UCSF

UC San Francisco Previously Published Works

Title

Toxic environmental chemicals: the role of reproductive health professionals in preventing harmful exposures.

Permalink

<https://escholarship.org/uc/item/237041dk>

Journal

American journal of obstetrics and gynecology, 207(3)

ISSN

0002-9378

Authors

Sutton, Patrice
Woodruff, Tracey J
Perron, Joanne
et al.

Publication Date

2012-09-01

DOI

10.1016/j.ajog.2012.01.034

Peer reviewed

OBSTETRICS

Toxic environmental chemicals: the role of reproductive health professionals in preventing harmful exposures

Patrice Sutton, MPH; Tracey J. Woodruff, PhD, MPH; Joanne Perron, MD; Naomi Stotland, MD; Jeanne A. Conry, MD, PhD; Mark D. Miller, MD, MPH; Linda C. Giudice, MD, PhD

Every pregnant woman in the United States is exposed to many and varied environmental chemicals. Rapidly accumulating scientific evidence documents that widespread exposure to environmental chemicals at levels that are encountered in daily life can impact reproductive and developmental health adversely. Preconception and prenatal exposure to environmental chemicals are of particular importance because they may have a profound and lasting impact on health across the life course. Thus, prevention of developmental exposures to environmental chemicals would benefit greatly from the active participation of reproductive health professionals in clinical and policy arenas.

Key words: environmental chemical, reproductive environmental health, toxic chemical

Among the US population, current indicators of reproductive adversity include a decline in the age of the onset of puberty,¹ declines in fertility and fecundity,^{2,3} increased rates of poor birth outcomes (such as babies born prematurely^{4,5}), increased rates of small for gestational age infants,⁶ increased rates of certain birth defects,⁷ and increased rates of childhood diseases (such as au-

tism,⁸ certain types of cancer,⁹ and obesity¹⁰), and declines in life expectancy (some communities have life expectancies already well behind those of the best-performing nations¹¹). Because these and other barometers of reproductive health and capacity have changed at a relatively rapid pace, they are unlikely to be explained by changes in genetic makeup.¹² Thus, we need to turn our attention to other factors that include the environment as possible contributors to these trends.

The environmental contributors to reproductive health begin in utero and include the social, physical, and nutritional environment and physical and chemical agents. Each of these factors interacts with the others and with intrinsic biologic factors (such as age, sex, and genes) to influence individual and population health outcomes.^{13,14} For example, environmental pollution interacts with stress to the detriment of long-term health¹⁵⁻¹⁷; the effects of exposure to toxic chemicals can be exacerbated or mitigated by nutritional status,¹⁸⁻²⁰ and exposure to toxic chemicals and good nutrition is influenced by social and other environmental factors such as injustice, poverty, neighborhood, and housing.¹⁸⁻²⁵

Disparities in these environmental contributors are of major health consequence.²⁶⁻²⁸ Many communities with the highest exposures also lack access to med-

ical care, good educational opportunities, good nutrition, employment, and other factors that may help to mitigate related impacts. Thus, the effect of a low-dose exposure to an environmental chemical may be quite different, depending on the population's degree of exposure to other environmental contaminants and underlying health status (Figure 1).²⁹

Within the field of obstetrics and gynecology, preconception and prenatal exposure to environmental chemicals (which is defined in this article as including synthetic chemicals and metals) is a key area of inquiry because (1) exposure to many and varied toxic chemicals among pregnant women in the United States is now the norm (Figure 2),³⁰ (2) developmental exposure to certain environmental chemicals is linked to a myriad of health consequences that can manifest across the lifetime of individuals and potentially be transmitted to the next generation (Table),⁵⁷ and (3) exposure to environmental chemicals can be mitigated and prevented. This article provides a brief overview of this new science that is relevant to practicing obstetricians, gynecologists, and other reproductive health professionals and outlines opportunities for the prevention of harm and associated costs in clinical and policy venues.

Exposure to environmental chemicals among pregnant women

In the past 70 years, there has been a dramatic increase in human exposure to both natural and synthetic chemicals. Over this period, US chemical production and use has increased over 16-fold.⁵⁸ Today, >80,000 chemical substances are listed by the US Environmental Protection Agency (EPA) as manufactured or processed in the United States or imported into the country,^{59,60} but this is probably an overestimate of the number of chemicals currently in commercial use. Approximately 3000-

From the Program on Reproductive Health and the Environment (Drs Woodruff and Perron and Ms Sutton), the Department of Obstetrics, Gynecology and Reproductive Sciences (Drs Stotland and Giudice), the Pediatric Environmental Health Specialty Unit (Dr Miller), University of California, San Francisco, CA; and the Department of Obstetrics and Gynecology, North Valley, Kaiser Permanente, Roseville, CA (Dr Conry).

Received June 30, 2011; revised Jan. 24, 2012; accepted Jan. 24, 2012.

Supported by New York Community Trust, the National Institute for Environmental Health Sciences (NIEHS: ES018135), and the Environmental Protection Agency (EPA STAR: RD83467801).

The authors report no conflict of interest.

Reprints: Patrice Sutton, UCSF Program on Reproductive Health and the Environment, 1330 Broadway, Suite 1100, Oakland, CA 94612. suttonp@obgyn.ucsf.edu.

0002-9378/\$36.00

© 2012 Mosby, Inc. All rights reserved.

doi: 10.1016/j.ajog.2012.01.034

4000 chemicals are identified as high-volume chemicals, which means that >1 million pounds of each of them are manufactured or imported annually.⁶⁰ Moreover, approximately 700 new industrial chemicals are introduced each year.⁶¹

Health care professionals and the public cannot assume, as they do with pharmaceuticals, that adequate in vitro and in vivo testing of environmental chemicals has been undertaken and considered by regulatory agencies before widespread human exposure occurs (Figure 3). The vast majority of chemicals in commerce have entered the marketplace without comprehensive testing and standardized information on their reproductive or other chronic toxicities.^{62,63} For example, in 1976 the US EPA was given the authority to regulate chemicals in commerce under the Toxic Substances and Control Act (TSCA). The EPA has used its authorities under the TSCA to require testing of <200 of the 62,000 chemicals in commerce when the TSCA became law.⁶⁴

The inadequacy of our current regulatory framework for chemicals in commerce is recognized by physicians and organizations of health professionals (such as the American Medical Association and the American Academy of Pediatrics⁶⁵⁻⁶⁷), governmental⁶⁸ and nongovernmental organizations,⁶⁹ and industry.⁷⁰

Toxic chemicals currently are distributed widely throughout homes, workplaces, and communities and contaminate food, water, air, and consumer products. A 2011 study that used population-based data from the National Health and Nutrition Examination Survey documented ubiquitous exposure among pregnant women in the United States to multiple chemicals.³⁰ The study found that virtually all pregnant women have measured levels of all of the following chemicals that can be harmful to human reproduction and/or development in their bodies: lead, mercury, toluene, perchlorate, bisphenol A (BPA), and some phthalates, pesticides, perfluorochemicals, polychlorinated biphenyls, and polybrominated diphenol ethers (PBDEs; Table).³⁰

FIGURE 1

The effect of biologic susceptibility and coexposure to other chemicals on the relationship between individual chemical exposure and adverse health outcomes

Reproduced, with permission, from Woodruff et al.⁷¹

Sutton. *Toxic matters. Am J Obstet Gynecol* 2012.

Several of these environmental chemicals in pregnant women, including phthalates, mercury, and PBDEs, are at levels that are associated with adverse health outcomes in human studies.³⁰ We have incomplete knowledge of what these exposures mean because the reproductive and other potential health impacts of daily exposure to this complex mixture of environmental chemicals have not been studied. This shortcoming is recognized by the National Academy

of Sciences to be a gap in current scientific methods that inform public policy that permits human exposure.²⁹ The National Academy of Sciences has also concluded that, in the absence of data, one cannot assume (as policy makers and regulators currently do) that there is a threshold or safe limit of exposure for chemicals that adversely impact reproductive or developmental health outcomes.^{29,79}

Many chemicals in pregnant women can cross the placenta; in some cases, such

FIGURE 2

Environmental chemicals in pregnant women in the United States

Adapted, with permission from Woodruff et al.³⁰

Sutton. *Toxic matters. Am J Obstet Gynecol* 2012.

TABLE

Examples of reproductive health impacts of prenatal exposure to environmental contaminants

Chemical	Exposure sources and pathways	Reproductive/developmental health impact
Bisphenol A	Chemical intermediate for polycarbonate plastic and resins; found in consumer products and packaging; exposure through inhalation, ingestion, and dermal absorption.	Recurrent miscarriage ³¹ Aggression and hyperactivity in female children ³²
Lead	Occupational exposure occurs in battery manufacturing/recycling, smelting, car repair, welding, soldering, firearm cleaning/shooting, stained-glass ornament/jewelry making; nonoccupational exposure occurs in older homes where lead-based paints were used, in or on some toys/children's jewelry, water pipes, imported ceramics/pottery, herbal remedies, traditional cosmetics, hair dyes, contaminated soil, toys, costume jewelry.	Alterations in genomic methylation ¹⁷ Increased likelihood of allergies ³³
Mercury	Coal-fired power plants are largest source in the United States; primary human exposure by consumption of contaminated seafood.	Reduced cognitive performance ^{34,35} Impaired neurodevelopment ^{36,37}
Polybrominated diphenylethers	Flame retardants that persist and bioaccumulate in the environment; found in furniture, textiles, carpeting, electronics and plastics that are mixed into, but not bound to, foam or plastic.	Impaired neurodevelopment ³⁸ Premature delivery, low birthweight, and stillbirth ³⁹
Polychlorinated biphenyls	Used as industrial insulators and lubricants; banned in the 1970s, but persistent in the aquatic and terrestrial food chains, which results in exposure by ingestion.	Development of attention deficit–hyperactivity disorder–associated behavior ⁴⁰ Increased body mass index ⁴¹ Reduced IQ ⁴²
Polyfluorochemicals	Widely used man-made organofluorine compounds with many diverse industrial and consumer product applications; examples are perfluorooctane sulfonate and perfluorooctanate, which are used in the manufacture of nonstick Teflon and other trademark cookware products and in food-contact packaging to provide grease, oil, and water resistance to plates, food containers, bags, and wraps that come into contact with food; persist in the environment; occupational exposure to workers and general population exposure by inhalation, ingestion, and dermal contact.	Reduced birthweight ⁴³
Perchlorate	Used to produce rocket fuel, fireworks, flares, and explosives and can also be present in bleach and in some fertilizers; primary pathway for exposure is through drinking water caused by contaminated runoff.	Altered thyroid function ⁴⁴
Pesticides	Applied in large quantities in agricultural, community, and household settings; in 2001, >1.2 billion pounds of active ingredients were used in the United States; can be ingested, inhaled, and absorbed by the skin; pathways of exposure include food, water, air, dust, and soil.	Impaired cognitive development Impaired neurodevelopment ^{45,46} Impaired fetal growth ⁴⁷ Increased susceptibility to testicular cancer ⁴⁸ Childhood cancers ⁴⁹
Phthalates	Synthetically derived; used in a variety of consumer goods such as medical devices, cleaning and building materials, personal care products, cosmetics, pharmaceuticals, food processing, and toys; exposure occurs through ingestion, inhalation, and dermal absorption.	Reduced masculine play in boys ⁵⁰ Reduced anogenital distance ⁵¹ Shortened gestational age ⁵² Impaired neurodevelopment in girls ⁵³
Toluene	Exposure occurs from breathing contaminated workplace air, automobile exhaust, some consumer products such as paints, paint thinners, fingernail polish, lacquers, and adhesives.	Decreased fetal and birthweight ⁵⁴ Congenital malformations ^{55,56}

Sutton. Toxic matters. *Am J Obstet Gynecol* 2012.

as methyl mercury, fetal exposure has been documented to be higher than maternal exposure.⁷²⁻⁷⁴ In 2010, the National Cancer Institute's President's Report on Cancer observed that "to a disturbing extent babies are born 'pre-polluted'."⁷⁵ Postnatally, maternal exposure to environmental chemicals may continue to expose a newborn infant through breast-feeding.⁷⁶⁻⁷⁸

Developmental vulnerability to environmental chemicals

Assumptions about the benign nature of "low-level" environmental exposures have been upended by the new science.^{29,79} We now know that the human reproductive system is particularly vulnerable to biologic perturbations that are caused by ambient levels of environmental chemicals when these exposures occur during critical or sensitive periods of development (ie, in utero and during infancy, childhood and adolescence).⁸⁰⁻⁸² This vulnerability is, in part, because these are times of extensive developmental changes, such as cellular proliferation and rapidly changing and/or undeveloped metabolic, hormonal, and immunologic capabilities.⁸³

For example, critical stages of central nervous system development occur from embryogenesis through adolescence. The periods of neuronal proliferation, migration, differentiation, and synaptogenesis are especially sensitive to disruption and permanent damage.^{84,85} Because these processes are unidirectional, interference at an early stage may result in disruption throughout the further cascade of reactions and interactions that propagate human development.^{84,85}

The range of potential adverse impacts from in utero exposure to exogenous chemicals is already well understood by clinicians who are familiar with thalidomide's congenital limb and gastrointestinal malformations⁸⁶⁻⁸⁸ and diethylstilbestrol's delayed effects of benign and malignant reproductive-tract abnormalities and increased risk of female breast cancer.⁸⁹⁻⁹¹ Diethylstilbestrol remains one of the most scientifically robust illustrations of the linkage between developmental exposure to a hormonally active exogenous chemical and adult disease.⁸³

FIGURE 3

Comparison of the evidence streams that are needed in clinical and environmental health sciences for an exogenous chemical to enter the marketplace

EPA, Environmental Protection Agency.

Adapted, with permission, from Woodruff et al.¹⁴⁶

Sutton. *Toxic matters*. Am J Obstet Gynecol 2012.

Of growing importance for patient health is that the exposure of pregnant women to endocrine-disrupting chemicals (EDCs) beyond diethylstilbestrol has proliferated, such that simultaneous exposure to many EDCs is ubiquitous among pregnant women in the United States today.³⁰ The EPA defines EDCs as compounds that interfere with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis (normal cell metabolism), reproduction, development, and/or behavior.⁹² Examples of EDCs that commonly are found in food, water, air, house dust, and/or personal care products include phthalates, BPA, PBDEs, perchlorate, and some pesticides.⁹³ Because hormonal regulation is critical to human reproduction, chemicals that perturb the system may cause permanent effects.⁹⁴⁻⁹⁹

For example, polychlorinated biphenyls and PBDEs can disrupt maternal thyroid function that is crucial for normal fetal development; in utero exposure to these chemicals has been associated with neurologic deficits in human and/or animal studies.^{38,100,101} Phthalates can interfere with testosterone; studies in animals and humans indicate that exposure to certain phthalates during critical times of development can increase the risk of adverse male reproductive development (in rats, undescended testicles and cryptorchidism and, in humans, a relationship with subtle measures of feminization in boys of women who have higher phthalate exposures during pregnancy).⁷⁹

The mechanisms of action that are related to developmental exposure to environmental toxicants are many and complex and can change depending on when in the pregnancy or other developmental stage the exposure or related insult oc-

curs.^{102,103} For example, environmental chemicals can interfere with the development of normal fetal lung structure and function by perturbing a variety of transcription factors and morpho-regulatory molecules during critical developmental stages.⁹⁶

Normal cell signaling can also be perturbed by EDCs, heavy metals, and other environmental chemicals through epigenetic mechanisms, which, although not changing DNA, disrupt gene expression that is integral to the orchestration of healthy human development.¹³ The relationship between the human genome and the environment has been analogized as genes acting to “load the gun” or create the potential for adverse health outcomes and as the environment acting as the “trigger” that activates the physiologic or pathologic network of biologic reactions or events that are responsible for human health and disease.¹³ Environmental modifications of gene expression can affect embryonic imprinting, cellular differentiation, and phenotypic expression.¹⁰⁴ Beckwith-Wiedemann, Prader-Willi, and Angelman are 3 syndromes that exemplify the significance of epigenetics in real life.¹⁰⁵⁻¹⁰⁷

Human research has begun to expand mechanistic data from animal studies on the effect of environmental chemicals on the epigenome and human health.^{17,108} However, as with preclinical testing of pharmaceuticals, the nonhuman system of evidence is the preferred method for the documentation and development of prevention strategies that are related to the health impacts of developmental exposure to environmental chemicals, because these studies can be undertaken before human exposure.¹⁰⁹ Environmental contaminants are not intended for human use, and it is unethical knowingly to expose humans to these chemicals under experimental conditions to assess for harmful effects.

The Table presents examples of the reproductive and/or developmental health effects from human studies of in utero exposure to environmental chemicals that are common in pregnant women today. Exemplary of these data, in 2009, the Endocrine Society reviewed the evidence of health impacts from EDCs and concluded that “the evidence for adverse reproductive outcomes (infertility, can-

cers, malformations) from exposure to EDCs is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis.”⁷⁶

New scientific discoveries (ie, epigenetics, cell signaling, and developmental programming) document the vulnerability of the developing human to contemporary levels of environmental chemicals. Environmental exposures during fetal development may lead to changes in organ structure, function, and/or metabolism that are permanent and impact lifetime health risk. For the practicing clinician, the new science means that an important outcome of pregnancy is not only a healthy newborn infant but also a human being who is programmed optimally for health from infancy through old age.

Implications of the new science for reproductive health clinicians

The nature and extent of the relationship between reproductive health and environmental chemicals is unfolding rapidly. The current strength of the evidence that links ubiquitous exposure to environmental chemicals to adverse reproductive and developmental health outcomes is sufficiently robust that leading scientists and reproductive health and other clinical practitioners have called for timely action to prevent harm.^{57,75,76,81} Among physicians, obstetricians and gynecologists are poised uniquely to intervene in critical stages of human development (ie, preconception and during pregnancy) to prevent harm.

Taking action to prevent harm in clinical settings

Obstetricians and gynecologists can serve as a science-based source of guidance on how to avoid potentially adverse exposures.^{110,111} As in other areas of clinical practice, communication of the science and areas of uncertainties about environmental chemicals can provide patients with the information they need to make informed choices based on the evidence and their values and preferences. Studies that are related to the communication of the results of environmental chemicals in breast milk and

other biomarkers lend empiric support to this approach.^{112,113}

Pediatricians have long been attuned to the opportunity that clinical practice offers to identify, evaluate, and counsel patients about preventing harm from hazardous environmental exposures. The American Academy of Pediatrics has had an environmental health committee for more than one-half of a century and publishes a clinicians’ handbook for the prevention of childhood diseases that are linked to environmental exposures.¹¹⁴

In light of the importance of preconception and prenatal environmental exposures to the health of the pregnancy and the child and adult that she or he will become, these pediatric approaches to the incorporation of environmental health into clinical care are equally applicable to reproductive health professionals. Based on our experience in clinical practice and through our engagement with health professionals, scientists, and the public, many patients who are pregnant or thinking about becoming pregnant are intensely and justifiably interested in their environmental exposures; at the same time, other women of childbearing age are unaware of the risk of their exposures. Clinicians should intervene as early as possible to prevent exposures during pregnancy by alerting patients to potential hazards and providing guidance on how to avoid toxic exposures. By the first prenatal care visit, disruptions of organogenesis may have already occurred.

Taking an exposure history is a key first step. Clinicians should always ask women of childbearing age about occupational exposures; the workplace may be an important source of toxic exposures among pregnant women. Legal exposure limits for most workplace chemicals are not designed to protect against harm to a pregnancy or the developing fetus. A variety of examples of how to take an exposure history exist¹¹⁵⁻¹¹⁸ and can be found at <http://prhe.ucsf.edu/prhe/clinical/index.html#eh>.

Clinicians should provide anticipatory guidance to all patients with information about how to avoid toxic exposures at home, in the community, and at work. Information and resources about envi-

ronmental hazards can be incorporated successfully into childbirth class course curriculum to help women and men make optimal choices for themselves and their children.¹¹⁹ Patient-centered brochures with tips for the prevention of toxic exposures and links to many additional resources can be found at <http://prhe.ucsf.edu/prhe/toxicmatters.html>.

Patient-centered actions can reduce body burdens of toxic chemicals. Research documents that, when children's diets change from conventional to organic food, the levels of pesticides in their bodies decline.¹²⁰ Likewise, recent studies found that avoiding canned food and other dietary sources of BPA can reduce measured levels of the chemical in children and adult family members¹²¹ and that short-term changes in dietary behavior may decrease exposure to phthalates significantly.¹²² It is important to recognize, however, that decisions on the individual level about avoiding toxic exposures are complex and often affected by external factors that limit making healthier choices.¹²³ Patient purchasing patterns can also send a signal to the marketplace that can help drive society-wide change. This was demonstrated by the burgeoning market in organic food,¹²⁴ in the explosion of the market for alternatives to BPA in food contact uses such as baby bottles,¹²⁵ and in the recent decision by Walmart Stores, Inc (Rogers, AR) to ban a flame retardant that is found in hundreds of consumer goods from its supply chain.¹²⁶

In addition, although reproductive health professionals can be certain that the environment influences patient health, the idea of adding yet another topic to a clinician's "to-do" list is likely to seem daunting. The reality of severely constrained patient-contact time and the lack of a reimbursement mechanism is compounded by the fact that medical education for obstetricians and gynecologists thus far has been largely devoid of training in reproductive environmental health beyond the dangers of alcohol, tobacco, and recreational drugs. However, reproductive health professionals do not need to be experts in environmental health to provide useful information to

patients and make referrals when hazardous exposures are identified. Existing clinical experience and expertise in the communication of the risks of treatment are also largely transferable to environmental health.

Many useful resources exist to support clinicians in communicating about environmental risks.¹²⁷ The Pediatric Environmental Health Specialty Units (PEHSUs) are a network of investigators across the United States who support clinical capacity that is related to environmental health.¹²⁸ The PEHSUs respond to requests for information throughout North America on the prevention, diagnosis, management, and treatment of environmentally related health effects in children and, as such, are poised to serve as a valuable resource for obstetricians and gynecologists in recognition of the inextricable relationship between reproductive and pediatric health.

Recent case examples in our (M.D.M.; T.J.W.; N.S.) experience include a woman who had a high blood lead level and was 16 weeks pregnant. She had an evaluation by public health workers with a home visit that did not identify a source and was referred to the PEHSU by her physician. We identified her use of an aruveydic medicine with a history of contamination with lead. We counseled her in general regarding possible health consequences for her baby and made her physician aware of the protocol for management of elevated blood lead in pregnancy. Another example was a mother and newborn infant who were identified as having elevated blood mercury levels. The PEHSU helped to determine that it was inorganic mercury and made the referral to the EPA region emergency response team who identified the source of mercury as face cream.

Taking action to prevent harm in policy settings

The role of clinicians in preventing exposure to environmental toxicants extends beyond the clinic or office setting.^{129,130} Society-wide policy actions are essential for the reduction of toxic exposures to pregnant women and other vulnerable populations because many exposures are not controllable on an individual level (ie, from air and water). In addition, en-

vironmental justice issues that are related to exposures to toxic substances cannot be redressed sufficiently by individual action. For example, women and men who are exposed to pesticides at work and in agricultural communities incur substantively higher exposures than the US population overall.^{131,132}

There are many examples that demonstrate that clinicians are in an excellent position to take action in policy settings. For example, our industrialized food system is associated with many and varied threats to reproductive and developmental health, including exposure to pesticides, chemical fertilizers, hormones in beef cattle, antimicrobials in beef cattle, swine, and poultry, fossil fuel consumption and climate change, toxic chemicals in food packaging and cookware, and the production and promotion of food that is unhealthy for pregnant women.¹³³ Policy interventions by the health care sector and physician's patient engagement offer mutually reinforcing opportunities to advance a healthy food system as a strategy to prevent adverse reproductive health impacts.¹³³

To this end, physician leaders have been instrumental in spurring efforts by health care institutions to support the development of urban agriculture programs, farmer's markets and local food-sourcing outlets to increase accessibility to healthier foods; health care institutions have undertaken procurement policies to create a sustainable and healthy food service model. Nearly 350 hospitals have taken the Healthy Food in Health-care Pledge in support of these efforts.¹³⁴ Because the food system purchasing power of the health care system is so large (approximately \$12 billion annually), clinicians who become engaged in changing their hospital food system procurement patterns can help leverage food system change more broadly. Other examples of institutional policy arenas for clinical action include the reduction of toxic chemicals in health care purchasing coupled to bringing policy gaps that impede less toxic procurement patterns to the attention of decision-makers (<http://www.saferchemicals.org/resources/business/kaizer-permanente.html>). Clinicians have also been engaged in reducing the use of pesticides in institutional pest-control

polices (<http://www.mdpestnet.org/projects/ipmHealthcare.html>).

Clinicians can also work towards policy change in their professional organizations. For example, professional organizations of physicians that include obstetricians and gynecologists have been active in calling for regulatory and other efforts to address exposure to toxic chemicals and many other environmental threats to human health. A compilation can be found at <http://www.prhe.ucsf.edu/prhe/pdfs/ProfessionalStatementsDatabase.pdf>.

In 2009, the Endocrine Society issued a position paper calling for improved public policy to identify and regulate EDCs and finding that “[u]ntil such time as conclusive scientific evidence exists to either prove or disprove harmful effects of substances, a precautionary approach should be taken in the formulation of EDC policy.”⁹⁹ The application of the precautionary principle in environmental health dates to the 1980s, and today precaution is an underlying principle of environmental health policy in the European Union, particularly in the realm of risk management.¹³⁵ The precautionary principle is defined in the following manner: “When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.”¹³⁶ Reversing the burden of proof so that chemical exposures are not presumed safe in the absence of scientific evidence would exemplify a precautionary approach to environmental chemicals.

Future directions

Just as the thalidomide tragedy led to strengthened regulatory oversight of the safety and efficacy of all prescription drugs,⁸⁶ recent advances in toxicity testing,¹³⁷⁻¹⁴² risk assessment,^{29,71,79,143,144} and efforts to address shortcomings in regulatory policy that is related to chemicals in commerce^{68-70,145} are likely to create important change in the amount, type, and availability of chemical toxicity data and related health impacts. These anticipated improvements underscore the need for a method to ensure the timely application of

these data to prevention. To this end, a method has been developed to evaluate the quality of evidence and strength of recommendations about the relationship between the environment and reproductive health in uniform, simple, and transparent summaries that integrate the best practices of evaluation in environmental and clinical health sciences.¹⁴⁶ The generation of clinical guidelines must proceed with the development and dissemination of validated methods to screen and counsel patients about their exposures and safer alternatives that will prevent exposure for all patients.

It is also expected that electronic medical records will revolutionize medical research by facilitating instant, comprehensive data that go back years into history and extend longitudinally into the future.¹⁴⁷ Harnessing these changes could greatly accelerate the creation of knowledge about the impact of the environment on our reproductive health and capacity. Obstetricians, gynecologists, and other reproductive health professionals can play a groundbreaking role by intervening in critical stages of human development to translate the new science into healthier pregnancies, healthier children, and healthy future generations. ■

REFERENCES

1. Wolff MS, Teitelbaum SL, Pinney SM, et al. Investigation of relationships between urinary biomarkers of phytoestrogens, phthalates, and phenols and pubertal stages in girls. *Environ Health Perspect* 2010;118:1039-46.
2. Swan SH, Hertz-Picciotto I. Reasons for infertility. *Fam Plann Perspect* 1999;31:156-7.
3. Brett K. Fecundity in 2002 NSFG women 15-24 years of age. Hyattsville, MD: National Center for Health Statistics;2008.
4. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand K. Cognitive and behavioral outcomes of school-aged children who were born preterm. *JAMA* 2002;288:728-37.
5. Hamilton BE, Martin JA, Ventura MA, et al. Births: preliminary data for 2009. *Public Health Resources* 2010. National Vital Statistics Report, vol 59, no. 3. Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_03.pdf. Accessed Feb. 14, 2012.
6. Donahue S, Kleinman KP, Gillman MW, Oken E. Trends in birth weight and gestational length among singleton term births in the United States: 1990-2005. *Obstet Gynecol* 2010;115:357-64.
7. Vu LT, Nobuhara KK, Laurent C, Shaw GM. Increasing prevalence of gastroschisis: population-based study in California. *J Pediatr* 2008;152:807-11.
8. Prevalence of autism spectrum disorders: Autism and Developmental Disabilities Monitoring Network, United States, 2006. *MMWR Surveill Summ* 2009;58:1-20.
9. US Environmental Protection Agency. America's children and the environment. Washington, DC: USEPA; 2010. Available at: http://www.epa.gov/envirohealth/children/child_illness/d6-graph.html. Accessed Feb. 14, 2012.
10. Centers for Disease Control and Prevention. Overweight and obesity. Atlanta: CDC; 2011. Available at: <http://www.cdc.gov/obesity/childhood/prevalence.html>. Accessed Feb. 14, 2012.
11. Kulkarni SC, Levin-Rector A, Ezzati M, Murray CJL. Falling behind: life expectancy in US counties from 2000 to 2007 in an international context. *Popul Health Metr* 2011;9:16.
12. Woodruff TJ, Schwartz J, Giudice LC. Research agenda for environmental reproductive health in the 21st century. *J Epidemiol Community Health* 2010;64:307-10.
13. Olden K, Freudenberg N, Dowd J, Shields AE. Discovering how environmental exposures alter genes could lead to new treatments for chronic illnesses. *Health Aff (Millwood)* 2011;30:833-41.
14. Huen K, Harley K, Brooks J, et al. Developmental changes in PON1 enzyme activity in young children and effects of PON1 polymorphisms. *Environ Health Perspect* 2009;117:1632-8.
15. Ren C, Park SK, Vokonas PS, et al. Air pollution and homocysteine: more evidence that oxidative stress-related genes modify effects of particulate air pollution. *Epidemiology* 2010;21:198-206.
16. Wright RJ, Visness CM, Calatroni A, et al. Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner-city cohort. *Am J Respir Crit Care Med* 2010;182:25-33.
17. Wright RO, Schwartz J, Wright RJ, et al. Biomarkers of lead exposure and DNA methylation within retrotransposons. *Environ Health Perspect* 2010;118:790-5.
18. Guilloteau P, Zabielski R, Hammon H, Metges C. Adverse effects of nutritional programming during prenatal and early postnatal life, some aspects of regulation and potential prevention and treatments. *J Physiol Pharmacol* 2009;60:17-35.
19. Kordas K. Iron, lead, and children's behavior and cognition. *Annu Rev Nutr* 2010;30:123-48.
20. Burke MG, Miller MD. Practical guidelines for evaluating lead exposure in children with mental health conditions: molecular effects and clinical implications. *Postgrad Med* 2011;123:160-8.
21. Cheadle A, Samuels SE, Rauzon S, et al. Approaches to measuring the extent and impact of environmental change in three California community-level obesity prevention initiatives. *Am J Public Health* 2010;100:2129-36.

22. Morello-Frosch R, Lopez R. The riskscape and the color line: examining the role of segregation in environmental health disparities. *Environ Res* 2006;102:181-96.
23. Schneider JS, Lee M, Anderson D, Zuck L, Lidsky T. Enriched environment during development is protective against lead-induced neurotoxicity. *Brain Res* 2001;896:48-55.
24. Weiss B, Bellinger DC. Social ecology of children's vulnerability to environmental pollutants. *Environ Health Perspect* 2006;114:1479-85.
25. Wright RO. Neurotoxicology: what can context teach us? *J Pediatr* 2008;152:155-7.
26. Morello-Frosch R, Zuk M, Jerrett M, Shamasunder B, Kyle AD. Understanding the cumulative impacts of inequalities in environmental health: implications for policy. *Health Aff (Millwood)* 2011;30:879-87.
27. Williams DR, Sternthal M. Understanding racial-ethnic disparities in health. *J Health Soc Behav* 2010;51:S15-27.
28. Marmot MG, Bell R. Action on health disparities in the United States Commission on Social Determinants of Health. *JAMA* 2009;301:1169-71.
29. National Research Council Committee on improving risk analysis approaches used by the US EPA, National Research Council Board on Environmental Studies and Toxicology, National Research Council Division on Earth and Life Studies. Science and decisions: advancing risk assessment. Washington, DC: The National Academies Press; 2009.
30. Woodruff TJ, Zota AR, Schwartz JM. Environmental chemicals in pregnant women in the US: NHANES 2003-2004. *Environ Health Perspect* 2011;119:878-85.
31. Sugiura-Ogasawara M, Ozaki Y, Sonta S, Makino T, Suzumori K. Exposure to bisphenol A is associated with recurrent miscarriage. *Human reproduction* 2005;20:2325.
32. Braun JM, Yolton K, Dietrich KN, et al. Prenatal bisphenol A exposure and early childhood behavior. *Environ Health Perspect* 2009;117:1945.
33. Jedrychowski W, Perera F, Mauger U, et al. Intrauterine exposure to lead may enhance sensitization to common inhalant allergens in early childhood: a prospective prebirth cohort study. *Environ Res* 2011;111:119-24.
34. Grandjean P, Weihe P, White RF, et al. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol* 1997;19:417-28.
35. Grandjean P, Weihe P, White RF, Debes F. Cognitive performance of children prenatally exposed to "safe" levels of methylmercury. *Environ Res* 1998;77:165-72.
36. Davidson PW, Strain J, Myers GJ, et al. Neurodevelopmental effects of maternal nutritional status and exposure to methylmercury from eating fish during pregnancy. *Neurotoxicology* 2008;29:767-75.
37. Lederman SA, Jones RL, Caldwell KL, et al. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. *Environ Health Perspect* 2008;116:1085.
38. Herbstman JB, Sjödin A, Kurzon M, et al. Prenatal exposure to PBDEs and neurodevelopment. *Environ Health Perspect* 2010;118:712-9.
39. Wu K, Xu X, Liu J, Guo Y, Li Y, Huo X. Polybrominated diphenyl ethers in umbilical cord blood and relevant factors in neonates from Guiyu, China. *Environ Sci Technol* 2009;44:813-9.
40. Sagiv SK, Thurston SW, Bellinger DC, Tolbert PE, Altshul LM, Korrick SA. Prenatal organochlorine exposure and behaviors associated with attention deficit hyperactivity disorder in school-aged children. *Am J Epidemiol* 2010;171:593-601.
41. Verhulst SL, Nelen V, Den Hond E, et al. Intrauterine exposure to environmental pollutants and body mass index during the first 3 years of life. *Environ Health Perspect* 2009;117:122.
42. Jacobson JL, Jacobson SW. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. *N Engl J Med* 1996;335:783-9.
43. Washino N, Saijo Y, Sasaki S, et al. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. *Environ Health Perspect* 2009;117:660-7.
44. Steinmaus C, Miller MD, Smith AH. Perchlorate in drinking water during pregnancy and neonatal thyroid hormone levels in California. *Journal of Occupational and Environmental Medicine* 2010;52:1217.
45. Rauh VA, Garfinkel R, Perera FP, et al. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. *Pediatrics* 2006;118:e1845-59.
46. Rauh V, Arunajadai S, Horton M, et al. Seven-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. *Environ Health Perspect* 2011;119:1196-201.
47. Whyatt RM, Rauh V, Barr DB, et al. Prenatal insecticide exposures and birth weight and length among an urban minority cohort. *Environ Health Perspect* 2004;112:1125.
48. Cohn BA, Cirillo PM, Christianson RE. Prenatal DDT exposure and testicular cancer: a nested case-control study. *Arch Environ Occup Health* 2010;65:127-34.
49. Wigle DT, Arbuckle TE, Turner MC, et al. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. *Journal of Toxicology and Environmental Health, Part B: Critical Reviews* 2008;11:373-517.
50. Swan SH, Liu F, Hines M, et al. Prenatal phthalate exposure and reduced masculine play in boys. *Int J Androl* 2010;33:259-69.
51. Swan SH, Main KM, Liu F, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environ Health Perspect* 2005;113:1056.
52. Latini G, De Felice C, Presta G, et al. In utero exposure to di-(2-ethylhexyl) phthalate and duration of human pregnancy. *Environ Health Perspect* 2003;111:1783.
53. Engel SM, Zhu C, Berkowitz GS, et al. Prenatal phthalate exposure and performance on the Neonatal Behavioral Assessment Scale in a multiethnic birth cohort. *Neurotoxicology* 2009;30:522-8.
54. Ahmed P, Jaakkola JJK. Exposure to organic solvents and adverse pregnancy outcomes. *Human reproduction* 2007;22:2751.
55. Wilkins Haug L. Teratogen update: toluene. *Teratology* 1997;55:145-51.
56. Jones HE, Balster RL. Inhalant abuse in pregnancy. *Obstetrics and gynecology clinics of North America* 1998;25:153-67.
57. Woodruff TJ, Carlson A, Schwartz JM, Giudice LC. Proceedings of the summit on environmental challenges to reproductive health and fertility: executive summary. *Fertil Steril* 2008;89:e1-20.
58. Morin NJ. Annual chemical production in the United States. Washington, DC: Federal Reserve Board; 2011.
59. US Environmental Protection Agency. TSCA chemical substance inventory: basic information. Washington, DC: USEPA; 2011.
60. US Environmental Protection Agency; Overview. Office of Pollution Prevention and Toxics Programs. Washington, DC: USEPA; 2007. Available at: <http://www.epa.gov/oppt/pubs/oppt101c2.pdf>. Accessed Feb. 14, 2012.
61. US Environmental Protection Agency. Master testing list: introduction. Washington, DC: USEPA; 2011. Available at: <http://www.epa.gov/opptintr/chemtest/pubs/mtlintro.html>. Accessed Feb. 14, 2012.
62. Vogel SA, Roberts JA. Why the toxic substances control act needs an overhaul, and how to strengthen oversight of chemicals in the interim. *Health Aff (Millwood)* 2011;30:898-905.
63. Wilson MP, Schwarzman MR. Toward a new US chemicals policy: rebuilding the foundation to advance new science, green chemistry, and environmental health. *Environ Health Perspect* 2009;117:1202-9.
64. Stephenson JB, US Government Accountability Office. Actions are needed to improve the effectiveness of EPA's Chemical Review Program: testimony before the Committee on Environment and Public Works, US Senate. Washington, DC: US Government Accountability Office; 2006.
65. Council on Environmental Health. Chemical-management policy: prioritizing children's health. *Pediatrics* 2011;127:983-90.
66. Landrigan PJ, Goldman LR. Children's vulnerability to toxic chemicals: a challenge and opportunity to strengthen health and environmental policy. *Health Aff (Millwood)* 2011;30:842-50.
67. American Medical Association. Resolution 404: modern chemicals policies. proceedings of the american medical association house of

delegates: 157th Annual Meeting. Chicago: American Medical Association; 2008.

68. US Environmental Protection Agency. Essential principles for reform of chemicals management legislation. Washington, DC: USEPA; 2010. Available at: <http://www.epa.gov/oppt/existingchemicals/pubs/principles.html>. Accessed Feb. 14, 2012.

69. Safer Chemicals HFC. The health case for reforming the toxic substances control act, 2011 (vol 2011). Available at: http://www.americanchemistry.com/s_acc/sec_article_acc.asp?CID=2178&DID=9939. Accessed Feb. 14, 2012.

70. American Chemistry Council. 10 principles for modernizing TSCA, 2011 (vol 2011). Available at: http://www.americanchemistry.com/s_acc/sec_article_acc.asp?CID=2178&DID=9939. Accessed Feb. 14, 2012.

71. Woodruff TJ, Zeise L, Axelrad DA, et al. Meeting report: moving upstream—evaluating adverse upstream end points for improved risk assessment and decision-making. *Environ Health Perspect* 2008;116:1568-75.

72. Barr DB, Bishop A, Needham LL. Concentrations of xenobiotic chemicals in the maternal-fetal unit. *Reprod Toxicol* 2007;23:260-6.

73. Rollin HB, Rudge CV, Thomassen Y, Mathee A, Odland JO. Levels of toxic and essential metals in maternal and umbilical cord blood from selected areas of South Africa: results of a pilot study. *J Environ Monit* 2009;11:618-27.

74. Stern AH, Smith AE. An assessment of the cord blood: maternal blood methylmercury ratio: implications for risk assessment. *Environ Health Perspect* 2003;111:1465-70.

75. Reuben SH, President's Cancer Panel. Reducing environmental cancer risk: what we can do now. Bethesda: National Cancer Institute; 2010.

76. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, et al. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocr Rev* 2009;30:293-342.

77. Jaga K, Dharmani C. Global surveillance of DDT and DDE levels in human tissues. *Int J Occup Med Environ Health* 2003;16:7-20.

78. Solomon GM, Weiss PM. Chemical contaminants in breast milk: time trends and regional variability. *Environ Health Perspect* 2002;110:A339-47.

79. National Research Council (US); Committee on the Health Risks of Phthalates. National Academies Press (US); 2008.

80. Crain DA, Janssen SJ, Edwards TM, et al. Female reproductive disorders: the roles of endocrine-disrupting compounds and developmental timing. *Fertil Steril* 2008;90:911-40.

81. Grandjean P, Bellinger D, Bergman A, et al. The Faroes statement: human health effects of developmental exposure to chemicals in our environment. *Basic Clin Pharmacol Toxicol* 2008;102:73-5.

82. Woodruff TJ, Janssen SJ, Guillette LJ, Giudice LC. Environmental impacts on repro-

ductive health and fertility. Cambridge; New York: Cambridge University Press; 2010.

83. Newbold R, Heindel J. Developmental exposures and implications for disease. In: Woodruff TJ, Janssen SJ, Guillette LJ, Giudice LC, eds. Environmental impacts on reproductive health and fertility. Cambridge, UK: Cambridge University Press; 2010.

84. Miller MD, Marty MA, Arcus A, Brown J, Morry D, Sandy M. Differences between children and adults: implications for risk assessment at California EPA. *Int J Toxicol* 2002;21:403-18.

85. Rice D, Barone S Jr. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. *Environ Health Perspect* 2000;108(suppl):511-33.

86. US Food and Drug Administration. This week in FDA history: July 15, 1962. Washington, DC: USFDA; 2009. Available at: <http://www.fda.gov/AboutFDA/WhatWeDo/History/ThisWeek/ucm117836.htm>. Accessed Feb. 14, 2012.

87. McBride WG. Thalidomide and congenital abnormalities. *Lancet* 1961;2:291-3.

88. McBride WG. Thalidomide embryopathy. *Teratology* 1977;16:79-82.

89. Hoover RN, Hyer M, Pfeiffer RM, et al. Adverse health outcomes in women exposed in utero to diethylstilbestrol. *N Engl J Med* 2011;365:1304-14.

90. Newbold RR. Lessons learned from perinatal exposure to diethylstilbestrol. *Toxicol Appl Pharmacol* 2004;199:142-50.

91. Palmer JR, Wise LA, Hatch EE, et al. Prenatal diethylstilbestrol exposure and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15:1509-14.

92. Kavlock RJ, Daston GP, DeRosa C, et al. Research needs for the risk assessment of health and environmental effects of endocrine disruptors: a report of the US EPA-sponsored workshop. *Environ Health Perspect* 1996;104(suppl):715-40.

93. The Endocrine Disruption Exchange. TEDX list of potential endocrine disruptors. Paonia, CO: 2011. Available at: <http://www.endocrinedisruption.com/endocrine.TEDXList.overview.php>. Accessed Feb. 14, 2012.

94. Colborn T, Dumanoski D, Myers JP. Our stolen future. New York: Penguin Books USA, Inc; 1997.

95. Colborn T, vom Saal FS, Soto AM. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environ Health Perspect* 1993;101:378-84.

96. Miller MD, Marty MA. Impact of environmental chemicals on lung development. *Environ Health Perspect* 2010;118:1155-64.

97. Chevrier J, Eskenazi B, Holland N, Bradman A, Barr DB. Effects of exposure to polychlorinated biphenyls and organochlorine pesticides on thyroid function during pregnancy. *Am J Epidemiol* 2008;168:298-310.

98. Miller MD, Crofton KM, Rice DC, Zoeller RT. Thyroid-disrupting chemicals: interpreting up-

stream biomarkers of adverse outcomes. *Environ Health Perspect* 2009;117:1033-41.

99. The Endocrine Society. Position statement: endocrine-disrupting chemicals. Chevy Chase, MD: Endocrine Society; 2009.

100. Herbstman JB, Sjodin A, Apelberg BJ, et al. Determinants of prenatal exposure to polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in an urban population. *Environ Health Perspect* 2007;115:1794-800.

101. Crofton KM. Thyroid disrupting chemicals: mechanisms and mixtures. *Int J Androl* 2008;31:209-23.

102. Cory-Slechta DA. Studying toxicants as single chemicals: does this strategy adequately identify neurotoxic risk? *Neurotoxicology* 2005;26:491-510.

103. Slotkin TA, Seidler FJ, Fumagalli F. Exposure to organophosphates reduces the expression of neurotrophic factors in neonatal rat brain regions: similarities and differences in the effects of chlorpyrifos and diazinon on the fibroblast growth factor superfamily. *Environ Health Perspect* 2007;115:909-16.

104. Weinhold B. Epigenetics: the science of change. *Environ Health Perspect* 2006;114:A160-7.

105. Ferguson-Smith AC. Genomic imprinting: the emergence of an epigenetic paradigm. *Nat Rev Genet* 2011;12:565-75.

106. Cassidy SB, Schwartz S, Miller JL, Driscoll DJ. Prader-Willi syndrome. *Genet Med* 2012;14:10-26.

107. Lalande M, Calcianno MA. Molecular epigenetics of Angelman syndrome. *Cell Mol Life Sci* 2007;64:947-60.

108. Pilsner JR, Hu H, Ettinger A, et al. Influence of prenatal lead exposure on genomic methylation of cord blood DNA. *Environ Health Perspect* 2009;117:1466-71.

109. Woodruff T. Bridging epidemiology and model organisms to increase understanding of endocrine disrupting chemicals and human health effects. *J Steroid Biochem Mol Biol* 2011;127:108-17.

110. Solomon G, Janssen S. Talking with patients and the public about endocrine-disrupting chemicals. *Endocr Disrupt Chem* 2007;289-307.

111. Solomon GM, Janssen SJ. Communicating with patients and the public about environmental exposures and reproductive risk. In: Woodruff TJ, Janseen SJ, Guillette LJ, Giudice LC, eds. Environmental impacts on reproductive health and fertility. Cambridge, UK: Cambridge University Press; 2010:214-26.

112. Wu N, McClean MD, Brown P, Aschengrau A, Webster TF. Participant experiences in a breastmilk biomonitoring study: a qualitative assessment. *Environ Health* 2009;8:4.

113. Wilson SE, Baker ER, Leonard AC, Eckman MH, Lanphear BP. Understanding preferences for disclosure of individual biomarker results among participants in a longitudinal birth cohort. *J Med Ethics* 2010;36:736-40.

114. Etzel RA, Balk SJ, American Academy of Pediatrics Committee on Environmental Health. Pediatric environmental health. Elk Grove Village, IL: American Academy of Pediatrics; 2003.
115. Chicago Consortium for Reproductive Environmental Health in Minority Communities. Prenatal environmental exposure history. Chicago, IL, 2011. Available at: http://www.hektoen.org/crehm/documents/crehm_hx_final%204-09.pdf. Accessed Feb. 14, 2012.
116. Agency for Toxic Substances and Disease Registry. Taking an exposure history. Atlanta: 2011. Available at: <http://prhe.ucsf.edu/prhe/pdfs/ATSDR%20CSEM%20Taking%20an%20Exposure%20History%20SS3046.pdf>. Accessed Feb. 14, 2012.
117. Huffling K. Environmental Exposure Assessment, 2011. Available at: http://www.healthandenvironment.org/partnership_calls/9910?res. Accessed Feb. 14, 2012.
118. Reigart R, Roberts J. Chapter 3. Environmental and occupational history. In: US Environmental Protection Agency. Recognition and treatment of pesticide poisoning. Washington, DC: USEPA; 1999.
119. Ondeck M, Focareta J. Environmental hazards education for childbirth educators. *J Perinat Educ* 2009;18:31-40.
120. 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;114:260-3.
121. Rudel RA, Gray JM, Engel CL, et al. Food packaging and bisphenol A and bis(2-ethylhexyl) phthalate exposure: findings from a dietary intervention. *Environ Health Perspect* 2011;119:914-20.
122. Ji K, Lim Kho Y, Park Y, Choi K. Influence of a five-day vegetarian diet on urinary levels of antibiotics and phthalate metabolites: a pilot study with "Temple Stay" participants. *Environ Res* 2010;110:375-82.
123. Adler NE, Stewart J. Reducing obesity: motivating action while not blaming the victim. *Milbank Q* 2009;87:49-70.
124. Organic Trade Association. Industry statistics and projected growth. Brattleboro, VT: 2010.
125. Bailin PS, Byrne M, Lewis S, Liroff R. Public awareness drives market for safer alternatives: bisphenol a market analysis report. Falls Church, VA: Investor Environmental Health Network; 2008.
126. Layton L. Wal-Mart turns to 'retail regulation' to ban flame retardant. *The Washington Post*. Feb. 27, 2011 A-4.
127. Miller M, Solomon G. Environmental risk communication for the clinician. *Pediatrics* 2003;112:211-7.
128. Trasande L, Newman N, Long L, et al. Translating knowledge about environmental health to practitioners: are we doing enough? *Mt Sinai J Med* 2010;77:114-23.
129. Gould R, Russell C. Taking action to prevent harm. *San Francisco Med* 2010;83:27-9.
130. Parker CL. Slowing global warming: benefits for patients and the planet. *Am Fam Physician* 2011;84:271-8.
131. Centers for Disease Control and Prevention. Fourth national report on human exposure to environmental chemicals. Atlanta: Centers for Disease Control; 2009.
132. Eskenazi B, Rosas LG, Marks AR, et al. Pesticide toxicity and the developing brain. *Basic Clin Pharmacol Toxicol* 2008;102:228-36.
133. Sutton P, Wallinga D, Perron J, Gottlieb M, Sayre L, Woodruff T. Reproductive health and the industrialized food system: a point of intervention for health policy. *Health Aff (Millwood)* 2011;30:888-97.
134. Health Care Without Harm. Healthy food pledge [Internet]. Reston, VA: Health Care Without Harm; [cited 2010 Dec 15]. Available at: http://www.noharm.org/us_canada/issues/food/pledge.php. Accessed Feb. 14, 2012.
135. Commission on the Precautionary Principle. Communication from the commission on the precautionary principle. Brussels: European Commission; 2000. Available at: http://ec.europa.eu/environment/docum/20001_en.htm. Accessed Feb. 14, 2012.
136. Raffensperger C, Tickner J. Protecting public health and the environment: implementing the precautionary principle. Washington, DC: Island Press; 1999.
137. Dix DJ, Houck KA, Martin MT, Richard AM, Setzer RW, Kavlock RJ. The ToxCast program for prioritizing toxicity testing of environmental chemicals. *Toxicol Sci* 2007;95:5-12.
138. Lein P, Locke P, Goldberg A. Meeting report: alternatives for developmental neurotoxicity testing. *Environ Health Perspect* 2007;115:764-8.
139. Stokstad E. Putting chemicals on a path to better risk assessment. *Science* 2009;325:694-5.
140. Judson RS, Houck KA, Kavlock RJ, et al. In vitro screening of environmental chemicals for targeted testing prioritization: the ToxCast project. *Environ Health Perspect* 2010;118:485-92.
141. Martin MT, Mendez E, Corum DG, et al. Profiling the reproductive toxicity of chemicals from multigeneration studies in the toxicity reference database. *Toxicol Sci* 2009;110:181-90.
142. National Research Council. Toxicity testing in the 21st century: a vision and a strategy. Washington, DC: The National Academies Press; 2007.
143. Weiss B, Cory-Slechta D, Gilbert SG, et al. The new tapestry of risk assessment. *Neurotoxicology* 2008;29:883-90.
144. Callahan MA, Sexton K. If cumulative risk assessment is the answer, what is the question? *Environ Health Perspect* 2007;115:799-806.
145. Wilson MP, Chia DA, Ehlers BC. Green chemistry in California: a framework for leadership in chemicals policy and innovation. *New Solut* 2006;16:365-72.
146. Woodruff TJ, Sutton P, The Navigation Guide Work Group. An evidence-based medicine methodology to bridge the gap between clinical and environmental health sciences. *Health Aff (Millwood)* 2011;30:931-7.
147. Halvorson GC. Electronic medical records and the prospect of real time evidence development. In: McClellan MB, McGinnis JM, Nabel EG, Olsen LM, eds. Institute of Medicine Annual Meeting: evidence-based medicine and the changing nature of health care. Washington, DC: The National Academies Press; 2007:128-32.