Environmental Contaminants and Reproductive Health

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Environment: production of chemicals has increased dramatically over past 60 yr; ≥43 chemicals measurable in pregnant women; some disturbing health trends have been observed over same period of time, including increase in childhood obesity, asthma, behavioral and/or learning problems, low birth weight, gestational diabetes, autism, and infertility

Endocrine disruptor: refers to substance that interferes with normal hormonal activity; includes some metals, industrial chemicals, and naturally occurring substances

Bisphenol A (BPA): endocrine disruptor commonly found in plastics and carbonless receipts used in grocery stores; BPA binds to estrogen receptor; 4 million tons of BPA produced annually in United States; compound functions as estrogen agonist or antagonist; epidemiologic studies—showed that executive function impaired in 3-yr-olds born to mothers exposed to BPA; these offspring, particularly girls, found to have increased anxiety, depressive symptoms, and impaired regulation of behavior; study of workers in factory that produced BPA—found reproductive effects in men

Phthalates: used to increase softness and pliability of plastics; endocrine disruptor with estrogen-like effects; study—investigated phthalates in pregnant women; anogenital index (AGI; distance between scrotum and anus; indicator of estrogen exposure in fetus) measured in male offspring; AGI normally higher in boys than in girls; study found that feminization of AGI had increased exposure to phthalates in utero—associated with decreased participation in masculine play in boys

Polybrominated diphenyl ethers (PBDEs): used as flame retardant in foam of upholstered furniture, plastic casing of electronics, and electronic wiring; PBDEs detected in food supply, especially fatty foods; levels of flame retardant in blood positively correlated with adverse outcomes in pregnancy, including low birth weight

Role of obstetrician: effects of most chemicals subtle; in most cases, lifetime of exposure required to cause cancer or other damage; survey showed that most practicing obstetricians in United States unlikely to ask about environmental exposure; however, research has shown that pregnant women want to know about exposure even if implications for health undetermined; American College of Obstetricians and Gynecologists—promotes education about chemical exposure; obstetricians should develop cross-disciplinary partnerships and refer patients to specialists when issues arise

Legislation: advocacy—obstetricians may advocate for patients before legislative bodies; societal change possible; examples—levels of lead in children decreased after lead ban; in California, levels of flame retardants in pregnant women decreased after statewide ban in 2006; proactive approach—despite these successes, improved approach to protecting population desirable; current approach to improving environment remains reactive; manufacturers of banned substances often synthesize new chemicals that may be no less harmful than banned chemicals; introducing regulations similar to those governing pharmaceutical industry could increase amount of testing done before chemicals introduced to market and encourage postmarketing studies

Decreasing exposure to chemicals: decreased levels of pesticides detected in patients who eat organic diets; decreased levels of BPA detected in patients who eat organic diets; decreased levels of PBDEs detected in pregnant women—levels of lead in children decreased after ban on leaded gasoline; in California, levels of flame retardants in pregnant women decreased after statewide ban in 2006; proactive approach—despite these successes, improved approach to protecting population desirable; current approach to improving environment remains reactive; manufacturers of banned substances often synthesize new chemicals that may be no less harmful than banned chemicals; introducing regulations similar to those governing pharmaceutical industry could increase amount of testing done before chemicals introduced to market and encourage postmarketing studies

What patients can do

Produce: patients may choose organic foods; Environmental Working Group (EWG) publishes annual list of “dirty dozen” (foods likely to be high in pesticide residue) and “clean 15” (foods likely to be low in pesticide residue); patients for whom organic shopping economically burdensome may concentrate on these lists

Packaging: substantial contact with plastic occurs in canned foods, sodas, and wet foods in plastic pouches or boxes; #3, #6, and #7 plastics probably worse than others; #1, #2, #4, and #5 probably less risky; plastics should not be placed in microwave because they may leach chemicals, especially into fatty foods

Fish: small fish usually have lower levels of mercury than large fish; amount of mercury in tuna debated; Food and Drug Administration recommends ≤1 serving/wk, but Consumer Reports has stated that tuna now contains increased levels of mercury and may be unsafe

Carbonless receipts: patients may decline receipt if not needed; patients who work in grocery store or similar environment

Educational Objectives
The goal of this program is to decrease the risk for poor reproductive health associated with environmental contaminants and advanced maternal age. After hearing and assimilating this program, the clinician will be better able to:

1. Explain the impact of chemical exposure on reproductive health.
2. Counsel patients about reducing the risk for exposure to chemicals during pregnancy.
3. List adverse pregnancy outcomes associated with advanced maternal age.
4. Explain the association between assisted reproductive technology and improved pregnancy outcomes.

5. Evaluate a woman >35 yr of age who is considering pregnancy.

Faculty Disclosure
In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose.
handling receipts should wear gloves and wash hands before eating; wearing gloves markedly decreases exposure.

Pesticides and solvents in household: alternative cleaning agents should be used; use of pesticides in home to control insects undesirable.

Personal care products: patients should avoid phthalates, fragrances with triclosan, and risky solvents; susceptibility higher in small and pubertal children than in adults; information about specific substances available from EWG app.

Dust: many chemicals found in household dust; dusting, vacuuming, and mopping helpful; removing shoes before entering home helps prevent noxious substances from being tracked into house (this practice particularly important in agricultural areas and urban neighborhoods, where exposure to outdoor toxins increasingly likely).

Old foam furniture: offending flame retardants most common in furniture manufactured from mid 1970 to 2005; such flame retardants also found in food containing animal fat (patients advised to reduce consumption of these foods).

Tobacco smoke: should be avoided; pregnant women especially should avoid secondhand smoke; safety of e-cigarettes undetermined, and many contain flavorings, phthalates, and other potentially harmful chemicals.

Lead: occupational exposure should be discussed; lead abatement should be done carefully to avoid aerosolizing lead; other sources of lead include treatments and pottery glaze from Mexico, treatments from Asia including cold remedies marketed for babies and children, and ayurvedic treatments and cosmetics from Middle East; lipstick contains small amounts of lead.

Resources: brochures and other resources available for patients with concerning occupational or home exposure or questions about exposure; patients can contact local Pediatric Environmental Health Specialty Units (pehsu.net) run by Environmental Protection Agency and Centers for Disease Control (CDC); CDC to offer app to help obstetricians educate patients about chemicals.

Suggested Reading


Updates on Advanced Maternal Age

Kirsten E. Salmeen, MD, Assistant Professor; Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, School of Medicine.

Definition: advanced maternal age (AMA) traditionally defined as 35 yr of age; this age represents point at which risk for pregnancy loss due to amniocentesis equivalent to risk for trisomy 21, and age after which rates of spontaneous conception fall dramatically; however, comparing risk for pregnancy loss with that for trisomy 21 not apt; advances in pregnancy screening have decreased the need for amniocentesis, and assisted reproductive technologies (ART) have improved; therefore, AMA should be seen as continuum rather than defined by specific age cutoff.

Risk factors: AMA may be associated with other risk factors such as maternal comorbidities, infertility, and multiple gestations related to ART.

Incidence and prevalence: In United States, 15% of births occur in women >35 yr of age and 3% of births occur in women >40 yr of age; incidence of AMA has increased slowly over past 15 yr.

Aneuploidy: risk for chromosomal anomalies increases 10-fold from 35 to 45 yr of age; rare autosomal dominant conditions associated with advanced paternal age.

Miscarriage: risk for spontaneous abortion in first trimester 40% at 40 yr of age and 80% at 45 yr of age; ART — appears to modify this risk; in 40-yr-old women using their own eggs during ART, risk for miscarriage reduced from 40% to 30%; in 45-yr-old women using their own eggs during ART, risk for miscarriage reduced from 80% to 65%; reduction in risk may be related to fact that women undergoing ART have embryo, and pregnancies with profound aneuploidies may not proceed to embryonic stage; ART associated with improvements in uterine lining that promote successful pregnancy regardless of source of egg; ART using donor eggs considerably improves pregnancy outcomes; =50% of women who undergo ART with donor eggs have successful pregnancy, regardless of age; ART clearly decreases risk for spontaneous abortion.

Perinatal morbidity: preterm birth, low birth weight, placenta previa, gestational diabetes, preeclampsia, and small-for-gestational-age infants associated with AMA, especially in women >40 yr of age; in United States, some risks difficult to assess because births in women >45 yr of age uncommon; studies offering estimates of perinatal risk difficult to interpret if underlying risk factors not controlled for.

Nonchromosomal congenital anomalies: AMA associated with 1.5- to 2-fold increase in risk; First and Second Trimester Evaluation of Risk (FASTER) trial found that AMA associated with minimal increase in risk for preterm birth, whereas different trial found significant increase.

Low birth weight: association between AMA and low birth weight underdetermined.

Preeclampsia: in observational trial of women >50 yr of age that did not include comparison group, rate of preeclampsia 35%.

Gestational diabetes: FASTER trial found that AMA associated with significant increase in risk for gestational diabetes, but other trials have not confirmed this.

Placenta previa: risk increases with age; 3-fold increase in risk demonstrated after adjusting for ART.

Cesarean delivery: some studies have found rates of 70% to 80% in older gravida; common indications for cesarean delivery include active phase arrest, arrest of descent, and non-reassuring fetal heart rate tracing; rate of elective cesarean delivery increased in AMA; risk factors for cesarean delivery include egg donation, which suggests that obstetricians may manage these patients differently than they do other women; study — oocyte recipients compared with controls who underwent IVF using own eggs; oocyte recipient status associated with increased frequency of cesarean delivery (odds ratio 2.78), and each additional year of maternal age associated with 13% increase in odds for cesarean delivery; assessment — AMA, and particularly donor oocyte status, not an indication for cesarean delivery.

Timing of delivery: study of ≈4000 patients — assessed association between intrauterine fetal demise (IUFD) and AMA; in women >40 yr of age, risk for IUFD increased after 40 wk gestation; large study sponsored by National Institute of Child Health and Human Development — hazard ratio for stillbirth at 41 wk gestation 0.75/1000 in younger women; same hazard ratio observed at 39 to 40 wk gestation in older women; assessment — fetuses of women >40 yr of age may benefit from earlier induction of labor.
Other risks associated with advanced maternal age: reported risks include increased probability of stay in intensive care unit, myocardial infarction, pulmonary edema, venous thromboembolism, postpartum depression, anxiety, and difficulty breastfeeding.

Assisted reproductive technologies: prevalence of ART in women >40 yr of age undetermined, but may exceed 90%; up to 30% of pregnancies conceived using ART result in twins, and 3% result in triplets; risk for monozygotic twinning also increased; ART associated with increased birth defects (relative risk 1.4), several perinatal risk factors, and increased rate of cesarean delivery.

Underlying health problems: some observed risks associated with MMA may be related to advancing age itself; risk for death increases sharply from 35 to 50 yr of age; leading causes of death in this population include heart disease, diabetes, and hypertension; rates of obesity, hypertension, and diabetes increase with increasing age; >60% of women >45 years of age have diabetes or prediabetes; rates of breast and colon cancers increase with increasing age.

Management: preconception evaluation — may include hemoglobin A1c, fasting glucose, thyroid-stimulating hormone, mammography, electrocardiography, lipid panel, blood pressure, and cardiac stress test; women should understand their risk for heart disease before undertaking pregnancy; hypertension and diabetes manageable, but severe heart disease may pose significant risk during pregnancy; early pregnancy evaluation — mode of conception should be ascertained because perinatal risk higher in women conceiving with ART; fetal number and chorionicity should be assessed; screening should include thyroid-stimulating hormone, glucose, and baseline laboratory studies for preeclampsia; when genetic counseling offered, adjustments for age of oocyte donor may be necessary; aspirin prophylaxis — aspirin reduces risk for preeclampsia by 17% in high-risk women; aspirin recommended in women >40 years of age who have other risk factors such as diabetes or hypertension; despite lack of randomized trials, aspirin should be prescribed for women >45 yr of age, for whom benefit likely outweighs risk; prenatal care — should include detailed fetal anatomic survey, fetal echocardiography if indicated, repeat glucose tolerance testing, third-trimester evaluation for fetal growth, and antenatal testing due to increased risk for IUFD; planning labor — mode of delivery should be discussed; labor and delivery need not be managed differently in older women; indications for cesarean delivery same in older gravidas as in younger women; induction of labor should be considered between 39 and 40 wk gestation.

Summary: age-related risks in pregnancy multifactorial; in women considering ART, strategies to minimize multiple gestations should be encouraged; multiple gestation more than doubles risk in AMA

**Suggested Reading**


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REPRODUCTIVE HEALTH

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1. According to a study, which of the following chemicals is(are) associated with feminization of the anogenital index in male offspring?
   (A) Bisphenol A (BPA)  (B) Phthalates  (C) Polybrominated diphenyl ethers (PBDEs)  (D) All the above

2. Which of the following chemicals is(are) used as a flame retardant?
   (A) BPA  (B) Phthalates  (C) PBDEs  (D) All the above

3. Which of the following organizations publishes an annual list of foods likely to be high in pesticide residue known as the “dirty dozen”?
   (A) Centers for Disease Control  (B) Environmental Protection Agency  (C) Food and Drug Administration  (D) Environmental Working Group

4. A person who eats an abundance of canned soup is at increased risk for contact with:
   (A) Mercury  (B) Plastic  (C) Lead  (D) Triclosan

5. In the United States, _______ of births occur in women >35 yr of age.
   (A) 3%  (B) 10%  (C) 15%  (D) 20%

6. From 35 to 45 yr of age, the risk for chromosomal anomalies increases:
   (A) 2.5-fold  (B) 5-fold  (C) 10-fold  (D) 15-fold

7. Assisted reproductive technology (ART) in advanced maternal age (AMA) is associated with a decreased risk for spontaneous abortion.
   (A) True  (B) False

8. AMA is associated with a 3-fold increase in risk for _______ after adjusting for ART.
   (A) Low birth weight  (B) Gestational diabetes  (C) Placenta previa  (D) Preeclampsia

9. The prevalence of ART in women >40 yr of age is estimated to be:
   (A) ≈25%  (B) ≈40%  (C) ≈65%  (D) ≈90%

10. Which of the following may pose a significant risk during pregnancy?
    (A) Hypertension  (B) Severe heart disease  (C) Diabetes  (D) A and C

Answers to Audio Digest Obstetrics/Gynecology Volume 62, Issue 23: 1-C, 2-D, 3-C, 4-B, 5-A, 6-A, 7-C, 8-D, 9-A, 10-D

Attention, CME/CE Participants

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