine disrupting nature of o,p'-DDT on nonhuman species. Many of the scientists working on these studies have appeared before EPA and international committees on endocrine disruption and several have attempted to make a link between hormonal effects in their study species and possible human effects [4].

Endocrine Disrupting Effects in Humans

Studies that have tried to link DDT levels in humans directly to endocrine effects were conducted in a much different way than those on other species. For one, the subject cannot be killed and dissected to look for more subtle variations in internal organ structure. Neither can one gather children and raise them in a laboratory. Therefore the studies that have been done about the effects of DDT on human subjects have been less controlled than their nonhuman counterparts.

Studies, such as the one conducted by Longnecker et. al. [9], have looked for correlations between maternal serum concentrations of DDT and DDE during pregnancy and certain hormone regulated abnormalities (preterm labor, gonad formation, etc.) in their children. Longnecker et. al. used blood collected almost 40 years ago from women who received prenatal care from university hospitals. They demonstrated a steadily increasing trend of preterm birth with serum DDE concentrations.

The benefit of this method is the sample size. Because the blood has already been collected along with a record of the women's and children's health, each additional

sample is relatively little work. This allowed them to use a sample size of 2613 women. The disadvantage is not being able to identify an accurate control group. Preterm birth has been associated with several health factors besides DDT, including but not limited to smoking, weight, height, and age. Separating the effects of DDT from other physical and sociological factors proves to be challenging problem. Although the authors of this study attempt to address it, it is difficult to know if they accounted for all of the other environmental factors that could lead to the observed outcome.

DDT was concluded to act as a lactation suppressant in a study conducted by Rogan *et. al*. [10]. In this case, soon to be mothers were asked to participate in the study and submitted breast milk and other samples on a regular basis for multiple years. The authors took great care to address possible accidental correlations in a variety of ways (primarily resulting in the same outcomes as previously calculated).

In general the human case studies evaluating DDT as an endocrine disruptor have been compelling, but only show a correlation, not a causal relationship. Other associations have been even less conclusive than the ones addressed here, such as seaman count, menstrual cycle irregularity, and birth weight [1].

There are two possible reasons why the link between endocrine disruption, birth related problems, and gender related birth defects has been much more clearly demonstrated in nonhuman species. The first might be that the species being studied are actually more susceptible to the endocrine disrupting properties of DDT and its metabolites than humans are.

The second possibility is that it is impossible to subject human subjects to substantial quantities of a toxin, force them to mate, and then kill and dissect their offspring. These

methods that are used on animal subjects lead to much more comprehensive and conclusive results because they allow scientist to examine tissue and look for a causal relationships.

However, statements such as the one quoted at the beginning of this paper from the Stockholm Convention on Persistent Organic Pollutants [3] indicate that international policy makers are prepared to take leap from the scientific proof a correlation between DDT concentrations and hormonal induced effects in humans to the assumption of a causal relationship.

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