14.1 Introduction

Over the last century and into the present, tens of thousands of chemicals have entered the environment, and the vast majority of the world's population is regularly exposed to a hodgepodge of these chemicals. Large numbers were designed to combat a wide variety of pest species, while others were generated as end-products, or as by-products of industrial applications. By design, a growing number of pesticidal chemicals act by impairing those mechanisms responsible for regulating reproduction in targeted plant and animal species. However, it is rarely the case that a pesticide affects only the intended population and precludes the emergence of resistance in that population. Unanticipated alterations in reproductive systems of non-targeted organisms are regularly detected. For chemicals that enter the environment as hazardous by-products of manufacturing processes, toxicities can vary considerably, and the sources of exposure to contaminants can also be quite different. Some exposures may be occupational, while others can be due to proximity to factories and waste disposal sites, or from exposures within residential structures. There are also concerns with the amount of pharmaceutical waste present in the environment.

The female reproductive system provides multiple targets for environmental toxicants, and there are clear examples of how each part of the system can be influenced by a range of chemicals. It should also be noted that the functional impact of a chemical will differ depending on the species involved and the parameters of exposure. Mammalian reproductive strategies exhibit varying degrees of dissimilarity that may temper or increase a toxicant's effectiveness. In addition to the existence of metabolic differences, distinct variations include the importance of seasonality, the presence or lack of spontaneously occurring ovarian cycles, the number of oocytes released at ovulation, the endocrine requirements for pregnancy maintenance, and the extent of maturation at birth. Nevertheless, despite such differences, mammalian reproduction is the end result of a dynamic process that develops during

gestation and continues postnatally. It is a process that is dependent on a functionally intact system of communication that manages activity within a physiological axis comprised of the brain, pituitary and gonads, while interacting with associated organs (the oviducts/Fallopian tubes and uterus) in the reproductive tract. Hormonal signals from the brain and pituitary are sent to the ovaries, which in turn communicate back. Both excitatory and inhibitory signaling is present within this hypothalamic-pituitary-ovarian (H-P-O) axis and both coordinate to regulate a recurrent maturation of ovarian follicles and the release of their oocytes at ovulation. Apart from some slight evolutionary modifications, the hormones that serve as the basis for communication within this axis are decidedly conserved in all mammals. Moreover, many chemicals have been shown to modify the synthesis, release, and receptor binding of specific hormones and, as a result, alter reproductive development and function in adulthood. Consequently, the issue of endocrine disruption by environmental compounds has emerged as a major concern in Reproductive Toxicology and has been a focus of international regulatory organizations charged with the registration of agricultural and industrial use chemicals. Portions of this chapter will therefore review basic relationships within the axis in order to provide a meaningful description of the effects of exogenous chemical exposure on reproductive function in the mammalian female.

Apart from some differences in the timing of endocrine signaling among the hypothalamus, pituitary and ovaries, this interspecies correspondence in communication within this axis suggests that the impact of a toxic insult in one mammalian animal species is frequently able to speak to effects in other members of the class. Whereas non-human primates present an animal model that most closely approximates human reproduction, their use in toxicological research has been limited by ethical and economic reasons. For a number of reasons, the great majority of reproductive studies with mammals have employed rodents as test subjects, and many have employed a variety of apical assessments,