

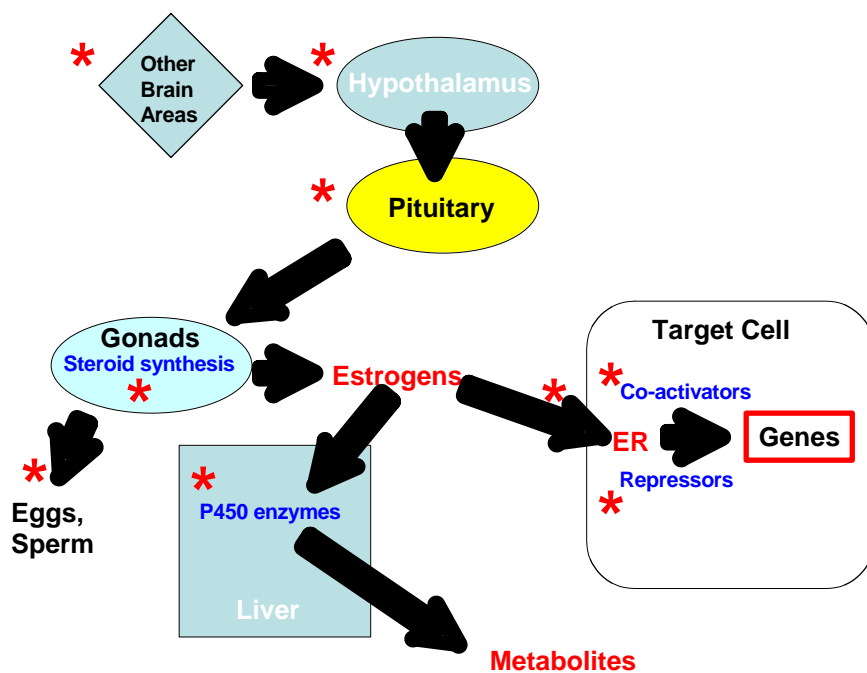
**XENOESTROGEN ACTIONS ON REPRODUCTION:  
IMPLICATIONS FOR HEALTH OF WILDLIFE AND HUMANS**

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**Abstract:** The endocrine systems of all vertebrates operate basically the same in controlling or modifying all aspects of physiology and behavior. Reproduction is controlled by the brain (hypothalamus) and pituitary gland that in turn control the activities of the gonads (ovaries and testes) responsible for synthesis of steroids including estrogens and androgens (the HPG axis). Hormones produce their effects by binding to specific protein receptors on target cells. If enough hormone is present and enough cells are stimulated, an effect characteristic of the hormone is observed in the animal. Xenoestrogens are endocrine-active chemicals that can alter endocrine function. Binding of natural estrogens or xenoestrogens activates receptors and stimulates other biochemical changes in target cells. Most known xenoestrogens activate estrogen receptors and consequently are additive in their effects when present in mixtures. Some may affect synthesis or metabolism of natural hormones or may modify events that occur after receptor activation through a variety of mechanisms (Figure 1).

One route of introduction of xenoestrogens into the environment is through wastewater treatment plants (WWTPs). The majority of natural and pharmaceutical estrogens excreted by humans as well as xenoestrogens from numerous domestic and industrial sources (e.g., detergents, plastics, cosmetics, etc.) enter WWTPs. Many of these compounds are retained in biosolids and a smaller portion typically appears in the wastewater effluent depending on the chemical and the type of wastewater treatment, retention times, etc. Treated wastewater effluent is discharged from the WWTPs directly into rivers and lakes or into estuarine environments. Biosolids frequently are used for fertilizer or dumped in landfills from which they can find their way into surface and ground waters. Xenoestrogens may have adverse reproductive effects in aquatic and terrestrial wildlife through sex reversals (altered sex ratios), production of intersexes (individuals with both male and female tissues), alterations in mating or parental behavior, and prevention of gonadal maturation or activity of the HPG axis (contraception). Additionally, their presence in wastewater represents a wakeup call for concerns about human health. Humans are exposed daily to xenoestrogens in food (e.g., phytoestrogens, PCBs, various pesticides) and from contact with detergents (e.g., nonylphenols) and plastics including plastic bottles, metal beverage can linings and food packaging (e.g., phthalates, bisphenol A, nonylphenols). Health care contributes estrogenic chemicals through pharmaceuticals and plastics used for surgical tubing, gloves, etc. In addition, many personal care products (e.g., shampoos, cosmetics, aftershave lotions) contain xenoestrogens including phthalates, nonylphenols, and bisphenol A. Xenoestrogens in downstream drinking water are too low to produce direct estrogenic effects in adult humans, but they can add to xenoestrogens from other sources. More importantly, the extreme sensitivity of the mammalian fetus to environmental chemicals encountered during pregnancy may have delayed effects that appear at puberty or adulthood or even in later generations. Numerous studies in mice and humans are reporting effects of extremely low concentrations of xenoestrogens on fetuses including effects that can appear in subsequent generations that were not exposed to the xenoestrogen.

Figure 1. Potential Sites (\*) of Xenoestrogen Action on the HPG axis. P450 enzymes are active in both the synthesis and metabolism of steroids such as estrogens. Co-activators and repressors are capable of altering the effectiveness of activated receptors (ER = estrogen receptor) in affecting gene activity and subsequent protein synthesis in target cells. Some metabolites may still be estrogenic.



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