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OB/GYN Clinical [ALERT]

Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Treatment and Prevention of Preeclampsia

By John C. Hobbins, MD

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

SYNOPSIS: A recent study suggested that sildenafil could temporarily stabilize patients with preeclampsia, while improving blood flow to and from the placenta.

SOURCE: Trapani A, Goncalves LF, Trapani TF, et al. Perinatal and hemodynamic evaluation of sildenafil citrate for preeclampsia treatment. *Obstet Gynecol* 2016;128:253-259.

Preeclampsia complicates 3-5% of all pregnancies and is the second most common cause of maternal death. Fetal effects can be devastating. Its etiology has been hard to crack. However, recently there have been a flurry of clinical papers dealing with the prediction, prevention, and treatment of preeclampsia. This recent study serves as a catalyst for a short discussion of what is new in preeclampsia investigation.

Trapani et al initiated a double-blind, placebo-controlled trial in Brazil involving 100 patients diagnosed with preeclampsia between 24 and 33 weeks of gestation. One-half were treated with sildenafil every eight hours and the other half received a placebo. All patients had uterine artery, umbilical artery, and middle cerebral artery waveforms obtained before and after treatment. Management and delivery decision-making were conducted by a common protocol. If needed, blood pressures were treated with beta-blockers in addition to methyldopa.

Data were available on all 50 patients in each group. The sildenafil-treated group (SG) spent four more days pregnant (14.4 days vs. 10.4 days; 95% confidence interval, 12.5-16.6). The SG group had a 22.5% and 18.5% reduction in pulsatility indices in the uterine and umbilical arteries, respectively, vs. 2.1% and 2.3% reductions in the controls. Mean maternal arterial pressures were significantly lower after treatment in the SG group. Two patients in the control group and one patient from the SG were dropped from the study because of possible side effects (headaches). There were no differences in immediate neonatal outcomes.

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■ COMMENTARY

A variety of maternal serum markers have been studied, but recently tyrosine kinase and placental growth factor (PGIF) have emerged as being rather efficient late predictors of true preeclampsia in patients suspected of developing the condition.[1] Uterine artery waveforms have fallen in and out of favor through the years as early preeclampsia predictors. Although the data suggest them to be only of modest efficacy as predictors of preeclampsia, in general, these waveforms in the second trimester do identify with good reliability patients destined to have preeclampsia severe enough to warrant delivery prior to 34 weeks.[2,3]

One of the reasons that there has been inconsistent enthusiasm for any predictor of preeclampsia is that attempts to prevent or treat the condition have yielded either unexciting or somewhat confusing results. The one medication that has gotten unfair treatment is low-dose acetylsalicylic acid (ASA). Despite earlier meta-analyses showing efficacy in preventing preeclampsia,[4] it was not until Bujold et al[5] showed that low-dose ASA had its greatest benefit when administered prior to 17 weeks that clinicians began to pay attention.[6] However, not all of the results have been positive. For example, a recent meta-analysis, in which Bujold was an author, suggested no benefit from a lower dose (60 mg) of ASA. Yet, to add to the confusion, in another paper published at about the same time, low-dose ASA was found to be cost-effective in high-risk patients.[7]

So, what is the clinician to think? All in all, the bulk of data do suggest the benefit of low-dose ASA (a baby aspirin of 81 mg) in patients at higher risk for pulmonary thromboembolism. In fact, in an effort to add icing on the cake, another group has even added low molecular weight heparin to an ASA regimen with some success.[8]

Others have attempted to go in another direction. Adult cardiovascular disease has some pathological similarities to preeclampsia, so why not try to approach the condition through that route? In a small pilot randomized trial,[9] the safety of using pravastatin to prevent the condition was seemingly validated. Efficacy studies undoubtedly soon will follow.

This sildenafil study makes some sense since preeclampsia causes peripheral vasoconstriction and, in addition to keeping the process at bay for an average of four days longer than controls, there was evidence sildenafil improved fetal and maternal blood flow on both sides of the placenta and there was a significant drop in maternal blood pressure. Who would have guessed that the very pricey "little blue pill" might have this completely different therapeutic potential?

> […the bulk of data suggest the benefit of low-dose ASA — a baby aspirin of 81 mg — in patients at higher risk for pulmonary thromboembolism….]

There are other preventive and therapeutic investigative activities in process, so stay tuned because breakthroughs may be on the horizon for preeclampsia. ■

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ABSTRACT & COMMENTARY

Early Menopause and CVD Risk: A Call for HRT?

By Jeffrey T. Jensen, MD

SYNOPSIS: A meta-analysis suggests that early menopause increases the risk of cardiovascular disease and all-cause mortality.

SOURCE: Muka T, Oliver-Williams C, Kunutsor S, et al. Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: A systematic review and meta-analysis. *JAMA Cardiol* 2016; Sep. 14. Doi: 10.1001/jamacardio.2016.2415 [Epub ahead of print].

The existing literature supports that menopause increases the risk of cardiovascular disease. However, whether early-onset menopause increases this risk further is controversial. Muka et al conducted a systematic review to identify studies evaluating age of menopause (exposure) and cardiovascular disease risk or mortality (outcomes). The search strategy identified 9,439 unique citations. After excluding reviews, letters, case reports, in vitro or animal studies, and studies without the proper exposure or outcomes, the authors screened 68 full-text manuscripts for eligibility and identified 33 pertinent articles reflecting the results of 32 (24 prospective cohort, two case-control, six cross-sectional) unique studies with data on 342,284 women. All but one of the included studies evaluated cardiovascular disease risk in relation to the age at onset of menopause, and four studies evaluated the risk in relation to time since onset of menopause.

In the pooled meta-analysis, compared to women with onset of menopause at age 45 years or beyond, those with very early onset of menopause younger than 45 years had a significant increase in coronary heart disease risk (adjusted relative risk [RR], 1.50; 95% confidence interval [CI], 1.28-1.76), cardiovascular disease mortality (RR, 1.11; 95% CI, 1.03-1.20), and all-cause mortality (RR, 1.19; 95% CI, 1.08-1.31), but not in stroke risk (RR, 1.23; 95% CI, 0.98-1.53) or stroke mortality (RR, 0.99; 95% CI, 0.92-1.07). In contrast, onset of menopause in the late 40s (45-49 years of age) compared with 50-54 years of age did not significantly increase risk in any of these categories. The results support premature or early-onset menopause as a risk factor for coronary heart disease, cardiovascular disease mortality, and overall mortality.

■ COMMENTARY

Meta-analysis offers many advantages to the investigator, but few rewards to the reader. Combining the results of previous studies yields impressive numbers of subjects and events that can provide statistical significance without the high costs associated with subject recruitment and follow-up in prospective studies, or drudgery of data cleaning and selection of appropriate controls for a case-control study. The routine disclaimer associated with meta-analysis applies to this paper — interpret these results with caution!

Although the paper by Muka et al received some press, the primary references already supported a relationship between early menopause and coronary heart disease risk. Lokkegaard et al used the Danish Nurse Cohort study to obtain data on age at menopause and cardiovascular disease.[1] These authors found that menopause before both age 40 years and 45 years was associated with an increased risk of ischemic heart disease, with the greatest risk seen in women with early oophorectomy. In the U.S. Multi-Ethnic Study of Atherosclerosis cohort of 2,509 women, surgical or natural menopause at age < 46 years of age increased the risk of both coronary heart disease (HR, 2.08; 95% CI, 1.17-3.70) and stroke (RR, 2.19; 95% CI, 1.11-4.32).[2] The meta-analysis extends this work by showing a significant increase in cardiovascular disease mortality and all-cause mortality among women with a very young age (< 45 years) of menopause. Keep in mind that these risk estimates are extremely small (11% for cardiovascular disease death and 19% for all-cause mortality).

So why focus on this paper at all? I presented evidence in last month's *OB/GYN Clinical Alert* from De Kat et al that a high-risk cardiovascular profile may develop during the perimenopause.[3] If so, early menopause may accelerate the progression of disease in women who accumulate cardiovascular risk factors during the perimenopause. Although we should not over-interpret the significance of the findings, death is a very serious outcome.

How should we counsel women with early menopause regarding hormone replacement therapy? In the Danish Nurse Cohort study, ever-use of hormone replacement therapy reduced the risk of cardiovascular disease, but only among those women with very early surgical menopause.[1] However, ever-use is a weak indicator of exposure, and may not reflect the benefit or risk associated with consistent longitudinal exposure. So more studies are needed to confirm benefit. In my practice, I counsel healthy postmenopausal women to strongly consider hormonal therapy, since delaying initiation may allow atherosclerotic changes to develop, increasing the risk of myocardial infarction and stroke.[4] Estrogens reduce the risk of atherosclerotic plaque formation.[5] As I have previously mentioned, as estrogen levels decline, this protection diminishes, and plaque accumulates, particularly in women with unfavorable lipid profiles and other cardiovascular risk factors. Age matters and so does progestogen exposure. The combined data from both the combined (conjugated equine estrogen [CEE]/medroxyprogesterone acetate) and estrogen-

only (CEE) arms of the Women's Health Initiative study showed a nonsignificant reduction in risk of myocardial infarction (RR, 0.76; 95% CI, 0.50-1.16) for women who initiated therapy less than 10 years post-menopause compared to the significant elevation of 1.28 (95% CI, 1.03-1.58) for women who began treatment 20 or more years post-menopause.[6] We also know that women 50-59 years of age randomized to CEE alone in the Women's Health Initiative showed a lower incidence of cardiovascular disease and all-cause mortality than those who received placebo.[7] Although a reduction in these risks was not observed in older women randomized to CEE only, there was no significant increase in risk.

The great reluctance of primary care physicians to recommend hormone replacement therapy for any women makes our jobs as gynecologists difficult. I feel we have sufficient evidence to strongly recommend hormonal therapy for healthy menopausal women. For our youngest patients experiencing early menopause, we must be even more strident in our messaging. ■

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ABSTRACT & COMMENTARY

Urinary and Bowel Symptoms in Women with Suspected Gynecological Malignancy

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

SYNOPSIS: Pelvic floor disorders are common in women before surgery for suspected gynecological malignancy.

SOURCE: Bretschneider CE, Doll KM, Bensen JT, et al. Prevalence of pelvic floor disorders in women with suspected gynecological malignancy: A survey-based study. *Int Urogynecol J* 2016;27:1409-1414. doi: 10.1007/s00192-016-2962-3. Epub 2016 Feb 12.

The main objective of this cross-sectional study was to describe the prevalence of pelvic floor disorders in women with suspected gynecological malignancy before cancer treatment. This was an analysis of the University of North Carolina at Chapel Hill Health Registry/Cancer Survivorship Cohort, a large hospital database. Subjects were identified and recruited for the cohort at the time of a new patient visit at the outpatient oncology clinics. Subjects for this study presented for treatment of gynecological malignancies and were recruited over an 11-month period. The main outcome measures were validated self-report pelvic floor symptoms questionnaires: the Rotterdam Symptom Checklist (RSC) and the International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS).

The authors enrolled 152 women who completed baseline assessments before surgery. The majority of subjects were Caucasian, parous, postmenopausal, and had private insurance. The most common gynecological malignancy types were uterine, ovarian, cervical, vulvar/vaginal, and other, in order of prevalence. Responses to the RSC and ICIQ-FLUTS revealed a high prevalence of urinary symptoms. Sixty percent of women reported symptoms of stress incontinence and 34% reported urge urinary incontinence. Nearly half the cohort reported any symptom of abdominal pain or constipation (46% and 43%, respectively).

■ COMMENTARY

Pelvic floor disorders are common in the general population. There are limited data suggesting a high prevalence of pelvic floor disorders in women following treatment for gynecologic cancers. The estimated rates of urinary incontinence following radiation therapy for cervical and uterine cancer range from 48% to 84%, respectively.[1,2] However, the baseline prevalence of concomitant pelvic floor disorders in women with suspected or diagnosed gynecologic malignancy is unknown.

This study of subjects undergoing new patient visits for gynecologic malignancy suggests that urinary incontinence

and bowel dysfunction is very prevalent in this population. These findings were similar to a 2013 cross-sectional study by Thomas et al that found more than half of 357 patients with gynecologic cancer reported baseline urinary incontinence and 11% reported feeling a bulge from their vagina.[3]

Although both studies used validated questionnaires, the current study did not use the Pelvic Floor Disorders Inventory (a validated and commonly used questionnaire in the urogynecology literature), outcomes measures did not include questions regarding pelvic organ prolapse symptoms, and study measures relied solely on patient report without clinical examination.

Despite several limitations, this study further adds to the small body of literature emphasizing the high prevalence of pelvic floor symptoms in women with gynecologic malignancy. This study highlights the importance of screening women presenting with gynecologic malignancy for pelvic floor disorders and including pelvic floor symptoms in perioperative planning and counselling. ■

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SPECIAL FEATURE

What's the Buzz about Measuring Ovarian Reserve?

By Robert W. Rebar, MD

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

It has been known for many years that fertility begins to decline after age 35 and particularly after age 40. Together with this decline in fertility is an increase in the incidence of miscarriage, largely because of an increase in aneuploid embryos.[1] However, these data hold for populations and not individuals: It has been difficult to predict when decreased fertility begins in any single woman and when she will become menopausal. Despite the ambiguities associated with the end of reproductive life, clinicians often are asked for advice and information about fertility potential. It is also known that the numbers of oocytes in a woman's ovaries are maximal at about 24 weeks in utero and decrease from that time forward.[2-4] Utilizing these bits of information, investigators have attempted to develop screening tests to measure the term "ovarian reserve." It is important for clinicians to understand the usefulness and limitations of these screening tests and to be able to interpret the results for themselves and their patients.

JUST WHAT IS OVARIAN RESERVE AND DIMINISHED OVARIAN RESERVE?

Personally, I find the term "ovarian reserve" itself confusing. It is intended to convey some estimate of both the number and quality of oocytes remaining in the ovaries and their capacity to result in a live-born infant.[5] However, measures developed to date really provide an estimate of the numbers of oocytes only and not of individual oocyte quality. The term "decreased or diminished ovarian reserve" (DOR) is intended to describe women with regular menses whose fecundability (ability to achieve pregnancy) is decreased compared to women of similar age. In reality, DOR can only be assessed by determining what transpires after the test is administered. Some studies have used response to ovarian stimulation and others have reported subsequent pregnancies. It is clear that all the tests developed and used to date are mere surrogates attempting to estimate ovarian reserve. Thus, the term DOR may refer to any of three related but distinctly different possibilities: oocyte quality, oocyte quantity, or reproductive potential.

What causes DOR? Most of the time, the cause or causes of DOR are unknown. It may be that many of those relatively young women with DOR really represent just the end of the normal bell-shaped curve; it also may be that such women have pathological processes yet to be identified. We know that certain genetic abnormalities (of which monosomy X and the fragile X premutation are the most well recognized), chemotherapy, radiation exposure of the ovaries, and cigarette smoking clearly lead to accelerated atresia and DOR.[5] To this day, it is not known if the sequence of events preceding ovarian failure is the same in women approaching menopause and in those with pathological process, but it is presumed that such is the case.

WHAT TESTS HAVE BEEN USED TO ASSESS OVARIAN RESERVE?

Soon after the development of immunoassays for measurement of reproductive hormones, it became apparent that menstrual cycles changed prior to menopause. One of the changes noted was a shortening of the menstrual

cycle, largely due to a shortening of the follicular phase.[6,7] This shortening of the follicular phase is accompanied by increased follicle-stimulating hormone (FSH) levels and by increased circulating estradiol levels in the early follicular phase. We now recognize that these changes are due to changes in the secretion of the glycoprotein hormones inhibin B and anti-Müllerian hormone (AMH), which are secreted by small ovarian follicles. (Inhibin B is secreted primarily by preantral follicles and AMH by primary, preantral, and antral follicles.) As the number of ovarian follicles decreases with age (or as a result of some stimulus such as radiation accelerating destruction), both AMH and inhibin B concentrations decrease. Decreased feedback to the hypothalamic-pituitary unit by the decreased inhibin B leads to increased FSH secretion in the late luteal and early follicular phases — and to the shortened follicular phases. Thus, FSH together with estradiol levels[8] during days 2-4 of the menstrual cycle, inhibin B levels,[9] and AMH levels[10] all have been used to estimate ovarian reserve. Recently, using data from a cohort study of 266 women, it has been reported that serial AMH levels can be used to predict the age of menopause in individual women.[11] However, this is both time consuming and costly and still does not predict the ability to conceive as menopause is neared. Moreover, this small study remains to be confirmed in a prospective trial.

One of the early dynamic tests used to assess ovarian reserve was the so-called clomiphene citrate challenge test (CCCT). In the CCCT, serum FSH is measured on cycle day 2-4 and on cycle day 10 of treatment with clomiphene citrate (100 mg daily) administered on cycle days 5-9.[12] An elevated FSH level before clomiphene administration suggests DOR. So, too, do increased FSH levels compared to normal age-matched women after clomiphene administration. This is because the smaller numbers of follicles that can be recruited in women nearing the end of their reproductive lives secrete less inhibin B and estradiol with less suppression of FSH secretion in response to clomiphene.

With improvements in ultrasound, it has become possible to examine direct changes in the ovary. Thus, one popular test is the antral follicle count (AFC) and another is ovarian volume.[13] The AFC describes the total number of follicles measuring 2-10 millimeters in diameter that can be seen during a scan in the early follicular phase in both ovaries. This number correlates with the number of oocytes remaining in the follicular pool and with the number of oocytes retrieved following stimulation. Obviously, ovarian volume decreases with age and also should correlate with ovarian reserve.

HOW HAVE THESE TESTS BEEN ASSESSED AND HOW EFFECTIVE ARE THEY?

Originally, ovarian reserve tests were intended to be used to screen women before they would begin a cycle of in vitro fertilization (IVF) to identify those women likely to respond to exogenous ovarian stimulation and to have good odds of becoming pregnant with treatment (because of the maturation and availability of several oocytes). The difficulty is that some centers have performed ovarian reserve tests on women with little likelihood of becoming pregnant, such as older women, and others have screened general populations of women seeking IVF, intending to discriminate those with good prognosis of conceiving with IVF from those with poor prognosis. Some studies have defined DOR on the basis of the response to exogenous ovarian stimulation and others have used pregnancy as an endpoint. Yet, now the usage of these tests has expanded to screen women who wish to have some estimate of their future fecundability.

One major problem is the fact that virtually all of these tests vary considerably from menstrual cycle to menstrual cycle.[5] Moreover, none of these tests predicts whether pregnancy is possible, even spontaneously. In addition, when considered statistically, the best predictor of future pregnancy remains the age of the woman. Evidence of DOR does not necessarily equate with the inability to conceive.

A Practice Committee Guideline from the American Society for Reproductive Medicine notes that a single FSH value has very limited reliability because of inter- and intra-cycle variability.[5] Moreover, the guideline notes that there is fair evidence to refute the notion that ovarian response and pregnancy rates will improve in cycles in which the early follicular phase FSH value is normal in women in whom a previously elevated level was recorded. Similarly, the evidence does not support the use of basal estradiol concentrations as a single screening test for DOR; however, estradiol levels do help with the interpretation of basal FSH levels. The guideline suggests that CCCT improves sensitivity for detecting DOR only mildly. It further suggests that the evidence is "mounting" to support the use of AMH as a screening test for poor ovarian response to gonadotropin stimulation. However, there is insufficient evidence to suggest it can be used to predict inability to conceive. Again similarly, the evidence that low antral follicle count (< 6) can be used as a screening test for poor ovarian response is fair, but there is insufficient evidence to support the use of AFC as a screening test for failure to conceive. There also is fair evidence that inhibin B and ovarian volume are not good screening tests for DOR. The guideline also notes that there is insufficient evidence to indicate that the combined results of multiple screening tests are more useful that any test separately. The guideline concludes by suggesting that the evidence indicates that there will be more false-positive test results as more low-risk women are tested.

WHAT CONCLUSIONS CAN WE REACH ABOUT OVARIAN RESERVE TESTING?

So what does all of the evidence mean? It means that these tests have very little value in providing predictions regarding the possibility of future pregnancy for individual women. It means that we are likely to worry more normal women unnecessarily when suspicious results are obtained on ovarian reserve testing of large numbers of women. I would suggest that ovarian reserve testing should not be used indiscriminately, but rather should be limited to women in

whom there is concern about their fecundability. Tests may well be offered to cancer survivors after radiation and/or chemotherapy and to women with a family history of early menopause or various genetic mutations known to affect fertility. Ovarian reserve testing also may be appropriate for women with severe endometriosis or a history of prior ovarian surgery. Tests can be offered to infertile women older than age 40 years considering in vitro fertilization to help them determine if the expense and commitment are justified. For those normal women who are compelled to cryopreserve their oocytes because of the absence of a suitable partner or some other reason, an argument also can be made for ovarian reserve testing prior to ovarian stimulation. On the other hand, there also is one theoretical study suggesting that oocyte cryopreservation is most efficient when performed at 38 years of age.[14] Almost all women are fertile until that age.

Ovarian reserve testing actually creates more questions than answers. Providing nuanced explanations to patients is difficult and challenging. These observations lead to the obvious final conclusion: Use these tests with caution — and in limited scope. A committee opinion from the American Society for Reproductive Medicine concludes that it is important to counsel women who desire to build families about the effect of increasing age.[15] Thus, women older than 35 years should be evaluated and treated after six months of failed attempts to conceive — and even earlier if there is an obvious impediment to fertility. In women older than 40 years of age who wish to conceive, immediate evaluation as well as any appropriate treatment based on the findings are warranted. ■

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11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box → ☒ None

Full Name	Complete Mailing Address

12. Tax Status *(For completion by nonprofit organizations authorized to mail at nonprofit rates) (Check one)*
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☑ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months *(Publisher must submit explanation of change with this statement)*

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13. Publication Title: OB/GYN Clinical Alert			14. Issue Date for Circulation Data Below: September 2016	
15.	Extent and Nature of Circulation		Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
a.	Total Number of Copies *(Net press run)*		183	170
b. Paid and/or Requested Circulation	(1)	Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. *(Include advertiser's proof and exchange copies)*	136	128
	(2)	Paid In-County Subscriptions Stated on Form 3541 *(Include advertiser's proof and exchange copies)*	0	0
	(3)	Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution	11	10
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c.	Total Paid and/or Requested Circulation *(Sum of 15b. (1), (2),(3),and (4))*		157	143
d. Free Distribution by Mail *(Samples, complimentary, and other free)*	(1)	Outside-County as Stated on Form 3541	11	12
	(2)	In-County as Stated on Form 3541	0	0
	(3)	Other Classes Mailed Through the USPS	0	0
e.	Free Distribution Outside the Mail *(Carriers or other means)*		5	5
f.	Total Free Distribution *(Sum of 15d. and 15e.)*		16	17
g.	Total Distribution *(Sum of 15c. and 15f)*		173	160
h.	Copies not Distributed		10	10
i.	Total *(Sum of 15g. and h.)*		183	170
j.	Percent Paid and/or Requested Circulation *(15c. divided by 15g. times 100)*		91%	89%

16. Publication of Statement of Ownership
☑ Publication required. Will be printed in the November 2016 issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: *David R. Fournier* Publisher & CEO — Date: 09/12/2016

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties).

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To earn credit for this activity, please follow these instructions:

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CME/CE QUESTIONS

1. Which of the following did *not* occur after treatment with sildenafil in preeclamptic patients?
a. Increase in length of pregnancy
b. Decrease in the umbilical artery resistance
c. Decrease in uterine artery resistance
d. Enhanced neonatal outcomes
e. Drop in maternal arterial pressures

2. In the Muka meta-analysis, compared to menopause onset beyond age 46, early-onset menopause was associated with:
a. an increased risk of fracture.
b. a reduction in the risk of lung cancer.
c. an increased risk of ischemic stroke mortality.
d. an increased risk of cardiovascular disease and all-cause mortality.

3. Women who present for care of gynecologic malignancy:
a. are unikely to have pelvic floor disorders.
b. should be screened for pelvic floor disorders before treatment.
c. have low rates of urinary incontinence.
d. have significant rates of pelvic organ prolapse.

4. Currently, which appears to be the best single measurement of ovarian reserve?
a. Antral follicle count
b. Basal FSH level on day 2-4 of the menstrual cycle
c. Anti-Müllerian hormone
d. Ovarian volume
e. Basal estradiol on day 2-4 of the menstrual cycle

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
- Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

[IN FUTURE ISSUES]

HPV Testing: An Approach Whose Time Has Come

When to Start Progestin-only Contraceptives After Medical Abortion