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Can farm animals help to study endocrine disruption?

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Abstract

The phenomenon of endocrine disruption can be regarded as part of the disciplines of toxicology and environmental toxicology. These two disciplines have generated guideline protocols on how various effects of chemicals should be tested as a basis for regulatory decisions. These protocols almost exclusively involve laboratory rodents and the data obtained are then used for human risk assessment. Would it be justifiable, then, to introduce or promote the use of other species in these test protocols? There are, at any rate rationales for studying effects in species other than laboratory rodents: (1) other species may better mimic the human system; (2) they may in some cases be more useful for studying a certain mechanism or phenomenon; (3) they may highlight the diversity of effects or sensitivity between species. However, there are at least two basic criteria that must be met for a species before it can be introduced in this context: (a) we must have a good understanding of the physiological system to be studied; and (b) we must have a number of tools to study effects on this system. When it comes to the reproductive system – regarding which most endocrine disruption has been reported – farm animals are second only, or in some respects superior, to laboratory rodents with respect to these criteria. This review gives examples of how farm animals can be of use in the study of endocrine disruption with a focus on the author's own data from studies in the pig.

Keywords: Endocrine disruption; Farm animals; Pigs; Male; Testosterone

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1. Endocrine disruption

An endocrine-disrupting chemical (EDC) has been defined as an exogenous substance that alters the endocrine system and consequently causes adverse health effects (IPCS Steering group, Joint IPCS/OECD Scoping Meeting on Endocrine Disrupters, 16–18 March 1998, Washington, DC, USA). The effects of this disruption may vary depending on when the exposure occurs from activational in the adult to organizational in the developing individual (reviewed by McLachlan [14]). The effects in the developing individual are mostly irreversible, whereas those in the adult may be reversible. Thus, the definition of EDCs relates to a mechanism of action for a variety of chemicals in humans, domestic animals and wildlife. Endocrine disruption is therefore of relevance both in human and experimental animal toxicology and in environmental toxicology. The classic example of endocrine disruption in humans is the side effect of the use of the drug diethylstilbestrol in pregnant women, whose in utero-exposed daughters showed an increased risk of developing clear-cell cervicovaginal cancer (reviewed by Giusti et al. [8]). In the environment, one of the first examples of endocrine disruption was eggshell thinning in peregrine falcons caused by DDE [18], although the mechanism was not understood until much later [12].

Currently the greatest cause for societal and scientific concern is the possible disruption of reproductive endocrinology, though other endocrine systems may also be affected. The focus here, therefore, will be on endocrine disruption affecting the reproductive system.

2. Rationales for studies in farm animals

Obviously there is an interest per se in how chemicals in the environment, including those in feedstuffs, may affect the reproductive performance of farm animals (reviewed by Sweeney and Rhind [23,19]). However, as indicated in the title, the scope of this article is to highlight how studies in such animals can contribute in a more general way to increasing our understanding of endocrine disruption.

To make a significant contribution to this scientific field, there are at least two criteria that have to be met for a “new” species that is to be introduced: (1) there needs to be a considerable body of knowledge about the reproductive physiology and pathology of the species of concern; and (2) we must also have a set of tools to assess this physiology and pathology. As a result of the paramount importance of reproductive performance in animal production, a solid scientific and technical platform has been established in this area, thereby fulfilling the two criteria mentioned.

The generality of data obtained from studies on EDCs in laboratory rodents can always be challenged with reference to the physiological diversity of the animal kingdom. This is true with regard to toxicology relating both to wildlife and humans. In the latter case, it is difficult for practical reasons to generate a regulatory system using other species than laboratory rodents. Even so, high-quality and detailed experimental studies in farm animals would reveal how universal findings in laboratory rodents actually are for EDCs.

Besides this general rationale for performing studies in species other than laboratory rodents, it may be speculated whether there could be certain advantages in conducting studies in farm animals rather than rodents. Such advantages may relate to the suitability of such animals as a model for humans or for studies on a particular mechanism or phenomenon.