Daria Z. Hall
Chemistry 505 – Environmental Chemistry
PIM #3 – Endocrine Disruptors
July 31, 2006

Introduction:

All living things contain chemical messengers that are known as hormones. Hormones play a critical role in the development and function of the reproductive, immune and nervous systems (*1*). The endocrine system is one of the body's main communication systems (like the nervous system). It controls and coordinates many body functions. Hormones are produced by endocrine tissues that are located in the sexual organs, pituitary, thyroid, and pancreas. These chemicals are then secreted into the blood as chemical messengers. Hormones work with the nervous system, reproductive system, and other organs to help control body energy levels, reproduction, growth and development, and responses to surroundings, stress and injury (*2*). There are, however, compounds, both natural and man-made, that can compromise this behavior. Compounds that change normal hormone behavior are known as endocrine disruptors. These chemicals have come to the forefront due to the increased number of cancers, reproductive problems, and developmental abnormalities, such as the increase in cases of breast cancer by forty percent since 1973 (*1*).

How do endocrine disruptors work?

Hormones are secreted into the bloodstream by endocrine cells. They travel throughout the body via the circulatory system, until they reach specific cells that can recognize that particular hormone. Only cells that bear the appropriate receptor protein will be responsive to that hormone; the cell will then react to the presence of the hormone. Before the cell can initiate a reaction, the hormone must bind to the cell receptor, sort of like a key into a lock (*3*).

Anything, either man-made or naturally occurring, that interferes with the endocrine system of hormone production and transmission is referred to as environmental estrogens or endocrine disruptors. Endocrine disruptor is perhaps a more fitting name since not all compounds affect estrogenic receptors. Some of the chemicals have androgenic, anti-androgenic, and thyroid-like activities, as well as others (*2*).

Endocrine disruptors work in several ways. The disruptor may mimic the shape of the hormone enough to bind to its receptors. This can occur with estrogens, androgens, and thyroid hormones, and could possibly cause over-stimulation. The disruptor may occupy the hormone's typical binding site, and instead of causing overproduction, it would prevent normal hormone activity. They could also interfere with the way that hormones or their receptors are made or controlled; for example, they could change the number of hormone receptors present, or change the amount of hormone produced. It has also recently been discovered that in addition to interfering with the binding of hormones to their receptors, some compounds can also accelerate the breakdown of natural hormones, or even promote the conversion of male hormones to female hormones (*1*).

What Are Different Types of Endocrine Disruptors?

Compounds that act as endocrine disruptors are many and varied. The compounds presented below are just a tiny sample of chemicals that have been implicated as endocrine disruptors. Some of these chemicals come from natural sources as well as man-made sources. For example, phytoestrogens are substances in plants that have hormone-like activity. Many of these compounds can be found in soy-derived products (*2*).

Other endocrine disruptors are man-made. These include bisphenol A (BPA). BPA is used in the manufacturing of compact disks, polycarbonate bottles, and other plastic products (*1*). It can leach out of these products when heated, which can be of particular concern given that BPS is found in food and beverage containers (*2*). Once free, it can bind to estrogenic receptors (*4*). Another class of chemicals that is suspect is compounds that are byproducts of industry. These include dioxins, furans, and polychlorinated biphenyls (PCBs). These are essentially industrial waste products, although PCBs are also used in electrical components as well. They tend to accumulate in the food chain (*1*). This means that as each higher order animal consumes a lower order animal, the contamination builds. Thus, there is typically an accumulation of these compounds in the fatty tissues of animals that are high in the food chain. The contamination can then be passed from mother to infant via the placenta or breast milk. These compounds tend to decrease estrogen levels (dioxins and PCBs), as well as increase thyroid stimulating hormone levels (PCBs) (*1*).

A major source of endocrine disruptors is pesticides. These include hexachlorocyclohexane (Lindane) and DDT and its metabolites. These compounds are used world wide, although DDT is no longer produced or used in the US. These compounds again tend to accumulate in the food chain. Lindane can also be absorbed through the skin when it is used as a treatment for head lice and it has anti-estrogenic actions. DDT and its metabolites affect androgen receptors (*1*).

Why Should Endocrine Disruptors Concern Us?

Endocrine disruptors are of major concern because they tend to be the antithesis of all toxicological knowledge. First, the effects can occur at very low dosage (*4*). The effectiveness of most toxins depends upon a minimum dosage for the effect to occur. In addition, the chemical may have the opposite effect at higher doses, so it is virtually impossible to predict its effects at varying dosages. For example, tamoxifen, a breast cancer drug, can act as an estrogen agonist or antagonist, depending on the dose (*1*). The dramatically low levels at which endocrine disruptors can have an affect are lower than current testing procedures are examining. In addition, these miniscule amounts suggest that there is no threshold at which these compounds would have no effect (*4*). These extremely low levels can harm infants and fetuses, while they may not harm adults (*1*).

Additionally, exposure is not limited to just one chemical. Humans and wildlife alike are exposed to hundreds of chemical throughout their lifetimes. This mixing of chemicals could produce unforeseen effects that would be different from each chemical taken separately (*1*). For example, in a study performed by Bergeron, et al. in 1994, the effects of chemical mixtures were studied by looking at the sex of turtle hatchlings. Typically, the

sex of the turtle hatchlings is dependent upon the incubation temperature. However, researchers painted the eggshells with both single chemicals and chemical mixtures, then incubated the eggs under conditions that would normally produce male hatchlings. Some of the mixtures produced female hatchlings, but when the chemicals in the mixture were applied separately, they had little or no effect (*5*).

Finally, the effects might not be noticeable upon direct contamination. Offspring of those organisms that have been contaminated may ultimately show the effects of the endocrine disruptors (*1*). Therefore, if the organisms in question are humans, the effects may not be seen for decades after the exposure to the chemical.

What Do Estrogen Disruptors Do?

As varied as are the chemicals that act as estrogen disruptors, so are the effects caused by those chemicals. Hormones play a critical role in the development and function of the reproductive, immune and nervous systems. When normal hormone activity is compromised during development, unalterable changes may occur in the development of organs, altering their structure, function or both. These effects have been thoroughly studied in both wildlife and laboratory animals. While there is evidence of undesirable effects on humans, not all feel that the evidence is conclusive (*1*).

One of the largest concerns is the role of endocrine disruptors in cancers of hormone sensitive tissue, such as breast cancer and vaginal carcinoma. Again, the effects of the endocrine disruptors are often unnoticeable until the offspring of those in contact with the chemicals demonstrate them. For instance, diethylstilbesterol (DES) was taken in the mid 20th century to prevent spontaneous abortions. The daughters of the mothers who took DES had increased rates of clear cell carcinoma of the vagina, which is typically a fairly rare cancer (*6*).

In addition, given the role of estrogen in the development and progression of breast cancer, there is an obvious concern that estrogen mimics would also be a problem. Not only would these chemicals be able to enter the body through food, water, and air, but they would also be bombarded by cosmetics containing these chemicals that would be applied to the underarm and breast area. They would provide a more direct pathway via dermal absorption to the breast. The cosmetics at fault could be substances such as aluminum salts, which are present in antiperspirants, triclosan, which can be found in deodorants, and sunscreens, along with many other compounds (*7*).

Conclusion:

Endocrine disruptors can have many negative effects on living organisms, human and wildlife alike. They can disrupt development, and cause reproductive, neural, immune and other problems. In addition, they are thought to cause a decline in fertility and an increase in diseases such as endometriosis and cancers (*2*). However, many remain unconvinced of their detriment to humans. It is imperative that further research occur to discover more about the effects of low dose endocrine disruptors, the results of mixtures of these disruptors, as well as their possible undesirable effects to humans.

Literature Cited:

1. *Environmental Endocrine Disruptors – What Health Care Providers Should Know*, URL http://www.envirohealaction.org/upload_files/enddisprimer.pdf (accessed July 27, 2006)
2. *Endocrine Disruptors,* URL http://niehs.nih.gov/oc/factsheets/pdf/endocrine.pdf (accessed July 27, 2006)
3. Campbell, N.A. *Biology*; Third edition; The Benjamin/Cummings Publishing Company, Inc: Redwood City, CA, 1993; pp 908-909.
4. *Our Stolen Future,* URL http://www.ourstolenfuture.org (accessed July 27, 2006)
5. Bergeron, J. M., Crews, D., McLachlan, J. A. *Environ Health Perspect.* **1994,** *102,* 780-781.
6. Herbst, A.L.; Ulfelder, H.; Poskanzer, D.C. *NEJM.* **1971,** *284,* 878-881.
7. Darbre, P.D. *Best Pract Res Clin Endocrinol Metab.* **2006,** *20,* 121-143.