PHYSICIANS FOR SOCIAL RESPONSIBILITY

Environmental Endocrine Disruptors

WHAT HEALTH CARE PROVIDERS SHOULD KNOW

Why You Need to Know About Endocrine Disruption

THE PUBLIC HEALTH LITERATURE tells us that a number of cancers, reproductive problems, and developmental abnormalities are on the rise. For example:

- In the past fifty years, the rate of new cases of testicular cancer in industrialized countries has increased by a factor of two to four.[1]
- The rate of new breast cancer cases in the United States has increased forty percent since 1973.[2]
- Also increasing, at least as tracked into the early 1990s, are abnormalities of sexual development, such as malformations of the genitals and urinary tract in males.[3]
- Since the 1950s, physicians have also observed that the age of initial breast and pubic hair development and the onset of menstruation in girls in the United States is occurring earlier than traditional norms.[4]

The increased frequency of these and other reproductive and developmental problems is puzzling. Improved diagnosis may account for some of the increase, but it is probably not the only explanation.

THE ENVIRONMENTAL CONNECTION

This same half-century has seen the advent of the large-scale production, use, and discharge of man-made chemicals into our environment. Yet most of the over 80,000 chemicals that have been produced in the United States have not been tested to determine whether they could harm human health.[5] Recent evidence confirms that environmental factors play a significant role in causing diseases such as cancer.[6] In addition, there is now more attention focused on a wide range of subtler, non-cancer effects of exposure to synthetic chemicals.

Many synthetic chemicals have been detected at low levels in the bodies of animals and in humans for years, but scientists have only recently begun to investigate whether such low dose exposures might be highly significant, especially during fetal and infant development. In the last decade, medical

This document addresses the following topics about endocrine disruption:

researchers and government officials have launched extensive new research efforts to consider this possibility. Government research programs in the U.S., Europe, and Asia, as well as chemical industry, academic, and NGO-led initiatives, have contributed to a large and growing body of evidence that some chemicals and other substances can alter or interfere with hormonal activity with significant health and developmental impacts. The National Academy of Sciences evaluated this evidence in 1999, finding that endocrine disruption is already occurring in wildlife and that further investigation is needed to evaluate possible risks to humans. In response to this emerging health threat, the U.S. Environmental Protection Agency is developing a program to begin screening and testing some substances for their ability to disrupt hormonal activity. Most recently, a panel of top scientists convened by the National Toxicology Program reported that low dose effects of endocrine disrupting agents—that is, effects at doses below those that are usually studied—have been demonstrated in laboratory animals. These experts have also called for revisiting current chemicals testing paradigms for reproductive and developmental toxicity.[7]

DO YOU HAVE THE ANSWERS?

Public awareness has been raised by news stories on "environmental estrogens" and "gender bender" chemicals. Patients may ask you, the health care provider, about possible connections between their exposure to chemicals in the environment and their health. For example, having heard in the news that breast milk is contaminated with toxic substances that have endocrine disrupting effects, parents may ask whether it is safe to breastfeed a baby. This booklet is meant to provide you with the latest information on the health effects of hormonally active substances in the environment and offer you help in communicating this knowledge to patients and communities.

WHAT ARE ENDOCRINE DISRUPTORS?

Any substance that alters normal hormonal levels or activity in the body may be labeled an endocrine disruptor. To date, most research on endocrine disruption has focused on synthetic chemicals that perturb the normal activity of estrogens, androgens, and thyroid hormones, but some chemicals disrupt other hormonal pathways as well. Some naturally occurring compounds, such as plant-based phytoestrogens, may also alter hormone homeostasis. Some heavy metals may also be endocrine disruptors.

HOW DO ENDOCRINE DISRUPTORS WORK?

Endocrine disruptors may interfere with the normal functioning of hormones in several ways. Ordinarily, a hormone binds exclusively to its receptor on or inside a cell, like a key fitting into a lock. It then activates a chain of events that results in a biological response. An endocrine-disrupting substance, however, may be shaped enough like the hormone to bind to its receptor. There, it may activate the receptor, initiating the chain of events as if the hormone were there. Or it may simply occupy the hormone's usual binding site, preventing normal hormone activity. Endocrine disruptors may also interfere with serum hormone-binding proteins that regulate the availability and activity of hormones. They may change the number of hormone receptors present in specific tissues, the amount of a hormone produced, or the rate at which hormones are broken down and excreted. In short, these substances augment, prevent, or otherwise alter the normal activity of hormones.

THE CHALLENGE OF ENDOCRINE DISRUPTION

Traditional toxicological testing has focused on the ability of substances to cause obvious harm to adult or developing animals at high doses. Some endocrine disruptors are able to impact the hormonal system at very low doses, causing subtle effects that

may not be readily apparent or that may be delayed, even into the next generation. The discovery that chemicals could cause harm to animals and possibly humans in such subtle ways and at low doses during windows of particular vulnerability has challenged traditional views of toxicity and exposed gaps in toxicity testing.

Fetuses and infants can be harmed by exposure to chemicals at levels that do not appear to harm adults. Different systems in the body may be more vulnerable to chemical disruption at different times during development. The experience of thalidomide in the late 1950s and early 1960s illustrates how crucial the timing of exposure can be in determining the effects of that exposure. This drug was prescribed to pregnant women to combat symptoms associated with morning sickness, and caused severe structural birth defects in thousands of children. As it turned out, the timing of thalidomide ingestion, rather than the total dose, influenced the babies' deformities. Although some of the mothers with limbless children had taken only two or three thalidomide pills during their entire pregnancies, the ingestion occurred during the fifth and eighth week of pregnancy when the babies' arms and legs were developing.

Recent studies involving the toxic pollutant dioxin show that its effects can be similarly dependent upon the timing of the dose. Pregnant rats fed one meal containing dioxin on day 15 of gestation—the time when sexual differentiation occurs—produced male offspring that showed signs of reproductive dysfunction, such as decreased epididymis and cauda epididymis weights and decreased daily sperm production.[8] Newborn female mice given the plant estrogen genistein (present in soy infant formula) or dosed with the synthetic hormone diethylstilbestrol (DES) develop a 30% rate of uterine cancer later in life.[9]

Endocrine disruptors can have effects at extraordinarily low doses. The hormonal system is complex and exquisitely regulated. Estrogen, for example, is active at levels as low as a few parts per trillion. Some synthetic compounds are present in human tissues at levels thousands or even millions of times higher. Although in many cases synthetic compounds are less potent than natural hormones, even weakly active substances may be biologically important. This is especially true during development, when minor changes in endogenous hormone levels may be significant. In addition, chemical changes that occur in the body, such as the hydroxylation of a class of industrial chemicals known as PCBs, may increase the potency of these compounds.

Making matters more complicated, some studies show that low concentrations of a hormone can have the opposite effect of higher concentrations. Therefore, it may not be accurate to extrapolate from the effects of a chemical at high doses to predict its effect at low doses. For example, the breast cancer drug tamoxifen can act as an estrogen agonist or as an antagonist, depending on the tissue and the dose. In another example, a 1997 study found that a 50 percent increase in free-serum estradiol in male mouse fetuses increased prostate size, while a 200 to 800 percent increase was associated with decreased prostate size.[10]

This same mouse study also reinforced the concept of hormone potency at extremely low doses: all of the increases in free serum estradiol were in the part per trillion range. Since then, additional studies in rodents have confirmed that male reproductive tract development is permanently altered by exposure to extraordinarily low doses of estrogenic agents, including some weakly estrogenic synthetic compounds, during vulnerable periods of fetal development. For example, bisphenol A (BPA), a component of polycarbonate plastic that is also used in sealants and adhesives, has been shown to alter male reproductive tract development of rodents

at exposure levels comparable to those experienced by humans. A 2001 expert report from the National Toxicology Program concluded that "there is credible evidence for low dose effects of BPA" and recommended further research in this area.[11]

Mixtures of chemicals can have effects that are different from those of individual chemicals. Although traditional testing and regulation of chemicals looks at the effects of one chemical at a time, humans are routinely exposed to mixtures of chemicals in the environment. Some evidence suggests that certain mixtures of chemicals could be more potent than the effects of the individual component chemicals would suggest. In one experiment, researchers used turtle eggs to determine whether exposure to endocrine disrupting chemicals could alter the sex of animals. Normally, the sex of turtle hatchlings is determined by incubation temperature. The researchers painted single chemicals and chemical mixtures on the shells and incubated the eggs under conditions that normally would produce males. Some chemicals tested produced female hatchlings when applied in a mixture, but had little or no effect when applied alone.[12]

WHAT ARE THE EFFECTS OF ENDOCRINE DISRUPTORS?

Hormones play a critically important role in the body, directing the development and influencing the function of the reproductive, immune, and nervous systems, among others. If normal hormonal activity is disrupted during development, organs may fail to develop properly, causing permanent changes in structure or function. Altered hormone levels or activity can also cause cells sensitive to that

TABLE 1. EXAMPLES OF ENDOCRINE DISRUPTORS*

Chemical	Uses	Routes of Exposure	Mechanism of Action	Observed Health Effects
Dioxins, furans, and related compounds	By-product of combustion, waste incineration, and industrial processes, such as the manufacture of chlorine-containing products and of paper.	Accumulates in the fatty tissues of humans and of animals high in the food chain. Fish, shellfish, beef, and animal and human milk contain higher levels. Passed from mother to infant via the placenta.	Aryl hydrocarbon receptor agonist; increases estrogen metabolism, decreases estrogen-mediated gene transcription, decreases estrogen levels, decreases testosterone levels by interfering with hypothalamic-pituitary-gonadal axis.	*Rodents* (*in utero* exposure): delayed puberty, increased susceptibility to mammary cancer (females); decreased testosterone, hypospadias, hypospermia (low sperm count), delayed testicular descent, feminized sexual behavior (males) *Humans:* decreased triiodothyronine and thyroxine levels, decreased testosterone levels (exposures in adults), cancer (exposures in adults); immune system dysfunction
Poly-chlorinated biphenyls (PCBs)	Used as insulators and hydraulic fluids in transformers and other electrical components, other industrial uses. Some also generated as byproducts of industrial processes.	Accumulates in the food chain. Fish from the Great Lakes and other contaminated bodies of water are known to contain high levels. Passed from mother to infant via the placenta and breast-milk.	Accelerated thyroxine metabolism, decreased thyroxine levels, elevated thyroid stimulating hormone levels (high doses: thyromimetic) Some PCBs occupy estrogen receptor with anti-estrogenic effects. Some are dioxin-like.	*Animals* (*in utero exposure):* birth defects, decreased fertility, decreased thyroid function *Humans* (*in utero exposure*): lower birthweight, delayed neurological development, IQ deficits

Chemical	Uses	Routes of Exposure	Mechanism of Action	Observed Health Effects
Hexa-chloro-cyclo-hexane (Lindane)	Insecticide. Various agricultural uses in the United States and worldwide. Used in shampoos to treat head lice.	Accumulates in the food chain. Found in Arctic sea mammals, and in human tissues. Can be absorbed through the skin when used as a treatment for head lice.	Anti-estrogenic	Epidemiological studies suggest spontaneous abortion, infertility, and menstrual disorders could be related to high serum levels of lindane. In utero exposure may alter reproductive behavior, decrease pregnancy rate, and/or reduce testis size, in sheep and mink.
Penta-chloro-phenol (PCP)	Wood preservative. Previously widely used in the U.S., today used primarily on power line poles, railroad ties, and fence posts. Used extensively worldwide.	Exposure can come from breathing contaminated air, drinking contaminated water, eating contaminated food, and touching wood products treated with PCP.	Competes with T4 for binding to transthyretin.	Animal experiments suggest that in utero exposure may be linked to impaired thyroid and reproductive function. PCP may affect the survival of rats exposed in the womb. PCP becomes contaminated with dioxins and furans during manufacture.
DDT and metabolites	Insecticide for agricultural use and mosquito eradication. No longer produced or used in U.S. but remains a widespread environmental contaminant.	Ingestion through food chain is primary route of exposure in countries, such as the U.S., where DDT is no longer used for pest control. Found in virtually all breast milk samples tested.	Metabolite (DDE) is an androgen receptor antagonist.	Neurodevelopmental impairment. Has estrogenic and anti-androgenic effects on the reproductive systems of various wildlife and laboratory animal species. Shortened period of lactation in women. Pre-term and small-for-gestational age births in humans.**
Bisphenol A	Used in manufacture of compact disks, polycarbonate bottles, lining of metal food cans, and dental sealants.	Potential sources of exposure include water and food packaged in polycarbonate bottles or cans, including baby bottles, and dental sealants.	Estrogen receptor agonist.	Prenatal exposure to low doses increase prostate size, prostate androgen receptor level, and decrease daily sperm production in male mice. Female mice exposed in the womb had changes in vaginal cells and in the estrous cycle.
Atrazine	Widely used herbicide.	Common contaminant of drinking water sources, especially in agricultural areas.	Reduces gonadotropin-releasing hormone from hypothalamus, reduces pituitary luteinizing hormone levels, interferes with metabolism of estradiol, blocks estrogen receptor binding.	*Rodents (females):* mammary tumors, abnormal ovarian cycling *Humans:* some evidence of breast and ovarian tumors

* Adapted from Solomon, Schettler. Endocrine disruption and potential human health implications. *CMAJ* 2000; 163(11): 1471–6.
** Longnecker MP, et al. *Lancet* 2001 Jul 14; 358(9276):110-4.

hormone to grow and proliferate improperly, possibly leading to cancer or organ dysfunction.

Evidence of the effects of endocrine disruptors comes from observations of wildlife, epidemiological studies of humans, and laboratory experiments using cells or laboratory animals. Endocrine disruptors cause a number of adverse health effects in animals. In humans, the evidence for some adverse health effects is overwhelming, while for others it is thus far only suggestive.

Endocrine disruptors may be associated with the development of cancers in hormone-sensitive tissues. From 1940 to 1971, the drug diethylstilbesterol (DES) was used to prevent spontaneous abortions. Years later, it was discovered that daughters of mothers who took the drug had increased rates of clear cell carcinoma of the vagina—normally an unusual cancer.[13] Animal experiments have demonstrated the carcinogenicity of many endocrine-disrupting chemicals, though the cancer-causing mechanism may or may not be related to the endocrine-disrupting properties. Recent studies support the possibility that other chemical exposures may play a role in cancer risk in humans. For example, one case-control study found that exposure to the insecticide dieldrin (which is banned in the U.S. but is still a common contaminant found in Americans' fatty tissues) was associated with an increase in the risk of breast cancer[14] and a shortened survival of women with breast cancer.[15]

Adverse reproductive effects have been observed in male populations, wildlife, and laboratory animals as a consequence of exposure to hormonally active chemicals. Male alligators living in one Florida lake contaminated with pesticides had one-third the testosterone level of males living in an uncontaminated lake. The males in the contaminated lake also had poorly organized testes and abnormally small penises.[16] These effects are consistent with structural and functional abnormalities found in rodents exposed perinatally to estrogenic and anti-androgenic chemicals and in wildlife exposed to endocrine disruptors. For example, male mice exposed prenatally to low doses of the chemical bisphenol A were found to have increased prostate weight, when compared to unexposed mice. These findings are of particular concern because they demonstrate that exposure of the fetus to low doses of environmental estrogens, comparable to human exposure levels, may adversely affect the adult reproductive system.[17]

In humans, sons of mothers exposed to DES show higher rates of some malformations of the genitals and urinary tract.[18] This finding suggests that endocrine disruption could be related to the doubling of the rate of hypospadias (a birth defect in which the urethra is does not emerge at the tip of the penis)[19] and the increase in cryptorchidism (when the testes fail to descend properly)[20] observed in the United States from 1970 to 1993 in some birth defect monitoring systems.

Chemicals could play a role in a number of reproductive abnormalities in females. Studies of Rhesus monkeys have shown that exposure to dioxin, a toxic byproduct of industrial processes, is associated with the development of endometriosis, a painful condition in which the lining of the uterus grows abnormally.[21] Rodent studies of surgically induced endometriosis and several human epidemiologic studies are consistent with the Rhesus monkey findings. It is thought that endometriosis has an immune system component. The effect of dioxin on the developing immune system is particularly strong at low doses.

Other female reproductive effects have also been documented. Fish consumption was associated with shorter menstrual cycle length, in a study of female anglers in the state of New York who consumed sport fish contaminated with PCBs and other chemicals.[22] Epidemiologic studies in a northern Mexican town and at three medical centers in North Carolina found that mothers with high levels of DDE, a metabolite of the insecticide DDT, in their milk and blood were more likely to have shortened duration of lactation.[23] Doses of bisphenol A brought on early puberty and altered the growth rate of female mice exposed in the womb.[24]

Endocrine disrupting chemicals could be contributing to a population-wide decline in fertility. Though analyses of trends in sperm counts over the past half-century remain controversial, some data sets, including a recent meta-analysis of 61 studies, indicate a statistically significant decline in sperm counts in some parts of the world.[25] If these declines are in fact occurring, it is possible that they could impair fertility. One recent study of healthy young Danish men found that 43 percent of them had sperm counts low enough to impair their ability to father children.[26] A study of sport fishers in the area around the Great Lakes, known to have highly contaminated fish, found that men who consumed more sport fish were more likely to report that they and their partner had failed to conceive after twelve months of trying.[27] Rats exposed in the womb to a single dose of dioxin had sperm counts as much as 74 percent lower than controls.[28]

Some of the class of industrial chemicals known as phthalates also cause reduced sperm counts and decreased fertility in rodents.[29] An expert panel convened by the National Toxicology Program recently completed a review of the reproductive effects of several phthalates, including di(2-ethylhexyl)phthalate (DEHP, which is added to many PVC plastic products to make them flexible). The panel concluded, based on laboratory animal studies, that there are serious concerns that DEHP can adversely affect the developing reproductive system of the male fetus or infant. There is evidence suggesting that these effects are mediated, all or in part, by hormonal mechanisms.[30]

Exposure to dioxins, toxic byproducts of incineration and industrial processes, may be associated with fewer male births. Nearly twenty-five years after an explosion at a chemical plant released large quantities of the common industrial pollutant dioxin in Seveso, Italy, the proportion of males born to exposed individuals remains reduced.[31] Increasing dioxin levels in the fathers was associated with an increased probability of having a female child. Fathers exposed when they were less than nineteen years of age had 62 boys per every 100 girls, compared to the worldwide average of 106 boys per every 100 girls. These findings, while intriguing, were based on a small population. A 1997 study of all live births in Canada and the United States from 1930 to 1990 noted that the proportion of males born decreased significantly after 1970.[32] This decline coincides with the peak in dioxin releases thought to have occurred in the United States around 1970.[33] Although a cause and effect relationship has not been proven, this evidence supports the hypothesis that dioxin exposures may result in a reduced proportion of male births.

Prenatal exposure to some chemicals is associated with deficits in IQ and memory, neurobehavioral effects, and delayed neuromuscular development in children. There is evidence to suggest that endocrine disruption may play a role in many of these adverse effects, although their underlying mechanisms have not yet been conclusively determined. The effects of prenatal exposure to PCBs, DDE (a metabolite of the insecticide DDT), and other contaminants from maternal consumption of contaminated fish or other food products have been studied in several populations in the United States and abroad. The first study showed that U.S. children born to women who ate more PCB-contaminated fish had lower IQ scores and poorer memory and attention.[34] This study has now been confirmed in five other populations, two in the United States and three in Western Europe.

Some have suggested that the adverse effects of PCBs on the nervous system could result from disruption of normal thyroid hormone activity. Animals exposed to certain PCBs and dioxins showed histologic changes in their thyroid glands similar to changes seen with the thyroid disease Hashimoto's

thyroiditis in humans.[35] Maternal exposure to PCBs is associated with decreased levels of T4, a thyroid hormone, in the blood and brain of the offspring rats.[36] PCBs are also associated with altered neurotransmitter levels, which may explain effects on the developing nervous system.

Other laboratory experiments in rodents have suggested that prenatal exposure to estrogenic compounds, including the synthetic estrogen diethylstilbestrol (DES) and the pesticides DDT and methoxychlor, can cause changes in reaction time and increased aggressive behavior of adults.[37]

A number of endocrine disruptors have also been found to have an effect on the immune system. As in the case with developmental neurotoxicity, it is not yet known whether the underlying mechanism for these effects is endocrine in nature.

HOW ARE PEOPLE EXPOSED TO ENDOCRINE DISRUPTING CHEMICALS?

Many known endocrine disruptors are found in the environment. These chemicals make their way to humans through food, water, and air. Pesticides, for example, can leave residues on foods or be washed from fields into drinking water supplies. Some plastic packaging can also deposit harmful chemicals, such as bisphenol A and phthalates, onto foods. Other endocrine-disrupting chemicals could be breathed in or absorbed through the skin. However, the vast majority of chemicals have not been tested for their endocrine-disrupting capabilities. As we learn more about the chemicals in our environment, we will likely identify additional sources of potentially hazardous exposures.

Chemicals can accumulate in fatty foods. Some endocrine-disrupting chemicals also have a tendency to bioaccumulate, becoming concentrated higher up the food chain. Foods high in animal fats, such as meat, fish, eggs, and dairy products, often contain significant levels of these contaminants. Processing can also introduce endocrine disruptors into food. The U.S. food supply is not routinely monitored for endocrine disrupting chemicals, though tests of common fast foods and foods purchased in U.S. supermarkets have revealed levels of contaminants such as dioxins and furans that exceed U.S. government standards.[38] In addition, human breast milk, with its high fat content, is known to store large amounts of some endocrine-disrupting contaminants. A nursing infant may receive ten to sixty times the adult daily dose of dioxins and PCBs per pound of body weight.[39]

Some pesticides that have endocrine-disrupting effects may be present in food and in the home. A number of pesticides are known or suspected to disrupt the endocrine system. People can be exposed to these pesticides by eating food with pesticide residues. Use of pesticides in the home and garden is another source of exposure. Although food in the United States is monitored for pesticide residues, EPA has only recently begun to assemble a program that will ultimately require that pesticides be assessed for some endocrine disruptor effects. It is possible that, within a few years, the use of pesticides that are now legal will be found to be unsafe.

Contaminants in drinking water may have endocrine-disrupting effects. Drinking water can be a significant source of exposure to pesticides and other endocrine disrupting chemicals. Surface waters, including many that are sources of drinking water, are highly vulnerable to chemical contaminants in runoff from agricultural, suburban and urban areas. Groundwater sources of drinking water can also be contaminated by infiltration of chemicals through the soil. Many contaminants are not removed by conventional treatment methods used by most municipal water utilities. In fact, many common contaminants are not even regulated in public drinking water supplies. Furthermore, EPA does not regulate

the quality of drinking water from private wells, and this water is rarely treated prior to consumption. Bottled water can also be a source of exposure to endocrine disrupting chemicals. For example, polycarbonate plastic, the strong, rigid material often used in bottles for water coolers, can leach the endocrine-disruptor bisphenol A into the water.[40] EPA will need to reassess drinking water safety standards as more data becomes available on the endocrine disrupting effects of contaminants.

Occupational exposure to chemicals may put workers and their families at risk. Special populations, such as industrial and agricultural workers and insecticide applicators, may be exposed to higher levels of endocrine-disrupting chemicals through their work. Workers may also track toxic chemicals home, exposing their families. Few Occupational Safety and Health Administration (OSHA) standards have been established for substances known to have the potential for endocrine disruption.

Plastic medical and consumer products may leach dangerous chemicals. Some plastics can leach chemicals suspected to have endocrine disrupting activity. Bisphenol A is a chemical with estrogenic properties. It is used in polycarbonate bottles, in the lining of metal food cans, and in dental sealants. Other additives, known as phthalates, are frequently added to polyvinyl chloride (PVC) plastics to make them pliable. Flexible PVC is used in a myriad of medical and consumer products, including medical tubing, teething rings, pacifiers, and shower curtains. An expert panel convened by the National Toxicology Program recently expressed serious concern that the developing reproductive tract of critically ill male infants could suffer adverse effects from potentially high exposures from medical equipment containing the phthalate DEHP. There is evidence from lab studies suggesting that endocrine-disrupting mechanisms might be responsible for effects on the developing male reproductive tract. At this time, substitutes are not widely available for much of this equipment.

Some communities may suffer disproportionately from chemical contamination. Racial minority and low-income communities face higher risks from environmental pollutants than the general population. Industrial plants that generate toxic chemicals, or incinerators that contaminate the local environment, are more likely to be situated in low-income areas. Mossville, Louisiana is one such area. A study by the Agency for Toxic Substances and Disease Registry (ATSDR) found that the median and mean concentrations of dioxin equivalents in the blood of the residents tested were higher than the 95th percentile of a comparison population.[41]

FOR MORE INFORMATION

You can find more information on endocrine disruption at:

- Physicians for Social Responsibility, www.psr.org
- Environmental Protection Agency, www.epa.gov/endocrine/
- National Institute for Environmental Health Sciences, www.niehs.nih.gov
- Center for Bioenvironmental Research at Tulane and Xavier Universities, www.tmc.tulane.edu/ecme/eehome/

READING LIST

- National Research Council, *Hormonally Active Agents in the Environment* (Washington DC: National Academy Press, 2000).
- Sheldon Krimsky, *Hormonal Chaos: The Scientific and Social Origins of the Environmental Endocrine Hypothesis* (Baltimore, MD: Johns Hopkins University Press, 2000).

- Greater Boston Physicians for Social Responsibility, *In Harm's Way: Toxic Threats to Child Development*, May 2000. Available from GBPSR, 11 Garden Street, Cambridge, MA 02138, www.igc.org/psr.
- Ted Schettler, Gina Solomon, Maria Valenti, and Annette Huddle, *Generations at Risk* (Cambridge, MA: MIT Press, 1999).
- Theo Colborn, Dianne Dumanoski, and John Peterson Myers, *Our Stolen Future: Are We Threatening Our Fertility, Intelligence, and Survival?* (New York, NY: Dutton, 1996)

Patient Q & A: Answers To Nine Common Questions

Q: How can I reduce my family's exposure to potentially harmful endocrine-disrupting chemicals in the environment?

Eat healthy foods. The food you eat is an important source of exposure to pesticides and other endocrine-disrupting compounds. Because some chemicals—including PCBs, DDT, and dioxins—tend to accumulate in animal fats, follow the recommended fish consumption guidelines (below) and eat less fatty meat, eggs, and dairy products. Remove fat, including the skin, from meats, fish, and chicken. Avoid processed foods made from ground meat and animal parts such as sausage, bologna, hot dogs, and canned, ground lunch-meats, which are very high in animal fats. Tossing out egg yolks and drinking skim milk can also reduce your intake of fats. This not only reduces the potential for chemical exposures, but also will help to prevent cancer and heart disease.

Eat at least five servings each day of a variety of fruits and vegetables. Buy organic food when possible. Carefully wash fruits and vegetables, and remove the outer leaves from lettuce. Washing produce with a mild solution of dish detergent can help remove pesticide residues.[42] Cut out the stem end of apples and other similarly shaped fruit to remove the "funnel" where pesticides can accumulate.

Practice sensible pest control. Treat fleas on pets using environmental controls and systemic treatments. Treat head lice with nit combs if possible. Less toxic pyrethroid-based lice products are preferable to lindane or malathion-based shampoos, although some pyrethroids may also have endocrine-disrupting properties.

Reduce your use of pesticides in your home and garden. If you hire a professional, you have the right to information about the available alternatives and the risks. However, even certified pesticide applicators are often completely unaware of the endocrine-disrupting properties and chronic, long-term risks of many of their products. You should inquire about what is proposed for use and do your own search for toxicity information. Keep away from areas freshly sprayed with pesticides.

Minimize the use of plastics. Endocrine disrupting chemicals in certain plastics may leach out during use. This is of particular concern when the plastic is used for food storage. To help decrease your exposure, minimize the contact between food and plastic. Do not microwave food in plastic containers. Heating food in plastic increases the migration of endocrine-disrupting chemicals into the food. Polycarbonate baby bottles may contain bisphenol A, an endocrine-disrupting chemical. Replace baby bottles made of polycarbonate (a hard, shiny clear plastic) with glass or polyethylene (an opaque, less shiny plastic).[43]

Concern over children's toys has led some manufacturers to change the formulation of teethers and pacifiers. Look for phthalate-free items at stores that have pledged to stop selling heavily-mouthed baby products that contain phthalates. (These stores include Kmart, Sears, Target, Toys R Us, and WalMart.)[44] However, other toys continue to contain these ingredients. Since the identity of additives in plastic products is not always known, you can reduce the potential for exposure by offering children non-plastic toys and keeping children from chewing on plastic products.

Q: Is it safe to eat fish?

Fish is a very nutritious food, but because many fish species are high on the food chain, they are vulnerable to contamination by chemical pollutants—some of them endocrine disruptors—that persist in the environment and accumulate in living organisms. While the levels of contamination are low in many fish, they may be higher in larger, long-lived fish, (such as swordfish), that concentrate pollutants, and in fish close to pollution sources (including many fresh water fish species and coastal ocean fish). See the box below and on page 12.

PATIENT GUIDELINES: HOW TO REDUCE RISKS FROM TOXIC CONTAMINANTS IN FISH

The following guidelines are intended to reduce risks from toxic contaminants while preserving overall health benefits. Since developing fetuses, infants and children are particularly vulnerable to toxic exposures, these guidelines are most important for pregnant and breast-feeding women, and for young children. However, because many pollutants build up in the body over many years, a woman's dietary habits throughout her early life profoundly influence the exposures of her future children. For that reason, these guidelines also apply to all women who may become pregnant in the future, as well as children and adolescents. The guidelines offered below should be viewed as provisional, since there has been very little testing of fish for contaminants, and therefore limited data on which to base recommendations.

Do not consume fish that are high in mercury such as swordfish, shark, king mackerel, tile fish, fresh tuna, and some fresh water fish, whose mercury levels approach or exceed 1 part per million.[45] [46] Many agencies recommend that fish with mercury levels of 0.5 parts per million or greater—such as sea bass, Spanish mackerel, and pike—not be consumed either.

Limit consumption of canned tuna and other moderate mercury fish. Consumption of fish with 0.3–0.4 ppm—such as canned white tuna (also known as albacore), red snapper, marlin and sunfish— should be limited to four ounces per week (about $^1/_2$ of a small can). Other canned tuna (sometimes labeled "light" tuna) has lower mercury levels, compared to white tuna. Consumption of canned light tuna, with mercury levels around 0.2 parts per million, should be limited to seven ounces per week (about one small can). Children can consume approximately the amount derived from the formula: maximum tuna consumption per week (in ounces) = child's body weight (in pounds) divided by 20.

The fatty fish dilemma: Healthy-heart nutrients with neurotoxic contaminants. Omega-3 fatty acids in fatty fish (marine omega-3s) provide valuable cardiovascular benefits, and may enhance brain development as well.[47] [48] [49] [50] However, due to the widespread contamination of fish with PCBs and dioxin, which are highly concentrated in fish fat, the benefits of omega-3 fatty acids are compromised by toxic threats. In particular, perinatal

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HOW TO REDUCE THE RISKS FROM CONTAMINANTS IN FISH

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exposures to PCBs/dioxins reduce memory and learning ability in later childhood. Though the effects of PCBs/dioxins on adults are relatively unexamined, a recent study raises concerns that adult consumption of PCB-contaminated fish may impair memory and learning in aging adults as well.[51]

Dietary (and other) strategies to reduce neurotoxic exposures while protecting cardiac health. The contamination of fatty fish with PCBs/dioxin poses a choice between two undesirable options: 1) avoid fatty fish and lose the benefit of a cardio-protective nutrient, or 2) eat the fish and risk the exposure to neurotoxic pollutants. In weighing these options, it is important to remember cardiac health can be enhanced by many dietary and lifestyle factors—exercise, a diet low in saturated fat and cholesterol, and avoidance of obesity and cigarette smoking. And, while marine omega-3 fatty acids appear to be cardio-protective, omega-3 fatty acids derived from plant sources have also been shown to be cardio-protective.[52] [53] [54] Plant sources of omega-3 fatty acids include soy and canola oils, tofu, soybeans, walnuts, and flax seeds.

Considering the importance of overall diet and exercise, a reasonable approach would be to limit intake of fatty fish consumption to 1–2 meals per month, and to compensate for the loss of marine omega-3s through the basic lifestyle measures for ensuring cardiovascular health. If one wanted to eat fatty fish more frequently, it is possible to compensate for increased PCB/dioxin exposure by reducing intake of PCBs/dioxins in other animal fats (eliminating fats in meat, chicken, dairy, and eggs. See "healthy eating" above.) However, since each gram of fish fat contains on average 5–20 times as much PCBs and dioxin as equal amounts of other animal fats[55] [56] substantial reductions in these animal fats are required to compensate increased consumption of fish fat.

Choose fish that are low in mercury *and* low in fat. Fish such as cod, haddock and pollack, are low in fat and mercury (averaging 0.1 parts per million). Such fish can be safely consumed in quantities of about 7–10 ounces per week

Minimize exposure to some pollutants by cutting away any visible fat and skin before cooking. Then bake, broil or grill in a raised pan or rack, and discard the drippings.[57] Avoid frying fish, as this can seal in pollutants. (*Note: This does not reduce mercury contamination*.)

Observe consumption advisories for fresh-water fish. More than half of the fish in inland lakes and rivers in the United States contain detectable levels of chemicals of concern because of local contamination. Dioxins, PCBs, and mercury are common contaminants. Contact your state health department about advisories before eating locally caught fresh-water fish. More information about fish consumption advisories is available from the U.S. EPA at www.epa.gov/ost/fish.

Q: Given that breast milk is contaminated with endocrine-disrupting chemicals, should I breast-feed my baby?

Breast milk provides the best nutrition for your baby, boosts immunity, and builds emotional closeness to the mother. These benefits far outweigh the risk that contaminants in your milk will harm your baby. Put another way, breast milk contamination may diminish the benefits of breast-feeding but does not cancel them out. If you need to use formula as a

supplement or substitute for breast-feeding, avoid soy-based formula unless at the advice of your physician.

Q: Should I be tested to find out if I have high levels of contaminants, such as DDT, PCBs, and dioxin in my body?

Testing to estimate your body burden of chemical contaminants is not recommended. The tests are expensive, and few clinical laboratories are capable of accurately performing such analyses. It is more important to focus on prevention and to minimize exposures.

Q: Could my infertility be caused by exposure to chemicals in the environment?

In most individual cases, no cause is identified for infertility. Some of the known causes of infertility include infection by a sexually transmitted disease, ingestion of certain drugs, inherited abnormalities, exposure to relatively high doses of certain toxic chemicals on the job, and stress-related hormonal imbalances. Infertility can also result from a combination of these factors affecting one or both partners. Many chemicals in the environment, including some endocrine disruptors, are known to have properties that could potentially influence fertility. Workplace exposures to other chemicals have been shown to cause infertility, though not through endocrine mechanisms. However, it has not been proven whether low-level exposure to environmental pollution can cause infertility in humans.

Q: Could exposure to environmental pollutants raise my risk of cancer?

Yes. New research suggests that environmental factors play a much greater role than previously thought in cancer risk. Some cancers are more influenced by genetic factors than others, but inheritance appears to contribute from 27 to 42 percent of the risk, and environmental factors make up the balance.[58] Much of the environmental risk is attributable to smoking, drinking, and diet. Viruses and pharmaceutical agents have also been implicated in some cancers. However, exposure to chemicals and to radiation in the environment also plays a role.

Chemical carcinogens cause cancer through a number of mechanisms, including DNA damage, promoting cell division, altering levels of growth factors, altering tissue differentiation, and hormone disruption. A number of common pollutants, including some ingredients in plastics, fuels, drugs, and pesticides, are known to cause cancers in animals and could do so in humans as well, by disrupting normal hormonal function. Natural hormones affect some cancers, particularly those of the reproductive tract. Exposure to endocrine disruptors may increase risk of these malignancies.

Q: Could my child's behavioral problem (or birth defect) be related to my exposure to chemicals in the environment?

The causes of most birth defects and behavioral disorders in individuals are often difficult to establish. We know from epidemiologic studies of populations that certain chemical exposures increase the risk of birth defects or behavioral problems but the cause in a particular individual is difficult to determine.

ADDITIONAL PATIENT INFORMATION

Physicians for Social Responsibility has produced a patient education brochure that outlines some easy choices pregnant women can make to protect their babies from avoidable risks of birth defects and other reproductive disorders. These include not drinking alcohol during pregnancy, avoiding smoking and second-hand smoke, avoiding contact with pesticides and harmful chemicals, and seeking medical advice before taking any drugs or medications. To order copies of the brochure for your practice, please contact PSR.

We do know that, in addition to genetic factors, environmental factors play a role. Accidental exposure to high doses of PCBs caused birth defects in the children of a population of Taiwanese residents. Much lower exposure causes altered behavior and IQ in offspring. Many other environmental contaminants, for example lead, mercury, alcohol, and some pesticides, affect behavior and learning. Some occupational pesticide and solvent exposures are also associated with birth defects in offspring.

Q: Is my water safe to drink?

Water from municipal systems is tested for a variety of chemicals and is generally safe to drink. Drinking plenty of water is important for good health, and in most cases the benefits outweigh the risk. However, some water supplies may contain chemical and/or microbial contaminants at levels that pose a health risk. Areas where substantial agricultural, municipal, or industrial discharges enter the water supply are at elevated risk of such contamination. People who have weakened immune systems may wish to consider alternatives to tap water, such as a water filter, bottled water, or boiled water, though each of these alternatives has its own advantages and disadvantages. Each year, your water utility is required to send you a drinking water quality report that lists contaminants detected in your water.

The federal government does not regulate private wells. You should test private water supplies regularly; EPA can provide contact information for the official who certifies water-testing laboratories in your state. Protect your water supply by keeping hazardous materials out of septic systems and contaminants away from your well. Avoid mixing or using pesticides, fertilizers, degreasers, and other pollutants near the well. Slope the area around the well to drain surface runoff away from the well.

More information can be found on the website of the Environmental Protection Agency (www.epa.gov/safewater), through the Safe Drinking Water Hotline (1-800-426-4791), and from PSR's primer on Drinking Water and Disease, available online at www.psr.org/dwater.html.

Q: Are natural plant hormones harmful?

Many plants—including grains (soybeans, wheat, rice), fruits (dates, cherries, apples), vegetables (carrots, potatoes, beans), and herbs (garlic, parsley)—produce hormonally active substances. Known as phytoestrogens, these substances can have estrogenic or anti-estrogenic effects. Some have used the presence of these plant-based hormones to argue that synthetic chemicals with hormonal activity are inconsequential. However, there are important differences between plant-based and synthetic chemicals.

Plant hormones are water-soluble and do not persist in the body. It has been suggested that phytoestrogens might actually counteract some of the effects of synthetic estrogens. There are differing opinions about phytoestrogens' role in health, though some evidence suggests that when consumed as part of an ordinary diet, phytoestrogens may actually be beneficial. For example, people in Asian countries with a traditional diet high in phytoestrogens have lower rates of menopausal symptoms, cardiovascular disease, and breast, ovarian, and endometrial cancers.

On the other hand, consuming very high levels of some phytoestrogens (by taking large amounts of phytoestrogen pills, for example) may pose health risks. Reproductive problems have been documented in laboratory, farm, and wild animals that ate very high (up to 100% of their diet) amounts of phytoestrogen-rich plants.[59] Infants consuming soy-based formula are exposed to high levels of phytoestrogens, and research on laboratory mice indicates that this could incur a risk of cancer. During the entire course of human evolution, save the last 100 years or so, infants have been fed solely on breast milk. It is possible that infants are not adapted to handle phytoestrogens and other substances in

artificial breast milk substitutes, and are thereby more sensitive than older children and adults. Although all the evidence is not in and more research is underway it is prudent to avoid the use of soy formula for infants if possible.

NOTES

1 Bergstrom R et al. *J Natl Cancer Inst* 1996; 88(11):727–33.
2 SEER Cancer Statistics Review 1973–1997.
3 Paulozzi LJ et al., *Pedatrics* 1997; 100(5):831–4; Paulozzi LJ. *Environ Health Perspect* 1999; 107:297–302.
4 Kaplowitz PB et al. *Pediatrics* 1999; 104:936–41; Herman-Giddens ME et al. *Pediatrics* 1997; 88(4):505–12.
5 Environmental Defense, *Toxic Ignorance*, 1997.
6 Lichtenstein P et al. *NEJM* 2000; 343(2):78–85.
7 National Institute of Environmental Health Sciences, National Toxicology Program (NTP). *Report of the Endocrine Disruptors Low Dose Peer Review*. May 2001.
8 Mably TA et al. *Toxicol Appl Pharmacol* 1992 May;114(1):118–26.
9 Newbold RR et al. *Cancer Res*. 2001 Jun 1; 61(11):4325–4328.
10 vom Saal FS et al. *Proc Natl Acad Sci USA* 1997; 94(5):2056–61.
11 National Institute of Environmental Health Sciences, National Toxicology Program (NTP). *Report of the Endocrine Disruptors Low Dose Peer Review*. May 2001.
12 Bergeron JM et al. *Environ Health Perspect* 1994; 102:780–1.
13 Herbst AL et al. *NEJM* 1971; 284(16):878–81.
14 Høyer AP et al. *Lancet* 1998; 352:1816–1820.
15 Høyer AP et al. *Journal of Clinical Epidemiology* 2000; 53:323–330.
16 Guillette LJ et al. *Environ Health Perspect* 1994; 102:680–8.
17 Nagel SC et al. *Environ Health Perspect* 1997; 105(1): 70–76.
18 Gill WB et al. *J Urol* 1979; 122:36–9.
19 Paulozzi LJ et al. *Pedatrics* 1997; 100(5):831–4.
20 Paulozzi LJ. *Environ Health Perspect* 1999; 107:297–302.
21 Rier SE. *Fundam Appl Toxicol* 1993; 21(4):433–41.
22 Mendola P et al. *Am J Epidemiol* 1997; 146(11):955–60.
23 Gladen BC, Rogan WJ. *Am J Pub Health* 1995; 85:504–8; Rogan WJ, Gladen BC. *Environ Health Perspect* 1985; 60:215–21.
24 Howdeshell KL et al. *Nature* 1999; 201:763–4.
25 Swan SH et al. *Environ Health Perspect* 1997; 105:1228–32.
26 Andersen AG et al. *Human Reproduction* 2000; 15(2):366–72.
27 Courval JM et al. *Environmental Research* 1999; 80:S183–8.
28 Mably TA et al. *Toxicol Appl Pharmacol* 1992; 114(1):118–26.
29 See, for example, Parmar D et al. *Toxicology* 1986; 42:47–55, and Agarwal DK et al. *Environ Health Perspect* 1986; 65:343–50.
30 National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction. *NTP-CERHR Expert Panel Report on Di(2-ethylhexyl)phthalate*. October 2000. Accessed on-line at http://cerhr.niehs.nih.gov/news/DEHP-final.pdf.
31 Mocarelli P et al. *Lancet* 2000; 355:1858–63.
32 Allan B et al. *Can. Med. Assoc. J.* 1997; 156(1): 37–41.
33 U.S. Environmental Protection Agency, Science Advisory Board. Science Advisory Board's review of the Draft Dioxin Exposure and Health Effects Reassessment Documents. Washington, DC, September 29, 1995.
34 Jacobson JL, Jacobson SW, *NEJM* 1996; 335:783–9.
35 Ness DK et al. *Toxicol Lett* 1993; 68:311–23.
36 Morse DC et al. *Toxicol Appl Pharmacol* 1996; 136:269–79.
37 Palanza P et al. *Pharmacol Biochem Behav* 1999; 64(4):665–72; Palanza P et al. *Neurosci Biobehav Rev* 1999; 23(7):1011–27.
38 Schecter A and Li L. *Chemosphere* 1997; 34(5–7):1449–57; Schecter A et al. *Chemosphere* 1997; 34(5–7):1437–47.
39 World Health Organization Regional Office for Europe. *Levels of PCBs, PCDDs, and PCDFs in breast milk*, Copenhagen, 1989.
40 *Consumer Reports* August 2000.
41 U.S. Agency for Toxic Substances and Disease Registry. *Exposure Investigation Report, Calcasieu Estuary, Lake Charles, LA*. CERCLIS NO. LA0002368173. November 19, 1999. http://www.atsdr.cdc.gov:80/HAC/PHA/calcas/cal_toc.html.
42 *Consumer Reports*, March 1999.
43 *Consumer Reports*, May 1999.
44 *Consumer Reports*, May 1999.
45 U.S. Environmental Protection Agency. *Mercury Study Report to* Congress. Volume IV: An Assessment of Exposure to Mercury in the United States. www.epa.gov/ttnuatw1/112nmerc/volume4.pdf, pages 150–162.
46 Environmental Working Group, US Public Interest Research Groups. *Brain Food*. 2001; 62. http://www.ewg.org/pub/home/Reports/brainfood/execsumm.html
47 Oomen C et al. *American Journal of Epidemiology* 2000; 151:999–1006.
48 Iso, H et al. *JAMA* 2001 Jan 17; 285(3):304-312.
49 Birch EE, Garfield S et al. *Dev Med Child Neurol* 2000 Mar; 42(3):174–81.
50 Makrides M et al. *Lipids* 1996 Jan; 31(1):115–9.
51 Schantz SL, Gasior DN, Polverejan E et al. *Environ Health Perspect* 2001; 109:605–611.
52 Ascherio A et al. *BMJ* 1996 Jul 13; 313: 84–90.
53 De Lorgeril M et al. *Lancet* 1994 Jun 11; 343(8911):1454.
54 Stone NJ. *Circulation* 1996; 94:2337–2340. (Statement of the American Heart Association).
55 UK Joint Food Safety and Standards Group. Food surveillance information sheet 105: Dioxins and PCBs in Foods and Human Milk. June, 1997. Table1 www.foodstandards.gov.uk/maff/archive/food/infsheet/1997/no105/105dioxi.htm
56 UK Joint Food Safety and Standards Group. Food surveillance information sheet 184: Dioxins and PCBs in UK and Imported Marine Fish. August, 1999. Table 7. www.foodstandards.gov.uk/maff/archive/food/infsheet/1999/no184/table3.htm
57 U.S. Environmental Protection Agency. *Should I eat the fish I catch? A guide to healthy eating of the fish you catch*. EPA 823-B-97-009, September 1997. http://www.epa.gov/ost/fish/fisheng.pdf.
58 Lichtenstein P et al. *NEJM* 2000; 343:78–85.
59 Center for Bioenvironmental Research of Tulane and Xavier Universities. Phytoestrogens. *Environmental Estrogens and Other Hormones*, http://www.som.tulane.edu/ecme/eehome/basics/phytoestrogens/.

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