Seminar: Endocrine Disruption: History, Fact and Fantasy of Gender Bending Chemicals

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Prenatal gender determination, sexual maturation during adolescence, and reproductive function in adulthood are all under hormonal control. Accordingly, hormonally active chemicals can potentially produce reproductive birth defects (such as gender ambiguity and hypospadias), abnormalities in sexual development and adult reproductive function, as well as alterations in the incidence of hormone dependent cancers (e.g., prostate, uterus, and breast). Such chemicals have been referred to as endocrine disruptors or ”gender benders.” Numerous observations in wildlife and humans are suggestive environmentally-induced endocrine disruption. Among these are: 1) “clover disease” or impaired fertility of grazing livestock; 2) demasculinized alligators in Lake Apopka, Florida and reproductive abnormalities in aquatic birds of the Great Lakes; 3) association between exposure to the synthetic estrogen, diethylstilbestrol (DES), in utero and vaginal cancer in human offspring; 4) association between kepone exposure of chemical plant workers and decreased sperm count; 5) a large (50%) decline in sperm production in the developed world over a 50 year period; and 6) an association between tissue levels of certain chemicals and the incidence of human breast cancer.

A diverse array of environmental substances (such as selected PCBs, alkylphenols, DDT derivatives, insecticides, pharmaceuticals and plant and fungal agents) exhibit hormonal activity, particularly in their ability to interact with the estrogen receptor (ER). The ER is a cellular protein which enables a target cell to recognize and respond to the estrogenic (female) sex hormone, estradiol. The “promiscuity” of the ER is the most prevalent mechanism for endocrine disruption and chemicals that interact with ER are referred to as environmental estrogens, xenoestrogens, or estrogen mimics. The binding of xenoestrogens to ER is usually very weak (0.1% or less) relative to estradiol. However, one such xenoestrogen, bisphenol A, a constituent of plastics and dental restorative materials, has been reported to produce enlargement of the prostate in adult mice exposed to low doses of the substance in utero.

Media coverage, as well as the book, Our Stolen Future (Colborn, Dumanoski, and Meyers), has raised the public awareness and concern about endocrine disruption. In view of the chemical diversity of potential “gender bending” chemicals, endocrine disruption is an issue of particular interest to numerous industries, such as plastics, food packaging, petroleum, pesticides, agricultural products, pharmaceuticals, and chemicals. The Food Quality Protection Act (FQPA) and the Safe Drinking Water Act (SDWA) (1996) mandated the EPA to implement the Endocrine Disruptor Screening Program (EDSP) in order to test for endocrine disruptive effects in over 87,000 substances or mixtures. Endocrine disruption is an issue relevant to the reproductive toxicity provisions of California Proposition 65. H.R. 852, the Environmental Health Research Act authorizes the NIEHS to fund necessary research to study “the effects of environmental toxins on endocrine development and hormone disruption.” In addition to activity in the US, the Commission of the European Communities (European Union) in its White Paper entitled “Strategy for a future chemicals policy” (February, 2001) regards endocrine disruptors as “substances of very high concern” on the basis of their association with such conditions as breast and prostate cancer, decreased sperm production and genital deformities.

In addition to this historical background, the seminar will address some or all of the following issues:

- Controversies surrounding observations suggesting endocrine disruption.
- The explanation of promiscuity of ER.
- What other factors influence the biological action of xenoestrogens?
- Can biological actions or adverse effects of xenoestrogens be predicted?
- What is the status of the EDSP?
- Are putative low dose in utero effects of bisphenol A in mice relevant to humans?
- What are the conclusions of certain expert panels on endocrine disruption?
- Do other hormones (e.g., androgens, progestins, thyroid hormone, and glucocorticoids) participate in endocrine disruption ?