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SPECIAL COMMUNICATION

International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals☆

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ABSTRACT

Exposure to toxic environmental chemicals during pregnancy and breastfeeding is ubiquitous and is a threat to healthy human reproduction. There are tens of thousands of chemicals in global commerce, and even small exposures to toxic chemicals during pregnancy can trigger adverse health consequences. Exposure to toxic environmental chemicals and related health outcomes are inequitably distributed within and between countries; universally, the consequences of exposure are disproportionately borne by people with low incomes. Discrimination, other social factors, economic factors, and occupation impact risk of exposure and harm. Documented links between prenatal exposure to environmental chemicals and adverse health outcomes span the life course and include impacts on fertility and pregnancy, neurodevelopment, and cancer. The global health and economic burden related to toxic environmental chemicals is in excess of millions of deaths and billions of dollars every year. On the basis of accumulating robust evidence of exposures and adverse health impacts related to toxic environmental chemicals, the International Federation of Gynecology and Obstetrics (FIGO) joins other leading reproductive health professional societies in calling for timely action to prevent harm. FIGO recommends that reproductive and other health professionals 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, and champion environmental justice.

1. Introduction

Widespread exposure to toxic environmental chemicals threatens healthy human reproduction. Industrial chemicals are used and discarded in every aspect of daily life and are ubiquitous in food, water, air, and consumer products. Exposure to environmental chemicals and metals permeates all parts of life across the globe. Toxic chemicals enter the environment through food and energy production, industrial emissions and accidents, waste, transportation, and the making, use, and disposal of consumer and personal care products.

For example, the industrialized food system is a major contributor to the introduction of toxic chemicals—from pesticides to plastics—into the environment [1]. Food is also a major pathway of exposure to environmental chemicals from human activities unrelated to agriculture [1]. Mercury pollution, primarily from the burning of coal, has far-reaching effects across the planet, including remote ecosystems [2]. Approximately 3 billion people in low-income countries are exposed to indoor air pollution from cooking and heating their homes using open fires and simple stoves that burn biomass (e.g. wood, animal dung, and

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crop waste) and coal [3]. Furthermore, in 2010, more than 8.6 million people were at risk of exposure to industrial pollutants at 373 toxic waste sites in India, Indonesia, and the Philippines alone [4].

World chemical manufacturing has grown rapidly over the past 40 years [5,6], with production projected to increase by 3.4% annually until 2030 [6]. There are now 70 000–100 000 chemicals in global commerce; approximately 4800 "high-production-volume chemicals" constitute the vast majority in global production [6,7]. Global pesticide use in agriculture reached 2.4 billion kg in 2007 [8]. In 2012, 9.5 trillion pounds (4.31 trillion kg) of industrial chemicals were manufactured in or imported into the USA [9]—equivalent to more than 30 000 pounds (13 000 kg) for every American.

The geography of chemical production is shifting away from high-income countries and toward low-income countries. By 2020, it is anticipated that low-income countries will lead the world in growth rate for high-volume chemicals [5,10]. The Organisation for Economic Co-operation and Development's outlook for environmental trends to 2030 identifies hazardous chemicals and waste as a "red-light" issue—i.e. not well managed, in a bad or worsening state, and requiring urgent attention [6].

2. Vulnerable people, communities, and populations

The potential health impact of a low-dose exposure to a toxic chemical is not the same for everyone. Communities as well as individuals vary in their vulnerability and in their risk for exposure. In addition to the timing and amount of exposure, risk depends on whether a person or population is in good or poor health, the presence or absence of other environmental chemical exposures and other stressors, and on other factors such as sex and genes [11,12]. In recognition of the fact that some are more vulnerable to toxic chemicals than others, the US National Academy of Sciences has concluded that, in the absence of evidence to the contrary, any level of exposure should be assumed to be potentially harmful—i.e. that there is no "safe dose" [11].

Exposure to toxic environmental chemicals and related health outcomes are inequitably distributed among populations within countries as well as between countries. For example, there is a higher burden of toxic exposures and resulting adverse health outcomes among Indigenous peoples in Canada, the USA, and other countries [13,14]. Poverty and exposure to toxic chemicals are tightly interwoven, and the nature of the risks and hazards of toxic chemicals vary by a country's level of development [15]. For instance, the rate of lower respiratory infections attributable to environmental causes is more than twice as high among low-income countries (42%) than among high-income countries (20%) [16]. Moreover, at every stage of development, the consequences of exposure to toxic chemicals—including morbidity and mortality, loss of family income and productivity, and environmental degradation—are disproportionately borne by people with low incomes [15].

Commerce and trade agreements influence the production and transfer of toxic chemicals within and across borders [17,18]. Occupational disparities also impact risk. For example, women and men exposed in the workplace to solvents, formaldehyde, ethylene oxide, anesthetic gases, pesticides, antineoplastic drugs, or to metals are at high risk for adverse reproductive health outcomes [19,20]. Racism, discrimination, and other social factors that can increase stress also influence exposures and associated health outcomes [21–23].

Preconception and prenatal exposure to toxic chemicals is a critical issue for both women and men of childbearing age. Women and men of reproductive age can encounter toxic chemicals at home, in the community, and in the workplace. Chemicals get into the body through breathing, eating, drinking, and/or penetration of the skin. Chemicals in pregnant women can also cross the placenta. For certain chemicals, such as methyl mercury, the levels in the fetus can be greater than those in the mother [24]. Furthermore, toxic chemicals can enter breastmilk after delivery: persistent organic pollutants and metals are found in the breastmilk of women around the world [25,26]. Once toxic chemicals enter the body, the reproductive health impacts can be many, can be varied, and can manifest across the lifespan of individuals and future generations.

3. Nature and extent of prenatal and preconception exposure to toxic environmental chemicals

A wide body of scientific evidence shows that the in utero environment is a critical bridge to future health outcomes [27]. Susceptibility to potential health impacts of toxic environmental chemicals may be heightened when exposure occurs during "critical" and "sensitive" periods of development, such as during pregnancy, childhood, and adolescence [28–32]. Although exposure to toxic chemicals at any point in life can be potentially harmful, there are time-specific vulnerable windows of human development when environmental factors, including nutrition, toxic chemicals, and other stressors, can dramatically alter developmental programming signals [29,33]. For example, prenatal exposure to lead, methyl mercury, or the pesticide chlorpyrifos interferes with one or more critical periods of human development leading to developmental neurotoxicity [34]. Consequently, even small exposures during a window of vulnerability can trigger adverse health consequences that can manifest across the life span of individuals and generations [29,31,35,36].

Exposure to toxic chemicals during pregnancy and lactation is ubiquitous. Research based on representative sampling of the population at large [37] has documented that virtually every pregnant woman in the USA has at least 43 different environmental chemicals in her body. Persistent organic pollutants are found in pregnant and lactating women across the globe [25,38,39]. A report by the US National Cancer Institute found that "to a disturbing extent babies are born 'pre-polluted'" [40].

4. Health impacts of preconception and prenatal exposure to toxic environmental chemicals

A key adverse health impact of ubiquitous exposure to environmental chemicals is disruption of hormones that regulate healthy human reproduction and development [41]. The potential for delayed onset of diseases due to prenatal exposure to hormonally active exogenous chemicals is firmly established by studies of the daughters and sons of pregnant women who took the drug diethylstilbestrol, a potent synthetic estrogen [42,43]. Although the mothers who took diethylstilbestrol seemed healthy, the drug caused a wide range of health impacts that became apparent only decades after the initial exposure, including clear cell adenocarcinoma of the vagina and cervix, structural reproductive tract anomalies, infertility, poor pregnancy outcomes, and breast cancer among prenatally exposed daughters [44], and hypospadias among prenatally exposed sons [45–47]. Similar relationships between environmental exposures incurred during pregnancy and adverse health impacts in later life have been documented in the field of human nutrition and in studies of wildlife [41,48–50].

Rates of non-communicable diseases (NCDs) such as cancer, cardiovascular disease, chronic respiratory disease, and diabetes are increasing, and the high rate of NCDs seen in high-income countries is now also emerging as a health crisis among middle- and low-income countries [51,52]. The global rise in the rate of NCDs encompasses increases in diseases and conditions related to the endocrine system—e.g. low semen quality, genital malformations, preterm birth and low birth weight, neurobehavioral disorders associated with thyroid disruption, endocrine-related cancers, early onset of breast development in young girls, and type 2 diabetes [41]. These trends have occurred in a timeframe inconsistent with a much slower pace of changes in the human genome, indicating that the environment has shaped these disease patterns [53].

The 2012 WHO/United Nations Environment Programme State of the Science on Endocrine Disrupting Chemicals states that "[c]lose to 800 environmental chemicals are known or suspected to be capable of interfering with hormone receptors, hormone synthesis, or hormone conversion" [41]. The document then explains that only a small fraction of these 800 chemicals has been tested for their capacity to affect the endocrine system of intact organisms [41]. Further, "[t]he vast majority of chemicals in current commercial use have not been tested at all" [41].

A wide range of adverse reproductive health impacts is associated with prenatal exposure to environmental chemicals that are currently in wide use, as well as exposure to chemicals such as polychlorinated biphenyls, which have been banned for decades but which persist in the environment. As compiled by the American College of Obstetricians and Gynecologists (ACOG) and the American Society for Reproductive Medicine (ASRM) [19], documented links between prenatal exposure to environmental chemicals and adverse health outcomes span the life course and include, but are not limited to, impacts on fertility and pregnancy, neurodevelopment, and cancer.

Box 1 presents examples of documented links between various health impacts and exposure to a toxic environmental chemical.

Box 1
Adverse health outcomes linked with preconception and prenatal exposure to environmental chemicals.[a]

Fertility and pregnancy

- Decreased semen quality with PCBs [54]
- Spontaneous abortion and fetal loss with solvents [55–58]
- Impaired fetal growth with pesticides [59]
- Fetal loss, low birth weight, and preterm delivery with air pollutants [60–66]
- Decreased fetal and birth weight, and congenital malformations with toluene [67–69]
- Shortened gestational age with phthalates [70]
- Low birth weight with PCBs [71]
- Reduced birth weight and fetal growth with perfluorinated compounds [72,73]

Neurodevelopment

- Impaired cognitive and neurodevelopment, increase in attention problems and attention deficit hyperactivity disorder behaviors at age 5 years, and reduction in working memory capabilities at age 7 years with pesticides [74–77]
- Impaired neurodevelopment in girls and reduction in executive function at age 4–9 years with phthalates [78,79]
- Intellectual impairment with lead [80]
- Reduced cognitive performance, impaired neurodevelopment, and reduced psychomotor outcomes with methyl mercury [81–85]
- Decreased placental expression of genes implicated in normal neurodevelopmental trajectories with increasing in utero exposure to fine particle air pollution [86]
- Reduced intelligence quotient score and a wide range of attention and executive function deficits with PCBs [87–91]
- Impaired neurodevelopment and reduction in sustained attention with polybrominated diphenol ethers [92,93]
- Attention problems at age 6–7 years with polycyclic aromatic hydrocarbons [94,95]
- Aggression and hyperactivity in girls, and reduction in executive functioning skills in girls aged 3 years with bisphenol A [96,97]

Cancer

- Maternal breast cancer risk with PCBs [98]
- Increased childhood cancers and susceptibility to testicular cancer with pesticides [99–101]

Abbreviation: PCB, polychlorinated biphenyl.

[a] Updated on the basis of the ACOG/ASRM Committee Opinion Exposure to Toxic Environmental Agents [19].

5. Global health and economic burden related to toxic environmental chemicals

The global health and economic burden related to toxic environmental chemicals is in excess of millions of deaths and billions of dollars every year. Exposure to ambient and household air pollution results in at least 7 million deaths a year worldwide [102]. The costs of pesticide poisonings over 15 years (2005–2020) among farm workers on small land holdings in 37 Sub-Saharan African countries are estimated by United Nations Environment Programme to be US$66 billion [103]. A 2015 analysis of the European Union's costs attributable to exposure to a select sample of endocrine-disrupting chemicals with only the highest probability of causation was conservatively estimated to be on average €157 billion per year [104–107]. In Nordic countries, adverse male reproductive effects due to routine exposure to endocrine-disrupting chemicals, including pesticides and the use of personal care or other consumer products, are estimated to cost €36 million per year of exposure [108]. In the USA, the cost of childhood diseases related to environmental toxins and pollutants in air, food, water, and soil, as well as in homes and neighborhoods, was calculated to be $76.6 billion in 2008 [109]. When exposures are widespread, even low-level environmental exposures can have large society-wide adverse consequences for health [110]. The available data underestimate the true burden of human disease, disability, and expenditures, and do not account for the impacts of toxic chemicals on the ecosystem that sustains human health and reproduction.

On the basis of accumulating evidence of exposures and adverse health impacts related to toxic environmental chemicals, including the potential for intergenerational harm, leading reproductive health professional societies have called for timely action to identify and reduce exposures and to address the consequences of such exposures [19,32,111,112].

6. Recommendation for prevention

Preconception and prenatal exposure to toxic chemicals in food, water, air, and consumer products is a determinant of maternal, child, and adult health worldwide. The International Federation of Gynecology and Obstetrics (FIGO) joins ACOG/ASRM [19], the Royal College of Obstetricians and Gynaecologists [111], the Endocrine Society [32,112], and the Society of Obstetricians and Gynaecologists of Canada in urging obstetricians, gynecologists, midwives, nurses, women's health nurse practitioners, and other reproductive health professionals to take timely action to prevent exposure to toxic environmental chemicals.

Reducing the disease burden of toxic environmental exposures from food, air, water, and other sources of pollution will contribute importantly to advancing the UN Millennium Development Goals of eradicating extreme poverty and hunger, reducing child mortality, improving maternal health, and ensuring environmental sustainability [16].

Successful strategies for prevention involve mutually reinforcing activities at the patient, healthcare provider, healthcare institution, and societal levels [19]. FIGO recognizes that clinical settings provide only limited time to address all the complexities of maternal and child health, and that by the time a woman sees a health professional for prenatal care, preventable exposures may have already occurred. Furthermore, individuals alone can do little to impact many exposures, such as air and water pollution. For example, improved public policy has been essential to reducing exposure to environmental tobacco smoke [113]. In addition, external factors may limit the capacity of individuals to make healthier choices [114]. As such, FIGO encourages prevention measures that support broad-based policy changes in exposure to toxic environmental chemicals that will lead to "prevention for all."

FIGO recommends that obstetricians, gynecologists, midwives, women's health nurse practitioners, nurses, and other health professionals should:

- Advocate for policies to prevent exposure to toxic environmental chemicals. Toxic chemicals and pollution move around the world in air, water, food, and consumer products; local, national, and/or international governmental policies can either support or undermine patient and population health associated with these exposures. Health professionals should actively engage in partnerships within their communities and nations, and across the globe to advance policies that effectively prevent exposure to toxic chemicals. Recommendations for protection of maternal and children's health from toxic chemicals would equally apply to reproductive health [115].
- Work to ensure a healthy food system for all. Healthy food is powerful medicine. Policies and practices among patients, healthcare providers and institutions, and societies that foster a healthy food chain should be encouraged, including drinking water free of toxic chemicals. This includes increasing the capacity for women and men who are planning a family, as well as pregnant and breastfeeding women, to eat fresh fruits and pesticide-free vegetables, legumes, and wholegrains daily, to avoid fast foods and other processed foods whenever possible, and to limit foods high in animal fat and fish containing methylmercury (e.g. shark, swordfish, king mackerel, and tilefish) [19,116].
- Make environmental health part of health care. Professionals should learn about the toxic chemicals and other harmful environmental exposures common in patients' communities and workplaces. Environmental exposure histories should be taken during preconception and first prenatal visits. Patients should be educated about how to avoid toxic environmental chemicals and providers should learn about resources in the community that can assist in education. Environmental hazards should be reported to appropriate agencies. Efforts now underway to ensure "Health Care Without Harm"—to transform the health sector worldwide so that it becomes ecologically sustainable and a leading advocate for environmental health and justice [117]—should be advanced. For example, healthcare institutions can play a critical role in preventing exposure to toxic chemicals by choosing clean energy and using purchasing power to shift the market towards safer alternatives to toxic chemicals in construction, food purchasing, and consumer products.
- Champion environmental justice. Exposure to toxic chemicals is a global phenomenon. However, as identified by ACOG and ASRM, "many environmental factors harmful to reproductive health disproportionately affect vulnerable and underserved populations and are subsumed in issues of environmental justice" [19]. "Environmental justice" is defined by the US Environmental Protection Agency as

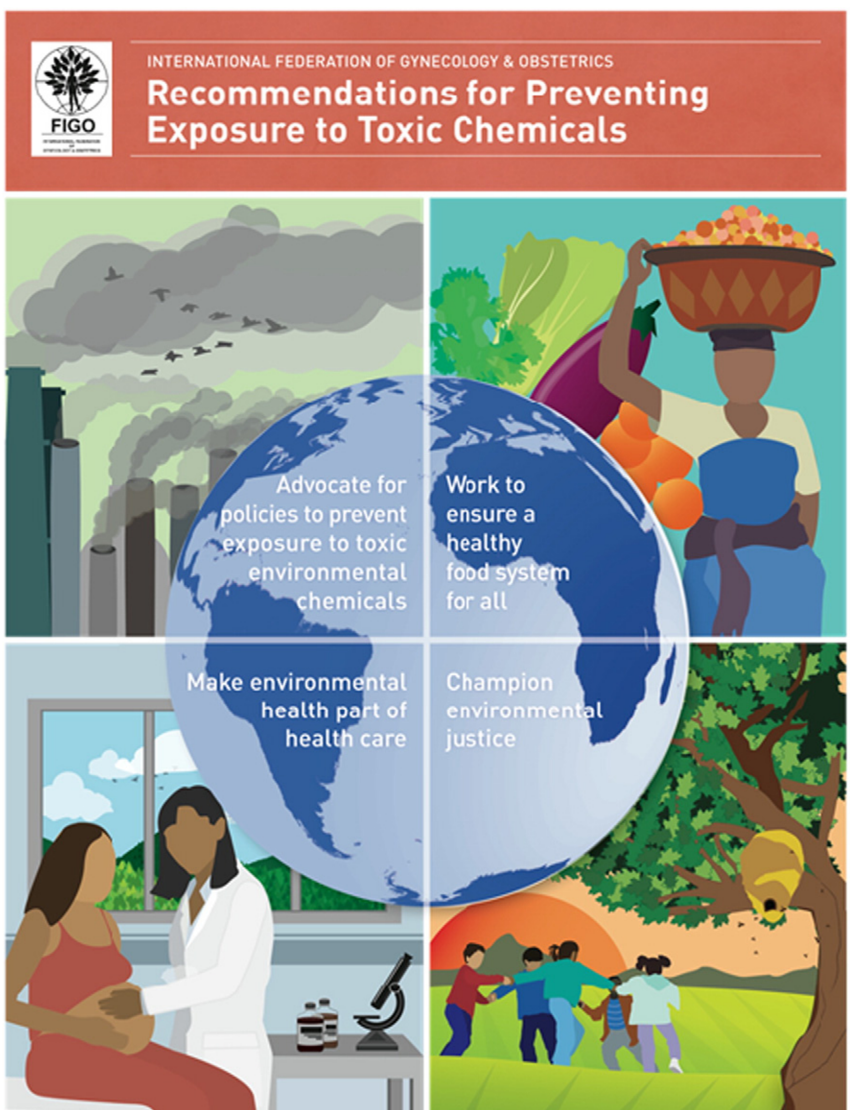

Fig. 1. FIGO's recommendations for healthcare providers.

"the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies" [118]. Health professionals who practice in high- and low-income countries should recognize that segments of their patient population likely bear a disproportionate burden of exposure to toxic chemicals, and they should champion policies and practices that secure environmental justice on a global scale.

FIGO's recommendations are portrayed in Fig. 1.

7. Conclusions

1. Exposure to toxic environmental chemicals is a feature of everyday life across the planet, and it harms the capacity for healthy human reproduction.
2. Preventing exposure to environmental chemicals is a priority for reproductive health professionals everywhere.
3. Environmental chemicals cross borders through trade, food, wind, and water, and there are inequities and injustices in how toxic chemicals move about the world.
4. A global perspective is needed to ensure equity and health for all.
5. Policies to address toxic chemicals must shift the burden of proof of safety of chemicals from the individual healthcare provider, the patient, and the public to the manufacturers before they are released into the environment.
6. Policies that address toxic chemicals should not result in the transfer of harmful exposures between and among current and future populations, but must protect the health of all vulnerable populations.
7. Policies that address toxic chemicals must protect the environment that sustains the potential for human existence across generations; human health and ecosystem health are mutually dependent on each other.

Conflict of interest

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