

Environmental influences on reproductive health: the importance of chemical exposures

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Chemical exposures during pregnancy can have a profound and life-long impact on human health. Because of the omnipresence of chemicals in our daily life, there is continuous contact with chemicals in food, water, air, and consumer products. Consequently, human biomonitoring studies show that pregnant women around the globe are exposed to a variety of chemicals. In this review we provide a summary of current data on maternal and fetal exposure, as well as health consequences from these exposures. We review several chemical classes, including polychlorinated biphenyls, perfluoroalkyl substances, polybrominated diphenyl ethers, phenols, phthalates, pesticides, and metals. Additionally, we discuss environmental disparities and vulnerable populations, and future research directions. We conclude by providing some recommendations for prevention of chemical exposure and its adverse reproductive health consequences. (*Fertil Steril*® 2016;106:905–29. ©2016 by American Society for Reproductive Medicine.)

Key Words: Chemical, environmental chemical, environmental exposure, pregnancy, reproductive health

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Scientific evidence has shown the adverse impacts of exposure to toxic environmental chemicals to human reproduction (1). Chemical exposures, especially during critical and sensitive windows of development such as pregnancy, can lead to a myriad of health consequences that can manifest across individuals' lifespan and potentially be transmitted to future generations (1, 2). Chemical exposures that occur during pregnancy can cross the placenta and can accumulate in the fetus (3). Accordingly, the next generations are born "prepolluted" (4) owing to these preconception and prebirth exposures. Preventing

harmful exposures to environmental chemicals is, therefore, a priority for reproductive health professionals around the world (5).

Industrial chemicals are present in our daily life and are ubiquitous in food, water, air, and consumer products. World chemical manufacturing has grown rapidly over the past few decades (6, 7), with a projected 3.4% annual rate in production increase until 2030 (7). Among the estimated 70,000–100,000 commercially available chemicals, almost 5,000 of them are produced in volumes exceeding 1 million tons per year (8). In the United States, the total reported production volume (domestically

manufactured and imported) of industrial chemicals in 2012 was 9.5 trillion pounds (4.31 trillion kg)—equivalent to more than 30,000 pounds (13,000 kg) for every American (5, 9). As of 2016 more than 65,000 chemical substances are listed for use by the US Environmental Protection Agency (10). Approximately 3,000 of these chemicals have annual production and importation above 1 million pounds (11). Unlike pharmaceuticals that require extensive in vitro and in vivo toxicity testing as well as human experimental studies before entering the marketplace and clinic, existing and new synthesized industrial chemicals currently can enter the marketplace, homes, schools, workplaces, and communities with only limited or even no assessment on their reproductive or other related toxic effects (12, 13). Recently (June 2016), President Obama signed the Frank R. Lautenberg Chemical Safety for the 21st Century Act, an amendment to the Toxic Substances Control Act (TSCA), which is the main law by which the government oversees industrial chemicals.

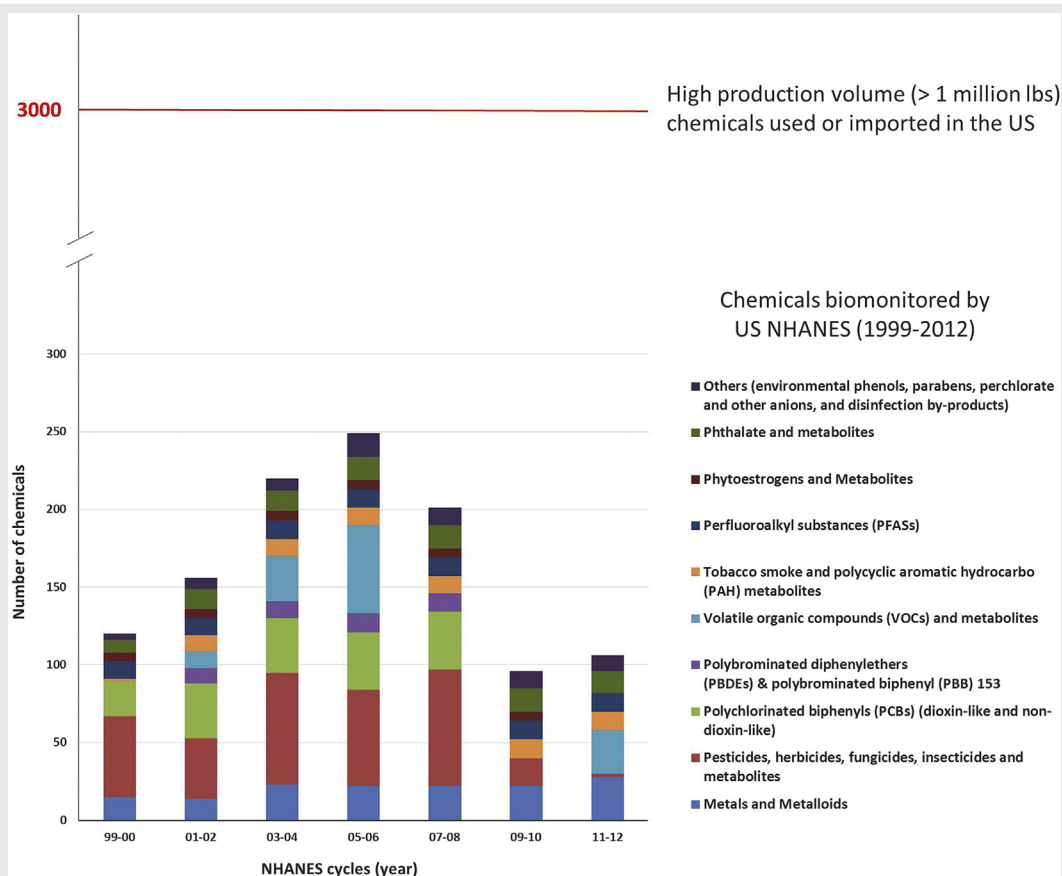
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FIGURE 1



Chemicals that are biomonitored by the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2012 based on the CDC 4th National Report on Human Exposure to Environmental Chemicals (Updated Tables, February 2015) and CDC NHANES website (www.cdc.gov/nchs/nhanes.htm) as of April 2016. Note: There will be more chemicals added for some biannual cycles in the future, especially later cycles, owing to delay in data analyses and releasing. Not all the chemicals currently biomonitored by NHANES are high production volume chemicals.

Wang. Environmental exposures and pregnancy. *Fertil Steril* 2016.

While there are significant changes, the law still does not require minimum set of data to be produced by manufacturers for new or existing chemicals, and its effectiveness remains to be evaluated. Further, there are not comprehensive data on where chemicals are used, so it is difficult to identify sources of exposures and the extent of exposures in the population. There are some data sources that allow characterization of certain exposures, such as air pollution monitoring, some monitoring of fish, and some portion of the water and food supply (14). In the United States there is a national biomonitoring program run by the US Center for Disease Control and Prevention (CDC) using the National Health and Nutrition Examination Survey (NHANES), which has increased the number of chemicals biomonitored over the past 15 years (Fig. 1) (15, 16).

Although we have made great progress in understanding the importance of chemicals in reproductive health and understanding exposures to pregnancy, we still have yet to comprehensively understand the full scope of the exposures and outcomes that may affect reproductive health. Understanding exposures is critical to both identify potential health risks and identify opportunities for intervention and preven-

tion of harmful chemical exposures. It is being increasingly recognized in numerous initiatives, including the Exposome (17), Precision Medicine Initiative (18), Genes, Environment and Health Initiative (19), and Children's Health Exposure Analysis Resource (20). Thus, using illustrative examples, this article aims to review the current evidence on environmental chemical exposures, including synthetic chemicals and metals, in pregnant women. We first provide an updated view on the relationship between environmental chemical exposure during pregnancy and potential adverse health consequences. We then summarize the current knowledge on the maternal body burden and fetal exposure to different environmental chemicals. After discussion on environmental disparities and future research directions, we conclude the article with recommendations for prevention of chemical exposure and its adverse health consequences.

HEALTH CONSEQUENCES OF PRENATAL CHEMICAL EXPOSURE

Chemical exposures have been linked to a range of adverse reproductive and developmental outcomes, including fertility-

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