cause them to exert diverse actions upon target cells. Some EDCs are agonists of hormone receptors expressed on neuroendocrine cells. For example, estrogen receptors can bind EDCs, including Polychlorinated Biphenyls (PCBs), phytoestrogens, pesticides, compounds in plastics such as bisphenol A, and other chemicals.\textsuperscript{4-6} Dioxins and some PCBs are potent agonists to the aryl hydrocarbon receptor (AhR),\textsuperscript{7} which is abundantly expressed in the brain. Other EDCs may act as antagonists to hormone receptors or as mixed agonist/antagonists. For example, PCBs can cause activation or suppression of thyroid hormone receptor activity depending upon the specific PCB mixture or dose. Phthalates are androgen receptor antagonists, and vinclozolin, a fungicide, acts, at least in part, as an anti-androgen.

Although not the subject of this review, it is important to mention that EDCs may exert their actions upon neurotransmitter systems that regulate neuroendocrine cells. PCBs have been shown to bind to serotonin, dopamine, and noradrenergic receptors.\textsuperscript{8} As these neurotransmitters act upon the hypothalamic releasing factors that control the pituitary gland, this is another mechanism for neuroendocrine disruption.

### 3. DEVELOPMENTAL EXPOSURE TO NEUROENDOCRINE DISRUPTORS

The timing of exposure to an EDC is crucial in determining its ultimate effect. It is recognized that there are critical developmental periods during which neuroendocrine systems are modulated by steroid and other hormones. For example, early life exposure to endogenous androgens or estrogens, particularly in fetal life and infancy, organizes the brain in a sexually dimorphic manner (i.e. resulting in morphological and functional differences between males and females) that becomes activated later in life.\textsuperscript{10-12} Exposure to exogenous substances such as EDCs is likely to have more profound detrimental consequences in developing organisms than in adults.\textsuperscript{12,13} This concept is now referred to as the “fetal/developmental basis of adult disease” and is highly applicable to neuroendocrine systems. For example, in the case of the HPG axis, early life exposures to environmental EDCs can permanently alter sexual development, resulting in females that are masculinized or defeminized and males that are feminized or demasculinized.\textsuperscript{14-17} As discussed below, these effects of EDCs on brain sexual differentiation are manifested as changes in reproductive development and may be detrimental to fertility and reproductive success. Therefore, the fetal/developmental basis of adult disease is a critical concept for neuroendocrine disruption.

### 4. ENDOCRINE DISRUPTION OF SEXUAL DIFFERENTIATION OF THE BRAIN

Neuroendocrinologists have known for decades...