Introduction

A growing number of health care providers report a rise in patients seeking treatment for infertility and other reproductive health issues (Luoma, 2005; Giudice 2006). Current research suggests that reproductive health may be supported or compromised by several factors including age, genetics, nutritional health, stress, and pharmaceutical use (Schettler et al., 1999). Mounting scientific evidence also suggests that chemicals and contaminants commonly found in the human environment, drinking water, and food supply can influence human fertility and reproduction, though in complex, often poorly understood ways. Several recent scientific discoveries about the effects of environmental pollutants on human reproductive health merit the attention and concern of health care providers treating patients with reproductive health issues (Giudice et al., 2005).

This bulletin provides an introductory overview of what role environmental exposures might play in fertility and reproductive health, with a special focus on evidence drawn from Alaska. This bulletin also provides resources and opportunities for further information about how clinicians can respond.

Health Outcomes of Potential Concern

Reproductive health outcomes with environmental links have been found in females and males of all ages. These issues are not only of concern to health care providers in gynecology or obstetrics, who may have patients struggling to conceive, but also, to pediatricians observing young children with malformed genitalia or early-onset or delayed menarche.

A host of symptoms or conditions are linked or suspected to be linked to environmental exposures. These include, among females (see Buck et al., 2006; Giudice et al., 2005):

- Premature ovarian failure
- Malformed reproductive organs
- Early or delayed menarche
- Infertility or compromised fertility
- Recurrent pregnancy loss
- Inability to carry baby to term, pregnancy compromise, birth defects, congenital abnormalities, and low birth weight
- Damage to fetal reproductive organs
- Premature menopause
- Uterine fibroids

Among males, key trends in reproductive health include (see Hauser 2006; Giudice et al., 2005):

- Undescended testes or malformed reproductive organs (e.g., cryptorchidism and hypospadias).
- Compromised sperm shape and quality, including issues of mobility, motility, and genetic integrity.
- Testicular dysgenesis syndrome, or TDS, is a suspected cluster of effects (undescended or malformed reproductive organs, testicular cancer, and decreased sperm quality) with a hypothesized common fetal origin (Skakkebæk et al., 2001).

Furthermore, after tracking a study group of Massachusetts men for twenty years, scientists observed an overall decline in testosterone levels that were not attributable to aging or lifestyle (Travison et al., 2007), further supporting the possibility that environmental exposures are affecting male reproductive health. More generally, there are also rising rates of diseases or conditions known to affect human fertility in which environmental exposures might also play some role in the etiology, including endometriosis, and ovarian, cervical, and testicular cancer (Giudice et al., 2005).

Sources of Environmental Exposures

Alaska Native peoples and others living in the circumpolar region bear a disproportionate burden of environmental contaminants (AMAP 1997; 2004; Berner 1999; Chary 2000). Several known or suspected reproductive toxicants, such as polychlorinated biphenyls (PCBs) and pesticides, have been detected in the Alaskan environment and food system, as well as in the blood of some Alaska Native people (Berner 1999; Carpenter et al., 2005;
Middaugh et al., 2000) and other circumpolar populations (AMAP 1997).

These chemicals and contaminants originate from both local and remote sources. Many chemicals and heavy metals are produced or released into the environment by industries located in the Lower 48 states and throughout the world, but because they are slow to degrade, and can travel vast distances in air and water currents, they tend to condense, concentrate, and then persist in the cold, northern climate. As a result, the circumpolar Arctic region has become a hemispheric sink for many pollutants and chemicals that may pose reproductive risks (AMAP 2004; Tenenbaum 1998). Of particular concern are pesticides, which are used elsewhere but accumulate in Alaska due to global fate and transport from southern latitudes.

Local industries and formerly-used defense sites are also current sources of exposure to heavy metals (e.g., lead and mercury) and industrial chemicals (e.g., PCBs) in Alaska (Button 2002). Thus, PCB exposures may result not just from global transport, but from formerly-used defense sites in Alaska as well (Carpenter et al., 2005).

These persistent pollutants enter the food chain, where they concentrate in the fatty tissues of predator species. As a result, many of these pollutants are found in the traditional subsistence foods that sustain a significant portion of the Alaskan population (AMAP 2004; Berner 1999; Chary 2000; Middaugh et al., 2000). Though a route of exposure, traditional foods remain the best source of sustenance for Alaska Native people as they are both nutritionally rich and culturally essential. Therefore, it is imperative that health care providers support local, national, and international initiatives to eliminate the use of chemicals known to accumulate in foods.

Humans also are exposed by inhaling air or drinking water that is contaminated by these pollutants. Such exposures can occur at home or on the job, outdoors as well as indoors, as many chemicals can collect in household air and dust (Rudel et al., 2003). In some cases, exposures can occur when substances containing reproductive toxicants are absorbed into the skin, such as phthalates (pronounced ‘thal-lates’), which are commonly added to self-care and beauty products (Rudel et al., 2003).

While researchers document these compounds in air, water, soil, foods, and consumer products, research also confirms that these substances enter the body. Ongoing population monitoring conducted by the U.S. Centers for Disease Control and Prevention (CDC) reports that the average American carries detectable levels of various reproductive toxicants that are also present in the environment (US CDC 2005). In general, many chemicals and pollutants, because of their chemical-physical characteristics, either build up in human systems or are ubiquitous so that, even if excreted by the body, constant re-exposure maintains elevated body levels.

Many chemical compounds are detected at levels known or suspected to affect the reproductive system. As scientists learn more about low-level effects of chemical exposures and the unique vulnerabilities of some individuals, the levels of current human burdens increasingly have flagged the attention of researchers and health care providers (Giudice et al., 2005). More recently, the effects of low-level exposures have garnered the attention of policy-makers. In many instances, however, there remain data gaps about whether and how low-level exposures affect the function of the human body (National Research Council 2006) and the reproductive system.

Researchers have not studied many compounds for their reproductive effects. A recent tabulation found that less than 10% of the 100,000 chemicals currently registered for commercial use have been studied for their human health effects, and only a fraction of those have been tested for how they affect reproductive health (Davis and Webster, 2002).

Timing of Exposures

The timing of exposure strongly influences the observed outcomes. Exposures to pesticides such as alachlor, atrazine, and diazinon, for example, were found to compromise sperm quality of human adult males (Swan et al., 2003b). Similarly, new research suggests links between men's exposures to a particular phthalate and lower sperm concentration and decreased mobility (Hauser et al., 2006).

Researchers also have found that exposures encountered in utero can shape the subsequent reproductive health of adults. Clinicians and scientists now know that the placenta does not shield the developing fetus from chemicals or pollutants the mother encounters (Colborn et al., 1996). For example, some conditions and disease of the reproductive tract have origins in exposures encountered during particular periods of fetal development (Giudice et al., 2005).

The effect of in utero exposures was first seen among the children of women who were, beginning in the 1940s, prescribed DES, a synthetic estrogen, to prevent miscarriage. Though not apparent at first, as exposed children reached puberty, a pattern of reproductive health problems emerged. Follow-up research has confirmed a host of outcomes in both the male and female children of women who took DES, including rare reproductive cancers and malformed reproductive organs, menstrual irregularities, and infertility or sub-fertility, i.e., difficulty conceiving (Schrager and Potter 2004).

Today, DES serves as one model for how exposures during critical periods of fetal development can affect reproductive health in later life stages.

A body of evidence now demonstrates that many chemicals humans routinely encounter in the environment can mimic or interact with the endocrine system, and like DES, can affect the fertility and reproductive health of offspring, though through other biological mechanisms (Colborn et al., 1996; McLachlan 2001). Synthetic or hu-
man-made substances can exhibit estrogenic, androgenic, or anti-estrogenic and anti-androgenic properties. That is, they can act like hormones, or block normal hormone function, which in turn, affects reproductive development (Colborn et al., 1996).

So-called 'endocrine disruption' of human reproduction by environmental chemicals has been demonstrated in animals, but more recently in humans as well. A 2003 study published in *The Lancet* found that women with higher *in utero* exposures to DDT—a pesticide banned from use in the US, but still used in other countries and present in circumpolar ecosystems (van Oostdam et al., 2004; Simonetti et al., 2001)—took longer to conceive once they reached reproductive maturity (Cohn et al., 2003). Researchers are also compiling evidence that phthalates encountered *in utero* affect adult male fertility later in life (Latin et al., 2006).

Environmental chemicals also interfere with the fertility of subsequent generations by altering how genes direct key biological processes. A recent study published in *Science* found that when pregnant female mice were exposed to two commonly used pesticides, vinclozolin and methoxychlor, the exposures compromised the fertility of male offspring in three subsequent generations (Anway et al., 2005). This is the first study to find multi-generational effects. Although the study was performed on mice and involved exposures that are higher than humans might encounter, it is biologically plausible that similar trends might be seen among humans since genetic processes are known to be reasonably similar in both species (Anway et al., 2005).

**Accumulating Evidence and Continued Research**

Though research is ongoing, reproductive environmental health researchers and clinicians agree there is already a substantial body of evidence implicating low-level exposures as a likely contributor to trends currently seen in reproductive outcomes (Giudice et al., 2005).

Supporting evidence comes from a wide variety of sources. Wildlife studies associate exposures to increased rates of malformed reproductive organs, infertility, and overall population declines (Colborn et al., 1996; Guillette and Moore 2006). In humans, the most compelling evidence comes from observations of reproductive outcomes following acute, high-level, occupational exposures (Colborn et al., 1996). For example, over thirty years ago, researchers demonstrated decreased fertility in male farm workers due to regular, occupational exposures to DBCP, an agricultural fumigant (Whorton et al., 1977; Slutsky et al., 1999).

Currently, researchers investigate what reproductive risks are posed by routine, low-level exposures to environmental chemicals. In addition, researchers also examine the effects of multiple, simultaneous exposures, which better account for the reality that humans encounter reproductive toxicants in complex mixtures (Denham et al., 2005). When substances interact, they may increase or mediate toxicological effects in unforeseen ways.

Compounds deemed high priority for research on reproductive effects include (Giudice et al., 2005):

- Commonly-used pesticides
- Chemical additives (used in production of plastics, e.g., Bisphenol A)
- Perfluorinated compounds (used in production of stain-resistant, water-repellant, or non-stick surfaces)
- Chemical additives to beauty and self-care products
- Polybrominated diphenyl ethers (PBDEs) (used as flame retardants in household upholstery and electronics).

Many of these substances are what scientists call 'emerging concerns.' They comprise a new class of persistent, bioaccumulative toxicants that have been studied far less than organochlorines such as PCBs and the pesticide, DDT. Research has already suggested some of these compounds are reproductive toxicants. For example, recent research found decreased sperm counts in male offspring of pregnant rats exposed to a single, low-dose of a ubiquitous brominated flame retardant. These effects were seen at levels already detected in samples of US women’s breast milk (Kuriyama et al., 2005).

Though ongoing research focuses on the reproductive toxicity of these emergent chemicals, new scientific evidence also advances our understanding of the reproductive concerns posed by PCBs, DDT, and other organochlorine exposures. Thus, these too, remain a priority concern as scientists continue to identify significant reproductive outcomes, how they affect the reproductive system, and at what levels.

**New Research in Alaska**

Though scientific research about how environmental factors affect human reproductive health in Alaska is limited, important trends can be inferred from studies conducted within the state.

For example, researchers recently documented a high rate of reproductive organ and testosterone-related problems among male, Sitka black-tailed deer on Kodiak Island. The study, published in *Environmental Health Perspectives*, argues that this unusual pattern is attributable to *in utero* exposures, when pregnant females ingested foods containing hormonally-active agents (Veeramachaneni et al., 2006).

Also in 2006, a team of UAA scientists examined whether exposure to perchlorate, which has many industrial and military applications, has reproductive effects on...
fish. Scientists suspect exposures are occurring in Alaska through imported produce and milk and possibly through seepage from military sites where munitions are stored, many of which have yet to be tested (O’Malley 2006). The UAA perchlorate-exposed fish exhibited altered patterns of sexual development and courtship behaviors. Also, exposed females developed both female and male reproductive organs and were capable of producing both eggs and sperm. This is the first study to demonstrate that perchlorate exhibits androgenic properties and impacts reproductive health (Bernhardt et al., 2006).

The first human studies of environmental exposures and reproductive health outcomes were published last year in The American Journal of Epidemiology and The International Journal of Circumpolar Health. Researchers examined the association between reproductive outcomes and open dumps located near many Alaska Native villages. They found that women from villages with open dump sites that were considered most hazardous 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 did 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 spotlights the role exposures could play in reproductive outcomes experienced by women entering your clinic. It also suggests that some exposures relevant to reproductive health outcomes stem from local, rather than only global sources.

Relevant epidemiological studies of reproductive health outcomes among other circumpolar populations are ongoing (e.g., Northern Contaminants Program, Canada; Project INUENDO in Greenland, Sweden, Ukraine, and Poland) as is research with populations who eat traditional, subsistence foods. One recent study conducted among the Mohawk of New York and Canada, who also rely on subsistence foods, suggests exposure to certain types of PCB congeners and lead was associated with changes in the timing of girls’ menarche (Denham et al., 2005). As new studies are published, they will contribute to our developing understanding of how environmental factors may be influencing human reproduction and fertility in Alaska.

**What Health Care Providers Can Do**

1. Request and organize grand rounds or workshops on reproductive environmental health.
2. Share case studies at medical meetings.
4. Routinely collect environmental and occupational histories. For more 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).
5. Learn more about exposure sources and reproductive toxicity of chemicals and environmental pollutants:
   - The Collaborative on Health and the Environment ([www.healthandenvironment.org](http://www.healthandenvironment.org)).

To investigate potential exposure outcomes common in Alaska, clinicians also could reference:

- The Toxics Release Inventory maintained by the Environmental Protection Agency, which reports major sources of toxins by zip code ([www.epa.gov/tri](http://www.epa.gov/tri)).
- Arctic Health, a resource portal maintained by University of Alaska Anchorage and the National Library of Medicine ([www.arctichealth.org](http://www.arctichealth.org)).
- Arctic Monitoring and Assessment Programme ([www.amap.no](http://www.amap.no)).
- Alaska Native Traditional Knowledge and Native Foods Database, run by the Alaska Native Science Commission, the Institute of Social and Economic Research (ISER) and the University of Alaska Anchorage. ([www.nativescience.org/html/arctic_contaminants.html](http://www.nativescience.org/html/arctic_contaminants.html))


   “The Collaborative on Health and the Environment (CHE) is a national, non-partisan partnership of individuals and organizations concerned with the effects of environmental contaminants on human and ecosystem health. CHE seeks to raise the level of scientific and public dialogue about the role of environmental contaminants and other

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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. CHE believes truth emerges through discussion and that civility among CHE partners is a condition of honest dialogue and learning.” For more information visit: www.healthandenvironment.org

CHE-Alaska formed as a regional group in December 2005 following the Alaska Conference on Health and the Environment and invites participation from health care professionals, researchers, health-affected individuals and 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


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

Association of Occupational and Environmental Health Clinics
1010 Vermont Avenue, NW, Suite 513
Washington, DC 20005
Website: http://www.aoec.org/
Phone: (888) 347-AOEC (2632)


Project INUENDO—Human Fertility at Risk from Biopersistent Organochlorines in the Environment. A research project supported by the European Commission. Examines couple fertility, semen quality and neonatal studies of reproductive hormone profiles among four populations in Greenland, Sweden, Poland and Ukraine. Website: http://www.inuendo.dk/

Physicians for Social Responsibility
Conducts trainings and workshops on environmental health for health care practitioners. Also, publishes ‘tool kits,’ pocket-sized, quick reference charts, and fact sheets on environmental health issues. Website: /www.psr.org

Also, for more resources, see Greater Boston Physicians for Social Responsibility at http://psr.igc.org

University of California at San Francisco, National Center of Excellence in Women’s Health, Program on Reproductive Health and the Environment. Website: www.ucsf.edu/coe/prhe.html

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

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Schettler, T., Solomon G., and Valenti, M. 1999. Genera-


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.

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.

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