

## **MECHANISMS AND EFFECTS OF ENDOCRINE DISRUPTION**

### **IN FISH: ARE THEY ECOLOGICALLY RELEVANT?**

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#### **EXTENDED ABSTRACT ONLY- DO NOT CITE**

##### **Introduction**

Considerable progress has been made in understanding the mechanisms by which environmental compounds may act to disrupt normal endocrine functioning in fish. And while compounds that interact with endogenous hormone receptors (i.e., the estrogen receptor) and their biological effects still dominate the literature, other potential EDC mechanisms continue to be investigated. In selected cases, EDC mechanisms have been correlated to, and in some cases causally linked to effects observed in feral fish populations, including compromised growth and reproduction, altered development, and abnormal behaviour. Some specific actions of EDCs in fish involve alterations in hormone biosynthesis, metabolism, bioavailability, or transport. Hormone action may be modulated by EDCs that compete with endogenous hormones for specific, high affinity receptors or EDCs may affect down-stream signalling events (Fairbrother et al., 1999; WHO/IPCS, 2002). The most popular examples of EDC-mediated effects in fish are, ultimately, the result of changes to reproductive, adrenal (interrenal), or thyroid physiology. Studies have demonstrated a wide range of effects from the molecular to the whole animal level. Yet, there is a lack of evidence to suggest that many of the effects are ecologically relevant in terms of their impact on population fitness. From a mechanistic perspective, this paper briefly discusses a few of the popularized effects of EDCs such as the induction of vitellogenesis, altered steroid biosynthesis, and compromised stress responses in fish.

##### **Induction of Vitellogenesis by Estrogenic Compounds**

Vitellogenin (vtg) induction in juvenile or male fish in the field has become one of the most notable and convincing biological responses of fish linked to exposures

to estrogenic compounds. Numerous studies indicate that several different estrogenic compounds in the complex effluent may be responsible, particularly natural (17 $\beta$ -estradiol (E<sub>2</sub>) and estrone) and synthetic estrogens (ethinylestradiol) or industrial chemicals (e.g., nonylphenol). As estrogens are the only known stimuli for the production of vtg, the presence of vtg in male or immature fish is a clear indication of exposure to estrogenic chemicals in the environment. Production of vtg requires the binding of estrogenic compounds to cytosolic estrogen receptors in the liver, followed by their translocation to the nucleus where they stimulate transcriptional activity. Some implications of elevated levels of plasma vtg at the individual level have been examined (e.g., retarded testicular growth, kidney damage, reduction of metabolic expenditure on growth and spermatogenesis, reduced E<sub>2</sub> levels), but there is no evidence to suggest that EDC-induced vtg production adversely affects population fitness (Kime, 1998; WHO/IPCS, 2002). Perhaps other adverse effects, such as testicular abnormalities, ovotestis or hermaphroditism, observed in feral fish exposed to estrogenic compounds have more potential than vtg induction to translate into effects at the level of the population.

#### **Reproductive Abnormalities Induced by Pulp and Paper Mill Effluent**

Reproductive abnormalities observed in fish residing downstream of pulp mills vary depending on the location and the species examined. In Canada, studies found that fish exposed to bleached kraft mill effluent (BKME) had delayed sexual maturation and reduced expression of secondary sexual characteristics, gonad size, and sex steroid levels. The mechanisms behind these alterations are not well understood and the active compounds in BKME have not been conclusively identified. The mechanism responsible for the demasculinizing effect may involve the concomitant decrease in plasma androgen levels, which are the result of BKME actions at multiple locations in the hypothalamus-pituitary-gonad axis (e.g., decreased pituitary gonadotropin levels, inhibition of steroidogenic enzymes within the gonad). Conversely, masculinizing effects (i.e., development of male-like gonopodium) of BKME have been observed in female mosquitofish in streams below mills in the United States. These effluents were found to contain degraded phytosterols that may act agonistically at the androgen receptor. Although this case clearly demonstrates that BKME is an EDC, there is little evidence to suggest that BKME affects the health or fitness of exposed populations. In fact, one study found that the viability of eggs and sperm and the viability of developing larvae of exposed suckers were normal (Fairbrother et al., 1999; WHO/IPCS, 2002).

## **Compromised Stress Response by Exposure to Heavy Metals**

In fish, stress results in the activation of the hypothalamus-pituitary-interrenal (HPI) axis, culminating in increased plasma cortisol concentrations. Field studies suggest that environmental contaminants may chronically stress fish resulting in a compromised HPI response. Yellow perch and northern pike from sites contaminated with PAHs, PCBs, and heavy metals were unable to produce cortisol in response to acute handling stress and their ACTH-producing cells were atrophied. The atrophy was speculated to be caused by prolonged hyperactivity of these cells. Recent studies on brown trout exposed to metals had comparable levels of cortisol compared with control fish; however, the metal-exposed fish were found to be hypersecreting ACTH and CRH to maintain baseline levels of cortisol. Similar studies demonstrated that fish chronically exposed to metals had a compromised stress response in acute stress trials. While chronic stress can result in elevated glucocorticoids and affect growth, reproduction, and immune responses, more research is necessary to determine the impact of EDC-induced compromised stress responses on the health of feral fish populations (WHO/IPCS, 2002).

### **Summary**

Determining whether the effects of EDCs are relevant to population fitness is complicated because many factors can adversely impact growth, reproduction, and survival. Food availability, disease state, competition, or habitat loss may impinge directly on many of the endocrine measures and physiological endpoints that are used to evaluate fish for the effects of EDCs. Understanding the mechanisms by which EDCs alter endocrine function in fish may provide researchers with a clearer view of the risks that the contaminants pose to fitness and health of feral fish populations, but there are numerous challenges inherent to this task. At present, there is uncertainty in how EDCs effects at the individual level may translate into effects at the level of the population. Further implementation of fish-based screening assays for endocrine-active compounds, as well as an increased emphasis on partial/full-life cycle exposure studies of fish to EDCs will aid in our understanding. It may be possible to better understand the risks posed by EDCs, particularly during critical periods of development, if more research efforts were directed at understanding basic endocrinological processes in a variety of fish species.

### **References**

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