

# **SPIRITUALITY AND SUSTAINABILITY**

## **Man-Made Chemicals and Health of the Unborn**

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Decades ago the Great Lakes in North America had many predatory birds that fed on fish in the lakes. Wildlife biologists noticed a dramatic decline in nests with live young, and between 1980 and 1983 there were very few birds that successfully reproduced. Biologists had known of the disastrous thinning effect of high levels of the pesticide, DDT, with the result that eggs would break prior to hatching ; also, chicks were being found dead with gross deformities. Now, with lower levels of pesticides and industrial chemicals in the lakes, the egg shell thinning and gross deformities were not seen, and most people assumed that the problem of pollution had been solved by the regulations enacted during the 1970s. But, something was still happening to reduce reproduction. One strange observation that, at first, there was no explanation for was that nests contained more than the typical 2 to 3 eggs, and instead, double clutches, nests with 5-6 eggs, were being found. In some areas in which this was observed, populations of Gulls were mostly females. There were very few males, and females were pairing with each other instead of with a male. Many of the eggs in these double clutches were not fertilized.

Where had all of the males gone? Why were these female Gulls exhibiting abnormal reproductive behaviors and pairing with other females? Michael Fry, an avian biologist, provided a possible answer when he measured the levels of DDT in Gull eggs found in nests, and then administered the same amount of DDT to Gull embryos that he had measured in eggs. The experimentally treated eggs were produced by Gulls that had not been exposed to man-made chemicals. The DDT caused sex reversal in males, making the male embryos appear as if they were females. However, all of the DDT exposed embryos were intersex (they had some male and female reproductive organs), and they were sterile. DDT ingested by a female Gull was being transported into her eggs and causing effects in male embryos that were similar to effects of treating embryos with the natural sex hormone, estrogen. Estrogen is critical as a regulator of sexual development in birds as well as all other vertebrate animals, including humans. The levels of DDT and other pollutants were no longer high enough to cause death or gross externally visible malformations, such as beaks that were crossed, but instead, more subtle damage not as easily detected was occurring in embryos that led to functional and behavioral abnormalities that became apparent much later in adulthood.

Biologists studying fish in the Great Lakes were also alarmed that so many different types of fish were showing abnormalities, including reduced fertility or sterility. There was not a top predator fish being found in the lower Great Lakes that did not show evidence of an abnormal thyroid. Entire populations of salmon and trout were not reproducing, and their reproductive organs were also abnormal. Thyroid hormone is essential for normal development, particularly of the brain, in all vertebrate animals.

At the same time that these observations were being made, I was conducting research showing that the sensitivity of fetuses to hormones, such as the most potent of the natural estrogens, estradiol, was remarkable. A change in the level of estradiol in the blood of a mouse fetuses of less than 1/10 of a trillionth of a gram per milliliter of blood (which we refer to in toxicology as 1/10 of a part per trillion) was sufficient to completely change the course of development of the brain and reproductive organs, resulting in changes in behavior and organ function throughout the remainder of life. Importantly, the potency of estradiol in mice is identical to its potency in humans.

As a background to this discussion of chemicals in the environment that can mimic natural hormones, I want to now tell you just a little about the endocrine system and how the hormone messengers that make up the endocrine system regulate the development of organs during prenatal life. The endocrine system consists of many different glands that produce hormones and many tissues in the body that have receptors that allow cells in the tissue to respond to a specific hormone. Most important is that the developing fetus cannot be thought

of as a little adult, who is capable of responding to changes in hormones by making physiological adjustments - the principle of homeostasis can not be applied to fetuses as it can to adults. As I just pointed out, fetuses are incredibly sensitive to hormonal disturbance. Why is this? Lets take as an example two sex hormones, testosterone (T) and estradiol (E) that have a dramatic influence on sexual development in humans and all other vertebrates. These hormones turn on and off genes in developing cells - not due to the presence or absence of the hormone, but based on minute changes in the amounts of these hormones in the fetal blood. Once a set of genes is turned on or off, they have been irreversible set and can never be altered again. For example, one consequence is that the relative amounts of testosterone and estradiol determines whether a fetus develops female reproductive organs or male reproductive organs - not a very subtle consequence of what would be considered by anyone to be minute changes in hormone levels. We refer to these effects as "organizational" changes, since the organs are permanently organized. The same thing happens in the brain, leading to differences in socio-sexual behaviors, such as aggression, activity levels, and sexual orientation. If you have raised both a boy and a girl you understand the consequence of these small differences in the levels of hormones in male and female fetuses.

Our dependence of hormones to regulate development has made us incredibly vulnerable to hormonal disruption during development. The recognition that environmental man-made chemicals could alter development led Theo Colborn contact me in 1990. Based on the very high sensitivity of fetuses to hormones that I was showing, Theo and I believed that it was possible that much lower levels of environmental pollutants than had previously been thought to cause effects might, in fact, account for the damage to wildlife that was being observed in the Great Lakes and elsewhere in the world. In 1991 Theo organized a meeting and subsequently published a book of the workshop proceedings at which the issue of endocrine disruptors was first addressed.

Why was this not previously found if the chemical revolution that led to the widespread use of man-made chemicals began in the 1950s. The reason is the very long generation time in people and many of the most affected species. If effects of endocrine disruptors are "programmed" during fetal life but do not become apparent until adulthood when attempts to reproduce continuously fail, it is logical that this problem is only now being widely recognized even though widespread exposure may have occurred decades ago.

Six years after the first workshop on endocrine disruptors there is now clear evidence that a wide variety of chemicals in use today can alter the endocrine system in developing animals and humans. These chemicals are showing up in unlikely places. They are present in a wide variety of products and are being released into the air we breath, the water we drink and the foods we eat. None of these chemicals was thought to be a "hormone mimic" when it was first synthesized for use as a pesticide or in some product, such as plastics or hand cream. It is only very recently that some of these chemicals have been discovered to be "environmental estrogens" that can mimic the hormone estradiol and alter development of the reproductive system. This can occur at doses thousands of times lower that the doses predicted by the crude testing methods currently used by industry to test the safety of the few chemicals that are actually directly tested for their effects in animals.

For example, based on prior animal tests with bisphenol A, the chemical used to make polycarbonate plastic, the plastic coating in metal cans, and in dental sealants used to protect teeth, daily intake of bisphenol A of 50 parts per million was estimated to be safe based on information provided by the chemical industry to the US government. We have reported that feeding a pregnant mouse a dose 25,000-times lower than this (2 parts per billion) for seven days resulted in a permanently enlarged prostate in male offspring as well as a decrease in daily sperm production. Female offspring showed early puberty. All of these effects are typical responses to an increase in estrogen levels during fetal life. The 2 parts per billion dose of bisphenol A is within the range of human daily consumption of this chemical in food, water and from use in dentistry as fillings and sealants, as reported by the plastics industry.

We have also directly tested the presumed safe daily intake level of a currently used pesticide, methoxychlor, and found that when fed to pregnant female mice, it also increased prostate size, decreased sperm count and increased aggressive behavior in male offspring. Incredibly, these findings with bisphenol A and methoxychlor represent the first actual experimental tests of the presumed safe intake doses for these chemicals. These doses had only been predicted to be safe based on hypothetical models of the biological response to chemicals. Because of the belief of toxicologists in these models, no one was actually testing to

see if the presumed safe levels were accurate and whether the doses of chemicals that we are actually ingesting are safe.

The implications of these findings for the process of testing chemicals for safety are profound. Clearly, current methods are leading to false conclusions with regard to safe levels of exposure to endocrine disrupting chemicals. The challenge will be for the establishment that has developed based on these flawed assumptions to accept this “paradigm shift”.

There are 3 changes that we are recommending to regulatory agencies with regard to chemical testing methods:

- Directly test environmentally relevant doses of chemicals. Also, after determining the mixture of chemicals in specific populations, test these mixtures for effects at the doses being monitored in wildlife and people.
- Directly test chemicals for developmental effects, particularly those that may not become apparent until much later in life.
- Examine offspring exposed via the mother for effects other than gross malformations and cancer, since changes in organ function, such as decreased sperm count, have not been examined using traditional toxicological testing methods.

Not all endocrine disrupting chemicals are estrogen mimics. Other chemicals, such as polychlorinated biphenyls (PCBs), that have been used in many products due to incredible resistance to heat, and dioxin, an industrial waste produced as a consequence of manufacturing chlorinated chemicals, can interfere with normal thyroid function during embryonic life. Not only have effects of PCBs been shown to occur in laboratory animals and wildlife, but a recent study in humans have shown that levels of PCBs in fetal blood predict the rate of postnatal neuromuscular development (which is delayed), a child’s behavior and even their IQ, which is lowered by 6 points if they were exposed as fetuses to the highest levels of PCBs. In one of a number of studies relating exposure to PCBs in the womb or via breast milk to subsequent abnormalities, mothers were recruited based on having eaten a few fish per month from the Great Lakes. But, sport fishing remains a multi-billion dollar a year business in this region, and governments and industries who profit from this activity by taxes, fishing licenses and selling products do not want to take action regarding the health risks posed by eating these fish.

Particularly frightening about PCBs and other highly persistent chemicals, such as DDT, which can remain active in your body for decades, is that they “bioaccumulate or biomagnify” as they are transported up the food chain and finally reach animals, such as humans, at the top of the food chain, who are thus the most heavily contaminated by these chemicals.

In addition, we now know with certainty that PCBs and other persistent chemicals are being transported around the globe via the atmosphere. Thus, whenever a chemical is released into the environment, its impact is not local but global. This is truly a world-wide problem that no laws that focus only on local communities will solve. One sad commentary on the approach to global pollution in USA is that whereas it became illegal to use DDT in the USA 25 years ago, it was not banned from production or sale by US companies abroad. Levels of DDT in the Great Lakes are now not decreasing due to atmospheric transport of DDT from use in other countries.

The finding that exposure of human fetuses to a man-made chemical predicts brain function later in life, and the confirmation of identical findings in animal experiments and studies of wildlife exposed to the same chemicals, now leaves no doubt that man-made chemicals in the environment can disrupt the endocrine system during development, with profound consequences for the functioning of the brain and reproductive system. The list of chemicals that can alter the normal functioning of the endocrine system in animals is growing, and this list is certain to get larger as testing for endocrine disruption finally becomes a part of the screening of chemicals for health effects. Now that there is overwhelming evidence of a problem, the

question is how are industry and government regulators responding to the information that scientists are producing?

At this time the position of the chemical industry is one of denial that a problem has been shown with regard to human health. There is, on the other hand, acceptance that wildlife and laboratory animals are showing effects. The assumption underlying this argument is that humans are somehow disconnected from the rest of the animal kingdom, and that chemicals can have dramatic damaging effects that can be demonstrated in every class of vertebrate: fish, frogs, alligators, Gulls, laboratory rodents and mammalian wildlife (such as mink), but, somehow we can believe that this does not mean that we should also expect to see effects in humans.

With regard to the likelihood of significant species differences in the capacity for environmental chemicals to cause endocrine disruption, there is consensus among biologists that at the molecular, mechanistic level, the response system to hormones (hormone receptors in cells) as well as the hormones that make up the endocrine system, are so fundamental to development and normal life that they have changed remarkably little over 300-million years of vertebrate evolution. Thus, the sex hormone estradiol in fish and humans is absolutely identical, and the receptor protein for estradiol in fish and human cells is fundamentally the same with regard to its response to estradiol. However, specific genes controlled by estrogen will differ in each species. Binding of natural estradiol or other man-made estrogenic chemicals to the estrogen receptor in fish has thus been shown to predict that a response (albeit a different response) will also occur in humans, and this has been known for decades, it is not a new finding! Thus, in a chemical is an endocrine disruptor in fish or any other vertebrate, it can reasonably be expected to disrupt the endocrine system in humans. If we reject the relatedness of humans to the rest of the living world, we open up the possibility that global pollution will be viewed as only a problem for plants and animals, but not for humans.

Industry representatives state that until "solid scientific proof" of effects in humans is obtained, they should not be expected to alter production or use of chemicals, such as bisphenol A, based only on information from animals. With regard to the standard of proof being set by industry whose products are being found to act as endocrine disruptors, we cannot and, hopefully, will never allow experiments to be conducted with people. Human effects are determined by the least sensitive of all methods of study, epidemiology, where effects at the population level are looked for. Finding relationships between exposure of women to endocrine disruptors prior to or during pregnancy and lactation and abnormalities in immune function, behavior, fertility, or other traits will require prospective studies that are only now being planned. Can we afford to wait decades until offspring from these studies are adults and showing problems to take corrective action. Or, do we take a "weight of evidence" approach, such as is now accepted for cigarette smoking and adverse health effects, and act now to begin reducing exposure to chemicals that are endocrine disruptors in animals. Remember, no study has provided "solid scientific proof" that cigarette smoking is dangerous to your health, since this would require a human experiment, which has not been conducted.

Industry in the United States has tremendous control over environmental laws enacted by congress, as well as the federal agencies that regulate chemicals. It has proven almost impossible to eliminate any chemical from the marketplace through federal regulatory action once it becomes economically valuable to an industry. Instead, civil lawsuits have been the only vehicle open to the US population to remove or restrict chemicals in commerce. A few examples are asbestos, Silicon and tobacco. Only through an intensive campaign of public education regarding the problem of global pollution and the long-term harm to the health of our children, those yet unborn, and all animal life, with resulting public and legal pressure on industry, will any positive response by the chemical industry occur.