Endocrine Disruptors as Water Contaminants:
Toxicological Implications for Humans and Wildlife

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Certain hormonally active chemicals, collectively called endocrine disrupting chemicals (EDCs), are known to mimic or block natural hormones in animals. The U.S. Environmental Protection Agency (EPA) defines environmental EDCs as xenobiotics (agents foreign to an organism) that interfere with the "synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior."

The discovery that certain compounds can mimic the natural hormones of animals was reported as early as the 1930s. However, the estrogenic activity of synthetic organic compounds was of little interest to the environmental community until several decades later when the pesticide DDT was implicated as the cause of deformed sex organs and skewed sex ratios in gulls living in contaminated areas. Additional studies have demonstrated that endocrine disruption in a wide variety of wildlife species, including marine gastropods, frogs, fish, and alligators, is associated with exposure to synthetic chemicals such as pesticides, steroids, surfactants, and plasticizers.

Initial attempts to identify the cause of feminization of fish exposed to sewage treatment plant effluents focused on synthetic organic chemicals with known estrogenic effects, such as plasticizers and surfactant degradation products. However, recent research suggests that natural estrogens and a common synthetic birth control pharmaceutical, ethinylestradiol, are the most potent estrogens in sewage effluent. In fact, researchers have demonstrated that ethinylestradiol can induce endocrine disruptive effects in fish at concentrations present in some municipal sewage effluents.

Endocrine disruption also can be caused by naturally occurring chemicals. Estrogens from plant sources, known as phytoestrogens, have been linked to reproductive failures in animals, such as sheep that graze on certain strains of clover. Various over-the-counter medicinal supplements, such as those recommended for estrogen replacement therapy in post-menopausal women, contain high levels of phytoestrogens. Industrial activities such as pulp and paper production also can release large quantities of phytoestrogens that may impact reproductive system function in fish. The degradation of vegetable matter and paper products in wastewater treatment plants also may contribute to releases of phytoestrogens into the aquatic ecosystem.

What Are the Human Effects?

The impacts of trace concentrations of EDCs on wildlife naturally lead to concerns about their potential effects on humans. The best-documented example of endocrine disruption in humans involved in utero exposure to the synthetic estrogen diethylstilbestrol (DES), a pharmaceutical administered to pregnant women to prevent miscarriage. Its use resulted in adverse reproductive impacts in human offspring, and it is no longer prescribed to pregnant women.

Although decreases in human sperm quality and quantity and increases in some cancers over the past 40 to 50 years have been attributed by some researchers to the presence of EDCs in the environment, the scientific community is far from consensus on the matter. Adverse human health effects from EDCs are unlikely to be caused by estrogenic chemicals in water, because their concentrations in water result in estrogen-equivalent doses that are minute compared to those due to phytoestrogens and other estrogenic compounds present in food sources. Estrogenic hormones in water also are less likely to cause adverse effects in humans, who ingest limited quantites of water, than in fish, which are constantly exposed to EDCs present in the aquatic environment.

Concerns also have been raised regarding human health effects associated with pollutants that interact with other hormone systems. Perchlorate, which has contaminated groundwater and surface waters throughout the United States and has a direct impact on the thyroid gland, is one such pollutant. The EPA currently is establishing a reference dose for perchlorate, which is expected to become the first drinking water contaminant regulated for endocrine disrupting toxicity.

Some scientists suggest that certain drinking water disinfection byproducts (DBPs) may act as EDCs. Several reports associate increases in spontaneous abortions and cancers in humans to elevated concentrations of halogenated DBPs. Additionally, the federal Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) suggests that DBPs be included among the mixtures evaluated for endocrine disruptive effects. Since DBPs generally are orders of magnitude greater in concentration than other contaminants and have been implicated as human reproductive toxicants, efforts to control EDCs and pharmaceuticals and personal care products (PPCPs) by oxidation may ultimately prove counterproductive due to increased potential for byproduct formation.

PPCPs Widespread in the Environment

Over the past several decades, a wide variety of PPCPs have been reported as environmental contaminants, including

antibiotics, X-ray contrast media, analgesics, antiseptics, insect repellants, and many other products. In the United States, a recent survey indicated widespread PPCP contamination of streams. Unfortunately, sparse data exist to explain the toxicological relevance of trace pharmaceutical compounds in the environment. Nevertheless, public perception regarding the presence of PPCPs in water supplies has focused attention on this issue despite the very low concentrations reported.

Lingo

androgenic compounds
compounds that mimic testosterone, the primary sex hormone in males

anti-estrogens, anti-androgens
compounds that may block the action of natural hormones

endocrine-disrupting compounds (EDCs)
agents produced outside an organism that interfere with the "synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior" (EPA)

estrogenic compounds
compounds that mimic estrogen, the primary sex hormone in females

pharmaceuticals and personal-care products (PPCPs)
(Also called organic wastewater contaminants, or OWCs) a general category of organic compounds found in wastewater that are being studied for their potential to cause endocrine-disrupting behavior. Includes prescription and nonprescription drugs, steroids, insect repellents, detergent metabolites, disinfectants, plasticizers, fire retardants, antioxidants, fragrances, polyaromatic hydrocarbons, and solvents.

phytoestrogens, phytoandrogens
estrogens and androgens from plant sources

U.S. Regulatory Issues

The Safe Drinking Water Act of 1974 requires the EPA to establish maximum contaminant levels for various drinking water contaminants, including some pesticides now known to have endocrine-disruptive activity. However, endocrine disruption was not specifically named in any U.S. legislation until 1995, when amendments to the Safe Drinking Water Act and Food Quality Protection Act mandated the screening of chemicals and formulations for potential endocrine activity before manufacture or use in certain processes where drinking water or food can become contaminated. To meet the requirements of this recent legislation, the EPA formed EDSTAC to recommend a conceptual framework, priorities, and screening and testing methodologies for EDCs. The committee's final report in 1998 recommended that human and wildlife impacts be considered and that estrogen, androgen, and thyroid endpoints be examined. In addition to screening for discrete chemicals, EDSTAC recommended evaluating mixtures of chemicals in breast milk, baby formulas, hazardous waste sites, pesticides and fertilizers, drinking water DBPs, and gasoline.

In 2001, the EPA formed the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) to evaluate the battery of tests suggested by EDSTAC. EDMVS is tasked with determining if a particular method is transferable to other laboratories, can be validated with representative chemicals, has sufficient sensitivity to endocrine endpoints, and has appropriate standard operating procedures. The screening battery recommended by EDMVS will be important to the water industry, as it will be designed to definitively identify EDCs. However, the current legislation does not regulate the water industry, only those industries producing or using raw chemicals. As a result, these actions may have little immediate effect on water and wastewater treatment regulations.

Federal regulations for pharmaceuticals in drinking water or natural waters currently are lacking. The Food and Drug Administration requires ecological testing and evaluation of a pharmaceutical only if an environmental concentration in water or soil is expected to exceed one microgram per liter or 100 micrograms per kilogram, respectively. In light of the recent data on the occurrence of PPCPs in the aquatic environment, it might be prudent to reconsider these policies. While extensive monitoring programs are underway, toxicological studies conducted at environmentally relevant concentrations are necessary to establish reasonable regulations. California is considering establishing regulations based on the potential impacts of EDCs and PPCPs, especially where municipal wastewater effluent is recycled for indirect potable reuse. A recent modification to California's draft regulations for indirect potable reuse states, "Each year, the PGRRP [planned groundwater recharge reuse project] shall monitor the recycled water for endocrine disrupting chemicals and pharmaceuticals specified by the Department, based on a review of the PGRRP engineering report and the affected groundwater basin(s)." Although the regulations have not been finalized, many practitioners of indirect potable reuse in California are establishing monitoring programs for EDCs and PPCPs. Because California's water reuse program often establishes precedents for programs throughout the world, other regulatory agencies will likely adopt similar language in their own water recycling programs.

Toxicological and Analytical Challenges

Without question, trace levels of contaminants such as EDCs and PPCPs make their way into water supplies by

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way of sewage effluents. Several reports indicate that aquatic organisms residing directly downstream from some effluent discharges are impacted by EDCs. However, these impacts usually are changes in biomarkers that have not been correlated to population-level effects. An example is induction of vitellogenin, a fish egg yolk precursor, in the blood of male fish exposed to exogenous estrogenic chemicals. Vitellogenin has no known function in male fish and its presence in their blood is considered evidence of endocrine disruption. However, vitellogenin induction is not known to affect reproductive performance in male fish (that is, it might not represent a clearly adverse effect).

It is important to determine if changes in biomarkers in organisms exposed to EDCs and PPCPs translate into adverse effects within the population. Furthermore, methodology for EDC testing has not been validated or standardized. For instance, a round-robin study on vitellogenin analysis commissioned by the EPA demonstrated that variability was unacceptably high, up to 173 percent. Very few reports have shown EDC/PPCP occurrences in drinking water. However, until the EPA testing program is in place, predicting which compounds actually have endocrine activity and therefore should be target analytes is difficult. For many compounds, analytical methods are not available to measure trace concentrations in water. When methods are available, few laboratories may have the capability to conduct the analyses. But advances in analytical technology will certainly lead to the discovery of more contaminants at lower and lower levels. Determining the toxicological relevance, if any, of these trace contaminants is critical to establishing reasonable treatment goals.

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