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Consequences of endocrine disrupting chemicals on reproductive endocrine function in birds: Establishing reliable end points of exposure

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Abstract

It has been difficult to establish reliable indices of exposure to endocrine disrupting chemicals (EDCs) appropriate for a variety of avian species because of a vast array of reproductive strategies. Data from mammals, reptiles and fish provide insight on likely mechanisms of action for EDCs. However, many of the effects of EDCs are weaker than the actions of the native hormones, making it difficult to assess adverse effects in domestic and wild birds. It is clear that differential sensitivity to EDCs exists across species, due to the timing and mode of exposure, compound toxicity and age of the individual. Our studies on EDCs are conducted in the quail model system, with focus on reproductive endocrine, neuroendocrine and behavioral responses. Studies have included EDC exposure, either by egg injection or via diet. Results from egg injection studies showed the following: (1) estradiol administered by embryonic day 12 demasculinized male sexual behavior, altered hypothalamic neurotransmitters and reduced hen day production and fertility in a dose dependent fashion, (2) methoxychlor (MXC) or vinclozolin impaired male sexual behavior in adult quail and (3) DDE exposure impaired reproductive and immune related end points. Two-generation studies were conducted on Japanese and northern bobwhite quail with dietary methoxychlor (MXC) exposure (0, 5 and 10 ppm) beginning in adults (P1), continuing in their offspring (F1), with F2 offspring raised on control diet. MXC exposure impaired male sexual behavior, hypothalamic catecholamines and plasma steroid hormones. Moreover, MXC exposure had reproductive consequences observable at both the lower and higher doses of MXC in

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F1 and F2 generations. These data demonstrate that embryonic EDC exposure interferes with sexual differentiation of neural systems that direct reproduction.

Keywords: Endocrine disrupting chemicals; Neuroendocrine measures; Reproductive end points; Immunotoxicology

1. Introduction

Endocrine disrupting chemicals (EDCs) include a number of environmental chemicals and chemicals found in plant products that interact with an endocrine system, often due to activity as a hormonal mimic. Unfortunately, it was not apparent that pesticides, herbicides, industrial chemicals and even plant hormones had endocrine activity in vertebrate species. Recognition of the potential activity of many of these compounds has led to research and review activities of national and international scope to characterize the effects of these chemicals [1–4].

There is somewhat unique challenge for those scientists attempting to characterize the potential impact for a single compound or a mixture of EDCs. First, toxicological tests may not detect the effects of EDCs because the measurement end points or variables under study are not sufficiently sensitive to endocrine disruption. This difficulty is compounded by the problem that many of the EDCs have fairly weak endocrine activity. Unfortunately, if the exposure is great enough to elicit a significant change in toxicological end points, it may also be at lethal levels. Conversely, if the measured response is below detection, it may be considered harmless. This conclusion may also be reached if there are differential sensitivities of various organisms, or if there are specific stages of the life cycle with greater vulnerability. Further, mixtures of EDCs, and consideration of the bioactivity of metabolites of an EDC complicate assessment of EDC impact. Therefore, there must be research based on mechanisms of action for classes of these compounds in order to attempt to address these issues that consider species specificity and life cycle sensitivity for suspected EDCs.

Given our current understanding of the activity of EDCs, many of the traditional measures for toxicity of compounds appear to be relatively insensitive in birds. Therefore, a document was written by the OECD Expert Group on assessment of EDC effects in birds in which measurement endpoints were identified from both current toxicological testing protocols. Basically, the current guidelines were expanded to include a number of critical measures that are important in development and function of the hypothalamic pituitary gonadal (HPG) system. Furthermore, the endpoints were assessed according to sensitivity as well as duration of visibility of impact (for review, see [3]). For example, embryonic exposure to a potent EDC is likely to have both short-term effects on neuroendocrine and endocrine impacts as observed at hatch as well as long-term effects that will persist in the maturing and adult animal. Due to the involvement of many of the neuroendocrine systems in regulating both reproductive and metabolic systems, the potential for impact by EDCs is significant even with differential sensitivities among individuals and between species [6–11]. In addition to efforts to characterize appropriate and reliable measurement