



Comprehensive Toxicology : Reproductive and Endocrine Toxicology

K. Boekelheide, R. Chapin, P.B. Hoyer, C. Harris, C.A. McQueen, A.J. Gandolfi, I.G. Sipes

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Section 1, the section on male reproductive toxicology, starts with a basic overview on the anatomy and physiology of the system. This is followed by reviews on the way molecules are evaluated for male reproductive toxicity in both the pharmaceutical and chemical industries, along with a strategy for evaluating the reproductive function of transgenic animals. The bulk of this section is devoted to reviewing mechanisms and manifestations of toxicants to particular targets within the male reproductive system (Sertoli cell, Leydig cell, etc.). Finally, a significant part evaluates areas of interest not often considered in the toxicologic context (fluid flow, the immune system, paracrine factors, etc.), as well as a part highlighting technical advances and what these mean for the field. Overall, this volume reviews the state of the science in a number of areas, explicitly provides strategies for investigators to use in addressing their own problems, and then looks forward to identify promising areas of future research. It is a most significant contribution to the field.

Section 2 provides a comprehensive overview of the field of female reproductive toxicology. Much interest has recently become focused on this area of toxicology, due to the increase in numbers of women in the workplace, and the impact of female fertility on reproduction issues. This section begins with an overview of female reproductive physiology, with an emphasis on the complexities of its hormonal regulation. Next, the various components of the female reproductive system are described in detail, along with known and potential sites of disruption by xenobiotics. Finally, assessment of human risk is discussed from the standpoint of classical methods of evaluation, as well as recently developed, novel experimental approaches.

Section 3 provides an overview of mammalian development, from fertilization to parturition and early postnatal maturation, in terms of the stage-selective anatomical and functional characteristics of each developmental phase that may underpin the ultimate manifestations of toxicity which have been observed. Several possible mechanisms of developmental toxicity are discussed in terms of the roles of biotransformation, pharmacokinetics, altered gene expression, neurobehavioral development, physiological conditions, and nutritional status. A selected list of chemical agents and environmental extremes known to produce persistent developmental abnormalities is reviewed by class and are discussed in terms of their known toxic effects and possible mechanisms of action. Strategies for the study of developmental toxicants *in vivo* and *in vitro* are described, as well as current screening and testing systems for the detection of additional potential disrupters of normal development. This section concludes with a summary and discussion of the critical needs for additional understanding and the future prospects for accurate prediction, prevention and assessment of risk in developmental toxicity.

Volume 10 concludes with five chapters that discuss the effects of chemicals on various endocrine tissues. These include the thyroid and parathyroid glands, the adrenal cortex and medulla, and the insulin secreting beta-cells of the pancreas. Since these tissues secrete hormones that cause profound biochemical and physiological effects on the body, the activities of these glands are tightly controlled, primarily by circulating factors. For example, trophic factors released by the pituitary gland upregulate the activities of the thyroid gland and the adrenal cortex. The pituitary gland is further regulated by releasing factors produced in the hypothalamus. Thus, the hypothalamus-pituitary-endocrine gland axis, provides for the fine regulatory control of hormone secretion. It is apparent, then, that chemicals can affect endocrine function either directly,

at the level of endocrine gland, or indirectly at the level of the hypothalamus-pituitary. However, the situation is even more complex. Since chemicals that alter the metabolism of the hormone (i.e. enzyme induction or inhibition in the liver) can cause an imbalance in the "axis", with dramatic effects on the endocrine gland and ultimately on other tissues of the body. The various chapters provide examples of drugs, model toxicants, and environmental pollutants that disrupt endocrine function. These disruptions result in such toxicities such as diabetes, hypertension, thyroid tumors, immune dysfunction, bone disorders, among others.

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