Are Environmental Sentinels Signaling?

Gerald A. LeBlanc

Department of Toxicology, North Carolina State University, Raleigh, NC 27695 USA

There is an increasing perception that environmental contamination by chemicals no longer poses a significant health threat and that relaxation of environmental regulations is warranted. However, many wildlife populations are showing signs of developmental, behavioral, and reproductive dysfunction due to environmental contamination by endocrine-disrupting chemicals. Scientists, regulators, and legislators must mobilize to identify current health threats posed by environmental pollutants, develop testing protocols that will detect such properties of new chemicals, and strengthen legislation designed to protect environmental health. Key words: chronic toxicity, endocrine disrupters, environmental sentinels, pesticides, reproductive toxicity.

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The year 1995 marked the 25th anniversary of both the U.S. Environmental Protection Agency and Earth Day. The inception of both institutions signaled the need to temper anthropogenic stresses on the environment or face unsettling consequences. Decades of environmental abuse culminated in the 1960s when public perception of the repercussions of unabated environmental pollution was heightened by Rachel Carson’s graphic depictions (1). The pressing environmental problems of 25 years ago were blatant. Among the most significant of these problems were chemical and sewage discharges making aquatic resources unsuitable for human use and habitation by aquatic organisms, and the use of pesticides, which posed a significant threat to nontarget species. In response, the Clean Water Act was instituted in 1972 to regulate waste discharge and to ensure that high water-quality standards were maintained. The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) was amended three times during the 1970s to provide safeguards against pesticide-mediated harm to human and environmental health. Such legislation provided the foundation upon which a sound and reasonable national environmental policy was established. This policy has resulted in significant improvement in environmental quality concurrent with population and economic growth. The success of the environmental protection policies of the United States is best exemplified when environmental quality of the United States is compared to that of industrialized countries of the former Soviet block and other countries where such policies were never significantly instituted (2–4).

With the current movement toward the reduction of government size and spending, the issue is often raised as to whether environmental legislation and supporting research programs could be relaxed without intolerable consequences. Major fish and wildlife kills due to chemical waste discharge and improper pesticide usage are now largely relegated to distant memory. If one accepts the thesis that fish and wildlife species serve as sentinels for the protection of human health from environmental contaminants, then human health must also be adequately protected from the adverse health effects of pollution. Such logic supports the contention that environmental legislation and research need not be expanded and could perhaps be relaxed. However, not factored into this argument is that, while the flagrant environmental problems of 25 years ago have been addressed, more subtle, though no less beguiling, environmental threats may persist. Central to this issue is the question, are environmental sentinels currently signaling the existence of such environmental hazards?

Toxicant-mediated endocrine disruption is one example of a toxicological hazard currently presenting itself in the environment. Endocrine-disrupting effects of environmental pollutants were first recognized when investigating mechanisms responsible for reproductive failure among some bird species exposed to organochlorine pesticides (5). The observation that exposure to some chemicals can lead to reproductive failure led to the promulgation of regulations under FIFRA and subsequently expanded to nonpesticide chemicals under the Toxic Substances Control Act requiring that the effects of chemical exposure on the production of viable offspring be determined. Such tests, conducted in standard test species of birds, fish, mammals, and invertebrates, involve chronically exposing the parent organisms to various concentrations of a chemical, then assessing the number of viable offspring produced (6). With fish, only subchronic testing, involving the assessment of the effects of the chemical on survival and growth of larval fish, is initially required. Assessments of reproductive toxicity are mandated only if the no-observed-effect level established during the subchronic toxicity test is greater than 1/10 the expected environmental concentration of the chemical (6). Retrospective assessments have shown that such approaches will adequately protect the environment against most chemicals (7). However, unique toxicological properties of some chemicals can result in undetected toxicity using these protocols. Endocrine-disrupting chemicals can be among these undetected toxicants because they may 1) elicit effects on the developing fetus that are not manifested until the mature organism enters its reproductive stage, 2) elicit specific biochemical/physiological changes that affect an organism’s reproductive capacity without affecting survival and growth as measured during subchronic testing, or 3) adversely affect endocrine processes characteristic of some species but absent in those surrogate species used in toxicity testing. Many pesticides, industrial chemicals, and wastes are among the toxicants that elicit such effects.

Shore birds such as gulls and terns typically produce broods of two or three eggs. Ornithologists began observing in the 1970s that broods of five or six eggs were not uncommon (8). This abnormal clutch size was found to be due to multiple females sharing a nest (9). This female–female pairing appeared to be due to a deficiency in reproducitively competent males (10). Laboratory investigations demonstrated that exposure to DDT feminized male gulls during embryonic development (11). Further, incidence of female–female pairing was higher in environments with significant DDT contamination (10). Thus, abnormal breeding behavior in these birds appeared to be due to reproductive deficiency in males caused by embryonic exposure to environmental pollutants. This observation is not only of historical relevance, as female–female pairing of terns has been noted recently in areas contaminated with polychlorinated biphenyls (PCBs) (12).

Female Poeciliidae fish inhabiting areas receiving pulp mill effluent have been observed to undergo masculinization. Most obvious is the modification of the anal fin in...
affected females to a gonopodidlike structure (used by males for sperm transmission) (13). Exposure to exogenous androgens has been shown to cause similar masculinization (14), and androgens generated by the action of bacteria on phytosterols present in the effluent are presumed to be responsible for this effect. Fish exposed to paper and pulp mill effluent can also experience altered steroid hormone titers (15), impaired gonad development (16), and reduced fecundity (17). Such effects, specific to reproduction, would not be detected in subchronic toxicity tests.

Propiconazole is a member of the imidazole-derivative class of fungicides. A common characteristic of these chemicals is their ability to inhibit enzymes responsible for steroid hormone biosynthesis and enzymes involved in steroid hormone metabolism (18,19). A consequence of this effect is severe reductions in some steroid hormone levels (18). This specific and potent effect has led to the consideration of some imidazole-derivatives for use as a male contraceptive (20). Propiconazole, which is used as an agricultural fungicide, shares these properties and thus has the potential to compromise reproductive success of chronically exposed organisms. These effects would not be detected in a subchronic toxicity test that did not evaluate reproduction. The Ecuadorian shrimp industry has called for a moratorium on the use of propiconazole for fear that it is responsible for the demise of shrimp populations (21).

Trichloroethylene has been used extensively for more than 20 years as an antifoulant in marine paints. Trichloroethylene has been identified as the causative agent responsible for imposex in many marine mollusk populations. Imposix is the imposition of sex characteristics of one gender onto another (a form of pseudohermaphrodisim). In the case of trichloroethylene-exposed mollusks, females develop a penis, vas deferens, and in severe cases, seminiferous tubules (22). Affected females can be rendered infertile because the vas deferens blocks the release of eggs from the oviduct. The mechanism responsible for this effect has not been conclusively established, but it seems to involve the neu- roendocrine regulation of sexual differentiation (23). Trichloroethylene can cause imposex at low part per trillion concentrations and has caused the extinction of some affected populations (22). Certain mollusk species may be particularly sensitive to the effect of trichloroethylene owing to unique aspects of sexual differentiation in these organisms (24).

Intersexuality also has been observed in some crustacean populations in the vicinity of sewage discharge, though causality has not been established (25). Peri- and neona-
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