PROTECT Puerto Rico Testsite for Exploring Contamination Threats

Bulletin

CRECE

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Body of Evidence: Reproductive Health and the Environment

Infertility and reproductive 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.[1] 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.

Information on these exposures and their health effects is important for health care providers because studies demonstrate that health care would be dramatically improved and medical care costs reduced if environmental pollution and chemical exposure were mitigated.[2] An increased awareness of the effects of environmental contaminants on patient health will allow health care providers to offer more timely and appropriate care, better understand potential causes of reproductive problems, better track and study reproductive outcomes, and 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 Puerto Rico. Finally, *Body of Evidence* provides resources and opportunities for clinicians and health care providers to educate themselves and their patients on the links between chemical exposures and reproductive health.

This version of *Body of Evidence* updates the 2012 publication of the Collaborative on Health and the Environment - Alaska (CHE-Alaska) and Alaska Community Action on Toxics, and frames it for a Puerto Rican audience. Since 2012, the volume of human health studies on environmental contaminants has grown significantly, although the general conclusions of the 2007 and 2012 Body of Evidence bulletins—that many chemical exposures are associated with reproductive health problems—remain unchanged.

1. Sources and Pathways of Environmental Exposures

Chemicals are ubiquitous in our daily lives, and over 85,000 chemicals are now in use in the

United States.[3] 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. Currently, 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 introduce new chemicals.[4,5] 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. Safety testing for so-called "inert" ingredients is not required, and they do not need to be labeled on 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 product can be measured in the human body using biomonitoring, which measures the presence and concentration of chemicals in human tissues.[6] The U.S. Centers for Disease Control and Prevention National Biomonitoring Program conducts nationwide biomonitoring studies every few years and has measured 265 chemicals in the blood or urine of thousands of Americans.[7] 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.[8]

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).[8,9] The NHANES survey detected chemicals such as polychlorinated biphenyls (PCBs), organochlorine pesticides, Perfluoroalkyl substances (PFAS), 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, which may interact with one another in unanticipated ways.

2. Environmental Exposures in Puerto Rico

Environmental contamination is of particular concern in Puerto Rico, which has 16 active Superfund sites and over 200 hazardous waste sites. In addition, many of these sites lie above unlined limestone aquifers, which leach hazardous chemicals into groundwater. Historic data shows that the groundwater sources in the north coast of Puerto Rico have been contaminated in this manner for over 40 years.[10] In addition, chlorinated volatile organic compounds were detected in over half of the groundwater samples, and almost three quarters of sampled wells.[11] Researchers also identified undocumented landfill sites, unidentified waste disposals and accidental spills. These findings have far-reaching impacts on the public; as a result, groundwater was discontinued as a source of drinking water in many parts of Puerto Rico as of 2005.[12]

3. Preterm birth in Puerto Rico

Puerto Rico has one of the highest preterm birth rates worldwide, where approximately 12% of all live births occur before 37 gestational weeks,[13] well above the average for the continental U.S. It has been shown that preterm birth can have long-term health implications, including atopic asthma in childhood[14], and chronic disease in adulthood, such as diabetes.[15] Yet the extent to which Puerto Rico's contaminated sites impact preterm birth remains unknown.

4. Health Outcomes of Potential Concern

Infertility and other reproductive health problems are on the rise in the U.S. and around the world. Nearly 11% of women of childbearing age had trouble conceiving[8]- a 20% increase since 1995.[16] 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.[9,17,18] 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.[19] Other scholars have noted increases in testicular cancer[20] and rates of sperm count abnormalities among young men in Europe[21] and declines in testosterone levels in urban Finnish[22], Danish[23] and American[24] men. In industrialized nations, there is an increase in reported male genitourinary conditions such as cryptorchidism and hypospadias[25], which some scientists link to exposure to endocrine disrupting chemicals.[26] Researchers report an earlier sexual maturation among U.S. girls, including the onset of breast development and menarche, over the past 30 years.[27]

Evidence from animal studies has identified chemicals of concern related to human reproductive outcomes. However, it remains 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, change jobs and locations, 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.[28] 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, and agricultural and industrial chemicals.

Chemicals can lead to adverse health outcomes by disrupting the endocrine system, by disrupting the nervous system's controls over the endocrine system, or by damaging reproductive tissues.[29] In women, exposure to environmental chemicals has been associated with:[30–32]

- 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 with:[29,30,33]

- Undescended testes (cryptorchidism)
- Malformed reproductive organs (hypospadias)
- Decreased sperm quality or quantity
- Testicular dysgenesis syndrome (TDS): a suspected cluster of effects including undescended or malformed reproductive organs, testicular cancer, and decreased sperm quality[34,35]
- Declining testosterone levels

5. 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.

5.1 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 and non-occupational exposures such as indoor pesticide exposure in children, as well as establishing biomonitoring programs to look for biomarkers of exposure to legacy chemicals such as DDT.

Pesticide exposure has been associated with prostate cancer,[36–40] decreased fetal growth and length of pregnancy,[41] endometriosis,[42] childhood leukemia and lymphomas,[43] and miscarriages, birth defects, changes in sperm quality, infertility,[44–47] and a decrease in testosterone levels.[48] Prenatal pesticide exposure has also been linked to changes in reproductive hormones such as sex hormone-binding globulin and testosterone in fetal cord blood.[49] The pesticide DDT was banned in the U.S. 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,[50] as well as urogenital malformation in boys[51] and an increased risk of breast cancer in women who were exposed before the age of 14.[52]

5.2 Bisphenol A

Bisphenol A (BPA) is used as an additive in polycarbonate plastics and as a lining in food cans. Research on BPA exposure in animals suggests cause for concern. A recent study found that environmentally-relevant doses of BPA in female mice caused potentially carcinogenic changes in reproductive tissues.[53] BPA exposure in adult laboratory animals has also been associated with egg chromosome abnormalities[54] and decreased semen quality.[55,56] In animals exposed during developmental stages, BPA has been associated with obesity and altered onset of puberty,[57] altered prostate development and enlarged prostate,[58–60] decreased semen quality,[56,61] and hormonal changes.[61] In addition, neonatal exposure to environmentally relevant doses of BPA in laboratory rats increased their susceptibility to prostate cancer after additional adult exposures to estrogenic substances.[62] In a study of Japanese women, researchers found BPA exposure linked to recurrent miscarriage.[63] A review concluded BPA could be considered an ovarian toxicant, and a potential uterine and testicular toxicant due to the various interferences found with exposure to BPA in animal and human studies.[64] The timing of the exposure could determine the impact on the ovaries, particularly during stages of pregnancy.[65]

5.3 Perfluoroalkyl substances

Perfluoroalkyl substances (PFAS) are used in consumer products containing non-stick, stain-resistant and waterproof coatings. Toxicological and animal studies show that PFAS can affect fetal development and growth, but human epidemiological work remains limited. Some studies have concluded that higher levels of some PFAS are associated with lower sperm counts,[66] increased risk of irregular menstrual cycles and longer time to conceive,[67] while associations with birth weight have been inconsistent.[68] Exposure to PFAS during fetal development is associated with hormonal changes,[69] reduced birth weight,[70] and miscarriage.[70,71] Higher levels of PFAA, the breakdown product of PFAS, are associated with altered hormone levels and decreased sperm

quality in men.[66] Some evidence suggests perfluorooctane sulfonate (PFOS, a type of PFAS) can impair sperm morphology in humans, potentially due to endocrine disruption.[72]

5.4 Phthalates

Phthalates are a class of plasticizers used in numerous consumer products including makeup, liquid soap, children's toys and flooring materials. Phthalate exposure is associated with early puberty in girls,[73] pre-term birth,[74] and cryptorchidism and decreases in the anogenital distance in boys.[18,34,75,76] Additionally, exposure as an adult has been found to lead to decreased semen quality,[77] reduced fertility,[78] endometriosis,[79,80] and miscarriage.[81] Di-(2-ethylhexyl) phthalate (DEHP) is widely used for PVC and in medical tubing. It has also been commonly associated with various reproductive effects, including changes in reproductive and thyroid hormones among pregnant women,[82] adverse effects on the health of follicles (possibly through oxidative stress), and alteration of ovarian steroidogenesis.[83]

5.5 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 U.S. 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 went 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,[84] increases in thyroid stimulating hormone in pregnant women,[85] decreased fecundability,[86] permanent impairment of spermatogenesis in offspring,[87] and elevated rates of cryptorchidism.[88]

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.[89] 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.[26] The thyroid appears to be the primary target of PBDEs; however, estrogen and androgen-mediated processes have also been shown to be affected by PBB exposure in animal studies, including changes in ovarian, testis, and epididymis weights in animals.[90]

5.6 Air pollution

Indoor and outdoor air pollution, including carbon monoxide, lead, ozone, and particulate matter is associated with many adverse health effects in children and adults, including reproductive problems. 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,[91,92] and is associated with reduced term birth weight and preterm delivery,[41,93] and congenital malformations.[94] Another study similarly showed that air pollution exposure during

development leads to low birth weight and preterm delivery.[95]

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.[96] 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.

5.7 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.[95] In a study of Russian boys, higher blood lead levels were associated with shorter height, lower weight and delayed onset of puberty stages.[97] 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.[98] A study showed that maternal blood lead levels correlated with umbilical cord blood lead levels, and additionally found that maternal blood lead was associated with pre-term birth and low birth weight.[99] Similarly, another study found an association between maternal blood lead levels and preterm birth among males only.[100] Infantile weight at 24 months was still decreased with prenatal exposure to lead in another study.[101]

5.8 Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) were used in a wide range of products, from coolants to wood floor finishes, before being banned in the U.S. in the 1970s. They are persistent organic pollutants and known carcinogens. Exposure to PCBs has been linked to endometriosis,[42] altered sex ratio,[102] decreased fetal growth,[41] earlier age at menarche,[98,103] and prostate cancer[104,105]. Exposure to PCBs at levels commonly found in the environment has been linked to reduced sperm motility.[33] In males, other health effects of PCB exposure include reduced fertility, delayed sexual maturation and testicular cancer.[32] A recent study of Native American men of the Mohawk tribe found that elevated levels of PCBs in blood serum were associated with lower testosterone levels.[106]

Prenatal exposure to PCBs has been associated with reduced sperm quality including abnormal morphology and decreased motility.[107] 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;[108] the magnitude of lower birth weight observed in this study is larger than that for cigarette smoking. One study found changes in sex hormone-binding globulin and testosterone in fetal cord blood with in-utero exposure to PCBs.[49]

6. Timing of Exposure and Transgenerational Effects

The timing of exposure to environmental contaminants has been linked to specific negative health 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.[95,109] 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 during development leads to altered sex ratio, altered onset of puberty, reduced fertility, and changes in fetal growth,[95] while exposure during adulthood can lead to

menstrual irregularities, reduced fertility, miscarriage, decreased semen quality, sperm chromosome abnormalities, and hormonal changes.

Many recent studies have highlighted the importance of exposures to chemicals in the pre-conception time window for reproductive and fetal development outcomes. Reviews describe life-long lasting effects on the epigenome and subsequent health effects due to stressors at the prenatal and early postnatal stages of life, including but not limited to obesity, mental health issues, heart disease, and other chronic conditions.[110–112] 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.[51] 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.[108]

Exposure to some chemicals may also trigger adverse health outcomes generations later. A 2012 study 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).[113] 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

7. Low-Dose, Synergistic, and Non-monotonic Dose Responses

The traditional toxicological paradigm of "the dose makes the poison" is increasingly found to be inadequate in explaining the effects 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 reported in a recent extensive review of the scientific literature on EDCs, "the effects of low doses cannot be predicted by the effects observed at high doses."[114]

8. 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[115] or the PBB

contamination of farm animals and the families that consumed them in Michigan.[116] In these case studies, researchers found that Seveso men exposed to dioxin had decreased sperm quality and motility.[117] 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".[117]

A significant body of research has also developed around women who took the synthetic estrogen diethylstilbestrol (DES) 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,[118] and reproductive tract abnormalities and testicular cancer.[119]

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.[120,121] 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.[122] Other studies have found that pesticide exposure led to elevated rates of prostate cancer in occupationally exposed farmworkers.[36–38]

9. Future Research

The evidence presented in this bulletin shows that researchers are increasingly able to use epidemiological studies to link environmental exposure to chemicals with reproductive health effects. 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.[103,123,124] 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.[124] Large research programs like the Children's Health Exposure Analysis Resource (CHEAR) provide resources to track the 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 – CRECE, the Center for Research on Early Childhood Exposure and Development in Puerto Rico, is one of these Centers that developed out of PROTECT.

10. Research in Puerto Rico

Research on environmental contaminants and reproductive health in Puerto Rico is limited. However, chemical contamination in Puerto Rico is an important local public health concern since most, if not all, of its inhabitants are exposed to phthalates and other emerging chemicals of concern. With funding from the National Institute of Environmental Health Sciences' Superfund Research Program, the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) Center, studies exposure to environmental contamination and its contribution to preterm birth rates in Puerto Rico. Our PROTECT team has chosen Puerto Rico as a research site due to its dangerously high rate

of preterm birth and the extent to which Puerto Rico has been subject to hazardous waste contamination.

The Superfund Research Program works with the Environmental Protection Agency (EPA), which oversees the remediation and restoration of the most hazardous waste sites in the country. PROTECT's overall goal and objective, in conjunction with the "Healthy People 2020" goal, is to reduce preterm birth in Puerto Rico by identifying potential causes of preterm birth and developing ways to mitigate exposures and protect human health and ecosystems. PROTECT's interdisciplinary collaboration allows for an array of scientific approaches to address environmental contamination and reproductive health. PROTECT and other investigators have begun to explore associations between toxicants found in urine and associated health risks among pregnant women in Puerto Rico, including chemicals called phenols and parabens, often used in consumer products.[125] A study among pregnant women in Puerto Rico found that exposure to BPA, select parabens, and the phenol triclosan (TCS) was associated with oxidative stress and inflammation and may serve as potential mechanisms by which exposure to these compounds may influence adverse birth outcomes and other health effects.[125] Similarly, urinary phthalates were also associated with increased levels of oxidative stress markers in pregnant women.[126] PROTECT has also linked phthalate exposure with reductions in reproductive and thyroid hormones in pregnant women, with the association appearing stronger in late stages of pregnancy.[82]

Elevated levels of PCB's, nickel, chromium and total chlordane have been found in sediment and fish in the Guànica Bay in the southwest region of Puerto Rico, due to the number of oil spills and pollution discharges that date back as far as the 1960's.[127,128] In fact, the PCB levels were the second highest reported PCB sediment level in the U.S. Seafood consumption could be an important route of exposure; median and 95% of urinary inorganic arsenic levels were higher in the Vieques Island off Puerto Rico, as compared to other countries.[129]

PROTECT researchers found generally lower levels of select pesticides in Puerto Rican women as compared to the U.S. national average,[130] and women were more likely to have elevated levels if they were less educated, unemployed, married, had consumed spinach or other collards in a 2-day period, and had used insect repellent during pregnancy.[131] Blood lead levels in Puerto Rican children was found to be comparable to the U.S. population, but was elevated in the summer months.[132] Human health studies in Puerto Rico have found evidence of reproductive health effects associated with environmental contaminants.[125] However, the research currently being conducted in Puerto Rico only serves as a foundation for what future research initiatives should and will address in terms of understanding what exposures, and how exposures of concern are associated with reproductive and other adverse health outcomes.

Climate change is another pertinent factor to consider when looking at environmental health concerns in the Puerto Rico context. Small islands such as Puerto Rico are especially vulnerable to climate change due to non-sustainable development practices, scarcity of natural resources, and non-sustainable urban sprawl—which lead to extensive soil erosion and sediment delivery to adjacent waters[133] and contamination in soil and groundwater.

11. 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 prevent, diagnose, and treat 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 Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) project. For more information, see http://www.northeastern.edu/protect/.
4. Encourage patients to avoid exposure to chemicals with known or suspected reproductive hazards and offer solutions for how patients can do this (e.g. the use of glassware).
5. Familiarize yourself with the unique needs of at-risk populations who may not receive detailed information on potential predictors of preterm birth. Health care providers can be the ones to pass on health advisories regarding medical and pregnancy history, demographic variables, and consumer products.
6. Routinely collect environmental and occupational histories.
7. Join the Puerto Rico March of Dimes, which works to prevent premature birth and birth defects, educate mothers, and provide support to families in need. For more information, please visit: http://www.marchofdimes.org/puertorico/

12. Additional Resources for Health Care Providers

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 provides a series of summaries about hazardous substances.
www.atsdr.cdc.gov/toxfaqs/index.asp

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

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. It also, publishes toolkits, quick reference charts, and fact sheets on environmental health issues. www.psr.org

Seattle Children's Research Institute 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*.

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

The Toxics Release Inventory, maintained by the Environmental Protection Agency, reports major sources of toxins 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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4. *Chemical Regulation: Options Exist to Improve EPA's Ability to Assess Health Risks and Manage Its Chemicals Review Program (GAO 05-458)*. (Government Accountability Office).
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