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Bulletin

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Body of Evidence: Reproductive Health and the Environment

Introduction

Infertility and reproductive health issues are growing health concerns in the United States and around the world. Many factors affect reproductive health, including diet, activity level, age, stress, and pharmaceutical use (Schettler et al., 1999). Environmental factors and exposure to chemicals also influence reproductive health. Mounting scientific evidence suggests that chemicals and contaminants commonly found in the human environment, drinking water, food supply, and occupational settings can influence human fertility, reproduction, early childhood development, and reproductive diseases, though in complex and often poorly understood ways.

These issues are important for health care providers because studies demonstrate that health care would be dramatically improved, and medical care costs reduced, if environmental pollution and exposure to chemicals were reduced (Edwards and Myers, 2007). An increased awareness of the effects of environmental contaminants on patient health will allow health care providers to offer more timely and appropriate care, to better understand potential causes of reproductive problems, to better track and study reproductive outcomes, and to protect patients from preventable harm.

This bulletin, *Body of Evidence*, provides an overview of the role that environmental contaminants may play in fertility and reproductive health. It also highlights the unique concerns and growing body of research on environmental contaminants and reproductive health in Alaska and the Arctic. Finally, this bulletin provides resources and opportunities for clinicians and health providers to educate themselves and their patients on the links between chemical exposures and reproductive health.

This issue of *Body of Evidence* updates the 2007 publication of the Collaborative on Health and the Environment-Alaska (CHE-Alaska) and Alaska Community Action on Toxics. Since then, the volume of human health studies on environmental contaminants has grown significantly, although the general conclusions of the 2007 *Body of Evidence* bulletin – that many chemical exposures are associated with reproductive health problems – remain unchanged.

Sources & Pathways of Environmental Exposures

Chemicals are ubiquitous in our daily lives, and over 84,000 chemicals are now in use in the United States (U.S. EPA, 2010). Chemicals developed and registered before the implementation of the Toxic Substances Control Act (TSCA) in 1976 were grandfathered in without requirements for environmental and health safety data, and manufacturers are not required to demonstrate environmental or health safety before their products go to market, nor to provide complete information on toxicity to develop and produce new chemicals (U.S. GAO, 2005; U.S. EPA, 2009). Pesticides are regulated under a different law, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which similarly allows pesticide manufacturers to market pesticide products without proof of safety. Once on the market, it is extremely difficult to remove a product even with evidence that it is harmful. Under FIFRA, pesticide manufacturers create their own labels with directions for use and warnings, but these are not reviewed for accuracy by a third party. So-called "inert" ingredients are not required to be tested for safety or be identified and listed on the labels of pesticide products, though these ingredients may be toxic.

People can be exposed to chemicals through diet, air, water, and skin contact. The presence of a chemical or its breakdown products can be measured in the human body using biomonitoring, which measures the presence and concentration of chemicals in human tissues (Morello-Frosch et al., 2009). The U.S. Centers for Disease Control and Prevention, National Biomonitoring Program, conducts nationwide biomonitoring studies every two years and has measured 212 chemicals in the blood or urine of thousands of Americans. Nearly all Americans have detectable levels of many chemicals in their bodies, including phthalates (used in perfumes and consumer products), perfluorinated compounds (PFCs; used in nonstick cookware), pesticides, and flame retardants (U.S. CDC, 2009). Researchers working with state governments, federal agencies, universities, nonprofits, and with industry also conduct biomonitoring research.

Many of the toxicants discussed in this bulletin are widely found in pregnant women, as seen in the large nationwide sample of CDC's National Health and Nutrition Examination Survey (NHANES) (Woodruff et al., 2011). This survey detected chemicals such as polychlorinated biphenyls (PCBs), organochlorine pesticides, PFCs, phenols, polybrominated diphenyl ethers (PBDEs), phthalates, polyaromatic hydrocarbons (PAHs), and perchlorate in 99–100% of pregnant women. Further, women have multiple exposures to many chemicals.

Environmental contamination is of particular concern in Alaska and elsewhere throughout the Arctic. Alaska's economy is and has been based on resource extraction, including mining and oil extraction – industries which are highly polluting. For example, in 2010 alone, Red Dog Mine operations in Northwest Alaska released nearly 3.2 million pounds of lead compounds into the environment (U.S. EPA, 2011). Additionally, atmospheric and oceanic currents transport chemicals used worldwide to the poles. Thus, pollutants used in the Northern Hemisphere accumulate in Arctic environments (Poissant et al., 2008). For example, high levels of PCBs and PBDEs have been measured in the Arctic environment due to long-range atmospheric transport (Yogui et al., 2009; de Wit et al., 2010).

Fish and sea mammals are important parts of the diet of many Alaska Native people (Jewett and Duffy, 2007), but fish in Alaska and elsewhere are contaminated with mercury and persistent organic pollutants. The Alaska Department of Health historically recommended unrestricted consumption of Alaskan fish, but as of 2007 recommended restricted consumption of certain larger, older fish and predatory species from Alaska waters (Verbrugge, 2007). Researchers have found that most Alaskan fish had relatively low levels of mercury compared to fish from other parts of the country and compared to the FDA's Action Levels (Verbrugge, 2007; Jewett and Duffy, 2007). A recent community-based participatory research project analyzed traditional foods from St. Lawrence Island, Alaska and found PCBs in rendered oils and blubber from all marine mammal samples at levels that trigger advisories for severely restricted consumption, based on EPA's fish consumption advisories (Welfinger-Smith et al., 2011). Another study (Hardell et al., 2010) of Alaskan fish from the Aleutian Islands found significant levels of PCBs at concentrations that trigger EPA consumption limits of between 7-22 meals per year for noncancer effects (i.e., health effects other than cancer, which may include reproductive toxicity, developmental toxicity, neurotoxicity, immunotoxicity, etc.).

Health Outcomes of Potential Concern

Infertility and other reproductive health problems are on the rise in the United States and around the world. In 2005, nearly 12% of women of childbearing age had trouble conceiving (CDC, 2005), a 20% increase since 1995 (Barrett, 2006). Infertility is growing rapidly among young women; twice as many women under the age of 25 reported difficulty conceiving and maintaining pregnancy in 2002 than in 1982 (Woodruff et al., 2010; Swan and Hertz-Picciotto, 1999; Chandra et al., 2005). A global analysis of studies of male sperm quality found a downward global trend in sperm counts, though the authors note that population- and location-specific studies are also needed (Merzenich et al., 2010). Other scholars have noted increases in testicular cancer (Bray et al., 2006) and rates of sperm count abnormalities (Jorgensen et al., 2006) among young men in Europe; declines in testosterone levels in urban Finnish (Perheentupa et al., 2006), Danish (Andersson, 2005) and American (Travison et al., 2007) men. In industrialized nations, there is an increase in reported male genitourinary conditions such as cryptorchidism and hypospadias (Toppari et al., 2001), which some scientists believe is linked to exposure to endocrine disrupting chemicals (Small et al. 2009). Researchers report a declining trend in the onset of breast development and menarche in girls in the United States over the past 30 years (Herman-Giddens, 2006).

There is growing evidence that chemical exposure is a cause of reproductive problems. Evidence from animal studies often suggests that a chemical may be of concern for human reproductive outcomes, but it is difficult to identify causal pathways of exposure and disease in humans. Laboratory animals can be exposed to carefully measured levels of only one chemical at a time, and their lifestyles can be tightly controlled. Humans, on the other hand, are exposed to thousands of chemicals simultaneously, have unique genetic makeups, move around, change jobs, and have varying lifestyles. Additionally, because many chemicals exist in the environment ubiquitously, there is no unexposed control group outside of the laboratory. These difficulties make human health research more uncertain, and often require precautionary actions based on preliminary evidence if human health is to be protected (Kriebel et al., 2001).
Despite these difficulties, the literature on human reproductive health outcomes is growing. Today, scientists suspect that many reproductive health symptoms, conditions, and diseases are linked to exposure to heavy metals, agricultural chemicals, or industrial chemicals.

In women, exposure to environmental chemicals has been associated (Giudice et al., 2005; Buck et al., 2006; Diamanti-Kandarakis et al., 2009) with:

- Premature ovarian failure
- Malformed reproductive organs
- Uterine fibroids
- Endometriosis
- Polycystic ovarian syndrome
- Ovarian and breast cancers

- Infertility or impaired fecundity
- Recurrent pregnancy loss
- Birth defects
- Low birth weight
- Premature menopause.

In men, chemical exposure has been associated (Giudice et al., 2005; Hauser, 2006; Ten et al., 2008) with:

- Undescended testes (cryptorchidism)
- Malformed reproductive organs (hypospadias)
- Decreased sperm quality or quantity
- Testicular dysgenesis syndrome (TDS), a suspected cluster of effects (undescended or malformed reproductive organs, testicular cancer, and decreased sperm quality) with a hypothesized common fetal origin
- Declining testosterone levels.

Chemicals can lead to environmental health problems by disrupting the endocrine system, by disrupting the nervous system's controls over the endocrine system, or by damaging reproductive tissues (Ten et al., 2008). In men, some scholars believe that exposure to endocrine-disrupting chemicals may be linked to testicular dysgenesis syndrome, a common causal pathway for a cluster of reproductive problems that emerge in adulthood (Bay et al., 2006; Skakkebaek et al., 2001).

Reproductive and developmental problems are of particular concern in Alaska. In 2008, the Alaska Department of Health and Social Services released a report documenting that the rate of birth defects in Alaska was twice as high as the national average (Alaska Department of Health and Social Services). As reported by the State of Alaska Epidemiology Bulletin, the prevalence of birth defects in Alaska is "twice as high as the 3% reported for the United States as a whole" (Alaska DHSS, 2008). Moreover, Alaska Native infants were found to have more than twice the risk of birth defects as compared to white infants in Alaska (Alaska DHSS, 2008). Dr. Bradford Gessner, Chief of Alaska's Maternal and Child Health Epidemiology Unit, stated this rate cannot be explained simply by the known risk factors of cigarette smoking, alcohol consumption, or maternal age (Bryson, 2008).

Chemical-by-Chemical Research Findings

Specific chemicals have been linked in human health studies to different reproductive health outcomes. The research outlined below is not exhaustive and is intended to call attention to some chemicals currently of concern.

Pesticides

Pesticides are synthetic chemical formulations designed to kill pests, including unwanted plants (herbicides), insects (insecticides), rodents (rodenticides), and molds/fungus (fungicides). These chemicals interfere with basic life processes and metabolism, thus harming "non-target" plants, animals, and people. Researchers have examined the effects of pesticide exposure on reproductive health, using occupationally exposed groups of farmworkers, or using biomonitoring to look for biomarkers of exposure to legacy chemicals such as DDT.

Pesticide exposure is associated with prostate cancer (Morrison et al., 1993; Meyer et al., 2007; Alavanja et al., 2003; Van Maele-Fabry et al., 2006; Mahajan et al., 2006), decreased fetal growth and length of pregnancy (Stillerman et al., 2008), endometriosis (Porpora et al., 2009), and miscarriages, birth defects, changes in sperm quality, and infertility (McCauley et al., 2006). The pesticide DDT was banned in the US in 1972, but use continues around the world mostly for malaria eradication. Exposure to DDT or its breakdown product DDE has been associated with fertility problems, miscarriage, early onset of menarche, and decreased sperm quality and quantity in highly exposed populations (Eskenazi et al., 2009), as well as urogenital malformation in boys (Lubick, 2010) and an increased risk of breast cancer in women who were exposed before the age of 14 (Cohn et al., 2007).

Bisphenol A

Bisphenol A (BPA) is used as an additive in polycarbonate plastics and as a lining in food cans. In a study of Japanese women, researchers found BPA exposure linked to recurrent miscarriage (Sugiura-Ogasawara et al., 2005). Research on BPA exposure in animals also suggests cause for concern. A recent study found that environmentally-relevant doses of BPA in female mice caused potentially carcinogenic changes in reproductive tissues (Newbold et al., 2009). BPA exposure in adult laboratory animals has also been associated with egg chromosome abnormalities (Hunt et al., 2003) and decreased semen quality (Al-Hiyasat et al., 2002; Sakaue et al., 2001). In animals exposed during developmental stages, BPA has been associated with obesity and altered onset of puberty (Howdeshell et al., 1999), altered prostate development and enlarged prostate (Timms et al., 2005; Gupta, 2000; vom Saal et al., 1998), decreased semen quality (Sakaue et al., 2001; Herath et al., 2004), and hormonal changes (Herath et al., 2004). In addition, Ho et al. (2006) found that neonatal exposure to environmentally relevant doses of BPA in laboratory rats increased their susceptibility to prostate cancer after additional adult exposures to estrogenic substances.

Perfluorinated compounds

Perfluorinated compounds (PFCs) are used in consumer products containing non-stick, stain-resistant and waterproof coatings. Toxicological and animal studies show that PFCs can affect fetal development and growth, but human epidemiological work remains limited. Some studies have concluded that higher levels of some PFCs are associated with lower sperm counts (Joensen et al., 2009), increased risk of irregular menstrual cycles and longer time to conceive (Fei et al., 2009), while associations with birth weight have been inconsistent (Steenland et al., 2010). Exposure to PFCs during fetal development is associated with hormonal changes (Lau et al., 2004), reduced birth weight (Butenhoff et al., 2004) and miscarriage (Butenhoff et al., 2004; Luebker et al., 2005). Higher levels of PFAA, the breakdown product of PFCs, are associated with altered hormone levels and decreased sperm quality in men (Joensen et al., 2009).

Phthalates

Phthalates are a class of plasticizers used in numerous consumer products ranging from makeup to liquid soap and children's toys to flooring materials. Phthalate exposure is associated with early puberty in girls (Wolff et al., 2010), pre-term birth (Meeker et al., 2009), and cryptorchidism in boys (Fisher et al., 2003; Bay et al., 2006; Sharpe et al., 2006). Additionally, exposure as an adult has been found to lead to decreased semen quality (Duty et al., 2003), reduced fertility (Lovekamp-Swan et al., 2003), endometriosis (Cobellis et al., 2003; Reddy et al., 2006), and miscarriage (Sharara et al., 1998).

Flame retardants

Polybrominated diphenyl ethers (PBDEs) are used as flame retardants in household and consumer products such as mattresses, upholstered furniture and electronics. The octa- and penta-BDE formulations were removed from production in 2005 in the US. The EPA negotiated a voluntary, three-year phase-out with two of the major manufacturers and the primary exporter to the U.S. of the deca BDE formulation, which will go into effect in 2013. However, people are exposed to these hazardous chemicals through imported and older products. Chlorinated Tris (TDCPP) and triphenyl phosphate are now used as PBDE replacements. Polybrominated biphenyl (PBB) was a flame retardant used in the 1970s until it was accidentally mixed with animal feed in Michigan, leading to widespread contamination of livestock and people. Several human health studies on various flame retardants have been published in the last several years. Researchers have found that PBDE exposure is associated with hyperthyroidism during pregnancy (Chevrier et al., 2010), decreased fecundability (Harley et al., 2010), permanent impairment of spermatogenesis in offspring (Kuriyama et al., 2005) and elevated rates of cryptorchidism (Main et al., 2007).

One major route of exposure to flame retardants is household dust. A recent study compared household dust levels to reproductive outcomes in male residents, and found that levels of chlorinated Tris in household dust were associated with reduced sperm count and altered levels of fertility and thyroid hormones in men (Meeker and Stapleton, 2010). The Michigan Long-Term PBB study tracks the health outcomes of exposed Michigan residents. Researchers have found that boys with cryptorchidism have higher rates of PBBs in maternal breast milk, and that *in utero* PBB exposure is associated with hernias and hydrocele (Small et al., 2009).

Air pollution

Air pollution, including carbon monoxide, lead, ozone, and particulate matter, is associated with many adverse health effects in children and adults, including reproductive problems. Both outdoor and indoor air pollution can be hazardous to health. A recent study found that exposure to traffic-generated air pollution (nitrogen oxides and particulate matter <2.5μm) during pregnancy increases the risk of preeclampsia and preterm birth (Wu et al., 2010), and leads to reduced term birth weight and preterm delivery (Stillerman et al., 2008). Another study showed that air pollution exposure during development leads to low birth weight and preterm delivery (Woodruff et al., 2008).

Many volatile and semivolatile organic compounds enter indoor air through vapor intrusion, from plumes of contaminants in the soil and groundwater. Benzene, a common industrial chemical and an additive to gasoline, is a known human carcinogen and causes blood disorders. Recently, researchers have found that occupational benzene exposure decreases sperm quality and leads to chromosomal abnormalities that impact human embryos and fetal development (Xing et al., 2010). This study found that these types of abnormalities are higher in men who are exposed to levels of benzene near the U.S. permissible limit for benzene air pollution.

Lead

Lead is a well-known neurotoxin, but extensive research has also identified its reproductive toxicity effects, including miscarriage, reduced fertility, hormonal changes, menstrual irregularities, abnormal sperm, and altered puberty onset (Woodruff et al., 2008). In a study of Russian boys, higher blood lead levels were associated with shorter height, lower weight and delayed onset of puberty stages (Hauser et al., 2008). A study of Native American youth from the Akwesasne Mohawk Nation showed that exposure to high lead levels was associated with risk of delayed menarche (Schell & Gallo, 2010).

Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) were used in a wide range of products, from coolants to wood floor finishes, before being banned in the US in the 1970s. They are persistent organic pollutants and known carcinogens. Exposure to PCBs has been linked to endometriosis (Porpora et al., 2009), altered sex ratio (del Rio Gomez et al., 2002), decreased fetal growth (Stillerman et al., 2008), earlier age at menarche (Schell & Gallo, 2010; Denham et al., 2005), and prostate cancer (Hardell et al., 2006; Prince et al., 2006; Ritchie et al., 2003; Charles et al., 2003). Exposure to PCBs at levels commonly found in the environment has been linked to reduced sperm motility (Hauser, 2006). In males, other health effects of PCBs exposure include reduced fertility, delayed sexual maturation and testicular cancer (Diamanti-Kandarakis et al., 2009). A recent study of Native American (Mohawk) men found elevated levels of PCBs in blood serum associated with lower testosterone levels (Goncharov et al., 2009).

Prenatal exposure to PCBs has been associated with reduced sperm quality including abnormal morphology and decreased motility (Guo et al., 2000). A recent study found that women with the highest exposures to PCBs in the months before they conceived gave birth to children who were substantially lower in birth weight (Murphy et al., 2010). The magnitude of lower birth weight observed in this study is larger than that for cigarette smoking.

Timing of Exposure and Transgenerational Effects

The timing of exposure to environmental contaminants has been shown to strongly influence associated outcomes. Researchers have found that exposures that occur during pre-conception, gestation, early childhood, and puberty can significantly shape the subsequent reproductive health of adults (Woodruff et al., 2008). Proceedings from the Summit on Environmental Challenges to Reproductive Health and Fertility divided results according to whether exposure occurred in adulthood or during development. For example, reviewers noted that exposure to pesticides as an adult can lead to menstrual irregularities, reduced fertility, miscarriage, decreased semen quality, sperm chromosome abnormalities, and hormonal changes, while exposure during development leads to altered sex ratio, altered onset of puberty, reduced fertility, and changes in fetal growth (Woodruff et al., 2008).

Two recent studies have highlighted the importance of exposures to chemicals in the pre-conception time window for reproductive and fetal development outcomes. Researchers in South Africa found that mothers who were exposed to DDT spraying 5-9 years before conception had a 33% greater chance of having a son with a urogenital malformation (Lubick, 2010). Another group of researchers found that PCB exposure is associated with adverse reproductive effects including time to pregnancy and menstruation, lower birth weight, birth defects, and developmental delays (Murphy et al., 2010).

Exposure to some chemicals may also trigger adverse health outcomes generations later. A 2012 study (Manikkam et al.) found evidence of epigenetic biomarkers for environmental exposures and transgenerational health effects in laboratory rats after ancestral fetal exposure to four classes of chemicals: pesticides (permethrin and insect repellant DEET), plastics (bisphenol A and phthalates), dioxin (TCDD), and hydrocarbons (jet fuel, JP8). In this study, the first, second and third generation offspring of rats who were exposed in the womb developed adult-onset diseases and changes in gene expression without directly being exposed to the same chemicals themselves. The offspring were assessed for pubertal onset and gonadal function. Researchers reported the following findings:

- Early-onset puberty in third generation females associated with ancestral exposure to plastics, dioxin and jet fuel
- Decreased ovarian primordial follicle pool size (a factor that leads to increased infertility in females) in third generation females associated with all chemicals studied
- Spermatogenic cell apoptosis in third generation rats from ancestral exposure to jet fuel
- Unique sperm epigenome alterations associated with each exposure, which may serve as exposure-specific epigenetic biomarkers.

Low-Dose Effects and Nonmonotonic Dose Responses

The traditional toxicological paradigm of “the dose makes the poison” is increasingly found to be inadequate for the behavior of endocrine disrupting chemicals (EDCs). Research has consistently shown that even low-dose exposures (doses in the range of what is commonly found in the environment) to EDCs are associated with adverse health effects, and that high doses to these same chemicals may trigger completely different health effects. In other words, even minute exposures to EDCs at critical times can be damaging. As Vandenberg et al. (2012) report in their recent extensive review of the scientific literature on EDCs, “the effects of low doses cannot be predicted by the effects observed at high doses.”

Using Occupational or Extreme Exposure to Understand Chemicals & Reproductive Health

As noted above, human health research on chemical exposure is incredibly complex because people are simultaneously exposed to many chemicals, often in low doses. To sidestep some of these difficulties, researchers can look for a group that was exposed to a particular chemical at higher levels or with greater consistency than the population as a whole. Such research has used extreme or one-time exposure events, like the industrial accident at the Seveso chemical manufacturing plant in Italy in 1976 that released large amounts of dioxin (Homberger et al., 1979) or the PBB contamination of farm animals and the families that consumed them in Michigan (Egginton, 1980). For example, researchers found that Seveso men exposed to dioxin had decreased sperm quality and motility (Mocarelli et al., 2008). They then compared their results to levels found throughout the world and found that effects were observed at exposure levels within one order of magnitude of those observed throughout the industrialized world. The authors conclude that exposure to dioxin “may be responsible at least in part for the reported decrease in sperm quality, especially in younger men” (70).

A significant body of research has also developed around women who took diethylstilbestrol (DES), a synthetic estrogen, during pregnancy to prevent miscarriage. DES led to a pattern of reproductive health problems as the women’s offspring reached puberty. Research with this unique cohort of people has found elevated rates of rare reproductive cancers, malformed reproductive organs, menstrual irregularities, infertility or sub-fertility (Schrager and Potter, 2004), and reproductive tract abnormalities and testicular cancer (Martin et al., 2008).

Groups of people who are occupationally exposed to chemicals also shed light on the connections between chemical exposure and reproductive health. For example, a study connected PCB exposure to reduced fertility, delayed sexual maturation, testicular cancer, and prostate cancer in a cohort of electrical utility workers who experienced high levels of exposure to PCBs (Ritchie et al., 2003; Charles et al., 2003). A study of women with occupational exposure to pesticides in Denmark found that their sons had considerably higher rates of reproductive problems, including cryptorchidism, decreased penile length, decreased testicular volume, and changes in hormone levels, compared to average Danish boys (Anderson et al. 2008). Other studies have found that pesticide exposure led to elevated rates of prostate cancer in occupationally exposed farmworkers (Morrison et al., 1993; Meyer et al., 2007; Alavanja et al., 2003).

Future Research

This body of evidence shows that researchers are increasingly able to use epidemiological studies to link environmental exposure to chemicals with reproductive health problems. Ongoing research investigates the reproductive risks posed by routine, low-level exposures to environmental chemicals. In addition, researchers are beginning to examine the effects of multiple, simultaneous exposures on health, which better account for the reality that humans encounter reproductive toxicants in complex mixtures (Denham et al., 2005; Woodruff et al., 2010). There is also an identified need for long-term, trans-generational studies to examine the impact on a lifetime of exposure and the inter-generational effects of chemical exposure (Woodruff et al., 2010). Large research programs like the National Children's Study aim to track the long-term impact of exposures on children's health and development outcomes. Smaller cohort studies done by the NIEHS/EPA Children's Environmental Health Centers also offer such potential.

Research in Alaska

Research on environmental contaminants and reproductive health in Alaska and elsewhere in the Arctic is limited, but as noted above, chemical contamination in Alaska is an important local concern since the frequent consumption of fish and sea mammals that make up the traditional Alaskan diet can lead to increased exposures in individuals (Van Oostdam et al., 1999).

Testing by the Alaska Department of Health and Social Services and other researchers has concluded that levels of mercury in Alaskan fish are low compared to elsewhere in the country and are generally not cause for concern (Verbrugge, 2007; Jewett and Duffy, 2007). However, another set of researchers came to more cautious conclusions. They examined levels of seven heavy metals in fish in the Aleutian Islands, and concluded that the levels of arsenic and mercury could pose a risk to human consumers (Burger et al., 2007b). The same researchers, in a larger project, looked at mercury levels in over 30 subsistence species in the Aleutians including fish, sea algae, birds, and marine mammals, and found significant differences in mercury levels across species (Burger et al., 2007). Mercury levels increased with weight in many of the organisms sampled. Over 40% of the fish and bird samples had mercury levels above 0.5 ppm. These authors concluded that Aleut women could easily consume enough subsistence foods in a single day to put them over the single-meal exposure limit of 2.0 ppm for pregnant women. They argued that rather than provide a blanket statement on whether it is safe to eat fish, it is more helpful for public health practitioners to provide people with information on mercury levels in a wide range of subsistence foods, to allow them to make informed decisions on their own.

There has been little epidemiological work done on reproductive health and the environment in Alaska. Two human studies on environmental exposures and reproductive health outcomes published in 2006 examined the association between reproductive outcomes and open dumps located near 197 Alaska Native villages. These studies found that women from villages with open dump sites that were considered "most hazardous" by EPA standards delivered babies who weighed less, were too small for their gestational age, were born too early, or had higher rates of some birth defects than babies born to women living in villages near less dangerous dump sites (Gilbreath and Kass, 2006a; 2006b). Though we know little about what exposure or combination of exposures contributed to these outcomes, or exactly how women were exposed, this research highlights the role that environmental exposures may play in reproductive health outcomes. Moreover, as discussed above, birth defects in Alaska are twice as prevalent as in the United States as a whole (Alaska DHSS, 2008).

The Arctic Monitoring and Assessment Program (AMAP) research studies on human health in the Arctic found that PBDE concentrations in maternal blood serum of Yupik women within the Yukon-Kuskokwim Delta area of Alaska are the highest known human PBDE concentrations in the Arctic, comparable to levels elsewhere in the U.S. (AMAP, 2009). Research results also indicate abnormal reproductive and developmental patterns among arctic communities in recent years that may be attributable to contaminant exposures. In Arctic Russia, high POPs levels were associated with low birth weight, premature births, and stillbirths, with possible changes in the sex ratios of children (AMAP 2009). Studies also suggest changes in the proportions of X and Y chromosomes in the sperm of men from Greenland and Scandinavia (AMAP 2009).

Human health studies in the Canadian Arctic have found evidence of reproductive health effects associated with environmental contaminants (Muir et al., 2005). One study found that Inuit women had higher levels of organic mercury in their cord blood than Caucasian women; another study found that PCB exposure in newborns of northern Quebec was associated with lower birth weight comparable to the effects of drinking and smoking during pregnancy. Additionally, the European Commission INUENDO project on human fertility and organochlorines in the environment found that, among Inuit women, increased time to pregnancy was associated with exposure to intermediate and high amounts of PCB and DDE (a metabolite of DDT) (Bonde et al., 2008).

What Health Care Providers Can Do

The links between environmental contaminants and reproductive health may still be uncertain, but they are a growing topic of scientific research and source of concern for many health care professionals. Health care providers play a key role by educating patients and helping to diagnose, treat and prevent health problems. Here are suggestions for concrete steps that can be taken by interested health care professionals:

1. Request and organize grand rounds or workshops on reproductive environmental health.
2. Share case studies at medical meetings and attend talks on environmental health topics.
3. Support research on birth defect trends with suspected environmental links using data available through the Alaska Birth Defects Registry. For more information, see www.epi.hss.state.ak.us/mchepi/ABDR/default.stm.
4. Encourage patients to avoid exposure to chemicals with known or suspected reproductive hazards.
5. Familiarize yourself with the unique needs of Indigenous populations who get a larger portion of their diet from marine wildlife. Health care providers can be the ones to pass on health advisories regarding diet issues, such as seafood consumption (Burger et al. 2007).
6. Routinely collect environmental and occupational histories. For information and suggestions about conducting an environmental history, consult Schettler, Solomon, Valenti, and Huddle's *Generations at Risk: Reproductive Health and the Environment* (1999), which includes a primer for clinicians (Chapter 10).
7. **Join the Alaska Collaborative on Health and the Environment** (CHE-Alaska). The Collaborative on Health and the Environment is a national, non-partisan partnership of individuals and organizations concerned with the effects of environmental contaminants on human and ecosystem health. CHE-Alaska formed as a regional group in December 2005 following the Alaska Conference on Health and the Environment. CHE-Alaska invites participation from health care professionals, researchers, health-affected individuals, patient groups, students, advocacy organizations, and any other individual or group concerned about protecting the health of current and future generations from environmental harm. For more information, please visit www.akaction.org.

Additional Resources for Health Care Providers

Alaska Community Action on Toxics (ACAT), Alaska's only environmental health and justice organization. Our mission is to assure justice by advocating for environmental and community health. We believe that everyone has the right to clean air, clean water, and toxic-free food.
www.akaction.org

ACAT's *Environmental Health Care Toolkit* is an evidence-based resource guide on proper diagnosis, treatment and prevention of health effects linked to environmental exposures, developed for health care providers and community health aides to use in rural health clinics. The toolkit provides facts about contaminants that may be present in the environment, how patients may be exposed, known or suspected symptoms and potential health effects of exposure, ways to reduce exposure, and steps for community health aides to take in their practice.
www.akaction.org/Tackling_Toxics/Body/Preventive_Medicine.html

Alaska Collaborative on Health and the Environment (CHE-Alaska), hosted by ACAT, sponsors regular statewide teleconference seminars and other public events featuring Alaskans and nationally-renowned scientists, health care professionals, and policy experts who are working on a range of environmental health concerns.
www.akaction.org/Tackling_Toxics/Alaska/CHE-AK.html

The Collaborative on Health and the Environment, a national, non-partisan partnership of individuals and organizations focused on the environmental factors that impact human health.
www.healthandenvironment.org

Above the Fold, a daily news update of key environmental health articles that can be customized to areas such as reproductive health, is available free by subscription. This digest provides instant links to the latest news on environmental health research.
www.environmentalhealthnews.org/subscribe.html

The Agency for Toxic Substances and Disease Registry Program provides a series of summaries about hazardous substances.
www.atsdr.cdc.gov/toxfaqs/index.asp

Alaska Native Traditional Knowledge and Native Foods Database, run by the Alaska Native Science Commission, the Institute of Social and Economic Research, and the University of Alaska Anchorage.
www.nativescience.org/html/arctic_contaminants.html

American Academy of Pediatrics Council on Environmental Health. *Pediatric Environmental Health* (3rd Edition). Etzel RA (Ed). Elk Grove Village, IL: American Academy of Pediatrics, 2012.
www2.aap.org/visit/cmte16.htm#manual

American College of Preventive Medicine Environmental Health Resource Center
www.acpm.org/education/environmentalhealth.htm

The American Fertility Association. *Infertility Prevention Program Handbook*. Contains a section on "Avoiding Environmental Toxins," which recommends avoiding exposure to phthalates, BPA, mercury, and benzene.

www.theafa.org/mediafiles/infertility-prevention-handbook-2012.pdf

Arctic Health, a research portal maintained by University of Alaska Anchorage and the National Library of Medicine.
www.arctichealth.org

Arctic Monitoring and Assessment Program, an international organization that provides information on threats to the circumpolar Arctic environment.
www.amap.no

Association of Occupational and Environmental Health Clinics
www.aoec.org

The CDC's National Report on Human Exposure to Environmental Chemicals, currently in its 4th report.
www.cdc.gov/exposurereport/

Children's Environmental Health Network (CEHN)
www.cehn.org

***Generations at Risk: Reproductive Health and the Environment*.** Ted Schettler, MD, Gina Solomon, MD, Maria Valenti, and Annette Huddle. 1999. Cambridge, MA: MIT Press.
www.psr.org/chapters/boston/resources/generations-at-risk-project.html

National Library of Medicine's Hazardous Substances Data Bank, which links databases on toxicology, hazardous chemicals, environmental health, and toxic releases.
www.toxnet.nlm.nih.gov

Physicians for Social Responsibility conducts trainings and workshops on environmental health for health care practitioners. Also, publishes toolkits, quick reference charts, and fact sheets on environmental health issues.
www.psr.org

Seattle Children's Research Institute researchers recently published a paper on clinicians' involvement in reproductive environmental health, which provides a guide outlining exposure risks and reduction tips for some of the most common environmental toxins:
Environmental exposures: How to counsel preconception and prenatal patients in the clinical setting. Sathyanarayana S, Focareta J, Dailey T, Buchanan S. 2012 (in press). *AJOG*.
www.ajog.org/article/S0002-9378%2812%2900151-2/

Science and Environmental Health Network (SEHN)
www.sehn.org

The Toxics Release Inventory, maintained by the Environmental Protection Agency, reports major sources of toxics by zip code.
www.epa.gov/tri

University of California at San Francisco, National Center of Excellence in Women's Health, Program on Reproductive Health and the Environment (PRHE) offers many resources for clinicians interested in incorporating environmental health into practice and becoming active in policy issues.
www.ucsf.edu/coe/prhe.html

PRHE researchers recently published the following paper, which describes the role of health professionals in preventing exposure to harmful chemicals and provides advice on steps that health professionals can take to prevent exposures at work, at home and in the community:

Toxic Environmental Chemicals: The role of reproductive health professionals in preventing harmful exposure. Sutton P, Woodruff, TJ, Perron J, Stotland N, Conry JA, Miller MD, Giudice LC. 2012 (in press). *AJOG*. Available at: www.ajog.org/article/S0002-9378%2812%2900065-8

Vallombrosa Consensus Statement on Environmental Contaminants and Human Fertility Compromise, October 2005.
www.healthandenvironment.org/infertility/vallombrosa_documents

World Health Organization. Children's Environmental Health Training Modules for Health Care Providers. Sub-package on Reproductive Health and Environment (2011).
www.who.int/ceh/capacity/training_modules/en/

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Alaska Community Action on Toxics (ACAT) is a statewide environmental health and justice organization established in 1997. Our mission is to assure justice by advocating for environmental and community health. *We believe that everyone has the right to clean air, clean water, and toxic-free food.*

We help communities implement effective strategies to limit their exposure to toxic substances and to protect and restore the ecosystems that sustain them and their way of life. We work to eliminate the production and release of harmful chemicals by industry and military sources, ensure the public's right to know, achieve policies based on the precautionary principle, and support the rights of Indigenous peoples.

Alaska Collaborative on Health and the Environment (CHE-Alaska)

The Collaborative on Health and the Environment (CHE) is a national non-partisan partnership of individuals and organizations concerned with the role of the environment in human and ecosystem health. CHE seeks to raise the level of scientific and public dialogue about the role of environmental contaminants and other environmental factors in many of the common diseases, disorders, and conditions of our time. CHE promotes interdisciplinary discussions, sharing of scientific evidence, outreach and education, and an agenda to bring about systemic change in improving environmental public health. Underlying all of CHE's activities is a commitment to strong, uncompromised science. We believe that the truth emerges through discussion and that civility among CHE partners is a condition of honest dialogue and learning. Visit us at: www.healthandenvironment.org.

CHE-Alaska formed as a regional group in December 2005 following the Alaska Conference on Health and the Environment. We invite participation from health care professionals, researchers, health-affected and patient groups, students, advocacy organizations, and any individual concerned about protecting the health of current and future generations from environmental harm. Visit us at: www.akaction.org.

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