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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Handheld Ultrasound for Assessing Fetal Size

By John C. Hobbins, MD

Professor, Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora

Dr. Hobbins reports no financial relationships relevant to this field of study.

SYNOPSIS: A recent study has shown abdominal circumference assessments with a portable handheld ultrasound machine to be superior to standard fundal height measurements in the prediction of small for gestational age and large for gestational age fetuses in utero and infants at birth.

SOURCE: Haragan AF, et al. Diagnostic accuracy of fundal height and handheld ultrasound-measured abdominal circumference to screen for fetal growth abnormalities. *Am J Obstet Gynecol* 2015;212:820-822.

Fundal height measurements for assessment of fetal growth have been the staple of providers seemingly forever, and there probably is not an obstetrical examining room in the country that does not have a paper tape measure within arm's length of the exam table. Now, there may be another clinical tool housed in the same area: a new portable handheld ultrasound device.

A team from the University of South Carolina pitted the tape measure against this mini-ultrasound instrument on 251 patients who were between 21 and 40 weeks' gestation. The idea was to see which method was a better predictor of aberrant fetal growth. Each patient studied had a fundal height (FH) measurement by an experienced provider. Any measurement of > 3 cm above gestational age (in cm per week) was considered large for gestational age (LGA). If the measurement was < 3 cm from gestational age, it was labeled as small for gestational age (SGA). In the same patients, a handheld ultrasound device was used by another provider to assess the abdominal circumference (HHAC). LGA was defined as an abdominal circumference > 95th percentile and SGA was < 10th percentile. All patients then had an estimated fetal weight (EFW) later by a registered sonographer using standard equipment and a commonly used formula. At birth, an infant weighing > 90th percentile for gestational age and gender was considered LGA and one weighing < 10th percentile was SGA.

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The results showed a high correlation (R = 0.939, *P* = < 0.001) between the HHAC and the EFW and abdominal circumference by the formal ultrasound examination. Seven fetuses (2.8%) were defined as LGA and seven fetuses (2.8%) were SGA by the formal ultrasound EFW. At the time of birth, 9.56% were LGA and 10.7% were SGA. Sensitivities for in utero SGA (by EFW) were 100% and 42.8% for HHAC and FH, respectively. Specificities were 85.2% vs 92.6%. For in utero (EFW) LGA, sensitivities were 57.1% vs 71.4% for the HHAC and FH. Regarding each technique's ability to screen for SGA at birth, the sensitivities for HHAC, FH, and EFW were 74%, 37%, and 21.4%, respectively. In the same order, specificities for SGA at birth were 89.7%, 95%, and 99.5%, respectively. For predicting LGA babies at birth, the HHAC had a sensitivity and specificity of 66.7% and 89.9%, compared with FH of 50% and 66.9%, respectively.

In short, the HHAC had the highest sensitivities of all methods when it came to screening for SGA in utero (low EFW) or at birth, but it did so at the highest false-positive rate of 15% and 11%, respectively. The FH picked up only 42.8% of SGAs in utero and 37% at birth. The huge surprise for me was how poorly the ultrasound EFW performed with screening sensitivities at birth for SGA of 21.4% and LGA of 25%.

■ COMMENTARY

Fundal height indirectly reflects everything in the uterus, while abdominal circumference goes right to a portion of the fetus that directly relates to how scrawny or corpulent he or she is. In fact, in fetuses that are labeled as SGA by EFW, I am always more interested in the abdominal circumference, which is always small (< the 5th percentile) in true SGA or large (> 95th percentile) in true LGA. The EFW formula can be skewed by a fetus with a head size or femur length that is well outside the mean for gestation — neither reflecting in most cases the nutritional status of the fetus. Also, the biparietal diameter and head circumference, two of the four components of the common formula used to calculate EFW, are often subject to error because of compression due to the fetal position or, late in pregnancy, the head being deep in the pelvis.

This study certainly makes the case for the use of small modern-day devices to screen for fetal size, and at the same time it could check amniotic fluid volume, monitor fetal behavior through biophysical profile, and quickly assess fetal heart rates, etc. This could even become the modern-day obstetrical provider's stethoscope. (Remember that prop that we now dust off occasionally to hang around our necks for PR pictures?) However, before jumping on this bandwagon, we have to think about one important item: cost.

These gadgets, marketed mostly to emergency department physicians, come in various sizes and some sell for < $5000. Online, I found one in particular that blew me away. The ad featured a small cordless transducer that talks to an iPad. With corporate competition, the cost of these ultrasound mini-machines may even drop down to a point where it would be affordable as a pocket accessory, coordinated to the color of every provider's scrub suit — the preferred clothing option of todays' physicians. For the time being, the paper tape measure still is useful, especially if this is in the hands of an experienced provider who can use this information in conjunction with clinical acumen. More than anything, however, this study shows how useful the abdominal circumference alone is in assessing fetal size. ■

ABSTRACT & COMMENTARY

Good News for a Change: No Association of Hormonal Replacement Therapy with Breast Cancer Before Age 50

By Jeffrey T. Jensen, MD, MPH

SYNOPSIS: Using data from the Two Sister Study, investigators found no association of past combined hormone replacement therapy with young-onset (before age 50) breast cancer, and a protective effect with estrogen-only therapy.

SOURCE: O'Brien KM, et al. Hormone therapy and young-onset breast cancer. *Am J Epidemiol* 2015;181:799-807.

To evaluate the impact of hormone replacement therapy (HT) on young-onset (< 50 year old) breast cancer, the authors used the Sister Study, a prospective cohort study of 50,884 women without breast cancer who had a full or half sister who had been diagnosed with breast cancer. Sister Study participants were enrolled between 2003 and 2009 and were 35-74 years of age living in the United States or Puerto Rico. A case-control study was performed. Cases were diagnosed with breast cancer within the past 4 years and before 50 years of age, and controls were full sisters of cases. After exclusions (e.g., sisters had to be within 7 years of age), there were 1419 eligible cases and 1665 eligible controls in the Two Sister Study sample. Cases included both invasive and in situ cancers. Participants were asked whether they had ever used any form of HT, and if so, the type of therapy and ages at which they started and stopped. Women who exclusively used creams, suppositories, or gels were considered nonusers. HT users were further subdivided according to duration of use (< 2 years vs ≥ 2 years), age at first use (< 40 years vs ≥ 40 years), and timing of first use relative to menopause. Since cases tended to be younger than controls, the investigators used propensity scores to adjust for differences in the opportunity to use HT. The authors used conditional logistic regression to estimate crude and adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the associations of each type of HT with breast cancer risk, using nonusers as the common reference. The adjusted models included birth order, menopausal status, presence of menopausal symptoms, hysterectomy/oophorectomy status, and length of recall between a woman's interview age and HT exposure assessment age.

Only 11% of controls and 8% of cases reported any use of HT. Of these, most (7% controls, 4% cases) used estrogen-only therapy (E-HT) with smaller proportions (4%, 2%) using estrogen plus progestin (EP-HT) therapy. As expected, use of HT was associated with early menopause, bilateral oophorectomy, and menopausal symptoms. Overall, the use of EP-HT was not associated with young-onset breast cancer (aOR, 0.80; 95% CI, 0.41-1.59). Adjustment for duration or recency of use and age at first use did not measurably modify the associations. In contrast, E-HT use was associated with protection against young-onset breast cancer (aOR, 0.58; 95% CI, 0.34-0.99). Of interest, the use of progestin-only HT was associated with a statistically nonsignificant increased risk of young-onset breast cancer (aOR, 1.51; 95% CI, 0.76-3.00).

The authors concluded that neither EP-HT nor E-HT increases the risk of young-onset breast cancer and that E-HT might be associated with a reduced risk.

■ COMMENTARY

According to the American Cancer Society, approximately 25% of breast cancers are diagnosed in women younger than age 50 years.[1] Previous research on whether hormonal therapy increases the risk of early breast cancer has been inconclusive. Shantakumar et al[2] found an increased risk with EP-HT (aOR, 3.51; 95% CI, 1.45-8.49) but not E-HT (aOR, 1.17; 95% CI, 0.23-5.88), and Palmer et al[3] also reported a nonsignificant increased risk for women younger than 50 years of age who took E-HT for at least 5 years (relative risk [RR], 1.6; 95% CI, 0.3-8.5). In contrast, Nelson et al[4] found a reduction in risk in women ages 40-49 years who did not have a uterus and reported HT use (likely E-HT). Results from the O'Brien study add to this literature and are consistent with the main findings in the Women's Health Initiative EP-HT and E-HT studies.

The finding that HT is not associated with early-onset breast cancer risk is highly relevant to clinical practice. First, let's put this into perspective. Although E-HT was associated with protection in this study, we should be highly cautious when epidemiologic studies provide risk estimates of less than two-fold (e.g., an elevation of risk of > 2.0 or reduction in risk of < 0.5). Therefore, the finding that E-HT actually protects women against breast cancer should be viewed with suspicion. However, the reduction seen is similar to that noted in the Women's Health Initiative (WHI) E-HT arm. Anderson et al found that the use of estrogen only for a median of 5.9 years was associated with a significantly lower incidence of invasive breast cancer compared with placebo (hazard ratio [HR], 0.77; 95% CI, 0.62-0.95), with no significant difference in risk reduction in those women diagnosed during the intervention phase (21% decrease) and post-intervention (25% decrease).[5] And even more impressively, fewer of the E-HT-treated women died from breast cancer (HR, 0.37; 95% CI, 0.13-0.91) or from any cause. You should also keep in mind that the magnitude of the effect of protection with E-HT (~60%) is actually larger than the magnitude of widely quoted increased risk with EP-HT (~25%)!

The absence of an increase of early breast cancer with EP-HT in the O'Brien study also provides reassurance. Most epidemiologic studies of this type suffer from recall bias that tends to push the risk estimate in the direction of harm, as women who are "cases" may be more likely to remember exposure than controls. Although the hazard ratio for breast cancer was significantly elevated in the WHI EP-HT arm (HR, 1.24; CI, 1.01-1.54), the magnitude of the increase is small, and statistical significance is lost in most of the subanalyses.[6] Another finding of great interest in the O'Brien study is the nonsignificant elevation of odds of early breast cancer seen in women prescribed EP-HT. The most likely indication would be abnormal uterine bleeding, and the most commonly prescribed drug would be medroxyprogesterone acetate (MPA), the same progestin used in Prempro™, the combination therapy of the WHI. Taken together, these data provide additional evidence against the use of MPA for HT. I recommend oral micronized progesterone or the levonorgestrel intrauterine system (off label) for my postmenopausal patients with a uterus.

So what did you hear from the media about this study? Probably crickets. Even the authors of this study seemed disappointed not to report an elevation of risk; the results

section of the abstract stated "unopposed estrogen use was inversely associated with the risk of young-onset breast cancer" rather than stating the effect was protective. Good news continues to be no news. But this is information you can use in the clinic tomorrow counseling young women faced with the decision of starting HT for premature menopause: Breast cancer risk concern should not be the deciding factor for the use of postmenopausal HT. In particular, for women who undergo surgical menopause at a young age, the results are directly applicable and highly reassuring, particularly if hysterectomy is also planned. ■

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ABSTRACT & COMMENTARY

When Do Combined Oral Contraceptives Start Working After Ulipristal Acetate Emergency Contraception?

By Rebecca H. Allen, MD, MPH

Assistant Professor, Department of Obstetrics and Gynecology, Warren Alpert Medical School of Brown University, Women and Infants Hospital, Providence, RI

Dr. Allen reports she is a Nexplanon trainer for Merck, a Liletta trainer for Actavis, and on the advisory board for Bayer, Actavis, and Vermillion.

SYNOPSIS: In this randomized, controlled trial of the effects of combined oral contraceptives on ovarian activity after taking ulipristal acetate, investigators found that some women needed up to 14 days to achieve ovarian quiescence. Therefore, abstinence or backup contraception should be used during that time.

SOURCE: Cameron ST, et al. The effects on ovarian activity of ulipristal acetate when 'quickstarting' a combined oral contraceptive pill: A prospective, randomized, double-blind, parallel-arm, placebo-controlled study. *Hum Reprod* 2015;30:1566-1572.

This double-blind, randomized, controlled trial was conducted in Scotland, Sweden, and the Netherlands between March and August 2012. Healthy female volunteers aged 18 to 35 years, with a body mass index (BMI) of < 30 kg/m^2 and regular menstrual cycles, were eligible to participate. Exclusion criteria were use of an intrauterine device or progestin-only method of contraception in the past 3 months, use of depot medroxyprogesterone acetate in the past 12 months, breastfeeding, pregnancy within the past 1 month, or any medications that may interact with study drugs. Women could be on combined oral contraceptives (COCs) prior to the trial. Following menses or withdrawal bleeding, transvaginal ultrasound was performed every 2 to 3 days until the lead ovarian follicle was > 13 mm in mean diameter. Women were then randomized to either ulipristal acetate (UPA) 30 mg or placebo. Women were given 1 packet of combined oral contraceptive pills (30 mcg ethinyl estradiol/150 mcg levonorgestrel) to start taking the same time the following day. The lead follicle was then followed every 2 to 3 days and estradiol/progesterone levels were measured until the follicle was ≤ 13 mm. Women kept daily bleeding diaries, and pill packets were checked for compliance. The time it took for women to reach ovarian quiescence (Hoogland score 1 to 3) was calculated. (*See Table 1.*)

Overall, 76 women were recruited and received either UPA (39) or placebo (37). There was no difference between the two groups in age or BMI. Approximately three-quarters of the sample had used COCs in the cycle before treatment. There was no difference between the two groups in terms of the proportion reaching ovarian quiescence by day 7 of COC treatment (17 [70.8%] UPA vs 14 [60.9%] placebo). All women in the study reached quiescence by day 14 of COC treatment. There was no difference between the two groups in the number of women who ovulated, with 12 (32%) in the placebo arm and 13 (33%) in the UPA arm.

■ COMMENTARY

Emergency contraception allows women the chance to prevent pregnancy in case of contraception nonuse or

Table 1

Hoogland Score[1]	Follicular Diameter (mm)	Estradiol (pmol/L)	Progesterone (nmol/L)
No activity	≤ 10	-	-
Potential activity	> 10	-	-
Non-active follicle-like structure	> 13	≤ 100	-
Active follicle-like structure	> 13	> 100	≤ 5
Lutenized unruptured follicle	> 13, persisting	> 100	> 5
Ovulation	> 13, ruptured	> 100	> 5

misuse. UPA is a progesterone receptor modulator that is more effective than levonorgestrel emergency contraception, but only available by prescription in the United States.[2,3] Because repeated acts of intercourse in the same cycle may lead to pregnancy, it is important to resume a regular contraceptive as soon as possible after using emergency contraception.[4] Some women choose to restart combined oral contraceptives immediately after taking UPA. Because UPA is a progesterone receptor modulator, there is a concern that UPA could impact the efficacy of COCs and/or that COCs could impact the efficacy of UPA.

Due to this concern, some experts recommend using abstinence or barrier contraception until the next menses.[4] Other experts recommend that a woman can initiate COCs, but she needs to abstain from sexual intercourse or use barrier contraception for 14 days or until her next menses, whichever comes first.[5] This is to allow 7 days for the UPA to be metabolized out of the body and 7 days for the COCs to induce ovarian quiescence. Given this uncertainty, the manufacturer funded this study to determine whether UPA interferes with COC's ability to induce ovarian quiescence.

This study has several strengths, including the randomized design and objective measure of ovarian activity. However, investigators were unable to determine exactly which day ovulation occurred because ultrasounds were performed only every 2 to 3 days. Nevertheless, this study provides important evidence for the expert opinion recommendations that currently exist in the literature. The Centers for Disease Control Selected Practice Recommendations for Contraceptive Use do suggest abstaining from sexual intercourse or using barrier contraception for 14 days after UPA use if hormonal contraception will be initiated immediately. The concern with waiting until the next menses to start hormonal contraception is that UPA may cause shortened cycles, prolonged cycles, or unscheduled bleeding. This may make identification of next menses confusing for women. In addition, the risk of unintended pregnancy if UPA fails and contraception is delayed needs to be taken into consideration.

Unfortunately, this study was not able to address whether COCs will affect the efficacy of UPA. The manufacturer's U.S. label states (updated March 2015) that because UPA and the progestin component of hormonal contraceptives both bind to the progesterone receptor, using them together could reduce the efficacy of either. After using UPA, they recommend waiting at least 5 days before initiating hormonal contraception.[6] More data are still needed regarding this issue. Given that UPA is superior to levonorgestrel emergency contraception, it should be the preferred oral emergency contraceptive, if available and accessible. Otherwise, let's not forget the copper intrauterine device as an emergency contraceptive that will not interact with hormones and provides both the most effective emergency contraceptive and long-term contraceptive. ■

[Given that ulipristal acetate is superior to levonorgestrel emergecy contraception, it should be the preferred emergency contraceptive, if available and accessible.]

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SPECIAL FEATURE

Environmental Influences on Male Reproductive Function

By Robert W. Rebar, MD

Professor and Chair, Department of Obstetrics and Gynecology, Western Michigan University Homer Stryker MD School of Medicine, Kalamazoo

Dr. Rebar reports no financial relationships relevant to this field of study.

SYNOPSIS: This special feature is intended to provide readers with information needed about the potential impact of the environment and lifestyle on male reproductive function so that they can better take histories and counsel couples presenting with questions about infertility.

The fact that various chemical substances found in the environment can impact reproductive function in men has been known for decades. In 1975, it was proposed that fertility was impaired in male workers exposed to excessive quantities of lead.[1] A few years later, reduced sperm counts were reported in employees working at a plant manufacturing the pesticide 1,2-dibromo-3-chloropropane.[2] In 1993, Colburn and colleagues suggested that endocrine-disrupting chemicals (EDCs), which mimic the effects of endogenous hormones or induce changes in the activity or levels of endogenous steroidogenic hormones, might impact the progeny of those exposed as well as the individuals themselves.[3] In the subsequent years, it has become apparent that EDCs are extremely common, being found in small amounts in foods as pesticides and fumigants, in insecticides and solvents, and as plasticizers in a number of household items. The majority of EDCs act either as an estrogenic substance or as an antiandrogen.

In fact, it is estimated that about 50,000 chemicals are used in consumer products and industrial processes in the United States; however, the actual number is uncertain because chemicals are not registered or proven safe before use.[4] Because the U.S. Environmental Protection Agency must demonstrate that a substance is dangerous after consumer release, only about 300 chemicals have been tested and fewer than 10 have had their usage restricted. Yet it is estimated that 10-30% of chemicals merit additional restrictions because of their risks to health. These numbers emphasize the difficulties in studying the impact of any one chemical on reproductive function.

Coincident with these reports was a series of alarming suggestions that sperm counts were decreasing over time in Western countries.[5,6] Whether there is indeed a worldwide decline in sperm quality remains controversial, but it is certainly plausible given the increasing prevalence of EDCs and remains a reason for concern.

PESTICIDES, BISPHENOL A, AND PHTALATES

As one example, eating produce containing higher quantities of pesticide residue (based on annual USDA reports) appears to be associated with lower sperm counts.[7] Researchers assessed pesticide residues in the diets of 155 men aged 26-51 years who were seen at a Boston fertility clinic and then analyzed these findings in relation to semen quality. Participants consumed a mean of 0.9 daily servings of high-pesticide fruits and vegetables and 2.3 servings of low-to-moderate pesticide produce. Although total produce intake was not associated with semen quality, men in the highest quartile of high-pesticide fruit and vegetable consumption had on average 49% fewer sperm, 32% fewer morphologically normal sperm, and 29% lower ejaculate volumes than men in the lowest quartile. (High-residue produce includes such items as strawberries, peaches, plums, blueberries, apples, pears, spinach, celery, and potatoes; lowest residue produce includes peas, lima beans, grapefruit, prunes, onion, beans or lentils, avocado, and corn.)

Diesters of phthalic acid, commonly called phthalates, have been one continuing source of concern because they are used in so many products, including personal care products (such as makeup, shampoos, and soaps), plastics, paints, and even some pesticides. Phthalates have been shown to disrupt reproductive tract development in male rodents by acting as an antiandrogen.[8] Because a number of studies suggested that prenatal exposure to various phthalates led to significant reductions in the anogenital distance (AGD) in rodents (and the AGD is uniformly less in females than in males in most species), Swan and colleagues[9] measured the AGD and recorded other genital measurements in male infants with varying phthalate exposure and reported that the AGD was also reduced in humans and that phthalates can affect human male reproductive tract development. Very recent studies have indicated that paternal phthalate and bisphenol A (BPA) exposure is associated with excess female births, and maternal phthalate and BPA exposure is associated with excess male births.[10]

EPIGENETIC CHANGES, SPERMATOGENESIS, AND MALE INFERTILITY

Several genes in the testes are regulated through epigenetic programming wherein changes occur in DNA methylation, histone modification, or chromatin remodeling. Alarmingly, it is now clear, for example, that exposure to the antiandrogenic endocrine disruptor vinclozolin (a fungicide that is used on fruits, vegetables, ornamental plants, and turf grass) during embryonic gonadal sex determination

in the rodent can alter this epigenetic programming and affect not only the developing offspring, but also subsequent generations.[11,12] Exposure to vinclozolin leads to transgenerational adult onset disease in the rodent, including spermatogenic defects, prostate disease, kidney disease, and cancer.[13] Might there be similar effects in human males exposed to some EDCs?

CIGARETTE SMOKING, ALCOHOL CONSUMPTION, AND MARIJUANA USE

Effects on human male reproduction do not appear limited to less commonly known chemicals. There are data suggesting that both cigarette smoking and alcohol consumption can affect male reproductive function, at least for those undergoing in vitro fertilization (IVF). Couples (one or both) who ever smoked had an adjusted relative risk (RR) of 2.41 of not achieving a pregnancy by IVF and of 3.76 of not achieving a live birth; couples smoking for more than 5 years had a RR of 4.26 of not achieving a pregnancy.[14] In this study, the number of oocytes retrieved decreased by 40% for couples and 46% for men smoking the week of IVF. It is not clear if the male partner's smoking affected retrieval of oocytes because of exposure of the female partner to tobacco passively or if another mechanism might be involved. A more recent study showed that cigarette smoking resulted in reductions in total testosterone, total sperm count, and progressive motility of sperm in Saudi Arabian men presenting to an infertility clinic.[15] A 2003 study indicated that each additional alcoholic drink (over the recommended 1-2 drinks) each day consumed by the male partner increased the risk of not having a live birth with IVF and gamete intrafallopian transfer.[16] More recent data from a self-administered questionnaire completed by 2545 couples undergoing 4729 cycles of IVF indicated that couples in which both partners drank four or more alcoholic drinks per week had a 21% lower live birth rate than those in which both partners drank less.[17]

Data also indicate that marijuana use by male partners affects reproductive outcomes.[18] If men smoked marijuana 11 to 90 times in their lives, there was a 15% decrease in infant birth weight with IVF and gamete intrafallopian transfer ($P = 0.03$); if they smoked more than 90 times, birthweight was decreased by 23% ($P = 0.01$). That timing of the marijuana use is important and showed that men who smoked in the 15 years previous to IVF had 16% smaller infants ($P = 0.03$).

Presumably these data regarding IVF can be extrapolated to men attempting to reproduce naturally and suggest an effect of cigarette smoking, alcohol, and marijuana on male reproductive function.

PHYSICAL ACTIVITY AND TELEVISION WATCHING

Other aspects of lifestyle also may have an impact on sperm count. In a study of 189 young men aged 18-22 years in Rochester, NY, activity levels and time spent watching television were assessed by questionnaire and correlated with sperm counts.[19] After multivariable adjustment, sperm concentrations in men in the highest quartile for moderate-to-vigorous physical activity (≥ 15 hours per week) were 73% higher than those in the lowest quartile for activity (< 5 hours weekly). In contrast, sperm concentrations in men in the highest quartile of TV watching (> 20 hours weekly) were 44% lower than those in the lowest quartile (0 hours weekly). Interestingly, only sperm concentrations and not sperm motility nor morphology were affected by either parameter.

IVF AND IMPRINTING DISORDERS

It now appears that IVF, with or without intracytoplasmic sperm injection, is associated with a slight increase in the risk of imprinting disorders in the progeny, including Angelman syndrome, Beckwith-Wiedemann syndrome, Silver-Russell syndrome, and isolated hemihypertrophy.[20] Although the relative risk is increased, the likelihood of having an affected child is actually small indeed. Imprinting disorders are the result of altered DNA methylation, and at this time it is not clear if there is an environmental toxicant in the laboratory affecting the egg, the sperm, and/or the early embryo and/or assisted reproduction itself, particularly the handling of the sperm, that increases epigenetic changes. What these data emphasize is that the environment plays a significant role in epigenetic changes in humans as early as the embryonic stage.

CONCLUSION

In our increasingly complex environment, we are exposed to an innumerable number of chemicals and our lifestyles are clearly changing. With the introduction of assisted reproduction, even our methods of reproducing are changing. It is becoming more and more apparent that all of these environmental influences impact reproductive function in men. Although it is true that the same influences discussed also appear to affect reproductive function in females, readers of this publication are more conversant with those changes occurring in women. Because reproduction involves couples, it is important for all obstetrician-gynecologists to be knowledgeable about the effects of various substances and lifestyle habits on male reproductive function as well as of the effects on subsequent progeny. This knowledge should allow clinicians to take more appropriate histories and to provide better counseling to couples with fertility problems. No doubt we will continue to read about new studies in this emerging field and be able to make better use of new information as we acquire it.

From this survey, it is obvious that it is impossible to avoid the many chemicals in common usage today. Still, if the male is involved in handling chemicals toxic to sperm, it certainly makes sense to suggest avoiding them as much as possible, perhaps by even finding alternative employment. With regard to pesticides and plasticizers, it makes sense to attempt to limit exposure, but altering lifestyle and diet dramatically does not seem warranted at this point. Leading an active life and making reasonable food choices seems most prudent. It also makes sense to counsel patients to at least moderate alcohol and tobacco consumption and to avoid the use of illicit drugs. ■

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CME QUESTIONS

1. Which method was the most sensitive in screening for babies born with birth weights below the 10th percentile?
a. Handheld abdominal circumference
b. Formal ultrasound estimated fetal weight
c. Fundal height
d. None was accurate enough to use clinically

2. The results for the Sister Study provide additional evidence that:
a. combined hormone replacement therapy doubles the risk of breast cancer in young women.
b. hormone replacement therapy is not associated with an increased risk of early breast cancer.
c. progestin therapy in the 40s decreases the risk of breast cancer.
d. both estrogen-only and combined hormone therapy increase the risk of early breast cancer.

3. In the study evaluating the interaction between ulipristal acetate and combined oral contraceptives, approximately what proportion of women achieved ovarian quiescence by day 7?
a. 30%
b. 40%
c. 70%
d. 100%

4. Endocrine-disrupting chemicals:
a. are rare in the environment.
b. destroy endocrine glands.
c. commonly act as estrogens or anti-androgens.
d. mimic the action of luteinizing hormone and follicle stimulating hormone.
e. are carefully regulated by the U.S. government.

[IN FUTURE ISSUES]

Morcellation: Has it Improved Outcomes or Put Women at Risk?