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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Contraception, Migraines, and Stroke

By Rebecca H. Allen, MD, MPH

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Dr. Allen reports she is a Nexplanon trainer for Merck, and has served as a consultant for Bayer and Pharmanest.

SYNOPSIS: In this case-control study, women with migraines with aura using combined hormonal contraception had six times the odds of experiencing ischemic stroke compared to women without migraines not using combined hormonal contraception. Use of combined hormonal contraception among women with migraines without aura was not associated with an increased risk of stroke over baseline.

SOURCE: Champaloux SW, Tepper NK, Monsour M, et al. Use of combined hormonal contraceptives among women with migraines and risk of ischemic stroke. *Am J Obstet Gynecol* 2016; Dec 26. doi: 10.1016/j.ajog.2016.12.019 [Epub ahead of print].

This is a case-control study of women aged 15-49 years whose data were collected in a U.S. national database of health claims and prescription drug claims entitled MarketScan Research Databases, Commercial Claims, and Encounters. Between 2006 and 2012, women with inpatient ischemic stroke codes were identified. Four controls were randomly selected for each case and matched by age in 2006. Both cases and controls had to be enrolled continuously in private insurance from Jan. 1, 2004, to the index date of the first stroke diagnosis. This ensured that adequate capture of migraine history and prior strokes was obtained. Women with pregnancy codes within six weeks prior to the index date of the stroke were excluded, as well as women with hysterectomy or sterilization from 2004 up to the index date. Migraine headaches were identified with both inpatient and outpatient codes, and migraine history had to be present before the index date. Current combined hormonal contraception (CHC) use was defined as a filled prescription for combined oral contraceptives, patch, or ring within 90 days prior to the index date. The number of women using the contraceptive patch and ring was too small for separate analyses. Other risk factors for ischemic stroke were identified, including age, obesity, smoking, diabetes, hypertension, ischemic heart disease, and valvular heart disease.

From 2006 to 2012, in the entire cohort, there were 25,887 ischemic strokes among 33,218,977 women. The overall average yearly cumulative incidence of stroke was 11 strokes per 100,000 women. Younger women had a lower incidence of stroke (1 per 100,000 women aged

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15-19 years) compared to older women (30 per 100,000 women aged 45-49 years). After applying inclusion and exclusion criteria, there were 1,884 cases matched to 7,536 controls. After adjusting for hypertension, diabetes, obesity, smoking, ischemic heart disease, and valvular heart disease, compared to women with neither migraine nor CHC use, the odds ratio (OR) of ischemic stroke was highest among women with migraine with aura using CHCs (adjusted OR, 6.1; 95% confidence interval [CI], 3.1-12.1). The odds of ischemic stroke also was elevated among women with migraine with aura *not* using CHCs (adjusted OR, 2.7; 95% CI, 1.9-3.7), women with migraine without aura using CHCs (adjusted OR, 1.8; 95% CI, 1.1-2.9), and women with migraine without aura *not* using CHCs (adjusted OR, 2.2; 95% CI, 1.9-2.7).

■ COMMENTARY

Although the absolute risk of ischemic stroke is low in women of reproductive age, as evidenced in the study discussed here, migraine with aura is an independent risk factor for stroke. Most studies have noted that women who have migraine with aura have a higher stroke risk than those who have migraine without aura.[1,2] The assumption is that aura is associated with vascular changes.[3] Use of combined hormonal contraception also increases the risk of stroke in women, although the absolute risk is still low.[4] The elevated risk of ischemic stroke likely is due to the hypercoagulable state caused by estrogen's effect on liver metabolism. The risk of stroke among women using combined hormonal contraception rises with increasing age, from 3.4 per 100,000 women-years in adolescents to 64.4 events per 100,000 women-years among women aged 45-49 years.[5]

The authors conducted this study to elucidate the risk of stroke among women using CHCs according to migraine type. The investigators found that CHC use by women with migraines with aura synergistically increases the risk of stroke. In contrast, use of CHC by women with migraines without aura did not increase the risk. This conclusion supports the 2016

Table 1: Diagnostic Criteria for Migraine With and Without Aura

Migraine without aura	**Migraine with aura**
Recurrent headache disorder manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea and/or photophobia and phonophobia.	Migraine headache plus recurrent attacks, lasting minutes, of unilateral fully reversible visual, sensory, or other central nervous system symptoms that usually develop gradually and usually are followed by headache and associated migraine symptoms.
Diagnostic criteria A. At least five attacks fulfilling criteria B–D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: • Unilateral location • Pulsating quality • Moderate or severe pain intensity • Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs) D. During headache at least one of the following: • Nausea and/or vomiting • Photophobia and phonophobia	**Diagnostic criteria** A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: • Visual • Sensory • Speech and/or language • Motor • Brainstem • Tetinal C. At least two of the following four characteristics: • At least one aura symptom spreads gradually over ≥ 5 minutes, and/or two or more symptoms occur in succession • Each individual aura symptom lasts 5-60 minutes • At least one aura symptom is unilateral • The aura is accompanied, or followed within 60 minutes, by headache D. Not better accounted for by another diagnosis, and transient ischemic attack has been excluded.

Adapted from: Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version) *Cephalalgia* 2013;33:629-808.

recommendation of the Centers for Disease Control and Prevention's U.S. Medical Eligibility Criteria for Contraceptive Use (USMEC).[6] The USMEC states that estrogen-containing contraceptives are contraindicated for women with migraine with aura given the devastating consequences of stroke. For women with migraine without aura, the USMEC recommends that the benefits of using CHCs outweigh the risks. Progestin-only methods and intrauterine devices also are safe for women with migraines of any type.

The study had several strengths, including use of a national database allowing sufficient cases of ischemic stroke to be identified and the ability to differentiate between migraine types. Nevertheless, even with this national database, the absolute numbers of women who had migraines with aura, took CHCs, and suffered a stroke were very small. Of note, all the women in this study had private insurance, which makes the study less generalizable. In addition, the use of diagnostic codes in large health claims database studies to classify exposures and outcomes can lead to misclassification. The design of this study also limited its ability to capture any information on women who had migraines but did not seek any medical attention. Finally, relying on filled prescriptions for evidence of contraceptive exposure may overestimate use.

Nevertheless, the findings of this study are consistent with the literature and USMEC recommendations, so where do we go from here? Migraine headaches are more common in women than men and peak at a prevalence of 24% among women aged 30-39 years.[7] Migraine without aura is the most common subtype, accounting for 75% of cases. Clearly, this is a common problem that obstetrician-gynecologists encounter. Given the USMEC contraceptive recommendations, it is very important for clinicians to be able to distinguish between classic migraines and migraines with aura. Nausea, vomiting, photophobia, phonophobia, or visual blurring occurring before or during a migraine headache do not constitute aura. According to the International Headache Society, an aura is the complex of neurological symptoms that occurs usually before the headache, but it may begin after the headache has begun.[8] A typical aura is reversible, lasts less than 60 minutes, and can consist of visual symptoms such as a zigzag figure (fortification spectrum, so named due to its resemblance to the walls of a medieval fortress) spreading across the visual field, sensory symptoms such as pins and needles, speech disturbances, or motor weakness (*see Table*). It is critical that we are very certain before diagnosing and labeling a woman with migraine with aura. Otherwise, we are reducing her contraceptive options for her entire life. ■

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ABSTRACT & COMMENTARY

Embryo Implantation

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 tracking embryos after embryo transfer has provided insight into why embryos have a greater tendency to ultimately implant in the lower uterine segment, thereby predisposing patients to a greater risk of placental complications.

SOURCE: Saravelos SH, Wong AW, Chan CP, et al. How often does the embryo implant at the location to which it was transferred? *Ultrasound Obstet Gynecol* 2016;48:106-112.

Have you wondered why patients using some forms of assisted reproductive technology (ART) have higher rates of placenta-related complications? A group from Hong Kong recently published information to explain why this may happen. The study was designed to track the location of an embryo from the time of transfer to its ultimate residence in the uterus at three weeks post-transfer.

Patients having embryo transfer (ET) were studied with 2-D and 3-D ultrasound examinations during the time of transfer, one minute later, and 60 minutes after ET. The last 3-D exam was conducted three weeks post-ET. An attempt was made to place three-day-old embryos into the middle portion of the uterus (10-20 mm from the fundus) under ultrasound guidance. The embryos were

accompanied by a tiny amount of air, and the location of the embryo was determined by the presence of bright echoes (representing the air bubbles) at one minute and 60 minutes. In addition, the investigators assessed the presence, frequency, and direction of uterine contractions at these same time intervals using three-minute ultrasound real-time clips. The frequencies of contractions were classified as "high" (> 2 per minute) or "low" (< 2 per minute). Last, at three weeks' gestation the final location of the implanted embryo was determined with 3-D ultrasound using planar reconstruction.

[This well-constructed paper may answer questions regarding why patients conceiving through ART are more prone to problems related to the placenta.]

Over the study period, 239 patients had ET procedures and 46% became pregnant, 71 of whom had adequate ultrasound information provided by the four ultrasound evaluations. The embryo location at three weeks was found to coincide with the bubble site in 29/71 (40.8%) at one minute and in 36/71 (50.7%) at 60 minutes. At 60 minutes, there was an 85% chance of the embryo staying at that original site if it was in the lower uterine segment. Those in the upper segments were more likely to move.

The contraction data were fascinating. Surprisingly, the direction of uterine contractions was not related to the ultimate implantation site, nor was the frequency of contractions at one minute related. However, a high frequency of contractions at 60 minutes was associated with a twofold increase in the chance of low implantation.

■ COMMENTARY

Why are we discussing a fertility paper in the obstetrical section of *OB/GYN Clinical Alert*? Because this well-constructed paper may answer important questions regarding why patients conceiving through ART are so much more prone to problems related to the placenta. Also, it can be a catalyst to a discussion of the obstetrical management of women who used ART.

The Saravelos et al study indicates that no matter how carefully one would avoid inserting an embryo into the lower uterine cavity, these embryos seem to have a higher tendency than spontaneously conceived embryos to alight in the lower uterine segment — and it may be due to increased uterine contractions at the time of, and/or shortly after, the procedure, driving the embryos downward.

Low embryo implantation begets low placental implantation. Patients undergoing in vitro fertilization (IVF) have a greater chance of placenta previa,[1] as well as accreta,[2] and a 10-fold increased risk of vasa previa.[3] They also have a greater chance of small for gestational age fetuses[4] and preeclampsia,[5] which may be due to the quality of placentation rather than the position of the placenta. Although maternal age is a factor, and more patients using ART are of advanced maternal age (AMA), the relationship between preeclampsia and ART seems to be even stronger than with age alone. The obvious relationship between ART and multiple gestations is worth a separate article, as is the increased risk of fetal anomalies.

Below are suggestions for managing patients after ET:
1. Whether or not the patient is AMA, a nuchal translucency (NT) exam is helpful at 10/6 weeks to 13/6 weeks, since fetuses with increased NTs are more likely to have cardiac abnormalities.
2. An anatomy scan at 18-20 weeks and an assessment of placental position are useful because of the higher risk for placenta previa. The placenta should be investigated for early signs of accreta, especially if the placenta is over an old cesarean scar. Except for the fetal heart, most fetal anomalies that have been linked to ART can be identified at this time.
3. During the above anatomy scan at 20 weeks, the cord insertion site always should be determined since vasa previa involving the cord always is velamentous. Also, the presence of an accessory lobe should be ruled out, since connecting vessels occasionally stray over the cervix.
4. A second trimester alpha-fetoprotein test can be useful, since more than 50% of patients with accreta will have very high levels of this fetal product.[6]
5. With IVF, some have recommended that a fetal echocardiogram be accomplished at 22 weeks since there is an increased rate of tetralogy of Fallot,[7] which on occasion can escape detection during an 18-week sonogram.
6. Another examination at 30 weeks is useful to track fetal growth and to look again for signs of accreta or the later development of vasa previa secondary to atrophy of placental tissue near the cervix. ■

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ABSTRACT & COMMENTARY

More Confusion Over Whether HRT Prevents Dementia

By Jeffrey T. Jensen, MD, MPH, Editor

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Dr. Jensen reports that he is a consultant for and receives grant/research support from Bayer, Abbvie, ContraMed, and Merck; receives grant/research support from Medicines 360, Agile, and Teva; and is a consultant for MicroChips and Evofem.

SYNOPSIS: A 20-year prospective cohort study from Finland did not provide strong evidence that hormone replacement therapy prevents dementia except among women who self-reported long-term use.

SOURCE: Imtiaz B, Tuppurainen M, Rikkonen T, et al. Postmenopausal hormone therapy and Alzheimer disease: A prospective cohort study. *Neurology* 2017; Feb 15.: doi: 10.1212/wnl.0000000000003696 [Epub ahead of print].

Several case-control and other epidemiologic observational studies support a decrease in the risk of dementia associated with use of postmenopausal hormone replacement therapy (HRT). Imtiaz et al used the Kuopio Osteoporosis Risk Factor and Prevention cohort to study the relationship between HRT use and the subsequent development of Alzheimer's dementia (AD). This population-based cohort included all women between 47-56 years of age who were residents of Kuopio Province, Eastern Finland, in February 1989. Out of a total population of 14,220 women in the area, 13,100 (92.1%) responded to a baseline survey and completed a health questionnaire that covered demographics; lifestyle; medical, surgical, and reproductive history; medications, including type and duration of HRT use; and other personal characteristics such as age, height, weight, smoking, alcohol consumption, occupation, and physical activity. Women who responded to the baseline questionnaire received follow-up queries every five years. The most recent sample from 2009 included responses from 8,195 women (62.6% of the original cohort). The primary outcome variable was clinically verified AD diagnosis. To assess this outcome, the authors used the Finnish Social Insurance Institution (SII) special reimbursement register that contains information on drugs used for chronic illnesses such as AD. This database likely captures most cases of AD, as Finnish Current Care Guidelines recommend that all persons with AD receive antidementia drugs (unless there is a specific contraindication). However, to receive reimbursement for drug costs, a medical statement of a clinically verified AD diagnosis must be submitted to SII. Systemic HRT use was assessed at each questionnaire by self-report, with number of years of use calculated. The authors also made use of the national prescription drug registry to verify HRT use.

Overall, women who developed AD during the 20-year follow-up interval were older and more likely to be menopausal at baseline. The average age at AD diagnosis was 72.3 years. While any history of HRT use did not change the risk of AD, a trend toward protection emerged with longer duration of self-reported use, with an approximately 50% reduction in risk seen in women reporting more than 10 years of HRT (adjusted hazard ratio [HR], 0.53; 95% confidence interval [CI], 0.31-0.91).

■ COMMENTARY

Does this observational study support or refute the hypothesis that HRT can reduce the risk of AD? The authors provided a cautious interpretation of their own data, concluding that "Our results do not provide strong evidence for a protective association between postmenopausal HRT use and AD or dementia, *although we observed a reduced AD risk among those with long-term self-reported HT*."

Although at first glance this looks like a negative study, on closer review, the data confirm the results of earlier research. The best data we have evaluating the long-term effects of HRT on AD come from the Cache County Cohort, a prospective study of incident dementia in men and women residing in a single county in Utah.[1] The Utah study enrolled an older group of subjects (men and postmenopausal women in their 70s) than the Kuopio cohort (perimenopause to early menopause). Both studies assessed HRT use and tracked incident diagnosis of AD. In the Cache County study, men and women were equally likely to develop AD up to about the age of 80, when the relative risk for women more than doubled. However, Utah women who reported any use of HRT had a reduced risk of AD compared with non-HRT users (adjusted HR, 0.59; 95% CI, 0.36-0.96), and the reduction in risk showed a strong linear relationship with duration of use becoming significant only among women using HRT for more than 10 years.

The absence of an overall effect of HRT on AD in the Kuopio Cohort could be due to the younger age of the Finnish women, who would have ranged from age 68-76 years at the time of the 2009 survey. That is roughly the age at which women in the Cache County cohort began

participation. Still, the magnitude of the protective effect of long-term (> 10-year) HRT on AD risk seen with both studies is remarkably consistent.

We recently reviewed data from the Elite-Cog[2] and KEEPS-Cog[3] studies. Both explored the hypothesis of a critical window for initiation of HRT and found no treatment-related benefit of HRT with respect to cognitive function. Although the outcomes of these studies do not support use of estrogen therapy to prevent subtle cognitive decline in postmenopausal women, this does not rule out a potential protective effect on the subsequent development of AD. The consistent finding so far from the Cache County and Kuopio cohorts is that duration of treatment matters, with at least 10 years of use an important goal of therapy. In both studies, current use of shorter duration did not reduce risk.

As we evaluate these results, we must consider the strengths and weaknesses inherent in study design. Both studies used a prospective cohort scheme that allowed incident diagnoses of AD, with the diagnosis validated using medical records. However, a healthy user effect could confound the results. The magnitude of the effect, about a 50% reduction in risk, approaches the threshold for resolution of this study design (two-fold difference) for consideration of clinical importance. Although cognitive benefits are not an indication for HT, healthy postmenopausal women should consider these results as they debate duration of treatment. Often, the timing of HRT discontinuation becomes an arbitrary decision when a woman no longer experiences bothersome symptoms. Women who tolerate therapy well may wish to continue treatment for at least 10 years to maximize protection against the development of AD. ■

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SPECIAL FEATURE

Group Prenatal Care

By Rebecca H. Allen, MD, MPH

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Dr. Allen reports she is a Nexplanon trainer for Merck, and has served as a consultant for Bayer and Pharmanest.

Group prenatal care is a different model for the delivery of prenatal care that typically consists of groups of eight to 12 women of similar gestational age who have each visit together. This contrasts with the one-on-one patient/provider prenatal care visits that are the traditional model. Women are enrolled in group prenatal care after they have had an individual initial prenatal visit and health risk assessment, and have completed the first trimester. Most programs enroll low-risk women who are able to attend the scheduled visits (eight to 10 visits lasting 90 to 120 minutes) and have childcare. The groups are run by an obstetric provider (nurse practitioner, nurse midwife, OB/GYN, or family medicine physician) and a co-facilitator (nurse, nutritionist, social worker, psychologist, health educator, or medical assistant). The visits consist of the standard maternal and fetal assessments followed by a group discussion regarding the prenatal education topic at hand. Women are encouraged to participate in the physical exam components, such as measuring their own blood pressure and weight. Most groups have the option of performing fundal height and fetal heart tone measurements in a semi-private area. There also can be individual consultations and exams as needed. Although there are different variations to group prenatal care, the first model that was established in the 1990s, CenteringPregnancy, is the most recognized and studied.[1] (*See Table 1.*) CenteringPregnancy (https://www.centeringhealthcare.org) provides a framework and assistance in starting a group prenatal care program for roughly $20,000 over the first two years; there is a $500 annual membership fee.[2] In addition, "Moms Notebooks" must be purchased for each participant for $22.

The advantages of group prenatal care include the promotion of a community of women who can support each other throughout the pregnancy and postpartum. Women also spend more time with a prenatal care educator than in a traditional model.[3] Group prenatal care also is associated with decreased wait times for appointments and high satisfaction levels for patients.[4] Group prenatal care has been implemented successfully for multiple different populations, including in adolescents, non-English speakers, incarcerated women, and women with HIV or gestational diabetes. For the practice, providers and educators can find efficiencies in meeting with a group to dispense routine prenatal information and answer questions.

The disadvantages of group prenatal care include the logistics in organizing the visits, enrollment and retention of participants, the need to find a large enough physical space for the meetings, and training facilitators. Some women face barriers to group prenatal care, such as transportation and childcare issues.[3] The implementation of a group prenatal

Table 1: 13 Essential Components of CenteringPregnancy

- Health assessment occurs within the group space.
- Women are involved in self-care activities.
- A facilitative leadership style is used.
- Each session has an overall plan.
- Attention is given to core content, but emphasis can vary.
- There is stability of group leadership.
- Group conduct honors the contribution of each member.
- The group is conducted in a circle.
- Group composition is stable, but not rigid.
- Group size is optimal to promote the process.
- Involvement of family support people is optional.
- Opportunity for socializing within the group is provided.
- There is ongoing evaluation of outcomes.

Adapted from: Rising SS, Kennedy HP, Klima CS. Redesigning prenatal care through CenteringPregnancy. *J Midwifery Womens Health* 2004;49:398-404.

care program requires significant administrative support and provider buy-in. The group size needs to be maintained at a certain level to make the visit cost-effective, and this also depends on the provider types utilized. Group prenatal care is billed and reimbursed similarly to individual prenatal care.

What about the medical advantages of group prenatal care? Group prenatal care programs have become very popular and are supported by the March of Dimes, the Centers for Medicaid and Medicare Services, and multiple states. The main reason is the claim that group prenatal care reduces the rate of preterm birth. This also brings in the cost-saving argument for the healthcare system as a whole. There have been two meta-analyses examining group prenatal care compared with traditional prenatal care. The Cochrane Collaboration evaluated four randomized, controlled trials (RCTs) of 2,350 women.[4] One trial contributed 42% of the participants. Although satisfaction with care was high, there was no significant difference between the two groups in preterm birth, low birth weight infants, or perinatal mortality. A second systematic review and meta-analysis included four RCTs and 10 observational studies.[5] This study found that, overall, the rate of preterm birth was no different (7.9% group vs. 9.3% traditional; pooled relative risk [RR], 0.87; 95% confidence interval [CI], 0.70-1.09). Group care was associated with a decreased low birth weight rate among observational studies (7.5% group vs. 9.5% traditional; pooled RR, 0.81; 95% CI, 0.69-0.96), but not among RCTs (7.9% group vs. 8.7% traditional; pooled RR, 0.92; CI, 0.73-1.16). There were no significant differences between the groups in NICU admission or breastfeeding rates. Nevertheless, among African-American women, a subanalysis of two high-quality studies (one RCT, one observational) showed lower rates of preterm delivery with group prenatal care (8% group vs. 11.1% traditional; pooled RR, 0.55; 95% CI, 0.34-0.88). There was no difference among Latinas. The authors speculated that the effect seen among black women, who have preterm birth rates twice as high as white women, may be due to the social support and stress reduction obtained through group prenatal care. In my opinion, this finding has led to the wide implementation of group prenatal care as a panacea for reducing preterm birth rates. Other medical outcomes of group prenatal care, such as beneficial effects on breastfeeding, depression, stress, and positive health behaviors, have been shown inconsistently.[3] There is some evidence for a positive effect on postpartum family planning and increased birth spacing. Some of the difficulty with evaluation clearly is linked to the different ways group prenatal care can be implemented and the quality of the groups.[6]

Although more RCTs are needed, there is no evidence that group prenatal care causes harm. It is a satisfying model to women who self-select into it and attend the visits. Therefore, it is certainly an alternative model of delivering prenatal care that should be studied and supported. However, there is evidence it can be difficult to recruit and retain women in the groups. It is certainly a challenge to change the entire paradigm of care delivery. In one study of 547 adolescents receiving group prenatal care in New York City, attendance at the groups averaged 60% and group visits were supplemented with individual visits.[7] Another study evaluating barriers to group prenatal care implementation cited several issues related to successful and unsuccessful sites.[8] In this study, only three of six sites randomized to start group prenatal care as part of a clinical trial were able to keep the program going after the trial ended. Successful sites were notable for an organizational culture that supported innovation and champions who were able to overcome obstacles. Unsuccessful sites were notable for lack of buy-in and financial support, as well as staff who were overwhelmed by logistical challenges such as lack of space, training facilitators, and scheduling patients into new templates. Clearly, group prenatal care programs should not be undertaken without adequate support on all levels, and such programs may not be appropriate for certain practices. In sum, group prenatal care is at least equivalent to individual prenatal care and is associated with high patient satisfaction. However, the evidence that it will solve the problem of preterm birth in the United States is not quite there. ■

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CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. **In the study by Champaloux et al, the risk of stroke in women with migraine without aura using combined hormonal contraceptives and women with migraine without aura *not* using combined hormonal contraceptives was roughly equivalent.**
   a. True
   b. False
2. **If embryos are found in the lower uterine segment at one minute and 30 minutes after transfer, they are more likely to stay there than if they were placed in the upper or middle segments.**
   a. True
   b. False
3. **Assisted reproductive technology has been associated with all but which one of the following conditions?**
   a. Vasa previa
   b. Small for gestational age
   c. Preeclampsia
   d. Placenta previa
   e. Aneuploidy
4. **If embryos are found in the lower uterine segment at one minute and 30 minutes after transfer, they are more likely to stay there than if they were placed in the upper or middle segments.**
   a. True
   b. False
5. **A reduction of risk of Alzheimer's dementia was seen in the Finnish study among women who self-reported:**
   a. ever use of postmenopausal hormonal therapy.
   b. more than 10 years of use of hormonal therapy.
   c. coffee consumption of more than 10 cups per day.
   d. an active lifestyle with a low-fat diet, exercise, and no smoking.

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]

Pregnancy Loss and Low-dose Aspirin: Helpful Under the Right Circumstances