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Statistical Modelling Suggests That Anti-Androgens in Wastewater Treatment Works Effluents are Contributing Causes of Widespread Sexual Disruption in Fish Living in English Rivers.

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Abbreviations:

E1: estrone
E2: 17β-estradiol
EE2: 17α-ethinyloestradiol
ER: estrogen receptor
NP: nonylphenol
NP1-nEO: nonylphenol ethoxylates (1-5 ethoxylate chain length)
SPE: solid phase extraction
WWTW: waste water treatment works
YAS: yeast androgen screen
YES: yeast estrogen screen

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Abstract

Background: The occurrence of feminised male fish downstream of some wastewater treatment works has led to substantial interest from ecologists and public health professionals. This concern stems from the view that the effects observed have a parallel in humans, and that both phenomena are caused by exposure to mixtures of contaminants that interfere with reproductive development. The evidence for a "wildlife human connection" is, however, weak: Testicular dysgenesis syndrome, seen in human males, is most easily reproduced in rodent models by exposure to mixtures of anti-androgenic chemicals. In contrast, the accepted explanation for feminisation of wild male fish is that it results mainly from exposure to steroid estrogens originating primarily from human excretion.

Objectives: We sought to further explore the hypothesis that endocrine disruption in fish is multi-causal, resulting from exposure to mixtures of chemicals with both estrogenic and anti-androgenic properties.

Methods: Hierarchical generalized linear and generalized additive statistical modeling were used to explore the associations between modeled concentrations and activities of estrogenic and anti-androgenic chemicals in 51 UK rivers and feminised responses seen in wild fish living in these rivers.

Results: In addition to the estrogenic substances, anti-androgenic activity was prevalent in almost all treated sewage effluents tested. Further, the results of the modelling demonstrated that feminizing effects in wild fish could be best modelled as a function of their predicted exposure to *both* anti-androgens and estrogens *or* to anti-androgens alone.

Conclusion: The results provide a strong argument for a multi-causal aetiology of widespread feminisation of wild fish in UK Rivers involving contributions from both steroidal estrogens and xenoestrogens and from other (as yet unknown) contaminants with anti-androgenic properties. They may add further credence to the hypothesis that

endocrine disrupting effects seen in wild fish and in humans are caused by similar combinations of endocrine disrupting chemical cocktails.

Introduction

Wildlife populations associated with the aquatic environment can be exposed to concentrations of endocrine-disrupting pollutants that are high enough to compromise their reproductive capacity (Reviewed by Vos et al. 2000) which may, in turn, have population-level consequences(Kidd et al. 2007). The widespread nature of these abnormalities has led to substantial interest from scientists and the general public. This concern stems, in part, from the hypothesis that reproductive diseases seen in humans are also caused by exposure to the same chemical contaminants (Skakkebaek et al. 2001). The actual evidence to support the wildlife-human connection is, however, weak. Moreover, in most cases there is little evidence to link cause and effect in even a single species, let alone multiple species. Some of the best evidence has been found in riverine fish populations where feminization of wild male fish (e.g. Jobling et al. 1998) is thought to be caused predominantly by exposure to steroidal estrogens in WWTW effluents originating from human and animal excretion (Desbrow et al. 1998; Routledge et al. 1998) with more minor contributions from other estrogenic chemicals found in WWTWs effluents, such as bisphenols and phthalates, nonylphenols (NP) and their ethoxylates and carboxylates (Gibson et al. 2005; Harries et al. 1997; Vajda et al. 2008; Vethaak et al. 2005). Supporting the role of these steroidal estrogens in the feminization of wild fish, recently, a very strong correlation was shown between the predicted steroid estrogen content of UK rivers and feminisation in wild fish (Jobling et al. 2006). Reproductive disorders also seen in human males are, however, best induced by exposing laboratory rodents to environmentally relevant concentrations of anti-androgens and estrogens rather than to estrogens alone (Skakkebaek et al. 2001; Sharpe and Skakkebaek, 2005), thus suggesting that the aetiology of human and fish –