HHS Public Access

Author manuscript

J Midwifery Womens Health. Author manuscript; available in PMC 2019 August 20.

Published in final edited form as:

J Midwifery Womens Health. 2016 July ; 61(4): 442–455. doi:10.1111/jmwh.12500.

Endocrine-Disrupting Chemicals & Reproductive Health

Marya G. Zlatnik, MD, MMS

Abstract

This review discusses the evidence linking industrial chemicals to a variety of health and reproductive outcomes is discussed. Industrial chemical production has increased over the last 30–40 years. Basic science, animal models, and epidemiologic data suggest that certain chemicals may act as endocrine disruptors (substances which interfere with normal hormonal action) and may play an etiologic role in a number of conditions whose incidence has also increased during this same period. These include low birth weight, gestational diabetes, obesity, certain cancers, certain birth defects, and neurodevelopmental disorders such as attention deficit disorder and autism. In addition, some environmental chemicals may have epigenetic effects, resulting in transgenerational health impacts. The epidemiologic and experimental evidence that links chemicals such as plasticizers such as phthalates and phenols, flame retardants, perfluorinated compounds, and pesticides, with adverse reproductive health outcomes is reviewed. Women's health care providers are the liaison between scientific research and their patients; they should educate themselves on the significance to health of environmental toxins. They are ideally positioned, not only to counsel and reassure pregnant women, but to suggest practicable changes in dietary and lifestyle habits to improve their health. Furthermore, women's health care providers should advocate for regulatory changes that protect women and their families from the health effects of environmental toxins.

Précis

This paper reviews the adverse effects of endocrine-disrupting chemicals on reproductive health and outlines patient counseling and advocacy points for clinicians.

Keywords

pregnancy; prenatal; environment; toxin; endocrine disruption; bisphenol; phenol; phthalate; polyvinyl chloride; perfluorinated compound; pesticide

INTRODUCTION

Modern living has spurred the increasing production of industrial chemicals over the last 30 to 40 years (N.J Morin, PhD, Assistant Director and Chief, Industrial Output Section, Division of Research and Statistics, Federal Reserve Board, written communication, February 2016), resulting in the current manufacture, or importation into the United States,

Corresponding Author: Marya G. Zlatnik, MD, MMS, 550 16TH Street, 7th Floor, Box 0132, San Francisco, CA 94143-0132 USA, Phone: 001-415-514-2167, Fax: 001-415-476-1811, Marya.zlatnik@ucsf.edu.

The author has no conflicts of interest to disclose.

of an estimated 30,000 pounds *per person* of these substances per year.[1] Exposure to industrial chemicals occurs through air and water pollution, contamination of the food chain, and consumer products.[2] In fact, a sampling of pregnant women in the United States showed that virtually every study subject had in her bloodstream at least 43 different environmental chemicals, including certain polychlorinated biphenyls, organochlorine pesticides, perfluorinated compounds, phenols, polybrominated diphenyl ethers, phthalates, polycyclic aromatic hydrocarbons, and perchlorate.[3] Over the last 30 years, the rates of many noncommunicable diseases, including obesity, diabetes, infertility, asthma, autism, attention deficit hyperactivity disorder, certain birth defects, childhood cancers, and cancers of the breast and reproductive tract have increased.[4] Although it is very likely that these increases are multifactorial, there is legitimate concern that exposure to industrial chemicals and other environmental toxins, especially those that affect endocrine function, plays a significant role.[2,5–7] The purpose of this paper is to provide an overview of the adverse effects of endocrine-disrupting chemicals on women's reproductive health, and offer clinicians some talking points for patient counselling and advocacy.

EVALUATING THE IMPACT OF CHEMICALS ON WOMEN'S HEALTH: ISSUES AND METHODOLOGY

Studying the impact of environmental chemicals on human health is complicated by several issues. Randomized controlled trials to conclusively establish the harms of specific chemicals would not be ethical. Without this preferred level of evidence, we must use animal or basic science models, in addition to epidemiologic data. Environmental exposures and their outcomes can be hard to assess. This is multifactorial: exposure to chemicals is typically not documented outside of industrial settings, and different people have different levels of sensitivity (stemming from nutritional status, life stage, metabolism, or genetics).[7] Additionally, the particular chemical involved may not be identifiable, even if an exposure was known to occur. The timing of exposure may be unclear or have occurred in the distant past. In the absence of human experimental data, the best evidence comes from consistent health effects in experimental animal models and human epidemiologic data.[2]

A new methodology, named Navigation Guide,[8] provides a systematic approach to synthesizing data from in vitro, experimental animal, and any available human studies. Its key elements are modeled after the Cochrane and Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodologies of systematic reviews in clinical medicine. These elements include a pre-specified protocol for selecting and rating the strength of the evidence, standardized and transparent documentation including expert judgment, a comprehensive search strategy, and assessment of "risk of bias," with the goal of minimizing subjectivity and bias while maximizing transparency and consistency.[8] There are only a few topics with published Navigation Guide systematic reviews,[9–11] as the method is new and time-intensive, but it is anticipated to elevate the standard of evidence assessment in environmental health research.[8]

Despite the challenges to obtaining proof that specific chemicals are harmful, enough circumstantial data has been amassed to concern many in the scientific community. Professional organizations, including the American Academy of Pediatrics, the Association

of Women's Health Obstetric, & Neonatal Nurses, the American College of Nurse-Midwives, and the American College of Obstetricians and Gynecologists, have joined the voices calling for attention to these concerns. Recommendations by these bodies are found in Table 1. There is consensus that women's health care providers should advocate for policies to prevent exposure to toxic environmental chemicals, as well as provide health care that includes education about, interventions to prevent, and addresses the consequences of, reproductive environmental toxins.

KEY CONCEPTS: ENDOCRINE-DISRUPTING CHEMICALS AND WINDOWS OF SENSITIVITY

An *endocrine-disrupting chemical* (EDC) is any substance that interferes with normal hormonal activity. The category includes some metals, many industrial chemicals, natural and synthetic hormones, pesticides, fungicides, herbicides, and pharmaceutical drugs; even personal care products may incorporate EDCs. In some cases, EDCs bind to the receptor for a natural hormone (for example, bisphenol A [BPA] can bind to the estrogen receptor).[18] Thus bound, an EDC can act as an agonist and activate the receptor in the same way as the normal ligand, or the EDC can bind to the receptor as an antagonist, and turn off the normal hormonal action of the receptor.[7] Alternatively, EDCs can interact with hormonal pathways, bypassing the receptor and activating or inactivating second messenger systems, or interfering with gene activation, or by changing levels of hormone-binding proteins.[7] To further complicate the scientific study of EDCs, some may act in multiple ways, depending on dose, tissue type, and sex.[2,18]

The timing of endocrine disruption during the individual lifespan is often important; there are windows of varying susceptibility, including during embryogenesis in early pregnancy as well as throughout fetal life, infancy, childhood, and adolescence.[5,18] Some periods of susceptibility result from rapid cell growth or differentiation; some are due to enhanced hormonal responsivity.[2] Pharmaceutical teratogens, for the most part, have their greatest impact during the first trimester, and ionizing radiation and lead poisoning are of greatest concern in young infants and children. Adolescence may be a time of increased sensitivity to endocrine promoters of cancers of the breast.[2] Awareness of these windows of susceptibility should alert women's health care providers to the importance of protecting reproductive-aged women from toxins that might have an impact upon their future health or fertility, as well as that of a future fetus, a current fetus, or a breast-feeding child.

The concern about EDCs and reproduction is heightened by emerging evidence suggesting that some toxins may have impacts that extend beyond the first generation. Multigenerational effects of EDCs were first established with the pharmaceutical estrogen diethylstilbestrol (DES). Daughters whose mothers took DES during pregnancy have a higher risk of several adverse reproductive outcomes, including rare vaginal cancers and cervical incompetence.[19] The grandsons of women who took DES in pregnancy appear to have a higher risk of hypospadias, suggesting that EDCs can cause transgenerational effects through epigenetic mechanisms.[20] Although other established human examples of transgenerational impacts of EDCs are rare, animal models predict we may see transgenerational effects of some EDCs in the future.[2,5]

Specific Examples of Endocrine-Disrupting Chemicals with Effects on Reproduction

Bisphenol A.—Bisphenol A, or BPA, an artificial estrogen developed by the same chemist who developed diethylstilbestrol,[21] is produced worldwide at a rate of greater than 5 billion pounds per year.[22] BPA's phenyl groups mimic estrogen and can bind to the estrogen receptor.[2] Animal and basic science experiments show that BPA can act as an estrogen agonist as well as an estrogen antagonist.[6] Human epidemiologic data suggest that BPA acts in humans as an estrogen agonist as well.[6] BPA has also shown "obesogenic" properties in animal models.[2]

Emerging data suggest that BPA can interfere with normal fetal neurodevelopment. A cohort study of 240 children published by Braun and colleagues[23] in 2011 explored the association of fetal exposure to BPA, as measured by maternal urinary samples (collected at ~16 and ~26 weeks' gestation and at birth) and childhood behavioral outcomes at age 3. Outcomes were measured by the Behavior Assessment System for Children 2 (BASC-2) Parent Rating Scale for preschoolers and the Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P), both of which are validated parent-report inventories of behaviors in community and home settings. In this study, fetal BPA exposure was associated with increased anxiety, depressive symptoms, and impaired behavioral regulation at age 3, and this finding was worse for girls than for boys.[23] The size of the effect measured was clinically significant (eg, for anxiety in girls, an increase in BPA level from the 10th to the 90th percentile was associated with an increase in anxiety score from the 30th to the 86th percentile). The validity of these results may be affected by unmeasured confounding, although the authors controlled for mother's race, education, marital status, household income, tobacco use, and maternal depression.[23]

BPA has also been shown to interfere with male reproduction.[6] An occupational cohort study in China compared workers in BPA factories (n=164) with factory workers not exposed to BPA (n=386). The BPA-exposed workers had a reduced frequency of intercourse, increased ejaculatory dysfunction, reduced satisfaction with their sex life, reduced sex drive, and reduced ability to have an erection. In the study, the average urinary BPA level was 58 micrograms per gram of creatinine versus 1.2 micrograms per gram of creatinine for the unexposed workers.[24] Of note, since these were occupational exposures, the subjects had higher BPA levels than would typical consumers.

Phthalates.—Phthalates are another class of chemicals[25] that have been implicated as endocrine disrupters.[7] Phthalates are used in multiple consumer applications, including personal care products such as lotion or shampoo, often as "fragrance", and as plasticizers to change the physical characteristics of base plastics, including products made with polyvinyl chloride, such as flooring, shower curtains, packaging, and some medical equipment.[25] Human cohort and experimental animal studies have demonstrated possible adverse effects on reproduction, including associations with poor semen quality and miscarriage.[26,27] Prenatal phthalate exposure, as measured by phthalate metabolite levels in maternal urine, has been associated with abnormal male genital development in the fetus. In animal models, anogenital distance is a sensitive index of demasculinization of the male reproductive tract. Multiple epidemiologic studies, including prospective cohort studies, have shown a

shortened anogenital distance (suggesting anti-androgenic influence) in boys whose mothers had higher urinary phthalate levels during pregnancy.[28,29] Some cohort studies have shown an association with smaller penile size as well.[30] These findings are reproducible in experimental studies with rodents.[31]

Prenatal phthalate exposure has also been associated with reduced "masculine play" in boys, as indicated in a follow-up study of a cohort of couples who had given blood and urine samples during pregnancy. At age 5, the boys' (n=74) play activities were assessed with a validated inventory of play styles (Pre-School Activities Inventory). An association was seen between prenatal exposure to anti-androgenic phthalates and less male-typical play behavior in boys.

The masculine play score dropped by 8% if a boy's mother's prenatal urinary phthalate metabolite concentration increased from the 10th percentile to the 90th percentile.[32] No effect was seen in the girls studied.[32] (The importance and validity of such measures as "masculine play score" should be interrogated elsewhere.) In another multicenter cohort study, long-term follow up of 163 children revealed higher maternal prenatal urine concentrations of monoisobutyl phthalate were associated with worse scores on several parent-reported behavioral measures for their sons at ages 6 to 10, including inattention, rule-breaking behavior, aggression, and conduct problems. No statistically significant effect was seen in girls.[33] A recent systematic review of 11 human studies suggests that higher levels of prenatal exposure to phthalate metabolites, measured as urinary concentrations, are associated with poorer cognitive and behavioral outcomes in children, especially boys.[34] These studies were all observational, so unmeasured confounding cannot be excluded, although most of the studies controlled for confounders such as age, gender, birth weight, history of breastfeeding, race, socioeconomic status, and maternal IQ or educational level.[34]

Phthalate exposure may also directly harm maternal health.[2] In a secondary analysis of a prospective cohort prenatal phthalate-exposure study, mono-benzyl phthalate (a metabolite of a high-molecular-weight phthalate, benzylbutyl phthalate, found in adhesives, sealants, vinyl tile, and possibly some personal care products[25]) concentrations were significantly associated with higher maternal diastolic blood pressure at <20 weeks gestation, with dose-response associations for systolic and diastolic blood pressures.[35] Additionally, of the 369 women studied, those in the top tercile of mono-benzyl phthalate at 16 weeks had an increased risk of developing pregnancy-induced hypertensive disorders (clinical diagnoses of gestational hypertension, preeclampsia, eclampsia, or HELLP syndrome).[35]

Flame retardants.—Flame retardants are another class of chemicals with suspected reproductive toxicity. Polybrominated diphenyl ethers (PBDEs) have been used extensively in foam and plastics to meet ignition standards in the United States, and they have been found in pregnant women's blood[3] and in cord blood.[38]Although some PDBEs have been taken off the market, they are persistent in humans and the environment.[19] Prenatal exposure to PBDEs was associated with adverse neurodevelopmental outcomes in offspring in a hypothesis-generating cohort study of 175 children.[36] In another cohort study of over 300 mothers and their children, higher maternal serum PBDE concentrations in the third trimester were associated with impaired attention at age 5 and poorer fine motor

coordination at ages 5 and 7. In addition, the study noted decrements in the IQ of offspring at age 7, as measured on validated neurobehavioral assessments completed by parents, teachers, and psychometricians.[37] In another longitudinal cohort study (n=210), children with higher cord blood concentrations of PDBEs scored lower on tests of mental and physical development, including the Bayley Scales of Infant Development and the Wechsler Preschool and Primary Scale of Intelligence.[38] The mechanisms by which PBDEs affect these outcomes are a subject of ongoing study, but endocrine disruption is suspected as a possible cause. PBDEs are thought to interact with steroid hormone receptors, and also to suppress normal thyroid hormone function.[39] Given that precisely regulated thyroid hormonal activity is implicated in normal fetal brain development,[40] these interactions may have a causal role in abnormal neurodevelopment. Similar neurodevelopmental abnormalities are seen in prenatally exposed mouse experimental models.[39,41]

Perfluorinated Compounds.—Yet another group of chemicals suspected to have reproductive effects are the perfluorinated compounds (PFCs),[2] which include a number of chemicals used for waterproofing, stain resistance, and lubrication, and include perfluorooctane sulfonate, perflurooctanoic acid, and perfluorohexane sulfonate. Some PFCs are found in food packaging and nonstick cookware.[42] Exposure has been associated with adverse health outcomes. In particular, increasing concentrations of perfluorooctanoic acid and certain other PFCs in maternal plasma were associated with reduced fecundity and infertility in a Canadian cohort of 1743 women.[43] Prenatal perfluorooctanoic acid exposure has also been associated with poor fetal growth in a number of experimental animal and human cross-sectional studies, confirmed by the Navigation Guide methodology.[9,10,44] How PFCs act as endocrine disruptors is an area of active study. Animal models and in vitro studies show interactions with estrogen-and androgen-receptors, thyroid hormones, and neurotransmitters.[2,45] In humans, PFC concentrations have been associated with alterations in thyroid function.[45]

Pesticides.—Pesticides have long been implicated in adverse reproductive outcomes.[46] The scope of pesticides with potential to disrupt endocrine systems is broad, and has been reviewed elsewhere.[7,47] In one example study, measurements of IQ at ages 5–7 were associated with fetal organophosphate pesticide exposure in a prospective cohort of 260 children. The difference between the highest and lowest quintiles of exposure was equivalent to 7 full-scale IQ points. The results were robust to adjustment for confounding by maternal age, intelligence and education level, breast-feeding duration, birth order, socioeconomic status, and marital status.[48]

Other sources of endocrine-disrupting chemicals.—It is beyond the scope of this paper to mention, much less describe in detail, all of the substances that are suspected endocrine disruptors. Air, water, and soil carry not only endocrine disruptors and other manufactured chemicals but also “natural” substances (such as arsenic or methane) that in unnatural situations may affect health.[2] Recent concern by the popular media and some scientists has focused on the health risks associated with a new oil and gas exploration technique (“fracking”). The handful of published studies that explore the effects of fracking on reproduction include research on pregnancy and proximity to fracking wells and have

identified varying associations with preterm birth and low birth weight.[49,50] Basic science studies, including in vitro cell culture assays and experimental studies in mice, have suggested that certain fracking chemicals may be endocrine disrupters.[51] These data are preliminary, but some health professionals have urged caution in the expansion of fracking to new sites.[52]

COMMUNICATING RISKS OF ENDOCRINE-DISRUPTING CHEMICALS

Preliminary questions

Answering the question of what to tell women about EDCs requires answers to several preliminary questions: What do women want to know, and how have we succeeded in responding to their requests? What *can* we tell them (ie, what do we know about EDCs and other environmental toxins?) And, last, how can we best go about conveying good information?

What do women want to know?—Biomonitoring and survey research studies provide some guidance on the information women want and need. Some women are unaware of the hazards of environmental toxins,[53,54] and some worry about potential toxins, but don't trust the resources they find in the public sphere. Furthermore, many find that their medical providers are not discussing these concerns.[53] Studies of both pregnant women and women in biomonitoring cohorts have shown that women want information on personal exposures to environmental chemicals, and they believe they have the right to know.[55] Moreover, one study found that 97% wanted exposure information even if the health implications of the information were unclear.[56] Respect for patients' autonomy should prompt women's health care providers to share their knowledge of the harms of endocrine-disrupting chemicals with those at risk.[55]

Given these study results, how well have we done in communicating risk to patients? First, it is undeniable that until recently, there has been less than optimal awareness, knowledge, or interest, among both health care providers *and* the public, on the everyday ubiquity of the chemicals under discussion here. Environmental health has only infrequently been a topic of discussion during routine health care. A mixed methods study of obstetricians' reticence to engage in such discussions by Stotland and colleagues[57] revealed two main themes: "bigger fish to fry," namely, other clinical or health concerns of higher priority than environmental concerns; and "Pandora's box," meaning discomfort with the possibility that the subject of environmental concerns may provoke questions for which these physicians have no answers.[57] Some providers worry about putting the burden of avoiding toxins on already stressed (and caffeine-, wine-, sushi-, and turkey-deprived) pregnant women.[57] Midwives' attitudes toward discussing environmental health with patients have not been explicitly studied. It is plausible that similar issues of competing clinical priorities, time limitations, and gaps in the evidence base are also barriers to midwives' counseling of women.

What should women be told?—The studies and evidence cited above document both the extent of our knowledge about EDCs and some of the lacunae. This information is useful only if and when it is mastered by health care providers. Informing ourselves precedes informing others. For providers grappling with how to communicate risks without causing

undue worry, it is useful to remember that the effects of these chemicals generally subtle, and that not everyone will be susceptible, such that often an effect is only clearly seen on population level. For a given toxin, if studies show a difference of 2–5 IQ points' difference based on an exposure, the impact on an individual is likely to be minimal. The additive impact, however, on a society comprised of individuals with slightly lower IQs, is significant. Another fact that may help to put this information into perspective for worried women: the exposures discussed in this review may have effects similar to that seen with a childhood lead level of 5 mcg/dl, now considered elevated, but which would have been much lower than the levels seen in the late 1970s when the median was 15 mcg/dl.[4]

Conveying good information—The first step might be establishing an environmental history for each individual patient. Table 2 is a suggested form, adapted from The Great Lakes Center for Children's Environmental Health, which provides not only an assessment of the patient's risk for use by both the health care provider and the patient herself, but also suggestions for making healthful choices. Taking an environmental history (see Appendix for a link to other suggested history forms) is a way of assessing patients' knowledge, toxin exposure risk, and concerns. Taking an environmental history from some women may reveal that they are not interested in change, or that their exposures are systemic and not easily addressed.

Nevertheless, for those women and their families who are eager and able to take personal action, studies show that individual-level actions can make a difference. A few experimental trials have shown decreased body burdens of specific chemicals in response to specific behavioral modifications such as dietary changes. In one crossover study, which took place in the cafeteria at the Harvard School of Public Health, two groups of volunteers were served 5 days of either fresh or canned soup and then five days of the other soup. Urinary bisphenol A levels were measured at the end of each period and were significantly lower when the subjects were served fresh soup.[58] Another study followed five Bay Area families over several days during which they ate their usual diet, and then were served three days of catered fresh organic food, without any exposure to BPA or plastics. This study also showed lower urinary BPA levels.[59] Similar studies have shown the effect of eating a diet of organic produce, with lowered urinary or serum levels of pesticides during consumption of organic rather than conventional produce.[60] These studies suggest that dietary changes (consuming fresh organic food, avoiding canned food) can lower exposure to BPA and pesticides. Of note, although women can be counseled based on the current evidence base, the potential for unintended consequences exists.[64] For example, if women choose water bottles made with "BPA-free" plastic in an attempt to avoid EDCs, they may inadvertently expose themselves to BPA replacements such as bisphenol S or bisphenol X, which are also thought to be EDCs.[65]

There is a caveat, however: no randomized controlled trials have been published to establish that any given personal action, such as eating fresh soup, will improve pregnancy outcomes. Until these data exist, however, the precautionary principle, which states that "when the health of humans and the environment is at stake, it may not be necessary to wait for scientific certainty to take protective action," suggests that actions based on the available literature may improve outcomes. Women ask for advice on avoiding environmental toxins,

and hope their clinicians will provide some guidance[53] even if clinicians do not have all the answers.[55] Table 3 provides some guidance on ways to avoid endocrine-disrupting chemicals, based on studies in humans and animals, as well as in vitro. The ability to avoid exposures to EDCs may be limited by a woman's socioeconomic circumstances, but many proposed steps are free or low cost and will be available to most women (washing hands prior to eating,[61–63] avoiding soda,[58,59] not microwaving in plastic,[63,66] limiting use of personal care products[62]). Additionally, a number of the recommended steps are often promoted for other health indications (washing hands prior to eating, limited processed foods and those high in animal fat, vacuuming house dust), and are expected to decrease exposures to other industrial and environmental chemicals which may be identified as endocrine disruptors in the future.[67]

Addressing special situations—Although many patient exposures are easy to address with the above steps, some situations require more urgent detoxification or complex care. If a patient has occupational or home exposures to lead, mercury, pesticides, or other chemicals, or questions that the provider cannot answer, the Appendix lists several resources and websites which have more in depth information available. The Program in Reproductive Health and the Environment (PRHE) at the University of California San Francisco has a series of educational brochures, including one called "Work Matters" that includes resources for addressing occupational exposures. PRHE's website also contains links to a number of resources for clinicians, including environmental health history forms.

Another valuable resource is the network of regional Pediatric Environmental Health Specialty Units (PEHSUs), distributed in the ten regions of the Environmental Protection Agency (EPA). This network was established in 1998, with the units based at academic centers throughout the country. The PEHSUs are jointly funded by the Agency for Toxic Substances and Disease Registry of the CDC (Centers for Disease Control and Prevention) and the EPA, and provide consultations with pediatric experts in environmental health and toxins. Since 2015, PEHSUs have included reproductive health experts on their staff. Other resources, noted in the Appendix, include occupational medicine specialists and toxicologists, in addition to the Occupational Safety and Health Administration. The Agency for Toxic Substances and Disease Registry, in conjunction with the PEHSUs, is creating an application for clinicians that will have a search function for obtaining information on environmental toxins.

The immovable bottom line, when knowledge, history, remedies, and resources are added up, is that the counsel offered to women by their health care providers must be a combination of sensitivity to the needs and abilities of each woman as well as a measure of educated commonsense. What we should tell each *individual* patient should reflect the study result noted above: Respect for patients' autonomy should prompt women's health care providers to share their knowledge of the harms of endocrine-disrupting chemicals with those at risk.[55]

Providers as Educators and Advocates

Given the ubiquity of industrial chemicals in our environment, what can providers do to decrease their patients' exposures? Although counsel provided to individual patients about the avoidance of specific toxins through consumer action may help the individual, it is limited in its ability to address the larger problem. This is particularly true in light of the disparate impact that environmental toxins have on disadvantaged women and families, and with environmental injustices that increase health disparities.[15] Midwives are encouraged to act as "change agents" to promote policies and regulations that protect the environment.[14]

History has shown that regulatory changes can have an impact upon the levels of toxic chemicals in humans. When lead was phased out of gasoline and paint in the early 1970s, lead levels in the blood of Americans dropped precipitously.[4] In 2006, PBDEs were banned in the state of California, and in 2013 research demonstrated lower levels in pregnant women over time.[68] Clearly, removing chemicals from use can reliably and measurably remove them from humans, with the caveat that some pollutants are persistent (eg, many perfluorinated compounds and polychlorinated biphenyls), and are slower to be removed from the environment and our bodies. However, chemicals that are removed from industrial use after health harms are found may be replaced with newer substances that also carry endocrine-disrupting or other health dangers.[64,65] Not surprisingly, such substitutions suggest moving to a *precautionary* approach to regulation, that is, at a minimum, testing chemicals for health effects prior to their use in commercial products such as toys or baby equipment. This approach is similar to that of the European Union, and the FDA's approach to pharmaceuticals. Ideally, chemicals with the potential to harm human health would not make their way into our food systems and homes prior to thorough testing for endocrine or other health effects. Recent legislation intended to reform the Toxic Substances Control Act is in conference committee to reconcile House and Senate versions of the bill; whether the final legislation will have much impact on the current regulatory framework is not yet known.[69]

Health care providers are used to thinking about behavioral changes that patients can make to improve their health. With toxic environmental exposure, however, individuals often must rely for protection upon on broad regulation or social consensus. For example, science provided evidence for tobacco's dangers; social pressure has made smoking both less desirable and more highly regulated. For environmental concerns that cannot be avoided through simple individual actions (eg, exposures in public settings, contamination of food systems by persistent organic pollutants, exposure to fracking in residential neighborhoods), educated patients can contact their elected representatives and policymakers to seek regulatory change.

Women's health care providers are well positioned to provide the impetus for action on research, regulation, and structural change, and history has shown the efficacy of citizen advocacy groups. The March of Dimes has outlasted its original mission of combating polio to become an advocate for maternal and child health. The Back to Sleep (now Safe to Sleep) initiative by the American Academy of Pediatrics predated some of the definitive research into sudden infant death syndrome, providing a fine example of wise precautionary action. Midwives, acting locally and focusing as a group on local concerns, can brainstorm about

resources and share ideas about communicating essentials to their patients. One possible action would be to lobby local businesses or government to open a farmers' market in a neighborhood devoid of stores selling affordable pesticide-free produce. If midwives identify a local toxic exposure of concern, such as lead in the municipal water supply, they can both provide counsel to individual women, but also work for local regulatory change by contacting their elected representatives or local media. Midwives, acting nationally as lobbyists, letter writers, and educators for congressional representatives, can have an impact that serves the welfare of women everywhere.

SUMMARY

Many chemicals present in consumer products, the US food supply, and the environment are suspected endocrine disruptors. Given the importance of endocrine function in reproduction and healthy offspring, evidence of endocrine disruption is of prime concern to women's health care providers. Some adverse health trends may or may not be related to environmental toxins, but the relevant basic science and epidemiology are of significant concern, warranting an approach based on the precautionary principle.

Wise counsel for the women whose health is our concern is perhaps our hardest task. As noted above, overly busy schedules and concern about provoking unhelpful fears often are obstacles to conveying important information. But the special ties between reproductive health care providers and the women they care for ought to be fertile ground for creative, educated, thoughtful and protective guidance and support.

Acknowledgements:

Funding for Dr. Zlatnik's work comes in part from the National Institute of Environmental Health Sciences (ESO22841), U.S. EPA STAR grant (RD83543301), and by the cooperative agreement award number 1 U61TS000237–01 from the Agency for Toxic Substances and Disease Registry (ATSDR). Its contents are the responsibility of the authors and do not necessarily represent the official views of the Agency for Toxic Substances and Disease Registry (ATSDR).

The U.S. Environmental Protection Agency (EPA) supports the PEHSU by providing partial funding to ATSDR under Inter-Agency Agreement number DW-75–95877701. Neither EPA nor ATSDR endorse the purchase of any commercial products or services mentioned in PEHSU publications

The author would like to thank Gail P. Zlatnik, PhD, for editorial assistance.

Appendix

APPENDIX:

Resources for further information

Resource	Type of information available	Available at: internet/telephone
CDC Guidance on lead in pregnancy	In-depth review of the impact and management of lead exposure in pregnancy.	http://www.cdc.gov/nceh/lead/publications/LeadandPregnancy2010.pdf
	Although lead affects fetuses and children are primarily through direct toxic effect, it can also cause endocrine disruption.	

Resource	Type of information available	Available at: internet/telephone
The Collaborative on Health and the Environment (CHE)	CHE is a nonpartisan organization with a mission to strengthen the science dialogue on environmental factors impacting human health and to facilitate prevention-oriented efforts to address environmental health concerns.	http://www.healthandenvironment.org/
	The website has a searchable database that summarizes links between chemical contaminants and approximately 180 human diseases or conditions. Searches can be made by disease or toxicant.	CHE Toxicant & Disease database http://www.healthandenvironment.org/tddb/
	Frequent webinars present current research on a variety of topics related to the impact of the environment on health.	
The Endocrine Disruption Exchange (TEDX) (includes List of Possible Endocrine Disruptors)	The TEDX List of Potential Endocrine Disruptors is a database of nearly 1000 chemicals with the potential to affect endocrine systems.	http://www.endocrinedisruption.org/
	Interactive timeline describes critical windows of development of various organ systems.	http://www.endocrinedisruption.org/prenatal-origins-of-endocrine-disruption/critical-windows-of-development/timeline-test/
Environmental Working Group (& Skin Deep website)	EWG's website has news and commentary on current environmental issues and consumer information.	http://www.ewg.org/
	EWG's Skin Deep is a searchable database of personal care products rated by the toxicity of their ingredients.	http://www.ewg.org/skindeep/
The Occupational Safety and Health Administration (OHSA)	OSHA is a federal agency that sets and enforces federal safety and health standards for the workplace.	(800) 321–6742 or www.osha.gov
NIH National Library of Medicine Household Products Database	A database of health and safety information regarding household products is searchable by product, ingredients, manufacturer, and health effects; includes information about contents of products, potential health effects, safety and handling.	http://householdproducts.nlm.nih.gov/products.htm
Pediatric Environmental Health Specialty Unit (PEHSU) network:	The PEHSU network has clinicians available for in-person patient or provider telephone consultation regarding any environmental exposures relevant to pregnancy and childhood.	http://www.pehsu.net PEHSU-East National Office (Federal Regions 1–5): Tel: (888) 227–1785 (Toll Free) PEHSU-West National Office (Federal Regions 6–10): Tel: (844) PEHSU-W9 or (844) 734–7899 (Toll Free) UCSF/ Western States PEHSU: 1-866-827-3478.
	The website has patient and provider factsheets on many topics of interest.	
University of California San Francisco's Program on Reproductive Health and the Environment (PRHE)	PRHE has an extensive website with information specifically for patients and families (available as downloadable brochures) and many resources and links for clinicians and researchers. Information for clinicians includes links to environmental history forms.	http://prhe.ucsf.edu/prhe/families.html Resources for clinicians: http://prhe.ucsf.edu/prhe/clinicalresources.html

Abbreviations: CDC, Centers for Disease Control and Prevention; NIH, National Institutes of Health.

References:

1. United States Environmental Protection Agency: Chemicals Snapshot Fact Sheet. 2nd edition Edited by United States Environmental Protection Agency: United States Environmental Protection Agency; 2012 http://www2.epa.gov/sites/production/files/2014-11/documents/2ndcdrsnapshot51914.pdf

2. Gore AC, Chappell VA, Fenton SE, et al. EDC-2: the endocrine Society's second scientific statement on endocrine-disrupting chemicals. Endocr Rev. 2015;36:E1–150. [PubMed: 26544531]

3. Woodruff TJ, Zota AR, Schwartz JM. Environmental chemicals in pregnant women in the United States: NHANES 2003–2004. Environ Health Perspect. 2011;119(6):878–885. [PubMed: 21233055]

4. Environmental Protection Agency US. America's Children and the Environment, Third Edition; Washington DC, 2013: U.S. EPA https://www.epa.gov/ace/ace-publications#order. Accessed March 27, 2016.

5. Schug TT, Janesick A, Blumberg B, Heindel JJ. Endocrine disrupting chemicals and disease susceptibility. J Steroid Biochem Mol Biol. 2011;127(3–5):204–215. doi:10.1016/j.jsbmb.2011.08.007 [PubMed: 21899826]

6. Peretz J, Vrooman L, Ricke WA, Hunt PA, Ehrlich S, Hauser R, Padmanabhan V, Taylor HS, Swan SH, VandeVoort CA, Flaws JA. 2014. Bisphenol A and reproductive health: update of experimental and human evidence, 2007–2013. Environ Health Perspect. 2014;122:775–786; 10.1289/ehp.1307728 [PubMed: 24896072]

7. Kabir ER, Rahman MS, Rahman I. A review on endocrine disruptors and their possible impacts on human health. Environ. Toxicol. Pharmacol. 2015; 40:241–258. [PubMed: 26164742]

8. Barrett JR. The Navigation Guide: Systematic Review for the Environmental Health Sciences. Environmental Health Perspectives. 2014;122(10):A283. doi:10.1289/ehp.122-A283. [PubMed: 25271710]

9. Johnson PI, Sutton P, Atchley D, Koustas E, Lam J, Sen S, et al. The Navigation Guide—evidence-based medicine meets environmental health: systematic review of human evidence for PFOA effects on fetal growth. Environ Health Perspect. 2014;122:1028–1039. doi: 10.1289/ehp.1307893. [PubMed: 24968388]

10. Koustas E, Lam J, Sutton P, Johnson PI, Atchley DS, Sen S, Robinson KA, Axelrad DA, Woodruff TJ. The Navigation Guide—Evidence-based medicine meets environmental health: systematic review of nonhuman evidence for PFOA effects on fetal growth. Environ Health Perspect. 2014;122:1015–1027. 10.1289/ehp.1307177 [PubMed: 24968374]

11. Vesterinen HM, Johnson PI, Atchley DS, Sutton P, Lam J, Zlatnik MG, Sen S, Woodruff TJ. Fetal growth and maternal glomerular filtration rate: a systematic review. J Matern Fetal Neonatal Med. 2015;28(18):2176–81. doi: 10.3109/14767058.2014.980809. [PubMed: 25382561]

12. Etzel RA, Balk SJ, eds. Pediatric Environmental Health. 3rd Edition Elk Grove Village, IL: American Academy of Pediatrics; 2012. ISBN (electronic): 978–1-58110–653-4.

13. American College of Nurse-Midwifery. Environmental Hazards in Pregnancy. J Midwifery Womens Health. 2006;51(1):57–58. Available at: http://onlinelibrary.wiley.com/doi/10.10167j.jmwh.2005.09.008/pdf Accessed 5-1-16 [PubMed: 16402445]

14. ACNM Board of Directors, Division of Standards and Practice Clinical Standards and Practice Documents Section. The Effect of Environmental Toxins on Reproductive and Developmental Health, 6 2015 Available from: http://www.midwife.org/ACNM/files/ACNMLibraryData/UPL0ADFILENAME/000000000292/Environmental-Toxins-June-2015.pdf. Accessed 5-1-16

15. The American College of Obstetricians and Gynecologists. Committee opinion number 575: exposure to toxic environmental agents. Obstet Gynecol 2013;122:931–5. http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Health-Care-for-Underserved-Women/Exposure-to-Toxic-Environmental-Agents. Published October 2013. Accessed September 20, 2014. [PubMed: 24084567]

16. AWHONN. Protecting the Health of Women and Children from Environmental Toxins; 2001 accessed January 21, 2016 at https://www.awhonn.org/awhonn/binary.content.do;jsessionid=31FCAC348C1D0166F323697B54855D63?name=Resources/Documents/word/5H2g_PS_ProtectHealthWomenChild.doc.

17. Di Renzo GC, Conry JA, Blake J, DeFrancesco MS, DeNicola N, Martin JN Jr, McCue KA, Richmond D, Shah A, Sutton P, Woodruff TJ, van der Poel SZ, Giudice LC. International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals. International Journal of Gynecology and Obstetrics. 2015; in press DOI:

18. Heindel J, Zoeller TR, Jobling S, Iguchi T, Vandenberg L, Woodruff TJ. Chapter 1. What is endocrine disruption all about? In: Bergman Å, Heindel JJ, Jobling J, Kidd KA, Zoeller RT, eds. State of the science of endocrine disrupting chemicals – 2012 An assessment of the state of the science of endocrine disruptors prepared by a group of experts for the United Nations Environment Programme (UNEP) and WHO.
19. Jobling S, Bjerregaard P, Blumberg B, Brandt I, Brian JV, Casey SC, Frouin H, Giudice LC, Heindel JJ, Iguchi T, Kidd KA, Kortenkamp A, Lind M, Ropstad E, Ross PS, Skakkebaek NE, Toppari J, Woodruff TJ, Zoeller RT. Chapter 2. Evidence for endocrine disruption in humans and wildlife. In: Bergman Å, Heindel JJ, Jobling J, Kidd KA, Zoeller RT, eds. State of the science of endocrine disrupting chemicals – 2012.
20. Kalfa N, Paris F, Soyer-Gobillard MO, Daures JP, Sultan C. Prevalence of hypospadias in grandsons of women exposed to diethylstilbestrol during pregnancy: a multigenerational national cohort study. Fertility & Sterility. 2011; 95: 2574–2577. Pubmed ID: 21458804. [PubMed: 21458804]
21. Dodds EC. The chemistry of oestrogenic compounds and methods of assay. Br Med J. 1937 2 20;1(3972):398–9. [PubMed: 20780496]
22. CDC National Biomonitoring Program Biomonitoring Summary, Bisphenol A, CAS No. 80057, 2013; accessed on ½1/16, at http://www.cdc.gov/biomonitoring/BisphenolA_BiomonitoringSummary.html
23. Braun JM, Kalkbrenner AE, Calafat AM, Yolton K, Ye X, Dietrich KN, Lanphear BP. Impact of Early-Life Bisphenol A Exposure on Behavior and Executive Function in Children Pediatrics. 2011;128:873–882.http://pediatrics.aappublications.org/content/pediatrics/early/2011/10/20/peds.2011-1335.full.pdf [PubMed: 22025598]
24. Li D, Zhou Z, Qing D, He Y, Wu T, Miao M, Wang J, Weng X, Ferber JR, Herrinton LJ, Zhu Q, Gao E, Checkoway H, Yuan W. Occupational exposure to bisphenol-A (BPA) and the risk of self-reported male sexual dysfunction. Hum.Reprod, 2010, 25, 2, 519–527. [PubMed: 19906654]
25. CDC National Biomonitoring Program Biomonitoring Summary, Phthalates, 2013; accessed at http://www.cdc.gov/biomonitoring/BzBPBiomonitoringSummary.html on 1/7/16.
26. Wang Y-X, You L, Zeng Q, Sun Y, Huang Y-H, Wang C, Wang P, Cao W-C, Yang P, Li Y-F, Lu W-Q. Phthalate exposure and human semen quality: Results from an infertility clinic in China. Environmental Research. 2015;142:1–9. [PubMed: 26087406]
27. Toft G, Jönsson BAG, Lindh CH, et al. Association between Pregnancy Loss and Urinary Phthalate Levels around the Time of Conception. Environmental Health Perspectives. 2012;120(3):458–463. doi:10.1289/ehp.1103552. [PubMed: 22113848]
28. Huang PC, Kuo PL, Chou YY, Lin SJ, Lee CC. Association between prenatal exposure to phthalates and the health of newborns Environ. Int. 2009;35:14–20.
29. Swan SH, Sathyanarayana S, Barrett ES, Janssen S, Liu F, Nguyen RH, Redmon JB; TIDES Study Team. First trimester phthalate exposure and anogenital distance in newborns. Hum Reprod. 2015;30(4):963–72. doi: 10.1093/humrep/deu363. Epub 2015 Feb 18. [PubMed: 25697839]
30. Sathyanarayana S, Grady R, Redmon JB, Ivicek K, Barrett E, Janssen S, Nguyen R, Swan SH; TIDES Study Team. Anogenital distance and penile width measurements in The Infant Development and the Environment Study (TIDES): Methods and predictors. J Pediatr Urol. 2015;pii: S1477–5131(15)00022–4. doi: 10.1016/j.jpurol.2014.11.018. [Epub ahead of print] PMID: 25824881
31. Foster PMD. Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. Int J Andrology. 2006;29:140–7. 10.1111/j.1365-2605.2005.00563.x
32. Swan SH, Liu F, Hines M, Kruse RL, Wang C, Redmon JB, Sparks A, Weiss B. Prenatal phthalate exposure and reduced masculine play in boys. Int J Andrology. 2010;33(2):259–69. doi: 10.1111/j.1365-2605.2009.01019.x. Epub 2009 Nov 16. PMID: [PubMed: 19919614]
33. Kobrosly RW, Evans S, Miodovnik A, Barrett ES, Thurston SW, Calafat AM, Swan SH. 2014 Prenatal phthalate exposures and neurobehavioral development scores in boys and girls at 6–10 years of age. Environ Health Perspect 122:521–528; [PubMed: 24577876]
34. Ejaredar M, Nyanza EC, Eycke KT, Dewey D. Phthalate exposure and childrens neurodevelopment: a systematic review. Environ Res. 2015;142:51–60. [PubMed: 26101203]

35. Werner EF, Braun JM, Yolton K, Khoury JC, Lanphear BP. The association between maternal urinary phthalate concentrations and blood pressure in pregnancy: The HOME Study. Environ. Health. 2015;14:75. [PubMed: 26380974]
36. Braun JM, Kalkbrenner AE, Just AC, Yolton K, Calafat AM, Sjödin A, Hauser R, Webster GM, Chen A, Lanphear BP. Gestational exposure to endocrine-disrupting chemicals and reciprocal social, repetitive, and stereotypic behaviors in 4-and 5-year-old children: the HOME Study. Environ Health Perspect. 2014;122:513–520; [PubMed: 24622245]
37. Eskenazi B, Chevrier J, Rauch SA, Kogut K, Harley KG, Johnson C, Trujillo C, Sjodin A, Bradman A. In Utero and Childhood Polybrominated Diphenyl Ether (PBDE) Exposures and Neurodevelopment in the CHAMACOS Study. Environ Health Perspect. 2013;121(2):257 10.1289/ehp.1205597 [PubMed: 23154064]
38. Herbstman JB, Sjödin A, Kurzon M, et al. Prenatal Exposure to PBDEs and Neurodevelopment. Environ Health Perspect. 2010;118(5):712–719. doi:10.1289/ehp.0901340. [PubMed: 20056561]
39. Costa LG, de Laat R, Tagliaferri S, Pellacani C. A mechanistic view of polybrominated diphenyl ether (PBDE) developmental neurotoxicity. Toxicol. Lett. 2014;230:282–294. [PubMed: 24270005]
40. Ahmed OM, El-Gareib AW, El-Bakry AM, Abd El-Tawab SM, Ahmed RG. Thyroid hormones states and brain development interactions. Int. J. Dev. Neurosci. 2008;26:147–209. [PubMed: 18031969]
41. Suvorov A, Girard S, Lachapelle S, Abdelouahab N, Sebire G, Takser L, Perinatal Exposure to Low-Dose BDE-47, an Emergent Environmental Contaminant, Causes Hyperactivity in Rat Offspring. Neonatology 2009;95:203–209. [PubMed: 18799892]
42. Fromme H, Tittlemier SA, Völkel W, Wilhelm M, Twardella D. Perfluorinated compounds: exposure assessment for the general population in western countries. International Journal of Hygiene and Environmental Health. 2008;212:239–70. doi: 10.1016/j.ijheh.2008.04.007. PMID: [PubMed: 18565792]
43. Vélez MP, Arbuckle TE, Fraser WD. Maternal exposure to perfluorinated chemicals and reduced fecundity: the MIREC study. Hum Reprod. 2015;30(3):701–9. doi: 10.1093/humrep/deu350. [PubMed: 25567616]
44. Fei C, McLaughlin JK, Tarone RE, Olsen J. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environ Health Perspect. 2007;115(11):1677–1682; doi: 10.1289/ehp.10506. [PubMed: 18008003]
45. Wang Y, Rogan WJ, Chen P-C, et al. Association between Maternal Serum Perfluoroalkyl Substances during Pregnancy and Maternal and Cord Thyroid Hormones: Taiwan Maternal and Infant Cohort Study. Environ Health Perspect. 2014;122(5):529–534. doi:10.1289/ehp.1306925. [PubMed: 24577800]
46. Carson R Silent Spring. Boston, MA: Houghton Mifflin Company 1962.
47. Mnif W, Hassine AIH, Bouaziz A, Bartegi A, Thomas O, Roig B. Effect of Endocrine Disruptor Pesticides: A Review. International Journal of Environmental Research and Public Health. 2011;8(6):2265–2303. doi:10.3390/ijerph8062265. [PubMed: 21776230]
48. Bouchard MF, Chevrier J, Harley KG, et al. Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year-Old Children. Environ Health Perspect. 2011;119(8):1189–1195. doi:10.1289/ehp. 1003185. [PubMed: 21507776]
49. Casey JA, Savitz DA, Rasmussen SG, Ogburn EL, Pollack J, Mercer DG, Schwartz BS. Unconventional Natural Gas Development and Birth Outcomes in Pennsylvania, USA. Epidemiology. 2015;XX: 00-00.
50. Stacy SL, Brink LL, Larkin JC, Sadovsky Y, Goldstein BD, Pitt BR, Talbott EO. Perinatal Outcomes and Unconventional Natural Gas Operations in Southwest Pennsylvania. PLoS ONE. 10(6): e0126425. doi: 10.1371/journal.pone.0126425.
51. Kassotis CD, Klemp KC, Vu DC, Lin C-H, Meng C-X, Besch-Williford CL, Pinatti L, Zoeller RT, Drobnis EZ, Balise VD, Isiguzo CJ, Williams MA, Tillitt DE, Nagel SC. Endocrine-Disrupting Activity of Hydraulic Fracturing Chemicals and Adverse Health Outcomes After Prenatal Exposure in Male Mice. Endocrinology. 2015;156:0000–000.

52. Hamilton M. Concerned Health Professionals releases reports outlining potential negative effects, Times Union, timesunion.com, published 9:37 pm, Thursday, July 10, 2014. http://www.timesunion.com/local/article/Opponents-report-lists-problems-5614012.php
53. Crighton EJ, Brown C, Baxter J, Lemyre L, Masuda JR, Ursitti F. Perceptions and experiences of environmental health risks among new mothers: a qualitative study in Ontario, Canada. Health, Risk & Society. 2013;15(4):295–312. doi:10.1080/13698575.2013.796345.
54. Barrett ES, Janssen SS, Redmon JB, Nguyen RHN, Kobrosly R, Swan SH, et al. Environmental health attitudes and behaviours: findings from a large pregnancy cohort study. Eur J Obstet Gynecol Reprod Biol. 2014;176:119–125; doi: 10.1016/j.ejogrb.2014.02.029. [PubMed: 24647207]
55. Morello-Frosch R, Brody JG, Brown P, Altman RG, Rudel RA, Pérez C. Toxic ignorance and right-to-know in biomonitoring results communication: a survey of scientists and study participants. Environ Health. 2008; 9:6.
56. Brody JG, Morello-Frosch R, Brown P, Rudel RA, Altman RG, Frye M, Osimo CA, Perez C, Seryak LM. Improving disclosure and consent: “is It safe?”: new ethics for reporting personal exposures to environmental chemicals. Am J Public Health. 2007;97:1547–1554. [PubMed: 17666695]
57. Stotland NE, Sutton P, Trowbridge J, Atchley DS, Conry J, et al. Counseling Patients on Preventing Prenatal Environmental Exposures -A Mixed-Methods Study of Obstetricians. PLoS ONE. 2014;9(6):e98771. doi:10.1371/journal.pone.0098771. [PubMed: 24964083]
58. Carwile JL, Ye X, Zhou X, Calafat AM, Michels KB. Canned Soup Consumption and Urinary Bisphenol A: A Randomized Crossover Trial. JAMA. 2011;306(20):2218–2220. doi:10.1001/jama.2011.1721. [PubMed: 22110104]
59. Rudel RA, Gray JM, Engel CL, et al. Food Packaging and Bisphenol A and Bis(2-Ethyhexyl) Phthalate Exposure: Findings from a Dietary Intervention. Environ Health Perspect. 2011;119(7):914–920. doi:10.1289/ehp.1003170. [PubMed: 21450549]
60. Lu C, Toepel K, Irish R, Fenske RA, Barr DB, Bravo R. Organic Diets Significantly Lower Children’s Dietary Exposure to Organophosphorus Pesticides. Environ Health Perspect. 2006;114(2):260–263. doi:10.1289/ehp.8418. [PubMed: 16451864]
61. Ehrlich S, Calafat AM, Humblet O, Smith T, Hauser R, Research Letter February 26, 2014: Handling of Thermal Receipts as a Source of Exposure to Bisphenol A. JAMA. 2014;311(8):859–860. doi: 10.1001/jama.2013.283735 [PubMed: 24570250]
62. Chen CY, Chou YY, Lin SJ, Lee CC. Developing an intervention strategy to reduce phthalate exposure in Taiwanese girls. Sci Total Environ. 2015;517:125–131. doi: 10.1016/j.scitotenv.2015.02.021. pmid: [PubMed: 25725197]
63. Huang P-C, Tsai C-H, Liang W-Y, Li S-S, Pan W-H, et al. Age and Gender Differences in Urinary Levels of Eleven Phthalate Metabolites in General Taiwanese Population after a DEHP Episode. PLoS ONE. 2015;10(7):e0133782. doi: 10.1371/journal.pone.0133782
64. Bui TT, Giovanoulis G, Cousins AP, Magnér J, Cousins IT, de Wit CA. Human exposure, hazard and risk of alternative plasticizers to phthalate esters. Science of the Total Environment. 2015; published online ahead of print 15 January 2016 http://www.sciencedirect.com/science/article/pii/S0048969715306963
65. Kinch CD, Ibhazehiebo K, Jeong J-H, Habibi HR, Kurrasch DM. Low-dose exposure to bisphenol A and replacement bisphenol S induces precocious hypothalamic neurogenesis in embryonic zebrafish. PNAS. 2015;112(5):1475–1480. doi:10.1073/pnas.1417731112 [PubMed: 25583509]
66. Lim DS, Kwack SJ, Kim K-B, Kim HS, Lee BM. Potential Risk of Bisphenol a Migration From Polycarbonate Containers After Heating, Boiling, and Microwaving, Journal of Toxicology and Environmental Health, Part A Current Issues. 2009;72(21–22):1285–1291.D0I: 10.1080/15287390903212329 [PubMed: 20077198]
67. Roberts JW, Wallace LA, Camann DE, Dickey P, Gilbert SG, Lewis RG, Takaro TK. Monitoring and reducing exposure of infants to pollutants in house dust. Rev Environ Contam Toxicol. 2009;201:1–39. doi: 10.1007/978-1-4419-0032-6_1. [PubMed: 19484587]
68. Zota AR, Linderholm LL, Park J-S, Petreas M, TGup T, Privalsky ML, Zoeller RT, Woodruff TJ. Temporal comparison of PBDEs, OH-PBDEs, PCBs, and OH-PCBs in the serum of second

trimester pregnant women recruited from San Francisco General Hospital, California Environ. Sci. Technol. 2013;46:11776–117849.

69. Veasy PF. Senate passes legislation to reform Toxic Substances Control Act. National Law Review. December 28, 2015; accessed ½3/16 at http://www.natlawreview.com/article/senate-passes-legislation-to-reform-toxic-substances-control-act.

Quick Points

- Virtually every pregnant woman in the US has at least 43 different environmental chemicals in her bloodstream.
- Common chemicals such as BPA, phthalates, flame retardants, and perfluorinated compounds can act as endocrine disruptors (chemicals which interfere with normal hormonal activity).
- Troubling health trends, including increases in abnormal neurodevelopment and infertility, may or may not be related to endocrine-disrupting chemicals, but the basic science & epidemiology are of enough concern to suggest employment of the “precautionary principle.” That is, when the health of humans and the environment is at stake, it may not be necessary to wait for scientific certainty to take protective action.
- Clinicians can and should educate women and advocate for safer chemical policies.

Table 1.

Statements from Professional Organizations regarding environmental toxins and endocrine-disrupting chemicals

Organization	Elements of statement
American Academy of Pediatrics (AAP) policy documents[a]	Several policy documents are relevant to endocrine disruption, including pesticides, pollutant chemicals and the thyroid, organic food, and chemical policy.
AAP *Pediatric Environmental Health*, 3rd edition[12]	Identify, prevent, and treat pediatric environmental health problems. Answer parents' questions about environmental hazards, among parents' top health concerns for their children.-
American College of Nurse-Midwives (ACNM): patient handout, "Environmental Hazards in Pregnancy"[13]	Counsel avoidance of pesticides, toxic cleaning supplies, nail salons, and lead contamination.
ACNM: position statement "The Effect of Environmental Toxins on Reproductive and Developmental Health"[14]	Increase awareness of environmental contaminants.
	Provide appropriate education and interventions for women exposed to environmental toxins.
	Encourage policy and research to promote a cleaner, safer environment.
American College of Obstetricians and Gynecologists (ACOG) and American Society for Reproductive Medicine (ASRM): joint opinion[15]	Take timely action to identify and reduce exposure to toxic environmental agents while addressing the consequences of such exposure.
Association of Women's Health Obstetric, and Neonatal Nurses (AWHONN): resource document[16]	Increase research and data collection regarding environmental toxins and the health of women and children.
	Promote regulatory and legislative action to protect the health of women and children based on data.
	Educate the public regarding environmental health risks.
	Ensure a global approach to providing a safe health environment for women and children.
International Federation of Gynecology & Obstetrics (FIGO)[17]	Advocate for policies to prevent exposure to toxic environmental chemicals.
	Work to ensure a healthy food system for all.
	Make environmental health part of health care.
	Champion environmental justice.

[a]The AAP website provides a number of different policy documents related to environmental health. They can be accessed at: http://pediatrics.aappublications.org/collection/council-environmental-health

Table 2.

Environmental exposure assessment for pregnant women[a]

Topics and Questions	Advice
General	
What do you do for work?	Always wear any recommended personal protective equipment for your type of work.
Are you exposed to any of the following at work:	Some work exposures, especially to metals, solvents, and radiation may be harmful. Contact an Occupational and Environmental physician with questions about workplace exposures. www.aoec.org
Metals or chemicals?	
Solvents or fumes?	
Radiation?	
Lead can cause brain damage, especially in babies and children.	Eating foods enriched with iron (red meats, chicken), calcium (dairy, green leafy vegetables), and vitamin C (oranges, tomatoes, green peppers) decrease the risk from lead.
Have you or anyone living in your house ever been treated for lead poisoning?	Family members should have their lead levels tested.
Do you live in a house built before 1978?	Have your home tested for lead if it was built before 1978. Chipping paint may release lead into the house.
Are there any plans to remodel your home?	Avoid remodeling or hire a certified contractor. Call 1–800-424-LEAD for more information.
Have you ever lived outside the United States?	Refugees or immigrants from resource-poor areas are more likely to have elevated lead levels.
Does your family use imported pottery for cooking, eating, or drinking?	Imported pottery or ceramics may contain lead, which can leach into food.
Have you used any herbal remedies such as azarcon, greta, pay-loo-ah, bo ying?	Do not use lead-containing home remedies.
Have you ever eaten any of the following:	Do not eat clay, soil, dirt, pottery, or paint chips because they may contain high levels of lead.
Clay?	
Soil or dirt?	
Pottery or paint chips?	
Mercury is another metal that can damage the developing fetal brain. Small children are also sensitive.	It's important to clean up mercury spills in a special way. https://www.childrensmercy.org/ClinicsandServices/ClinicsandDepartments/PharmacologyandToxicology/Environmental_Health_Specialty_Unit/Cleaning_Up_Liquid_Mercury_Spills/
Is there a mercury thermometer in your home?	Use a digital or mercury-free thermometer.
In general, do you eat fish more than twice a week?	Eat a variety of fish low in mercury twice a week. Contact local health dept. about local fish advisories.
Do you eat any of the following types of fish:	Do not eat shark, swordfish, king mackerel or tilefish because they contain high levels of mercury.
Shark or swordfish?	
King Mackerel or tilefish?	
Albacore (“white” tuna)?	Albacore tuna contains more mercury than canned light tuna; do not eat more than 6 oz per week of albacore tuna.

Topics and Questions	Advice
Air pollution is harmful to pregnant women who are "breathing for two" and also for babies, and children.	
Do you plan on having painting done in your home during your pregnancy?	Avoid exposure to paint fumes, wood strippers, and other products containing solvents.
Do you live near an industrial site or busy roadway?	Avoid outdoor exercise on high air pollution days.
Do you use a wood burning stove or kerosene or gas space heaters?	Ensure adequate ventilation of wood burning stoves, fireplaces, and space heaters (crack a window if necessary).
Does anyone who lives in your home or who will be caring for the baby smoke?	Make your home smoke-free. Also, avoid public places where smoking is allowed.
Pesticides have many potential health harms, both for babies and adults.	If you can afford fruits and vegetables grown without pesticides (including organic), you and your family will be exposed to less of these harmful chemicals.
Do you use pesticides (bug killers, weed killers, rat poison) such as Raid, 'Weed & Feed' or OFF:	For more information go to the National Pesticide Information website, http://npic.orst.edu/
Inside your home?	Avoid sprays, foggers, and bug bombs.
Outside your home?	Use Integrated Pest Management methods to control pests. http://www.ipm.ucdavis.edu/PMG/menu.homegarden.html
On your pets?	
Healthy food and water are very important during pregnancy and for growing children.	
Do you use water or baby bottles made out of hard plastic or polycarbonate (labelled #7)?	Polycarbonate plastic (even that labeled "BPA-free") often contains BPA or similar chemicals which can interfere with hormones in the body, especially in developing fetuses.
Do you eat canned foods or food microwaved in plastic?	The linings of food cans may contain a BPA-like additive. Microwaving in plastic increases the leaching of chemicals into food. Microwave in glass containers or ceramic bowls. Use a plate to cover a dish rather than plastic wrap.
Does your water come from a well?	Well water should be rested routinely for contaminants.
If your house is old, does it have lead pipes?	Run the tap for 60 seconds to flush out sitting water.
Chemicals in personal care products, fragrances, and household cleaners may be harmful to pregnant women or fetuses.	These products may contain chemicals such as phthalates which are thought to cause developmental problems for growing fetuses.
Do you use fragrant personal care products such as perfume, body spray, lotion, or shampoo/conditioner?	Use fewer products, and purchase fragrance-free if possible.
Do you use chemicals at home or work for cleaning or scent?	Practice safe handling techniques if you have to use strong chemicals. Try to use less-toxic alternatives for cleaning such as vinegar, soap, and baking soda. Avoid air fresheners and scented candles.

[a]Source: Great Lakes Center for Children's Environmental Health (Region 5 PEHSU), adapted with with permission from Susan Buchanan, MD and available from: http://www.uic.edu/sph/glakes/childrenshealth/downloads/Env%20history%20form%2010–2013.pdf

Table 3.

Suggested actions to decrease individual exposure to endocrine disrupting chemicals

Goal of Action	Simple Steps	Expected Outcome
Avoid eating or drinking toxins	Wash hands with plant-based soap prior to eating, as toxins present on hands may be orally ingested.	Decreased contamination of hands with BPA,[61] phthalates,[62,63] and other potential toxins
	Choose organic produce and wash produce to remove pesticide residue. NOTE: If organic is too expensive, choose items from the "Clean Fifteen" list. http://www.ewg.org/foodnews/cleanfifteenlist.php	Less pesticide residue[60]
	Avoid processed foods, including fast food, which are often exposed to plastic during manufacture or storage. Fatty foods and meat are more likely to contain flame retardants.	Less exposure to plasticizers, flame retardants[58,59]
	Limit foods high in animal fat. Persistent organic pollutants are fat soluble, and may be found in the food chain. Flame retardants have a half-life of 1–3 years in human fat.	Lower exposure to persistent organic pollutants[4,39]
	Avoid foods with substantial plastic contact, particularly if the food is wet, including canned foods, sodas, wet foods in plastic pouches or boxes.	Lower exposure to BPA, phthalates, and other plasticizers[58,59]
	Avoid plastics thought to have more health risks including PVC, polystyrene, and polycarbonate (labeled with plastic recycling numbers 3, 6, and 7, respectively). Plastics labeled "BPA-free" may contain other plasticizers such as bisphenol S that are also thought to have endocrine-disrupting properties. Stainless steel and glass are considered safer alternatives.	Lower exposure to BPA, phthalates, and other plasticizers[63–66]
	Do not microwave in plastic. Heating increases leaching of chemicals, especially with fatty foods. Use a paper towel or glass lid to cover food in the microwave.	Lower exposure to BPA, phthalates, and other plasticizers[63,66]
Avoid toxins in the home.	Limit pesticide and solvent use in home. Clean with soap and vinegar. Use baking soda for ants. Keep counters clean. Use integrated pest management strategies (a process intended to address pest problems while minimizing risks to people and the environment by minimizing chemical use while taking advantage of natural inhibitors of pest activity) in the garden. See http://www.ipm.ucdavis.edu/PMG/menu.homegarden.html	Less pesticide exposure
	Decrease house dust, which may contain toxic chemicals. Take shoes off outside. Dust, damp mop, or vacuum (with a HEPA filter) twice weekly (daily for high risk dust or crawling baby). These steps are especially important when dust is likely to be high risk: to have toxins, such as in agricultural areas and urban neighborhoods, or when the patient or household member works in occupation with pesticides, solvents, lead, or other toxins.	Less exposure to lead, flame retardants, pesticides, phthalates, and other toxic chemicals, as well as allergens and endotoxin.[39,67]
	Get rid of old foam furniture or replace the foam in the cushions. Flame retardants are worst in pre-2005 foam. The risk appears to be higher if the foam is crumbling. If furniture cant' be replaced, damp mop or vacuum with a HEPA filter. NOTE: Foam cushions can be replaced by contacting Safer Foam Exchange at http://greensciencepolicy.org/responsible-furniture-disposal/#exchange	Less exposure to flame retardants.[39,67]
Avoid toxins on your skin.	Avoid carbonless receipts. Dont' take receipt if you dont' need it. Cashiers should wear gloves when working with receipts and wash hands thoroughly prior to eating. Many receipts contain phthalates or BPA.	Decreased urinary BPA levels.[61]
	Be thoughtful about body products: avoid phthalates (often listed as fragrance), parabens, and triclosan. Risk stratify (it's more important to avoid these during "windows of susceptibility," such as pregnancy, lactation, infancy, puberty. Chemicals meant to stay on the skin may result in higher doses than those washed off. NOTE: Online resources include the Skin Deep database from www.ewg.org and the California Safe Cosmetics Program Database https://safecosmetics.cdph.ca.gov/search/	Decreased exposure to phthalates, parabens, and other endocrine-disrupting chemicals.[2,3,774]

Abbreviations: BPA, bisphenol A; HEPA, High-efficiency particulate air; PVC, polyvinyl chloride.