Advanced Paternal Age Counseling and Concerns

Ranjith Ramasamy, MD, Jaden Kohn, MD, MPH, and Jeffrey K. Than, BS
IN THIS ISSUE

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THE EDITORS ARE PLEASED TO ANNOUNCE the availability of our new parent company’s continuing education activities. We’ve picked this one especially for our Contemporary OB/GYN readers - bit.ly/ManyFacesOpioidAbuse

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ON THE COVER:
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Congenital syphilis makes a comeback

Faced with the rapid increase in a potentially deadly—but preventable—congenital disease, it’s time for states to take action to require appropriate screening.

Rates of congenital syphilis have taken an ominous uptick over the past few years and are now at a 20-year high. The Centers for Disease Control and Prevention (CDC) reports that rates of primary and secondary syphilis in the general US population have increased 72.7% from 5.5 cases per 100,000 in 2013 to 9.5 per 100,000 in 2017 when a total of 30,644 cases were reported.1 The number of cases of congenital syphilis have increased simultaneously. After years of decline reaching a nadir in 2012, cases of congenital syphilis increased from 362 in 2013 to 918 in 2017 including 64 stillbirths and 13 infant deaths.1 During this time, the largest rate increases occurred in the Western United States (362.5%). Rates were highest among blacks (58.9 cases per 100,000 live births), followed by Native (indigenous) Americans (35.5 per 100,000), Hispanics (33.5 per 100,000), whites (9.7 per 100,000), and Asians/Pacific Islanders (4.3 per 100,000).

The consequences of congenital syphilis are so severe, and its prevention so straightforward, that this increase represents a public health tragedy. Thus, it is time to ensure that all pregnant women are adequately screened and expeditiously treated to eliminate this disease entirely. Fortunately, a few states are leading the way in curbing this epidemic and provide useful lessons for the rest of the nation.

Syphilis

Syphilis is caused by the spirocheteTreponema pallidum. Primary syphilis is marked by presence of a chancre that heals in 3 to 6 weeks. Secondary syphilis, manifest by lymphadenopathy and/or a maculopapular rash on the palms, soles and mucous membrane, occurs in a quarter of cases 6 weeks to 6 months after the chancre first appeared and lasts 2 to 5 weeks. Early latent syphilis occurs in the first full year, and late latent occurs thereafter. Tertiary syphilis is now rare with its classical gumma lesions and cardiac defects while neurosyphilis can begin with early disease and slowly progress to paresis if untreated.

Screening can employ either traditional or reverse sequence approaches.2 The former includes initial nontreponemal testing such as a quantitative Rapid Plasma Reagin (RPR) assay followed by confirmatory treponemal testing (e.g., Fluorescent treponemal antibody absorption test (FTA-ABS) or T. pallidum particle

Redefining postpartum care How to improve care for mother and child during the “fourth trimester.” Read more on page 17.

Reproductive risks of advanced paternal age As couples start their families at an older age, ob/gyns should know how to counsel patients on the associated risks of APA. Read more on page 12.
agglutination assay [TPPA]). Reverse sequence screening begins with an initial treponemal chemoluminescent or enzyme immunoassay with reflex testing of positive results (false positive results occur in 50% to 90% of cases) using a non-treponemal test such as quantitative RPR. If the RPR is positive it is diagnostic, but if negative, a final TPPA or FTA-ABS study is required to exclude the diagnosis.²

Treatment depends on the stage of the disease. For primary, secondary, and early latent disease a single dose of penicillin G benzathine (2.4 million units) is given intramuscularly. For late latent and tertiary disease, three weekly doses are required. Neurosyphilis requires inpatient parental therapy. While non-penicillin treatments (e.g., tetracycline) can be used in non-pregnant women, only penicillin G benzathine is appropriate in pregnancy. Thus, if pregnant patients are allergic, desensitization is needed. The biggest risk of treatment is the Jarisch-Herxheimer reaction occurring within 2 hours of treatment which can trigger preterm labor.

Congenital syphilis

Transplacental passage of Treponema pallidum can occur at any stage of the disease with the greatest risk occurring with primary, secondary, and early latent disease.³ It can also occur at any gestational age. Because it is the fetal immune reaction that produces the pathological stigmata, more severe effects are seen in the second half of pregnancy. Fetal manifestations include hepatomegaly, placentomegaly, anemia, hydrops, and death. There is an 80% risk of congenital syphilis if mothers remain untreated. Fortunately, adequate and prompt treatment is almost always curative.

Thus, the key to prevention is detection. Women at highest risk include those who have a partner in a high-risk sexual network, and those with a history of incarceration or substance abuse. However, Trivedi and associates analyzed national case report data including risk behavior statistics and concluded that half of affected women had no traditional risk factors.³ Nonetheless, the current recommendation by the CDC and the American College of Obstetricians and Gynecologists (ACOG) is for universal screening at the first prenatal appointment with re-screening in the third trimester and at delivery for women at high personal risk or who live in areas with high rates of syphilis.⁴

There is clear evidence that such screening reduces risk. A recent US Preventive Services Task Force (USPSTF) report noted that increasing screening of pregnant women in Shenzhen, China from 89.8% to 97.2% between 2002 and 2012 reduced prevalence of congenital syphilis from 109.3 cases per 100,000 livebirths to 9.4 per 100,000.² This resulted in a reduction in adverse outcomes from 42.7% of affected pregnancies to 19.2%. The primary “harm” associated with screening are false-positive results primarily

While non-penicillin treatments can be used in non-pregnant women, only penicillin G benzathine is appropriate in pregnancy.

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when using the “reverse sequence” strategy and relatively rare false negatives (2.9%) from traditional screening using the RPR as a screen due to the “prozone phenomenon.” The latter occurs when undiluted serum contains high titers of nonspecific antibodies which bind antigen sites preventing flocculation. The USPSTF concluded that screening “for syphilis in pregnant women is associated with reduced incidence of congenital syphilis and available evidence supports the need for reflexive testing for positive test results.”

Causes of the current epidemic and novel mitigation strategies

So why have rates of congenital infection climbed despite universal first-trimester screening and the availability of a very effective treatment? One explanation is failure to perform third-trimester screening because the patient is not known to be high risk. Providers can be hesitant to ask uncomfortable questions about sexual histories. Reinfection is another cause as many providers assume a treated patient will remain infection-free and do not retest previously treated patients in the third trimester. Moreover, as noted, up to half of all cases occur in low-risk women. Albright et al. used a decision support model to show that universal re-screening in the third trimester would be a cost-effective way of reducing associated morbidity. For example, re-screening all pregnant women in the United States would prevent 60 cases of congenital syphilis annually, seven stillbirths and four neonatal deaths at a cost of $419,842 for each case prevented. Louisiana requires rescreening in the third trimester for all pregnant women and the Arizona Department of Health recently began recommending universal screening at the first prenatal visit, in the third trimester and at delivery. In response to high rates of congenital infection, especially in Caddo Parish which includes Shreveport, Louisiana has become an exemplar in the fight against congenital syphilis. The state established regional review boards to identify factors leading to cases and propose effective interventions. Of the 79 cases occurring there over an 18-month period, roughly one-third involved providers failing to perform adequate screening. The state has now hired a nurse practitioner to conduct grand rounds and raise provider awareness about screening. In about another third, treatment was either not given (e.g., the patient never returned for care), was incomplete or was delayed. Because treatment for late latent disease requires three weekly doses of penicillin with the need to repeat the series if more than a week elapses between therapies, the state is assessing whether visiting nurses administering injections at home improves adherence. However, in 40% of cases affected patients never received prenatal care for a variety of reasons (e.g., lack of awareness of their condition, no transportation, fear of receiving care related to substance abuse or domestic violence). Tackling these social determinants presents a far bigger challenge with no simple solutions.

Take-home message

Rates of congenital syphilis have been rising sharply over the past few years from multiple causes. At a minimum universal screening should be done at the first visit with re-screening in high-risk women in the third trimester and at delivery. However, I believe the time has come for all states, and certainly those with the highest incidence, to require universal re-screening in the third trimester and a third screen at delivery in high-risk women.

Dr. Lockwood, editor in chief, is Senior Vice President, USF Health, and Dean, Morsani College of Medicine, University of South Florida. He can be reached at DrLockwood@mmhgroup.com

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Nearly 1 in 5 pregnancies are complicated by a perinatal mood disorder, but screening remains infrequent and underutilized.

Read more about postpartum care on page 17 and get a patient screening handout on page 50.

Do you screen your postpartum patients for postpartum depression?

Nearly 1 in 5 pregnancies are complicated by a perinatal mood disorder, but screening remains infrequent and underutilized. Read more about postpartum care on page 17 and get a patient screening handout on page 50.

59%
71 said Yes

41%
50 said No

TAKE THE SURVEY AT contemporaryobgyn.net/PPDscreen
Reproductive risks of advanced paternal age

Older age in men may impair conception and it can also have implications for fetal wellbeing, birth outcomes, and long-term health of offspring.

by RANJITH RAMASAMY, MD, JADEN KOHN, MD, MPH, AND JEFFREY K. THAN, BS

With the growing trend of couples choosing to start their families at a later age, ob/gyns must be prepared to counsel patients regarding the effects of advanced paternal age (APA) on reproductive outcomes and on their future offspring. Compared to data from 1993, the proportion of live births to fathers aged 35 to 54 increased by 15% over 10 years, with the trend continuing to climb.1 In the United States, among fathers aged 35 to 39, 40 to 44, and 45 to 49 years, birth rates increased 61%, 63%, and 52%, respectively.2 Socioeconomic factors, increased life expectancy, and growing accessibility of assisted reproductive techniques (ART) all have contributed to the rise in paternal age.3 Although a woman’s natural fertility terminates with menopause, spermatogenesis continues throughout life.4

Although APA is commonly defined as age 40 years or older, no universally accepted criteria for it exist. The American College of Medical Genetics (ACMG) has not established an age cutoff for APA and does not currently recommend additional screening or diagnostic intervention for offspring of older men.5 Specifying a clear paternal age for APA is complicated by the heterogeneity of the reproductive outcomes and offspring risks noted in the literature. As noted by Ramasamy et al., many studies do not define an age threshold for APA and those that establish a threshold span a wide range of ages.6

While fathering children at an older age remains a viable option, couples should be counseled on the effects of APA that could impair conception, such as altered sperm parameters and reproductive hormones, and data supporting increased risk of adverse outcomes such as congenital birth defects, neurocognitive disorders, and fetal deaths. This review summarizes recent findings surrounding the reproductive risks of APA.

Reproductive outcomes

Possible impairment of reproductive outcomes is an important implication of APA. With an age-related decrease in testosterone, older men experience decreases in libido, sexual function, and sexual frequency, reducing opportunities for conception.7-10 Fur-
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ther, a review of the literature from 1980 to 1999 found a decrease in semen volume (3%-22%), sperm motility (3%-3%), and percent normal sperm (4%-18%) in 50-year-old men compared with 30-year-old men. In addition, controlling for female age, actual rates of pregnancy fathered by men over age 50 year were 23% to 38% lower than those in men younger than age 30. Similarly, a meta-analysis of 90 studies quantifying the effect of male age on ejaculate traits (n=93,839) found statistically significant age-associated declines in semen volume, percent motility, progressive motility, morphology, and unfragmented cells, while sperm concentration had no associated changes with increasing male age. A retrospective study performed by Hossain et al. also identified significant decreasing trends in semen volume and sperm motility with increased paternal age. Similarly, a large prospective study identified decreases in sperm motility with increased paternal age. Further, lifestyle factors accrued over the life of the male—such as obesity, smoking, and marijuana use—also may contribute to impaired reproductive outcomes, though this remains an active area of research. These changes in semen parameters can be associated with fertility impairment in older men, but the association remains unproven.

**Paternal age and ART outcomes**
The changes in semen parameters seen in older men may impact outcomes of ART. In couples who underwent ART, McPherson et al. found that women aged 35 with a partner older than age 40 had an approximately 10% decrease in live birth rate compared with women of similar age who had younger partners (n=4,057). In a retrospective study of 859 cycles of in vitro fertilization (IVF) and 1632 of intracytoplasmic sperm injection (ICSI), Chapuis et al. identified a significantly decreased rate of clinical pregnancies in men older than age 51 (28.2%) compared with men aged 20 to 29 (41.5%). However, this result may be confounded by the older maternal age in this study (36.5±4.9 years).

**Altered reproductive outcomes in older men may be related to increased DNA fragmentation in sperm, with as much as 80% of fragmentation attributed to oxidative stress.**

After adjusting for female age, a retrospective study of 4,025 embryos from 1,169 IVF cycles found a significant decrease in euploidy rate compared to men aged 35 to 40 and younger than age 35. However, a recent multicenter study of 1,202 IVF/ICSI cycles (6,934 embryos) found no association between advancing paternal age and embryo aneuploidy. Further, a large retrospective study of 2,204 intrauterine insemination cycles, 1,286 standard IVF/ICSI cycles, and 1,412 ovum donation IVF/ICSI cycles identified no association between male age and implantation, pregnancy, and miscarriage rates among maternal age groups. APA does not appear to conclusively impact ART outcomes, and certainly not to the extent contributed by advanced maternal age, but it remains an area of active research.

**Paternal age and fetal health**
APA may also increase the risk to the fetus during pregnancy—particularly increased risk of spontaneous abortion and very preterm birth. Adjusting for maternal age, Kleinhaus et al. (2006) identified a 60% increase in odds of spontaneous abortion in fathers aged 40 or older when compared with fathers aged 25 to 29. Compared with that in men aged 20 to 24, a risk of very preterm birth (< 32 weeks) was increased by 70% in men aged 40 to 44 whose partners were aged 20 to 29. Similarly, another study demonstrated increased odds of very preterm births among fathers aged 45 to 49 compared with fathers aged 25 to 29, for both mothers aged 20 to 24 (91%) and mothers aged 25 to 29 (72%). Altered reproductive outcomes in older men may be related to increased DNA fragmentation in sperm, with as much as 80% of DNA fragmentation attributed to oxidative stress. Singh et al identified a 15% increase in highly damaged DNA and 20% increase in DNA break number in sperm from men aged 36 to 57 compared with men aged 20 to 35 (n=66). A similar study found a significantly higher DNA fragmentation index (DFI) in men aged ≥ 45 compared with men aged < 45 years (P < 0.01 for all comparisons, n=1,125); in particular, men aged ≥ 45 had a more than two-fold increase in DFI compared with men aged < 30 (32.0±17.1% vs. 15.2±8.4%). In addition, a recent meta-analysis of 26 studies identified a strong negative effect of male age on the percentage of sperm cells with unfragmented DNA (r = -0.209, 95% CI -0.287, -0.128).
Interestingly, the effect size of male age on DNA fragmentation was the largest of the study. However, while sperm from older men have a loss of DNA integrity, likely secondary to oxidative stress, conclusions about the impact on reproductive outcomes remain unclear.

**Medical comorbidities**

Because spermatogenesis is a continuous and ongoing process throughout the reproductive lifetime, spermatozoa are prone to acquiring DNA mutations, particularly due to the oxidative stress in aging men. This increased rate of mutation places the sperm of older men at risk of acquiring mutations that impact the health of their offspring. After the discovery of a link between APA and achondroplasia, an increasing number of disorders have been identified to be associated with increasing paternal age. Of note, incidence of chromosomal aneuploidies—an abnormal number of chromosomes—increases with the age of the father. When controlling for random variation, a study on genome-wide de novo single-nucleotide polymorphism (SNP) mutation rates in offspring similarly demonstrated two mutations per year of paternal age. In women aged 35 and greater, Fisch et al identified a two-fold increase in the rate of neonates with Trisomy 21 when the father was aged ≥ 40 compared with ≤ 24 years. Similarly, when controlling for maternal age, men aged ≥ 50 had a two-fold greater odds of a child with Down syndrome compared with men aged 25 to 29. In addition, one case-control study indicated that a 10-year increase in paternal age increased the odds of Klinefelter syndrome by 35%. Overall, APA appears to account for a small proportion of chromosomal aneuploidies.

Much of the literature similarly supports a correlation between paternal age and risk of neurocognitive disorders. Four hypotheses have been suggested to explain this increased risk with APA:

1. Increased frequency of de novo mutations;
2. Age-related epigenetic alterations in sperm;
3. Selection into late fatherhood secondary to paternal psychiatric disorders or subclinical predisposition; and
4. Environmental characteristics.

A recent review suggests that these etiologies—both inherited predisposi-
tion and de novo events—may all contribute to the complex neurocognitive disorders associated with APA. A large study of individuals born in Denmark over a 51-year span (n=2,894,688) identified a 34% increase in risk of any psychiatric diagnosis in offspring of fathers aged 45 or older compared with offspring of fathers aged 25 to 29. A similar study composed of individuals born in Sweden over a 28-year span (n=2,615,081) compared siblings and identified an increased risk of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder, psychosis, bipolar disorder, suicide attempts, substance abuse, failing a grade, and low education attainment in offspring born to fathers aged 45 or older compared with fathers aged 20 to 24. Of note, risks for ADHD (hazard ratio [HR] 13.13, 95% CI 6.85-25.16) and bipolar disorder (HR 24.70, 95% CI 12.12-50.31) were particularly increased. A meta-analysis of 12 studies similarly found increased risk of schizophrenia associated with fatherhood at aged 30 or older compared to age 25 to 29, with the highest effect size in men aged 50 or older (RR 1.66, 95% CI 1.46-1.89).

The literature most strongly supports a link between APA and ASD. D’Onofrio et al. (2014) identified a nearly 3.5 times higher risk of ASD in offspring born to fathers aged 45 or older. A recent meta-analysis of 27 studies similarly found a 55% increased risk of ASD in the highest paternal age category; an increase of 10 years in paternal age was associated with a 21% increase in risk of ASD. This association has been supported by several other studies spanning a wide range of populations and databases.

The neurocognitive implications of APA, particularly increased risk of ASD, must be considered when counseling patients regarding APA.

In addition to neurocognitive disorders and chromosomal aneuploidies, APA has associated risk of medical comorbidities and advanced paternal age

<table>
<thead>
<tr>
<th>Chromosomal Aneuploidy</th>
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<th>Risk</th>
<th>Reference</th>
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</thead>
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<tr>
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<td>≥ 40 (≤ 24)</td>
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<td></td>
<td>≥ 50 (25-29)</td>
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<td>Cleft palate</td>
<td>≥ 40 (20-39)</td>
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<tr>
<td>Central nervous system neoplasms</td>
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TABLE 1
Associated risk of medical comorbidities and advanced paternal age

CONTINUED ON PAGE 44
Redefining postpartum care
A paradigm shift toward the continuum of well women’s health

Ob/gyns, support staff, and patients all need to be educated about the needs of the mother/child dyad during the “fourth trimester.”

by HAYWOOD L. BROWN, MD

Postpartum follow-up is important to the well-being of the mother, her infant, and their long-term health. As such, the postpartum visit must gain a renewed sense of importance for the woman and her providers. The new mother must adapt physically and emotionally to changes that have occurred from childbirth. The initial postpartum follow-up should occur within 3 weeks after childbirth and is the start of an individualized plan for the continuum of care that encompasses counseling, services, interconception and contraceptive management for reproductive life planning, and support to optimize immediate and long-term health.

Approximately 60% of maternal deaths occur postpartum. In fact, women are more likely to die of pregnancy-related conditions in the weeks following birth than during pregnancy or intrapartum. This burden falls disproportionately on women of color, with black women being three to four times more likely to die of pregnancy-related causes than white women.1 For example, risk of thromboembolic events and maternal death is greatest in the first 2 to 4 weeks postpartum.2 Cesarean delivery approximately doubles the risk of venous thromboembolism, but in an otherwise normal patient, risk is still low at approximately 1 per 1,000 patients.

Early postpartum follow-up within the first 3 weeks following childbirth is especially important for mothers with preexisting health conditions such as hypertension, diabetes, and gestational diabetes, heart conditions, depression, substance addiction, and other medical complications that might have been exacerbated by pregnancy and those women who suffered a near-miss maternal morbidity. Maternal near-miss morbidity is defined as a catastrophic obstetric event where the pregnant woman comes close to death but survives. For every woman who has a pregnancy-related death there

DR. BROWN is professor, obstetrics and gynecology, and associate dean, Morsani College of Medicine, University of South Florida, Tampa.
are approximately 50 to 100 episodes of severe maternal morbidity affecting more than 50,000 women in the United States every year. It is estimated that as many as 40% of women do not have postpartum follow-up. Attendance is even lower for women with limited resources and where access to perinatal care is a challenge, as in many rural communities in the United States. In these settings it would be potentially helpful for improving postpartum participation to coordinate the infant follow-up visit with the woman’s postpartum visit. Telehealth can also be used to help facilitate follow-up. It is also interesting that women who deliver in a rural hospital setting have an associated higher rate of postpartum hemorrhage. It is essential that these women have postpartum follow-up for counseling on recurrence risk and reproductive life counseling to decrease risk in subsequent pregnancy.

Potential ramifications of lack of postpartum follow-up include early discontinuation of breastfeeding, undiagnosed postpartum depression and anxiety disorders, lack of family planning and increased recurrence risk for preterm birth (PTB), preeclampsia and gestational diabetes. Lack of follow-up contributes to racial disparity in prematurity and infant mortality. Risk for recurrent PTB is more likely for those women with a short interpregnancy intervals within 12 months of delivery and subsequent conception. Four of 10 mothers with

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Candidates for follow-up within the first 3 weeks postpartum</th>
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| **Hypertensive disorders** | - No later than 7 to 10 days  
- 3 days for those with preeclampsia with severe features* |
| **Risk for postpartum depression** | - Screen and evaluate for medication and referral |
| **Cesarean delivery** | - Evaluation for wound healing and complications |
| **Lactational challenges** | |
| **Substance abuse/addiction** | - Monitor opioid maintenance therapy and risk for opioid overdose |
| **Chronic conditions** | - Diabetes, heart disease, those at higher risk for thromboembolism |

*Alliance for Innovation in Maternal Health (AIM) Safety Bundle for Severe Hypertension in pregnancy

Medicaid coverage do not come in for a postpartum follow-up visit. This vulnerable population does not have the opportunity to receive care and support for common problems such as postpartum depression and breastfeeding challenges. Multiple barriers prevent women with Medicaid from accessing postpartum care. In 19 states, Medicaid coverage for pregnancy ends at 60 days postpartum, cutting women off from access to care during this critical period. When women do not come in for a postpartum visit, they do not have an opportunity for education and to receive information about nutrition, exercise, and pregnancy spacing. For example, a woman with no postpartum follow-up who has experienced a postpartum hemorrhage and anemia is more vulnerable to maternal morbidity and mortality if she has an unplanned pregnancy before she has an opportunity to return to a healthier state.

**Strategies to improve breastfeeding initiation and continuation**

The 2020 breastfeeding objectives are to increase the proportion of infants who are breastfed at any time to 81.9%, at 6 months to 60.6%, exclusively through 3 months to 46.2% and exclusively through 6 months 25.5%. Rates of exclusive breastfeeding between 3 and 6 months are lowest for black infants and infants of mothers who are young, unmarried, less educated, and who live in rural areas. Current low rates of breastfeeding continuation and exclusivity, particularly for black infants, suggest that infants and mothers are not receiving maximum health benefits. These differences contribute to infant, childhood, and adult health disparities. Breastfeeding benefits include decreased risk for childhood and adult obesity and decreased risk

Between 2014 and 2017, 33 hospitals enrolled in the CHAMPS program from Boston Medical Center’s Center for Health Equity, Education and Research. The program was intended to decrease racial disparities in breastfeeding by using a community and hospital collaborative strategy to improve maternity care practices and implement the Ten Steps to Successful Breastfeeding Initiative.
for diabetes, hypertension, and cardiovascular disease.12-14

A recent study examined how effective a hospital- and community-based initiative could be in reducing racial disparities while at the same time helping participating hospitals achieve a Baby-Friendly designation.15 Between 2014 and 2017, 33 hospitals enrolled in the CHAMPS (Communities and Hospitals Advancing Maternity Practices) program from Boston Medical Center’s Center for Health Equity, Education and Research.15 The program was intended to decrease racial disparities in breastfeeding by using a community and hospital collaborative strategy to improve maternity care practices and implement the Ten Steps to Successful Breastfeeding Initiative. Enrolled hospitals received intensive quality improvement and technical assistance intervention to enhance compliance. The authors found that the average rate of breastfeeding initiation at CHAMPS-enrolled hospitals rose from 66% to 75% and the average rate of breastfeeding exclusivity rose from 34% to 39%. The disparity between African-American and white infants regarding breastfeeding initiation disparity decreased by 9.6% over 31 months. Among black infants, rates of breastfeeding initiation and exclusivity increased from 46% to 63% and 19% to 31%, respectively.15

Some specific barriers for breastfeeding continuation after hospital discharge include lack of knowledge by mothers and providers of the dose-related health benefits, the knowledge that small quantities of colostrum in the first days after delivery are sufficient to meet the needs of a term newborn, inadequate family and social support, comfort level with formula feeding, employment and childcare practices, and lack of breastfeeding role models. Early postpartum contact by phone and/or face time or office visit within the first weeks following birth allows breastfeeding mothers and providers the opportunity to identify breastfeeding challenges and to provide lactation counseling and support that improves breastfeeding continuation and exclusivity rates.5

A cutoff score of 13 [on the EPDS] is a very reliable indicator of postpartum depression.

Postpartum depression
Depression is more common in women than in men and peaks for women during the reproductive years.16 Perinatal depression, which includes pregnancy and the 12 months following childbirth is a common medical complication affecting one in seven women. Previous studies indicate that approximately 10% of pregnant and postpartum women met the criteria for perinatal depression.17 Women with lower income, lower educational attainment, and unintended pregnancy are at even higher risk for depression during pregnancy and postpartum.18 Women with a history of depression or anxiety are candidates for early postpartum follow-up. Other high-risk factors include a previous history of postpartum depression, stressful life event, traumatic birth events (near-miss morbidity), premature birth of an infant with a need for neonatal intensive care and/or birth defects, and low levels of social support.

In the United States, the Edinburgh Postnatal Depression Scale (EPDS) is the validated screening tool for postpartum depression most commonly used in current clinical practice.19 It takes approximately 5 minutes to complete and has a high sensitivity and specificity for depression diagnosis. A cut-off score of 13 is a very reliable indicator of postpartum depression. System-wide recommendations for postpartum depression detection are to ensure that all pregnant and postpartum women are screened to optimize detection, referral, and treatment; educate providers on risk factors; and have focused preconception discussions about the impact on pregnancy and pregnancy complications for those with preexisting mental disorders.

Women with perinatal depression are at higher risk for suicide. Women whose screening suggests suicidal thoughts warrant prompt evaluation, monitoring, psychiatric intervention and treatment. Women on medications for anxiety or depression during pregnancy should be evaluated for worsening symptoms and should not discontinue medications during pregnancy nor postpartum due to concerns for fetal or infant harm from placental transfer of the medication or from breastfeeding. Medications should be adjusted or initiated based on individual patient circumstances and symptoms in conjunction with a mental health provider for maximum benefit and follow-up.
In recent years, suicide has become a more common cause for maternal mortality in the postnatal period. There has been a decline in suicide deaths per 100,000 live births over the last couple of decades with the introduction of national guidelines for screening for depression and recommendations for prediction, detection and treatment of mental disorders during pregnancy and up to 1 year postpartum. However, suicide continues to contribute to approximately 1.5 of 100,000 maternal deaths in the United States. Deaths from opiate addiction and overdose have recently contributed to the rise in maternal mortality.

Women with addiction, especially those on opioid maintenance therapy, are prone to overdose and require special attention in the postpartum period. Particularly in women with chronic pain disorders, medications for postpartum pain management should be carefully prescribed and monitored. Women being treated for pain with opioids are especially vulnerable and should be evaluated in the first 2 to 3 weeks for medication adjustment and referral to experts in pain management for follow-up.

Achieving a healthier weight
The postpartum and inter-conception period is an opportunity to address obesity/overweight during pregnancy and goals for achieving a healthier adult weight. In a large systematic review and meta-analysis of over 1 million pregnant women, 47% had gestational weight gain in excess of the Institute of Medicine (IOM) (now National Academy of Medicine) recommendations. Women who have weight gain exceeding IOM guidelines during pregnancy are at two to four times higher risk of being overweight or obese. Excessive weight gain is associated with an increased risk for complications in a future pregnancy and increased risk for hyperlipidemia, diabetes, hypertension, cardiovascular disease, and early mortality. As such, implications for lack of weight loss postpartum combined with short pregnancy intervals include generational obesity, hypertension, diabetes, and the potential for early death.

Sexuality
A return to normal sexual intimacy postpartum is an expectation for most couples. Dyspareunia is reported by 41% to 67% of women 2 to 3 months postpartum depending on the severity of perineal trauma at delivery. Typical healing and perineal pain resolve by 3 months; however, some women will experience dyspareunia for a longer period. Urinary and perineal incontinence is highly prevalent in the postpartum period. The highest frequency is seen in women who have a severe perineal laceration involving the anal sphincter and those with instrument/operative vaginal deliveries. Publications from the Pelvic Floor Network Childbirth and Pelvic symptoms (CAPS) study put the prevalence of fecal incontinence at 17% in primiparous women who delivered vaginally with a recognized anal sphincter tear compared to 8.2% for those who delivered vaginally without anal sphincter tears. Urinary incontinence prevalence was 31.2% for all women irrespective of perineal injury. These symptoms have a significant impact on quality of life postpartum and several months to years after delivery.

Women with perineal lacerations, especially severe laceration or injury, should have early postpartum follow-up and be asked about flatus, fecal, and urinary incontinence. Because of embarrassment, a woman might be reluctant to volunteer that she has symptoms and/or downplay the severity. As such, it is important for providers to be aware of the prevalence of incontinence postpartum and provide reassurance and prompt referral to a subspecialist when appropriate so that early intervention can be initiated.

It is important for providers to engage in a conversation regarding the emotional and sexual expectations of couples during pregnancy, discuss normal variation and fluctuation in sexual activity during pregnancy, and provide anticipatory guidance on the postpartum changes that impact sexual function.

Family planning and pregnancy spacing
Pregnancy spacing of 12 to 18 months is associated with improved birth outcome in subsequent pregnancy especially, in women who experience an adverse pregnancy outcome such as PTB. Furthermore, the ideal recommended pregnancy interval is
**Indication**

EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Safety and efficacy have not been established in other nerve blocks.

**Important Safety Information**

EXPAREL is contraindicated in obstetrical paracervical block anesthesia. Adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via interscalene brachial plexus nerve block were nausea, pyrexia, and constipation. If EXPAREL and other non-bupivacaine local anesthetics, including lidocaine, are administered at the same site, there may be an immediate release of bupivacaine from EXPAREL. Therefore, EXPAREL may be administered to the same site 20 minutes after injecting lidocaine. EXPAREL is not recommended to be used in the following patient population: patients <18 years old and/or pregnant patients. Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease.

**Warnings and Precautions Specific to EXPAREL:**

Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL. EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks other than interscalene brachial plexus nerve block, or intravascular or intra-articular use. The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.

**Central Nervous System (CNS) Reactions:**

There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesia. CNS reactions are characterized by excitation and/or depression.

**Cardiovascular System Reactions:**

Toxic blood concentrations depress cardiac conductivity and excitability which may lead to dysrhythmias, sometimes leading to death. Allergic Reactions: Allergic-type reactions (eg, anaphylaxis and angioedema) are rare and may occur as a result of hypersensitivity to the local anesthetic or to other formulation ingredients. Chondrolysis: There have been reports of chondrolysis (mostly in the shoulder joint) following intra-articular infusion of local anesthetics, which is an unapproved use. Methemoglobinemia: Cases of methemoglobinemia have been reported with local anesthetic use.

Please refer to brief summary of full Prescribing Information on adjacent page. Full Prescribing Information is available at www.EXPAREL.com.

**FOR MORE INFORMATION, PLEASE VISIT WWW.EXPAREL.COM OR CALL 1-855-RX-EXPAREL (793-9727).**

INDICATIONS AND USAGE
EXPAREL is indicated for single-dose infiltration in adults to produce postoperative local analgesia and reduce patient-reported pain following various surgical procedures. EXPAREL may be administered simultaneously in the same syringe, and bupivacaine HCl may be administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more.

NON-INTERCHANGEABILITY WITH OTHER FORMULATIONS OF BUPIVACAINE

The chemical composition and physical form of the lipid component. Such differences affect a drug's functional properties relative to those of the unencapsulated or free drug. Different formulations of bupivacaine are not bioequivalent even if the milligram strength is the same. Therefore, it is not possible to convert dosing from any other formulations of bupivacaine to EXPAREL.

DOSE AND ADMINISTRATION

Important Doze and Administration Information

• EXPAREL is intended for single-dose administration only. Infusion is not recommended even if the milligram strength is the same. Therefore, it is not possible to convert dosing from any other formulations of bupivacaine to EXPAREL.

• DO NOT dilute EXPAREL with water for injection or other hypotonic agents, as it will result in disruption of the liposomal particles.

DOSE ADMINISTRATION

Contraindications

• Do not administer EXPAREL if it is suspected that the vial has been frozen or exposed to high temperature (greater than 40° or 104°F) for 24 hours or longer.

• Inspect EXPAREL visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if more than one vial of EXPAREL is being used in the same patient.

RECOMMENDED DOING IN ADULTS

Local Analgesia via Infiltration

The recommended dose of EXPAREL for infiltration in adults is up to a maximum dose of 268mg (50 mL), and is based on the following factors:

• Size of the surgical site
• Volume required to cover the area
• Individual patient factors that may impact the safety of an analgesic therapy

As general guidance in selecting the proper dosing, two examples of infiltration dosing are provided:

1. In patients undergoing bunionectomy, a total of 108 mg (6 mL) of EXPAREL was administered with 7 mL infiltrated into the tissues surrounding the bunion, and 1 mL infiltrated into the subcutaneous tissue.

2. In a patient undergoing bilateral mammoplasty, a total of 268 mg (20 mL) of EXPAREL was diluted with 10 mL of saline, for a total of 30 mL, divided into bilateral mammary fat pads (this is subject to local variability in technique and face and slowly infiltrating one aliquot to each of the even numbers to produce a field block.

Pharmacokinetics

Bupivacaine HCl is amphoteric, and therefore may be absorbed from acidic, neutral, and basic solutions. Bupivacaine HCl is only partially soluble in water, and hence, the drug must be dissolved in a solvent, such as saline. None of the materials studied had an adverse effect on EXPAREL. As general guidance in selecting the proper dosing, two examples of infiltration dosing are provided:

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POSTPARTUM CARE

18 months after a cesarean delivery and 12 to 18 months after a vaginal birth.5,28 Counseling on a method of contraception should occur during the prenatal period and the woman’s choice confirmed in the immediate postpartum period prior to her hospital discharge. This is important because so many women do not present for postpartum follow-up. While women are encouraged not to engage in intercourse until “6 weeks postpartum,” approximately 25% are having unprotected intercourse before that 6-week visit. Most first menstrual cycles after birth are anovulatory, and for those women who are not breastfeeding, ovulation and the risk of pregnancy significantly increases from the first cycle after giving birth to almost 90% with the second menstrual cycle after childbirth.

Immediate postpartum long-acting reversible contraception (LARC) is becoming more of an option for women after vaginal delivery and cesarean. LARC provides pregnancy spacing with fewer contraceptive failures than other methods of birth control. The rate of expulsion is lower than 10% with “post-placental” insertion of an intrauterine device (IUD), that is, placement within 10 minutes after placental delivery. For implantable contraception, the most effective progesterone-only method, there is minimal risk associated with placement within the first several days or weeks postpartum. Some described side effects for implants include irregular bleeding, headaches, dizziness, weight gain, and acne.

For women with post-placental IUD insertion, an early postpartum examination within the first 3 weeks should be done to check for expulsion and trim the IUD string. Early postpartum is also a perfect time to place LARC with follow-up at 12 weeks for further discussion on reproductive life planning.

Pregnancy complications and long-term health
There are several pregnancy complications that increase risk for cardiovascular disease (CVD), including pre-eclampsia, gestational diabetes, PTB and intrauterine growth restriction (IUGR).29 For example, women with a history of preeclampsia have an approximate 4-fold higher incidence of later development of chronic hypertension and a two-fold elevated risk of heart disease, stroke, and venous thromboembolism.29,30 A combination of recurrent preeclampsia, PTB or IUGR carries a cardiovascular risk later in life comparable to obesity or smoking.29 Hence, the American College of Obstetricians and Gynecologists (ACOG) recommends annual blood pressure, fasting glucose, lipid and body mass index checks and counseling on reducing risk for early-onset CVD for women with specific pregnancy complications such as preeclampsia and gestational diabetes.5

Gestational diabetes (GDM) impacts between 5% and 10% of all pregnancies and women with it have a seven-fold risk for development of Type 2 diabetes. ACOG recommends screening women with GDM 4 to 12 weeks postpartum for diabetes and pre-

### TABLE 2 Components of the postpartum plan

<table>
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<th>The visit</th>
<th>Reproductive life plan</th>
<th>Pregnancy complications</th>
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<td>Timing, date, and location for first follow-up visit between 2-4 weeks, comprehensive follow-up no later than 12 weeks</td>
<td>Family planning/contraception</td>
<td>Obstetrical morbidities and recurrence risk counseling</td>
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<tr>
<td>Infant feeding plan</td>
<td>Chronic health conditions</td>
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Gestational diabetes (GDM) impacts between 5% and 10% of all pregnancies and women with it have a seven-fold risk for development of Type 2 diabetes. ACOG recommends screening women with GDM 4 to 12 weeks postpartum for diabetes and pre-
diabetes with an oral glucose tolerance test.\textsuperscript{5,31} In a study by Eggleston et al. of 447,556 women across 50 states of whom 7.2\% had GDM, 75\% had no follow-up screen within 1 year.\textsuperscript{32} In another study of women with GDM, only 23.4\% received any kind of glucose test by 6 months postpartum.\textsuperscript{33} Unfortunately, the screening recommendation for diabetes for those women with GDM in the postpartum period is not consistently followed and education on the importance of follow-up testing for diabetes has important implications for long-term wellness. Finally, PTB occurs in 8\% to 12\% of pregnancies and is a leading contributor to infant mortality disparity. What is unappreciated is that women who deliver a low-birth-weight infant, either preterm or term with growth restriction (< 2500 g) have a two-fold higher risk for cardiovascular disease and death.\textsuperscript{34}

**Conclusion**

Adjustment to childbirth in the first several weeks postpartum can be challenging for many mothers, especially as they navigate the physical and emotional changes and sleep deprivation associated with caring for a newborn. Most women must make these adjustments without support from a family member during the first several weeks after childbirth.

Redefining the postpartum period and using it to promote the continuum of well women’s care will require a paradigm shift. A concerted effort must be made to educate patients, providers and support staff about the importance of the immediate needs of mother and child postpartum and what a woman might expect or experience in the first several weeks after giving birth. This is especially important for women on Medicaid and those with concerns about access to care and or who might not have culturally congruent support at home. Community health workers and, for some women, postpartum doulas can assist in filling this void in the first days and weeks after childbirth, particularly for vulnerable populations. The postpartum visit appointment should be discussed and scheduled during the last month of pregnancy and reemphasized at the time of hospital discharge. The continuum of care is particularly important for women with pregnancy complications that place them at higher risk for later development of hypertension, diabetes and heart disease. Ob/gyns and their team of providers are uniquely qualified to provide immediate postpartum evaluation and counseling and to annually evaluate women as they proceed through the reproductive years and beyond.

Finally, Medicaid finances nearly 50\% of all births in the United States. Advocating for policies that extend Medicaid at least 3 months and hopefully 12 months after childbirth would improve the continuum of women’s health care.

**DISCLOSURES** The author reports no potential conflicts of interest with regard to this article.

**FOR REFERENCES VISIT**

contemporaryobgyn.net/RedefiningPostpartumCare

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**CHECK OUT OUR HANDOUT OF THE MONTH:** In the United States, the Edinburgh Postnatal Depression Scale (EPDS) is the validated screening tool for postpartum depression most commonly used in current clinical practice.\textsuperscript{19} It takes approximately 5 minutes to complete and has a high sensitivity and specificity for depression diagnosis. A cut-off score of score of 13 is a very reliable indicator of postpartum depression. **Find a copy of the Edinburgh Postnatal Depression Scale patient questionnaire and scoring information on PAGE 50**
Counseling on complex contraception dilemmas

This installment in our series looks at postpartum contraceptive options for a pregnant patient with comorbidities

by CHARISSE M. LODER, MD, MSC, AND KIRSTEN BONAWITZ, BS

Prenatal visits are an opportunity to discuss future fertility plans and contraceptive planning following delivery. As ob/gyns, we have a responsibility to ensure that women feel empowered to make contraceptive decisions that best fit their needs and desires. Thus, it is important to review patients’ medical comorbidities as well as their preferences and beliefs during prenatal care to develop a postpartum contraceptive plan.

A provider’s contraceptive counseling approach has implications for the patient-physician relationship, patient satisfaction, and contraceptive continuation. Studies have shown that patient satisfaction with counseling is correlated with higher rates of contraceptive use and greater satisfaction with contraceptive choice.\(^1\) High-quality, fair counseling should incorporate the concept of shared decision-making—in which the provider and the patient work collaboratively, with the provider offering medical information and expertise and the patient stipulating her experiences and preferences—in order to select a method that is safe, effective, and meets the needs, desires, and expectations of the patient.\(^2\) It is also important to recognize that disparities exist in contraceptive care because of racial, ethnic, and economic differences.\(^3\) In addition, there is the potential for bias in contraceptive counseling or recommendations.\(^4\)

Patient satisfaction with counseling is correlated with higher rates of contraception use.

CASE

Nina, a 34-year-old G4P3 at 28 weeks’ gestation, presents for her prenatal appointment. Her medical history is complicated by chronic hypertension, controlled with labetalol and nifedipine, and Crohn’s disease without medications. She has an obstetric history significant for three preterm deliveries at 36, 35, and 34 weeks due to induction of labor for pre-eclampsia with severe features. Nina also has a complicated surgical history, with multiple bowel surgeries and a small bowel resection due to Crohn’s disease. She feels that this pregnancy will complete her childbearing and is interested in discussing birth control options. In addition, she is concerned because she will lose her health insurance 60 days after delivery and she wants to have an effective contraceptive method in place beforehand.

Dr. Loder is a clinical instructor, Michigan Medicine, University of Michigan, Ann Arbor.

Ms. Bonawitz is a research assistant at Michigan Medicine, University of Michigan, Ann Arbor.
FOR THE TREATMENT OF MODERATE TO SEVERE VASOMOTOR SYMPTOMS (VMS) DUE TO MENOPAUSE IN WOMEN WITH A UTERUS

FIRST OF ITS KIND: INTRODUCING THE ONLY FDA-APPROVED BIO-IDENTICAL COMBINATION HORMONE THERAPY

TWO BIO-IDENTICAL* HORMONES PRECISELY COMBINED

*Bio-identical hormones are structurally identical to the hormones produced within a woman's body. The relevance of risks associated with the use of synthetic hormones compared to bio-identical hormones is not known but cannot be excluded.

INDICATION
BIJUVA™ is a combination of estradiol and progesterone indicated in a woman with a uterus for the treatment of moderate to severe vasomotor symptoms due to menopause.

IMPORTANT SAFETY INFORMATION

WARNING: CARDIOVASCULAR DISORDERS, BREAST CANCER, ENDOMETRIAL CANCER, AND PROBABLE DEMENTIA

See full prescribing information for complete boxed warning.

Estrogen Plus Progestin Therapy
- Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia
- The Women’s Health Initiative (WHI) estrogen plus progestin substudy reported increased risks of stroke, deep vein thrombosis (DVT), pulmonary embolism (PE), and myocardial infarction (MI)
- The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer
- The WHI Memory Study (WHIMS) estrogen plus progestin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age or older

Estrogen-Alone Therapy
- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens
- Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia
- The WHI estrogen-alone substudy reported increased risks of stroke and DVT
- The WHIMS estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age or older
OFFER HER VMS RELIEF WITH THE CONVENIENCE OF BIJUVA

The first and only FDA-approved combination of bio-identical estradiol and bio-identical progesterone in a single, once-daily oral capsule.

Reduction in moderate to severe VMS (hot flashes) with improvements in Menopause-specific Quality of Life and sleep measures.

A steady state of estradiol that reduces moderate to severe VMS with progesterone to reduce the risk to the endometrium.

IMPORTANT SAFETY INFORMATION (CONT’D)

CONTRAINDICATIONS
• BIJUVA is contraindicated in women with any of the following conditions: undiagnosed abnormal genital bleeding; known, suspected, or history of cancer of the breast; known or suspected estrogen-dependent neoplasia; active DVT, PE, or history of these conditions; active arterial thromboembolic disease (for example, stroke, MI), or a history of these conditions; known anaphylactic reaction, angioedema, or hypersensitivity to BIJUVA or any of its ingredients; known liver impairment or disease; known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders.

WARNINGS AND PRECAUTIONS
• An increased risk of PE, DVT, stroke, and MI has been reported with estrogen plus progestin therapy. Should these occur or be suspected, therapy should be discontinued immediately. Risk factors for arterial vascular disease and/or venous thromboembolism (VTE) should be managed appropriately.
• The WHI substudy of daily estrogen plus progestin after a mean follow-up of 5.6 years reported an increased risk of invasive breast cancer. Observational studies have also reported an increased risk of breast cancer for estrogen plus progestin therapy after several years of use. The risk increased with duration of use and appeared to return to baseline over about 5 years after stopping treatment (only the observational studies have substantial data on risk after stopping). The use of estrogen plus progestin therapy has been reported to result in an increase in abnormal mammograms requiring further evaluation.

Please note that this information is not comprehensive. Please see Brief Summary of the Full Prescribing Information, including the BOXED WARNING, on the following pages.


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To learn more about BIJUVA or request samples, visit BijuvaHCP.com or call 1-877-533-8096.
In patients with cardiovascular disease and dementia, the risk of developing cardiovascular disease or dementia is increased with estrogen plus progestin therapy, but the relationship is not fully understood. Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.3, and Clinical Studies (14.4, 14.5) in full prescribing information)].

BREAST CANCER

Estrogen plus progestin therapy may increase the risk of breast cancer in postmenopausal women. In postmenopausal women treated with estrogen plus progestin, the risk of breast cancer was increased compared to placebo in the WHI estrogen plus progestin substudy. In this study, the risk of breast cancer increased with duration of use, and appeared to return to baseline over about 5 years after stopping treatment (only the observational follow-up). The increased risk for estrogen-alone therapy, after several years of use, the risk increased with duration of use, and appeared to return to baseline over about 5 years after stopping treatment (only the observational follow-up).

In postmenopausal women who took daily oral estradiol (0.625 mg) plus medroxyprogesterone acetate (MPA) (2.5 mg) compared to placebo, there was a statistically significant increased risk of breast cancer compared to placebo (23 versus 15 per 10,000 women-years) [see Clinical Studies (14.4) in full prescribing information]. A subgroup analysis of women 50 to 59 years of age suggested a statistically non-significant reduction in CHD events (CE 0.625 mg)-alone compared to placebo in women who received daily estradiol receiving daily CE (0.625 mg) plus MPA (2.5 mg) compared to placebo (41 versus 34 per 10,000 women-years). An increased in relative risk was demonstrated in year 1 and a trend toward an increased relative risk was reported in years 2 through 5 [see Clinical Studies (14.4) in full prescribing information].

Exposure to estrogen plus progestin increases the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including endometrial sampling, should be undertaken in all patients who report symptoms suggestive of endometrial cancer (e.g., abnormal uterine bleeding, pelvic or abdominal pain, postmenopausal bleeding, or discharge), and in any postmenopausal patient in whom use of estrogen plus progestin therapy is being considered. A woman is at increased risk of endometrial cancer if she has ever been exposed to estrogen therapy in the absence of a concurrent progestogen or an increase in sex hormone binding globulin (SHBG) or if she has a documented history of endometrial hyperplasia or carcinoma. In the WHI estrogen plus progestin substudy, the risk of endometrial cancer was increased compared to placebo (35 versus 17 per 10,000 women-years). Statistically significant increases in risk for both DVT (26 versus 13 per 10,000 women-years) and PE (18 versus 8 per 10,000 women-years) were also demonstrated. The increased risk of VTE and the risk of breast cancer was increased compared to placebo (23 versus 15 per 10,000 women-years). Although only the increased risk of DVT reached statistical significance (23 versus 15 per 10,000 women-years), the increase in VTE risk was demonstrated during the first year and persisted (see Clinical Studies (14.4) in full prescribing information). Should a woman be found to be pregnant, estrogen plus progestin therapy should be discontinued immediately. In the WHI estrogen-alone substudy, the risk of VTE was increased for women receiving daily CE (0.625 mg)-alone compared to placebo (30 versus 22 per 10,000 women-years), although only the increased risk of DVT reached statistical significance (23 versus 15 per 10,000 women-years). The increase in VTE risk was demonstrated during the first 2 years [see Clinical Studies (14.4)]. Should a woman be found to be pregnant, estrogen plus progestin therapy should be discontinued immediately. If feasible, discontinuation should be at the time of, or within 2 weeks of, the first positive pregnancy test.

In women who reported prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 versus 25 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 versus 36 cases per 10,000 women-years for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.24, and the absolute risk was 41 versus 33 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 versus 25 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 versus 36 cases per 10,000 women-years for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.24, and the absolute risk was 41 versus 33 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 versus 25 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 versus 36 cases per 10,000 women-years for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.24, and the absolute risk was 41 versus 33 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 versus 25 cases per 10,000 women-years, for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 versus 36 cases per 10,000 women-years for CE plus MPA compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.24, and the absolute risk was 41 versus 33 cases per 10,000 women-years, for CE plus MPA compared with placebo.
dose. Most studies show no significant increased risk associated with use of estrogens for less than 1 year. The greatest risk appears associated with prolonged use, with an increased risk of 15- to 24-fold for 5 to 10 years or more. Consideration should be given to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.

There is no evidence that the use of natural estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen dose. Adding a progestogen to estrogen therapy in postmenopausal women has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.

Ovarian Cancer

The WHI estrogen plus progestin substudy reported a statistically non-significant increased risk of ovarian cancer (RR 1.5; 95% CI, 1.2 to 1.9). The relative risk of ovarian cancer for CE plus MPA versus placebo was 1.18 (95% confidence interval [CI], 0.9 to 1.5). The absolute risk for CE plus MPA versus placebo was 4.3 per 100,000 women-years.

In the WHIMS estrogen-alone ancillary study of WHI, a population of 5,200 postmenopausal women aged 70 to 79 years of age was randomized to daily CE (0.625 mg) plus MPA (2.5 mg) or placebo. After an average follow-up of 4 years, 40 women in the CE plus MPA group and 21 women in the placebo group were diagnosed with ovarian cancer. The relative risk of ovarian cancer for CE plus MPA versus placebo was 2.05 (95% CI, 1.21 to 3.48). The absolute risk of probable dementia for CE plus MPA versus placebo was 45 versus 22 cases per 10,000 women-years [see Use in Specific Populations (8.5), and Clinical Studies (14.5) in full prescribing information].

In the WHIMS estrogen-alone ancillary study of WHI, a population of 2,947 hysterectomized women 65 to 79 years of age was randomized to daily CE (0.625 mg) alone or placebo. After an average follow-up of 5 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE versus placebo was 1.49 (95% CI, 0.83 to 2.66). The absolute risk of probable dementia for CE plus placebo was 37 versus 25 cases per 10,000 women-years [see Use in Specific Populations (8.5), and Clinical Studies (14.5)]. When data from the WHIMS estrogen plus progesterone arm were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.76 (95% CI, 1.19 to 2.60). Since both ancillary studies were conducted in women 65 to 79 years of age, it is unknown whether these findings apply to younger postmenopausal women [see Use in Specific Populations (8.5), and Clinical Studies (14.5) in full prescribing information].

Gallbladder Disease

A 2- to 4-fold increase in the risk of gallbladder disease requiring surgery in postmenopausal women receiving estrogens has been reported.

Hypertension

Estrogen administration may lead to severe hypertension in women with breast cancer and bone metastases. If hypertension occurs, use of the drug should be stopped and appropriate measures taken to reduce the serum calcium level.

Visual Abnormalities

Retinal vascular thrombosis has been reported in women receiving estrogens. Discontinue medication pending examination if there is a sudden partial or complete loss of vision, or a sudden onset of photopsia, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, estrogens should be permanently discontinued.

Addition of a Progestogen When a Woman Has Not Had a Hysterectomy

Studies of the addition of a progestin for 10 or more days of a cycle of estrogen administration, or daily with estrogen in a continuous regimen, have reported a lowered incidence of endometrial hyperplasia, which may be a precursor to endometrial cancer. These include an increased risk of breast cancer.

Elevated Blood Pressure

In a small number of case reports, substantial increases in blood pressure have been attributed to idiosyncratic reactions to estrogens. In a large, randomized, placebo-controlled clinical trial, a generalized effect of estrogens on blood pressure was not seen.

Hypertriglyceridemia

In women with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Consider discontinuation of treatment if pancreatitis occurs.

Hepatic Impairment and/or Past History of Cholestatic Jaundice

Estrogens may be poorly metabolized in women with impaired liver function. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, caution should be exercised, and in the case of recurrence, medication should be discontinued.

Hypercalcemia

Estrogen administration leads to increased thyroid-binding globulin (TBG) levels. Women with normal thyroid function can compensate for the increased TBG by making more thyroid hormone, thus maintaining free T4 and T3 serum concentrations in the normal range. Women dependent on thyroid hormone replacement therapy who are on estrogen may require increased thyroid hormone dosage.

These women should have their thyroid function monitored in order to maintain their free thyroid hormone levels in an acceptable range.

Fluid Retention

Estrogens and progestins may cause some degree of fluid retention. Women with conditions that might be influenced by this factor, such as a cardiac or renal dysfunction, warrant careful observation when estrogens plus progestins are prescribed.

Hypocalemia

Estrogen therapy should be used with caution in women with hypoparathyroidism as estrogen-induced hypocalcemia may occur.

Exacerbation of Endometriosis

A few cases of malignant transformation of residual endometrial implants have been reported in women treated post-hysterectomy with estrogen-alone therapy. For women known to have residual endometriums post-hysterectomy, the addition of progestin should be considered.

Hereditary Angiopiodema

Exogenous estrogens may exacerbate symptoms of angiopiodema in women with hereditary angiopiodema.

Exacerbation of Other Conditions

Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangioleomata and should be used with caution in women with these conditions.

Laboratory Tests

Serum follicle stimulating hormone (FSH) and estradiol levels have not been shown to be useful in the management of moderate to severe vasomotor symptoms.

Drug Laboratory Test Interactions

Accelerated prothrombin time, partial thromboplastin time, and platelet aggregation time; increased platelet count; increased factors II, VII, prothrombin, and traces of fibrinogen and fibrinogen activity; increased plasminogen and activity. Increased thyroid-binding globulin (TBG) levels leading to increased circulating total thyroid hormone as measured by protein-bound iodine (PBI), T4 levels (by column or by radiomimun assay) or T3 levels by radiomimun assay. T3 resin uptake is decreased, reflecting the elevated TBG.

Free hormone concentrations, such as testosterone and estradiol, may be decreased. Other plasma proteins may be increased (angiotensins/renin substrate, alpha-1-antitrypsin, ceruloplasmin), increased plasma high-density lipoprotein (HDL) and HDL2 cholesterol subtraction concentrations, decreased low-density lipoprotein (LDL) cholesterol concentrations, increased triglyceride levels. Impaired glucose tolerance.

ADVERSE REACTIONS

In a single, prospective, randomized, placebo-controlled, double-blind trial, the most common adverse reactions with BIJUVA (incidence > 3% of women and greater than placebo) were breast tenderness (10.4%), headache (3.4%), vaginal bleeding (3.4%), vaginal discharge (3.4%) and pelvic pain (3.1%).

DIURETIC DRUGS

Inducers and inhibitors of CYP3A4 may affect estrogen drug metabolism and decrease or increase the estrogen plasma concentration.

USE IN SPECIFIC POPULATIONS

Pregnancy

BIJUVA is not indicated for use in pregnancy. There are no data with the use of BIJUVA in pregnant women, however, epidemiologic studies and meta-analyses have not found an increased risk of genital or non-genital birth defects (including cardiac anomalies and limb reduction defects) following exposure to combined hormonal contraceptives (estrogen and progestins) before conception or during early pregnancy.

Lactation

BIJUVA is not indicated for use in females of reproductive potential. Estrogen are present in human milk and can reduce milk production in breast-feeding females. This reduction can occur at any time but is less likely to occur once breast-feeding is well-established.

Pediatric Use

BIJUVA is not indicated in children. Clinical studies have not been conducted in the pediatric population.

Geriatric Use

There have been sufficient numbers of geriatric women involved in clinical studies utilizing BIJUVA to determine whether those over 65 years of age differ from younger women in their response to BIJUVA.

An increased risk of probable dementia in women over 65 years of age was reported in the Women’s Health Initiative Memory ancillary studies of the Women’s Health Initiative OVERDOSAGE

Overdosage of estrogen plus progestogen may cause nausea, vomiting, breast tenderness, abdominal pain, drowsiness and fatigue, and withdrawal bleeding may occur in women. Treatment of overdose consists of discontinuation of BIJUVA therapy with institution of appropriate symptomatic care.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Abnormal Vaginal Bleeding

Inform postmenopausal women of the importance of reporting abnormal vaginal bleeding to their healthcare provider as soon as possible [see Warnings and Precautions (5.2) in full prescribing information].

Possible Serious Adverse Reactions with Estrogen Plus Progestrone Therapy

Inform postmenopausal women of possible severe adverse reactions of estrogen plus progestrone therapy including cardiovascular disorders, malignant neoplasms, and probable dementia [see Warnings and Precautions (5.1, 5.2, 5.3) in full prescribing information].

Possible Less Serious but Common Adverse Reactions with Estrogen Plus Progestrone Therapy

Inform postmenopausal women of possible less serious but common adverse reactions of estrogen plus progestrone therapy such as breast tenderness, headache, vaginal discharge, and pelvic pain [see Adverse Reactions (6.1) in full prescribing information].

Missed Evening Dose of BIJUVA

Advise the patient that if she misses her evening dose, she should take the dose with food as soon as she can, unless it is within two hours of the next evening dose.
CONSIDERING NINA’S MEDICAL HISTORY, WHAT CONTRACEPTIVE METHOD MEETS HER DESIRE TO AVOID PREGNANCY, MINIMIZE RISKS, AND ADDRESSES HER INSURANCE COVERAGE CONCERNS FOLLOWING DELIVERY?

A. Postpartum sterilization
B. Combined hormonal contraception
C. Depot medroxyprogesterone acetate (DMPA)
D. Immediate postpartum intrauterine device

Nina has indicated a desire to avoid additional pregnancies and a concern for lack of health insurance coverage in the future. Therefore, you and she may decide together to focus your counseling on long-acting reversible contraception (LARC), such as the intrauterine device (IUD) and the subdermal implant, and permanent contraception.

It is important to explore this patient’s and her partner’s interest in male sterilization or vasectomy, the safest and most effective form of permanent contraception, because permanent sterilization would help Nina to achieve her fertility goals. Female sterilization, however, may not be the safest contraceptive method, because Nina’s surgical history may complicate a surgeon’s ability to complete a tubal ligation or may put her at increased risk of surgical complications. LARC is both safe and extremely effective. Both the IUD and implant can be placed immediately postpartum, which may relieve this patient’s concerns about postpartum follow-up and insurance coverage. Alternatively, you can place the LARC at her postpartum visit.

**TABLE 1** Postplacental IUD insertion step by step

**Manual insertion following vaginal delivery**

- Perform time out and verify that there are no contraindications to placement: hemorrhage or intrauterine infection
- Change into sterile gloves
- Remove IUD from packaging and grasp with dominant hand between two fingers
- Stabilize the uterus abdominally using the non-dominant hand
- Advance IUD to the fundus, open fingers, rotate hand 15 degrees, and withdraw
- Consider abdominal ultrasound to confirm placement
- Visualize cervix to confirm location of strings: Copper: strings should not be visualized LNG-IUS: strings should be trimmed at the level of the cervix

**Ring forceps-assisted insertion following vaginal delivery**

- Perform time out and verify that there are no contraindications to placement: hemorrhage or intrauterine infection
- Change into sterile gloves
- Grasp the anterior cervix with a ring forceps using the non-dominant hand
- Remove IUD from packaging and grasp IUD firmly along the stem with ring forceps without fully clamping down on the device
- Advance IUD to the fundus and move non-dominant hand to the abdomen to stabilize the uterus
- Open ring forceps, rotate 45 degrees, and sweep laterally and out to avoid dislodging the IUD
- Consider abdominal ultrasound to confirm placement
- Visualize cervix for location of strings: Copper: strings should not be visualized LNG-IUS: strings should be trimmed at the level of the cervix
- Remove forceps from the cervix

**Placement at time of cesarean delivery**

- Perform time out and verify that there are no contraindications to placement: hemorrhage or intrauterine infection
- Remove IUD from packaging and trim IUD strings to 12 cm
- Grasp the IUD firmly along the stem of the device
- Stabilize the uterus using the non-dominant hand or with the aid of an assistant and advance the IUD through the hysterotomy to the fundus
- Remove hand and ensure that the strings are in the lower uterine segment
- Close the hysterotomy, taking care not to incorporate the IUD strings

*Abbreviations IUD = intrauterine device; LNG-IUS = levonorgestrel intrauterine system
In regard to other contraceptive methods, combined hormonal contraception is contraindicated with this patient’s history of chronic hypertension. Progestin-only pills are safe; however, they may not be ideal, as they require daily dosing within a short window of time. DMPA is an option but, it may not be accessible to Nina if she loses health insurance. Her prenatal visit today is a good opportunity to explore her interest in LARC methods and timing of placement, her and her partner’s interest in vasectomy, and potential risks of female sterilization.

Reproductive life planning
One consideration in contraceptive counseling is the patient’s reproductive life plans, including wanting to avoid pregnancy or planning for a future pregnancy and its timing. A conversation about reproductive expectations provides an opportunity for the provider and patient to review medical comorbidities and for preconception counseling to be undertaken for women who want to become pregnant. The American College of Obstetricians and Gynecologists (ACOG) recommends that ideally, pregnancies be spaced by 18 months to allow for adequate physiologic preparation for a subsequent pregnancy and bonding between mother and child.5 Shorter interpregnancy intervals are associated with higher risk of preterm birth and low birth weight.6 Many women resume sexual activity prior to 6 weeks postpartum, and those who wait to initiate contraception may be at risk for short-interval pregnancy.7

Immediate postpartum LARC
Placement of LARC after birth before the mother is discharged allows a woman to leave the hospital with a highly effective contraceptive method. The U.S. Medical Eligibility Criteria for Contraceptive Use (US MEC) lists immediate postpartum LARC as category 1 or 2 for healthy breastfeeding or non-breastfeeding women, meaning that it is safe to use.8

Coverage and reimbursement
Until recently, reimbursement was uncommon for LARC devices and placement procedures in the inpatient setting. However, growing awareness of the importance of these procedures has pushed many states to revise their Medicaid policies to include reimbursement for immediate postpartum LARC in addition to the global fee for delivery.3 Additional efforts are being made to advocate for immediate postpartum LARC reimbursement from commercial payers.10 Ob/gyns should inquire about insurance coverage and discuss financial concerns with their patients so that information can be incorporated into the contraceptive plan prior to delivery and IUD insertion.

IUD insertion
Immediate postplacental insertion (IPPI) of an IUD is not only convenient for the patient, but also safe and effective for postpartum contraception (Table 1). It is important to review the advantages and disadvantages of such insertion (Table 2).15 IPPI is not associated with increased risks when inserted during the postpartum stay. It is safe for women who want to breastfeed.8 Studies have shown that infant weight at 1 year, infant intake of breast milk, and volume and content of breast milk produced are not impacted by immediate postpartum insertion of the implant.11-13 In addition, there are few logistical barriers to immediate postpartum insertion. The implant can be inserted in the delivery room or at any time before discharge using the same technique as for interval insertion.14 There are no contraindications associated with postpartum insertion of the contraceptive implant.14

Implant placement
The contraceptive implant is an effective form of LARC that poses no increased risks when inserted during the postpartum stay. It is safe for women who want to breastfeed.8 Studies have shown that infant weight at 1 year, infant intake of breast milk, and volume and content of breast milk produced are not impacted by immediate postpartum insertion of the implant.11-13 In addition, there are few logistical barriers to immediate postpartum insertion. The implant can be inserted in the delivery room or at any time before discharge using the same technique as for interval insertion.14 There are no contraindications associated with postpartum insertion of the contraceptive implant.14

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<thead>
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postplacental IUD insertion is safe for mother and infant during breastfeeding. Recent studies have shown that receiving an immediate postplacental hormonal IUD has no effect on time to lactogenesis, and there are no differences in reports of breastfeeding at 8 weeks postpartum between women whose IUDs were inserted immediately after delivery of the placenta and those in whom insertion was delayed. One disadvantage of IPPI compared to delayed insertion is a higher expulsion rate (approximately 2%-27% in the first postpartum year).

**Contraindications to IPPI**
There are few contraindications to IUD placement in general, including anatomic anomalies such as arcuate uterus, bicornuate uterus, or didelphys uterus; active pelvic infection; cervical cancer; and gestational trophoblastic disease. Postplacental IUD placement is contraindicated under the following conditions: intrauterine infection, postpartum hemorrhage, and puerperal sepsis.

**Procedure for IPPI**
**Assessment**
Before beginning the insertion procedure, a brief history should be taken to assess for exclusion criteria, which include recent (within the last 3 months) or active intrauterine infection, known uterine cavity abnormality, and any absolute contraindications (e.g. Wilson’s disease). A postpartum history also should be taken to assess for exclusion criteria such as intrapartum fever greater than 38.0°C or clinical concern for chorioamnionitis, postpartum hemorrhage, and retained placenta requiring manual removal or dilation and curettage. Finally, timing should be confined to within 10 minutes of placental delivery. At that point, the IUD packaging can be opened for placement.

**Insertion technique following vaginal delivery**
A postplacental IUD can be inserted manually or with the aid of ring forceps (Table 1). First, grasp the IUD and advance it through the cervix. Next, place a hand abdominally to stabilize the uterine fundus. Advance the IUD to the fundus with confirmation from the abdominal hand. Release the IUD, taking care to avoid dislodging it from the fundus. At the provider’s discretion, ultrasound can be used to confirm the IUD location. Finally, inspect the vagina for proper string visualization. Because the Copper IUD strings are 12 cm, they are not expected to be visualized at or through the cervix after insertion; if the strings are visible, consider reinsertion of the IUD to ensure fundamental placement. Most strings will pass spontaneously through the cervix and can be visualized and trimmed at a follow-up visit. The levonorgestrel (LNG)-IUS strings are longer, however, and should also be trimmed to the level of the cervix after insertion.

**Insertion technique following cesarean delivery**
If inserted following cesarean delivery, an IUD should be manually placed at the top of the uterine fundus. Before closing the uterine incision, place the strings in the lower uterine segment (LNG-IUS strings may need to be trimmed prior to placement). When the cervix is dilated, the strings will usually descend spontaneously through the cervix in the weeks following delivery. If the cervix is closed, strings may be left in the lower uterine segment or passed through the cervix with ring forceps. If a ring forceps is used, recheck to make sure the IUD remains at the fundus of the uterus before closing the uterine incision. The strings may be trimmed at a follow-up visit.

**Special considerations**
All pregnant patients should be screened for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and if the results are positive at any point, they must be treated prior to IUD placement. If a patient has not been screened prior to admission for delivery, a urine screening can be done then. If the results are found to be positive post-insertion, the patient can be treated with the IUD in place. Any clinical evidence of infection warrants consideration of IUD removal followed by treatment.

If postpartum endometritis is diagnosed after IUD insertion, remove the IUD and treat with intravenous antibiotics. The patient can then be counseled about the option of having an

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**Counseling on complex contraceptive dilemmas**
The first in our new series discusses how to effectively balance contraception needs and seizure control in patients with epilepsy.

[contemporaryobgyn.net/ContraceptionCounseling](contemporaryobgyn.net/ContraceptionCounseling)
Technology Matters:

How the Pap Test Protects Your Patients

The Pap test reduces the incidence of cervical cancer and its precursors for women around the world but has limitations in sensitivity and accuracy.

Liquid-based cytology improves detection of dysplasia and cervical malignancy while producing fewer unsatisfactory or insufficient results. This supplement examines the science, development and clinical benefits of ThinPrep® — the first FDA-approved, liquid-based cytological testing method for women aged 30 and older.

Read the supplement at contemporaryobgyn.net/thinprep
interval IUD insertion at a postpartum visit. Women with postpartum sepsis can have an interval IUD insertion 3 months after successful treatment of intrauterine infection. Ultrasound follow-up is not required after postplacental IUD insertion. There are no data on malpositioned IUDs following postplacental insertion. Data from interval postpartum insertion have found no increased risk of pregnancy with a low-lying LNG-IUS, and there are no data to support increased risk of pregnancy with a low-lying Copper IUD.

Follow-up
Before discharge, patients who have had postplacental IUD insertion must be instructed about its side effects, possible complications, and warning signs. They all should receive education on IUD expulsion and should be advised to call with expulsion concerns. Almost all expulsions occur in the first 3 months after insertion. In addition, patients should be aware that in the next few weeks, the IUD strings may descend to the introitus and that they can be shortened at a follow-up visit. All patients who have a postplacental IUD placement should be offered a visit in 2 weeks for a string check because the strings may be at the level of the introitus as the uterus subinvolutes postpartum. Women with postplacental IUD insertion should still be scheduled for routine postpartum follow-up at 4 to 8 weeks.

Choosing the best method
Postpartum contraceptive counseling is a multistep process that should be patient-centered (Table 3). For our patient Nina, discussing a contraceptive plan during her prenatal visits allows you to identify her fertility and contraceptive preferences and counsel her in a way that respects reproductive autonomy while minimizing coercive practices. LARC may be a good option for a woman like Nina who wants extremely effective contraception immediately following delivery. Immediate postpartum LARC is easy to place and one of many safe and effective options for postpartum contraception that can help to optimize birth spacing and decrease risk of unintended pregnancy. With relationship-building and thoughtful counseling, you can identify a safe postpartum contraceptive method that meets the needs and goals of patients like Nina.

DISCLOSURES The authors report no potential conflicts of interest with regard to this article.

FOR REFERENCES VISIT contemporaryobgyn.net/PostpartumContraception
EXPERT PERSPECTIVES ON PRACTICE BULLETINS

by ASHLEY S. ROMAN, MD, MPH

Dr. Roman is Director, Division of Maternal Fetal Medicine, Program Director, Maternal Fetal Medicine Fellowship and associate professor of obstetrics and gynecology, NYU Langone Health, New York, NY

The new American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin on chronic hypertension in pregnancy replaces the prior ACOG task force hypertension in pregnancy report from 2013, which covered the full range of hypertensive diseases in pregnancy in an extremely thorough way. However, several factors prompted a needed update with a dedicated focus on chronic hypertension in pregnancy, particularly the new recommendations issued by the American College of Cardiology (ACC) and the American Heart Association (AHA) on the diagnosis and management of hypertensive disease in adults.

Diagnosis

Chronic hypertension in pregnancy is defined as any one of the following:
1. Hypertension diagnosed or present before pregnancy, whether or not a woman is on antihypertensive medication
2. Elevated blood pressure prior to 20 weeks of gestation on two occasions at least 4 hours apart. For the purposes of this diagnosis, a threshold of 140 mm Hg systolic or 90 mm Hg diastolic or both is used.

The basic core of these recommendations is unchanged from the ACOG task force report. However, it is unclear how to align the recent ACC/AHA guidelines with these pregnancy-related recommendations. The ACC/AHA criteria for diagnosing hypertension in adults now classify blood pressure into four categories based on blood pressure results, with stage 1 hypertension (and recommendation for treatment) starting at a lower blood pressure threshold than we typically use for pregnancy, systolic blood pressure of 130 to

The purpose of this document is to clarify the criteria used to define and diagnose chronic hypertension before or during pregnancy, to review the effects of chronic hypertension on pregnancy and vice versa, and to appraise the available evidence for management options. The purpose of these revised best practice recommendations is to provide a rational approach to chronic hypertension in pregnancy based on new research and relevant pathophysiologic and pharmacologic considerations.
139 mm Hg or diastolic blood pressure of 80 to 89 mm Hg.

While there is no consensus on how to apply the ACC/AHA recommendations to pregnancy, there does not appear to be benefit to initiating antihypertensive medication during pregnancy or low-dose aspirin for preeclampsia prevention for women who meet criteria for stage I hypertension during pregnancy based on a recent secondary analysis of a multicenter randomized controlled trial. However, data are limited on outcomes and preventative measures in women with stage I chronic hypertension. Therefore, according to ACOG, it is reasonable to continue managing patients who met the criteria for a diagnosis of hypertension based on ACC/AHA recommendations (including stage I hypertension) prior to pregnancy as chronically hypertensive during pregnancy.

The bulletin also addresses another hot diagnosis: white coat hypertension. Women with white coat hypertension are hypertensive during office visits but otherwise normotensive. They should be observed carefully during pregnancy as they are at increased risk of developing preeclampsia and gestational hypertension. Ambulatory blood pressure monitoring may be helpful when making decisions about starting antihypertensive medications in these patients.

**Risks**

Chronic hypertension carries risks to both mother and fetus during pregnancy, with severe and uncontrolled hypertension associated with the highest risks for both. For the mother, there is an increased risk of mortality, cerebrovascular accidents, pulmonary edema, and renal failure; however, the absolute risk of these complications remains low. Fetal risks include increased risk of stillbirth or perinatal death, fetal growth restriction, preterm birth (mostly ascribed to an increase in indicated preterm deliveries), and congenital anomalies, with the highest risk of these abnormalities correlating with presence of maternal end-organ damage.

**The prepregnancy period...**

**the ideal time to initiate care**

**Prepregnancy management**

The prepregnancy period remains the ideal time to initiate care—to look for end-organ damage, assess medications, look for signs of secondary hypertension (such as underlying renal, endocrine or vascular disease) and refer the patient for evaluation if needed, discuss the role of low-dose aspirin for preeclampsia prevention, improve blood pressure control prior to conception, and modify other risk factors that are seen in conjunction with chronic hypertension, such as diabetes mellitus and obesity.

**Antepartum management**

Antepartum management is targeted toward blood pressure control, reducing risk of complications such as preeclampsia, identifying maternal and fetal complications early, and determining optimal timing of delivery. At the first prenatal visit, baseline labs should be sent, including serum aspartate aminotransferase and alanine aminotransferase, serum creatinine, serum electrolytes, blood urea nitrogen, complete blood count, and spot urine protein/creatinine ratio or 24-hour urine for total protein and creatinine. Electrocardiogram or echocardiogram should be ordered as appropriate. Patients with either chronic hypertension or white coat hypertension should be advised to initiate low-dose aspirin (81 mg daily) between 12 and 28 weeks (optimally before 16 weeks) and continue it until delivery for prevention of preeclampsia.

For patients not already on an antihypertensive medication, antihypertensive therapy should be initiated when the systolic blood pressure is 160 mm Hg or more, diastolic 110 mm Hg, or both. The target range is 120 to 160 mm Hg systolic and 80 to 110 mm Hg diastolic. Lower targets may be desirable in women with signs of end-organ damage.

**Which antihypertensives are best during pregnancy?**

Nifedipine and labetalol are recommended above other antihypertensive medications. Methyldopa may be used but appears to be less effective than nifedipine or labetalol in achieving blood pressure control. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are generally not recommended due to the risks of fetal renal dysgenesis and calvarial hypoplasia. Other medications, such as conidine and prozozin, can be considered as second-line agents. Acute treatment of severely elevated blood pressure can be achieved using intravenous (IV) labetalol, IV hydralazine, and/or oral nifedipine. The Practice Bulletin provides several different algorithms for achieving urgent blood pressure control. Care should be taken to avoid overcorrection of blood pressure leading to hypotension, which can affect uterine perfusion.

**Fetal surveillance**

Third-trimester ultrasound to assess fetal growth is advised in women
with chronic hypertension. In terms of additional evaluation such as subsequent growth ultrasounds or fetal surveillance with nonstress testing or biophysical profiles, the Practice Bulletin does not make a solid recommendation due to limited data.

Timing of delivery
Timing of delivery depends on whether a patient is on antihypertensive medication and the degree of blood pressure control. For all patients, delaying delivery later than 39 0/7 weeks should only be considered after a careful evaluation of the risks and benefits.

- **Chronic hypertension not on antihypertensive medication:** not earlier than 38 0/7 weeks
- **Chronic hypertension on antihypertensive medication with good control:** not earlier than 37 0/7 weeks
- **Chronic hypertension with superimposed preeclampsia without severe features:** at 37 0/7 weeks; if at a later gestational age than 37 0/7 weeks, then upon diagnosis.
- **Chronic hypertension with superimposed preeclampsia with severe features:** not later than 34 0/7 weeks; if at a later gestational age than 34 0/7 weeks, then upon diagnosis.
- **Immediate delivery after maternal stabilization is recommended if any of the following are present at any gestational age in women with superimposed preeclampsia:** uncontrollable severe hypertension, eclampsia, pulmonary edema, disseminated intravascular coagulation, new or worsening renal insufficiency, placental abruption, or abnormal fetal testing.

Intrapartum management

- **Fetal monitoring:** Continuous fetal monitoring during labor is advised in women with chronic hypertension at higher risk of adverse outcomes (e.g., those who require any blood pressure control or with other short-term or long-term sequelae).

  - **Axial anesthesia:** Axial anesthesia is safe even in the setting of severe hypertension. Unless contraindicated by thrombocytopenia, it should be used for cesarean delivery as general anesthesia may pose higher risks for women with severe hypertension.

Postpartum management
A patient’s blood pressure should be evaluated in the first 1 to 2 weeks after delivery, either with an early outpatient office visit or with home blood pressure monitoring. Target blood pressure is systolic blood pressure of 150 mm Hg or less and diastolic blood pressure of 100 mm Hg or less. The patient can be maintained on the medication used in pregnancy or she can be transitioned back to her pre-pregnancy medication. Medications such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are compatible with breastfeeding. NSAID use appears to be safe in postpartum patients with chronic hypertension. Methyldopa should be avoided because it often can be associated with depression.

Unresolved controversies
Diagnosing superimposed preeclampsia: Up to 20% to 50% of women with chronic hypertension develop superimposed preeclampsia. Diagnosing superimposed preeclampsia in patients with chronic hypertension can be a challenge. It can be difficult to determine whether a surge in blood pressure represents worsening chronic hypertension or superimposed preeclampsia. ACOG indicates that laboratory testing can be helpful in distinguishing between the two by evaluating platelet count, liver function tests, and uric acid levels.

What’s new?
ACOG recommends an individualized approach in considering who meets a diagnosis of chronic hypertension. Women diagnosed with stage I hypertension prior to pregnancy may be managed as chronic hypertensives in pregnancy even though they don’t meet the threshold of 140 mm Hg systolic or 90 mm Hg diastolic.

White coat hypertension is associated with an increased risk of adverse obstetrical outcomes and merits close observation at minimum with ambulatory blood pressure monitoring.

Women with a diagnosis of chronic hypertension should be started on low-dose aspirin (81 mg daily) between 12 and 28 weeks (optimally before 16 weeks) to be continued until delivery. While women with stage I chronic hypertension as defined by ACC/AHA guidelines may be managed as chronically hypertensive during pregnancy, data are limited on outcomes and interventions to reduce the risk of preeclampsia, and further research is necessary to define optimal care.

Recommendations for timing of delivery depend on whether a patient is on antihypertensive medication, degree of blood pressure control, and presence or absence of superimposed preeclampsia. Many women with chronic hypertension now meet criteria for early term delivery.

DISCLOSURES The author reports no potential conflicts of interest with regard to this article.

FOR REFERENCES VISIT contemporaryobgyn.net/PregnantHypertension
Experimental vaccine for HPV-associated CIN2/3

by BEN SCHWARTZ

Vaccination is effective for preventing infection with certain subtypes of human papillomavirus (HPV), but nonsurgical, nonablative therapies are needed to control HPV disease. Results of a recent study in Gynecologic Oncology suggest that a therapeutic vaccine may be effective and safe for clearing cervical intraepithelial neoplasia (CIN) 2/3 irrespective of HPV subtype.

The multicenter, prospective, randomized, double-blind, parallel-group, study enrolled women aged 18 years and older who had a histologically confirmed diagnosis of HPV-associated CIN2/3. Women who had received a prophylactic HPV vaccine were excluded. The vaccine tested was the Tipapkinogen Sovacivec (TS) therapeutic HPV vaccine and follow-up in the placebo-controlled trial was done for 2.5 years.

Participants in the study were randomized 2:1 (TS vaccine:placebo). They received the drug or placebo via subcutaneous injection in the thigh three times over 15 days. Cytologic and high-risk HPV testing was done at 3 and 6 months. The primary efficacy endpoint was individual histological resolution at 6 months when excisional therapy was performed.

In the trial, 129 subjects received vaccine (mean age 30.1 years) and 63 received placebo (mean age 29.8 years). The authors noted that the rate of complete resolution of CIN2/3 was significantly higher in the vaccine group than in the placebo group regardless of HPV type (24% vs 10%, P < 0.05). The vaccine also outperformed the placebo in instances of just CIN3 regardless of the HPV type (21% vs 0%, P < 0.01).

EXPERT PERSPECTIVE

“This report of an experimental THERAPEUTIC HPV vaccine (in contrast to the prophylactic vaccine that is currently recommended by the Advisory Committee on Immunization Practice of the Centers for Disease Control and Prevention to be administered routinely at age 11 or 12) is very exciting to me as a clinician. This vaccine offers the potential that in the future, we may be able to treat pre-malignant cervical lesions of high-grade cervical intraepithelial neoplasia in a non-surgical manner. That would be a huge benefit for our patients. I will stay tuned for more reports on the safety and efficacy of this therapeutic vaccine.”

Paula J. Adams Hillard, MD  Professor, Department of Obstetrics and Gynecology, Stanford University School of Medicine Director, Gynecology, Lucile Packard Children’s Hospital, Stanford, Calif.
A new study in *Lancet Diabetes & Endocrinology* that leveraged nearly two decades of research has tested the hypothesis that metformin prevents late miscarriage and preterm birth (PTB) in women with polycystic ovary syndrome (PCOS).

From 2000 to 2017, the research group oversaw three controlled studies comparing the impact in pregnant women with PCOS of metformin versus placebo. PregMet2, the largest of the studies, took place between October 19, 2012 and September 1, 2017. The authors also performed a post-hoc analysis of pregnancy outcomes in which they pooled data from PregMet2 with individual participant data from two previous trials, which had shown a significant reduction in late miscarriage and PTB in women with PCOS taking metformin.

Administered at 14 hospitals in Norway, Sweden, and Iceland, PregMet2 was a randomized, double-blind trial. Participants were women aged 18 to 45 with PCOS who were pregnant with singletons. They were randomly assigned (1:1) to receive oral metformin 500 mg twice a day or placebo during the first week of the study and metformin was increased to 1000 mg twice a day from week 2 until delivery.

The composite primary outcome of the study—late miscarriage and PTB—occurred in 12 (5%) of 238 women in the metformin group and 23 (10%) of 240 women in the placebo group ($P = 0.08$).

No significant differences were found for secondary endpoints, including gestational diabetes (60 [25%] women in the metformin group and 57 [24%] women in the placebo group were diagnosed). No significant between-group differences in serious adverse events were observed in either mothers or offspring.

In the post-hoc pooled analysis, 18 (5%) of 397 women in the metformin group had late miscarriage or PTB compared with 40 (10%) of 399 in the placebo group ($P = 0.004$).

Based on their findings, the authors believe that metformin treatment reduces risk of late miscarriage and PTB in pregnant women with PCOS. However, they were surprised that metformin did not prevent gestational diabetes in this population, given that metformin is an insulin sensitizer and is predominantly used in treatment of type 2 diabetes.

**Ben Schwartz** is the associate editor of *Contemporary OB/GYN*.

**SOURCE**


Should ob/gyns use metformin to treat pregnant women with PCOS?

**by BEN SCHWARTZ**

A new study in *Lancet Diabetes & Endocrinology* that leveraged nearly two decades of research has tested the hypothesis that metformin prevents late miscarriage and preterm birth (PTB) in women with polycystic ovary syndrome (PCOS).

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**Ben Schwartz** is the associate editor of *Contemporary OB/GYN*.

**SOURCE**

Clinical trials of romosozumab, a drug recently approved by the US Food and Drug Administration, showed that it significantly reduced risk of new fractures in postmenopausal women. Clinicians should be aware, however, that the monoclonal antibody (mAb)—marketed as Evenity—carries a “black box” warning about increased risk of heart attack, stroke, and cardiovascular death.

Romosozumab is given in a total dose of 210 mg, administered as two separate subcutaneous injections at the same time. Treatment is once monthly and limited to 12 doses because the anabolic effect of the drug, which blocks the protein sclerostin and increases new bone formation, wanes after that period.

Romosozumab increased risk of [CV] death, heart attack, and stroke in the second trial but not the first trial.

In two clinical trials of more than 11,000 women with postmenopausal osteoporosis, romosozumab was tested against placebo and followed by treatment with denosumab and with alendronate, respectively. In both studies, the mAb significantly reduced risk of fracture.

“Romosozumab represents a new very potent osteoporosis therapeutic option for patients at very high risk of fractures,” said Kenneth G. Saag, MD, principal investigator of one of the two phase 3 clinical trials that established the safety and efficacy of the drug. “As is true with all therapies, the benefits much be weighed with the potential risks and decisions should be made incorporating patient preference.”

Women who took the drug for a year in the first trial, published in 2016, had a 73% lower risk of a new vertebral fracture than patients on placebo. That benefit was sustained in the second year of the trial, when patients in both arms were switched to denosumab. In the second trial, published in 2017, 1 year of treatment with romosozumab followed by 1 year of alendronate resulted in a 50% lower risk of new vertebral fracture than 2 years of alendronate alone. In that study the mAb also was found to reduce risk of nonvertebral fractures compared with alendronate alone.

Common side effects of the mAb seen in the two trials were joint pain and headache. Romosozumab increased risk of cardiovascular death, heart attack, and stroke in the second trial but not the first trial. In the 2017 study, serious cardiovascular events were observed in 2.5% of patients on romosozumab versus 1.9% on alendronate. The authors noted that sclerostin is constitutively expressed in the aorta but its function in the vasculature is unknown, and that in some studies but not two meta-analyses, alendronate was associated with a reduction in risk of cardiovascular disease.

Judith M. Orvos, ELS, is an editorial consultant for Contemporary OB/GYN.

EXPERT PERSPECTIVE  
“Romosozumab is a new option for patients at high risk for fracture associated with osteoporosis and offers the advantage of rapid and significant increase in bone density which may subsequently be maintained with conventional bisphosphonate therapy. Preliminary data suggests that it may be associated with increased cardiovascular risks which is biologically plausible since it is a monoclonal antibody that targets sclerostin, a glycoprotein expressed by osteocytes and in the aorta. Current use should ideally include patients at very high risk for fracture without underlying cardiovascular disease until risk vs benefits are more completely delineated.”

Steven J. Ory, MD  Professor of Obstetrics and Gynecology, Florida International University, Miami, Partner, IVF Florida, Margate.

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FDA proposes updates to mammography regulations

by JUDITH M. ORVOS, ELS

The public comment period is open for a US Food and Drug Administration (FDA) proposal to make major updates to the agency’s regulations on mammography. The changes reflected in the amendment to the Mammography Quality Standards Act of 1992 are aimed at addressing mammographic technology, enhancing quality standards, and improving the way results of screening are handled throughout the healthcare system.

Included in the description of the new rule are projections of the financial impact of the changes. They relate to new breast density reporting requirements that FDA believes could result in fewer deaths and lower costs for breast cancer treatment. Annualized benefits over 10 years, according to the agency, range from a low of $16.27 million to a high of $534.03 million. Annualized costs to mammography facilities over 10 years are estimated to range from $34.96 million to $59.40 million.

If passed, the rule would require, among other things, that:

- Mammographic reports to patients, healthcare providers and others within specific timeframes;
- Changes be made to explanatory language for “benign” findings and that three new categories of mammographic assessment be added to existing language to help mammographic facilities more precisely classify and communicate results of exams; and
- If a facility is closing or will no longer perform mammography, it makes arrangements to give patients and health-care providers access to mammographic images and reports.

In a press announcement about the proposal, FDA said that the agency is proposing specific language for mammographic reports that would explain how breast density can influence mammography accuracy and encourage patients with dense breasts to talk with a health care provider about how it relates to breast cancer risk and their unique situation. The new categories of mammographic assessment include “known biopsy proven malignancy,” which would help identify cases in which cancer being mammographically evaluated for therapy is already known and identified.

The public has until June 26, 2019 to comment on the proposed rule, which would be the first amendment to the Mammography Quality Standards Act in more than 20 years. The provisions would be effective 18 months after date of publication of the final rule in the Federal Register.

Judith M. Orvos, ELS, is an editorial consultant for Contemporary OB/GYN.

SOURCE


EXPERT PERSPECTIVE

As of May 2018, 34 states required that information on breast density also be provided to patients. The current amendment would mandate that the lay summary provided to patients identify whether the patient has low- or high-density breasts and include a prescribed paragraph on the significance of breast density. The FDA predicts that breast density reporting requirements will reduce delays in diagnosis, leading to earlier breast cancer detection with reductions in cancer treatment costs and mortality.

Ilana Cass, MD Vice Chair, Associate Clinical Professor, Department of Obstetrics and Gynecology, Cedars-Sinai Medical Center Los Angeles, CA, Calif
Why I chose a MIGS fellowship

The choice to pursue a fellowship isn’t always straightforward, but one resident explains why she is choosing to follow her passion.

by MEENAL MISAL, MD

“It’s honestly just a waste of time.”

“Why would you do a fellowship for something that you already know how to do?”

“MIGS isn’t even accredited.”

My chiefs and attendings read my mind when I was wrestling with the idea of applying for a fellowship in minimally invasive gynecology (MIGS) as a second-year resident.

I’ve loved surgery since medical school, so I was excited about my first surgical cases as an intern. I anticipated a steep learning curve, but by the end of the year, I felt like I’d barely taken a step. Much of the surgical teaching during my residency, as in most high-volume programs, is provided by private attendings. Skill levels vary, which I think is largely a product of the ob/gyn educational system. In most residencies, a great deal of time is spent on obstetrics, outpatient clinic, or night float coverage. We spend barely a year dedicated to gynecologic surgery. Contrast that with general surgery residents, who spend 5 years training in the operating room.

Now in my fourth year, I feel comfortable leading straightforward cases, but there’s no way I’m ready to tackle complex endometriosis or gigantic fibroid uteruses. Neither are most other ob/gyns straight out of training, and it’s the reason in-residency tracking and generalist fellowships are gaining traction.

On the other hand, watching surgical subspecialists operate is amazing. The way they navigate distorted anatomy, identify tissue planes, and troubleshoot unexpected challenges is beautiful. I want to grow up to be capable of that. But gynecologic oncology and urogynecology were not for me, and an unaccredited fellowship in MIGS seemed risky. I could graduate from residency and go directly into practice making $200,000+ a year. Or I could continue with my training making a PGY-5 salary, delaying financial stability for another 2 years.

AAGL established the first MIGS fellowship in 2001, with just seven spots and now there are 48 programs. In 2018, MIGS was the most competitive fellowship, with 1.7 applicants per position (compared to 1.4 applicants per position in gynecologic oncology, historically the most competitive fellowship). In April, the American Board of Medical Specialties approved AAGL’s application for a focused practice designation in minimally invasive gynecology, which would require those seeking such a designation to complete a minimum of 100 MIGS procedures in patients with benign and complex gynecologic conditions. This step towards recognizing those that have significant experience in gynecologic surgery reflects what may be a response to an anticipated shift in the field from maintaining full ob/gyn practices to specializing in either obstetrics or gynecology. It is conceivable that eventually, physicians without fellowship training will not perform any gynecologic surgery. That would be a major change, but I think we all can agree that patients deserve the best
chance at a good outcome, and on that point, the data favor high-volume surgeons.2

With the advent of more medical treatment options for fibroids, heavy menstrual bleeding, and pelvic pain, the volume of gynecologic surgery across the country has fallen.3 Therefore, by default, more surgeons are becoming low-volume surgeons.4 So, even if I planned to hone my surgical skills in practice with the aid of a senior partner, the opportunity to progress might not really exist. If you operate once a month, how will you maintain your skills? Maybe it’s not absolutely necessary to do a fellowship, but there is no denying that doing three to five surgical cases a day, 5 days a week for 2 years, will accelerate your skills.

In the end, I decided to apply for the MIGS fellowship because I want to be the best surgeon I can be. I want my patients to get the best surgery for them. I don’t want to take shortcuts for my convenience or because of my skill level. I don’t want to fulgurate endometriosis and call it a day. I don’t want to do a supracervical hysterectomy because I’m afraid of the ureter. I don’t want to leave the fallopian tubes behind on a vaginal hysterectomy. I want my cases to be elegant, beautiful, purposeful.

Advanced Paternal Age CONTINUED FROM PAGE 16

been associated with an increased risk of congenital anomalies and cancer in the offspring.3 These findings are summarized in Table 1.32-35, 41-50

Conclusions
With a growing trend of delaying fatherhood, couples must be informed of the increased risks of producing abnormal offspring associated with APA. The ACMG currently recommends a prenatal counseling session regarding potential risks of APA such as Trisomy 21 and individualized genetic counseling for specific concerns. The process of conception in older men may be complicated by decreased libido or altered sperm characteristics. APA may or may not impair the outcomes of ART; some evidence suggests impaired ability to conceive and decreased rates of live birth in conceptions by older men, but any decreases in fertility attributed to APA are minor in comparison to those of advanced maternal age. The fetus may be at increased risk of spontaneous abortion and very preterm birth. Increased oxidative stress may be linked to higher rates of DNA fragmentation in older men, but data on the impact on reproductive outcomes remain inconclusive.

Lastly, in the offspring of older men, certain medical comorbidities have also been identified, including ASD and acute lymphoblastic leukemia. Although the effect of APA on reproductive outcomes and medical comorbidities in the offspring remains an active area of research, we recommend that physicians discuss these risks—particularly Trisomy 21, psychiatric diagnoses, and ASD—with couples with male partners aged 40 or older. Studies differ in their definition of APA when assessing risk for chromosomal aneuploidies versus neurocognitive outcomes. Establishing a consensus definition of APA will help guide management and counseling of patients.

DISCLOSURE The authors report no potential conflicts of interest with regard to this article.

FOR REFERENCES VISIT contemporaryobgyn.net/AdvancedPaternalAge
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Mastering revenue cycle management

Ob/gyns can reduce the amount of time spent collecting revenue, but they need to research which plan fits their practice’s needs best.

by JAMES F. SWEENEY

Doctors are fond of complaining that they didn’t go to medical school in order to practice business, but independent physicians do spend much of their time on their practices’ finances.

That requires mastering revenue cycle management (RCM), the financial process practices use to administer all the functions associated with claims processing, payment, and revenue generation.

At the level of the individual patient, RCM begins when that patient makes an appointment and ends when all claims and payments resulting from the appointment and subsequent services have been settled. At a higher level, it means ensuring that the practice generates enough income to pay expenses and yield a profit.

Revenue cycle management has never been easy, but the move to value-based care and reimbursement, as well as more risk-based payer contracts, has made it harder than ever. A 2016 survey by research firm Black Book found that 90 percent of small, independent practices were unprepared financially and technologically to implement value-based care.

Difficult thought it may be, efficient and disciplined RCM is key to an independent practice’s ability to remain so. “Effective revenue cycle management isn’t going to guarantee your practice’s financial success, but neglecting revenue cycle management might result in its failure,” says Melissa Lucarelli, MD, a family physician in Randolph, Wis.

A move to outsourcing

As RCM becomes increasingly demanding, more practices are turning to vendors to handle part or all of it.

The Black Book study predicted that the U.S. market for physician and ambulatory RCM outsourcing and extended business office services would grow by 42 percent between the end of 2016 and the beginning of 2019. The same survey of 2,000 independent physician practices found that 59 percent of providers intended to outsource some or all of their billing.

“High-impact drivers of the physicians practice outsourcing market include the increasing emphasis on compliance and risk management, and the need for more efficient and cost-effective processes,” Black Book managing partner Doug Brown says in the study.

The rising costs of operating a practice also underscore the importance of RCM. A 2018 Medical Group Management Association study found that over the past 5 years, median operating costs for primary care practices have risen by 13%, from $391,798 to $441,559 per physician. And while revenue can fluctuate, expenses such as salaries, rent, insurance, and equipment payments must be paid on a regular schedule.

Outsourcing RCM is comparable to a primary care physician referring a patient to a specialist, says Todd Van Meter, senior vice president, ambulatory care, for Optum360, a revenue cycle management firm based in Eden Prairie, Minn.

The specialist has greater resources, knowledge, and expertise to handle the task than does the generalist, he says. And unlike a practice whose primary mission is providing healthcare, a ven-
dor is focused solely on RCM, making it easier for them to stay current on regulatory and reporting requirements while discovering new efficiencies.

Lucarelli says outsourcing much of her RCM has been a boon for her small, rural practice. “These are tasks we could do and we used to do, but the system does the heavy lifting and the drudgery stuff that keeps us away from the medical stuff we want to do,” she says.

Lucarelli uses her EHR vendor, Athenahealth, for coding, billing, verifying insurance coverage, interfacing with payers, and other functions. She adds that outsourcing the RCM function has made it possible for her to reduce the practice’s back office staff from four to two, a part-time billing clerk who posts claims and an office manager.

The system has been particularly helpful for meeting reporting requirements under the Merit-based Incentive Payment System, as well as providing upgrades, such as free interfaces with labs. “There is no way that I would go back to the old way and be able to provide medical care the way I want to,” she says.

Keeping it in the practice
Not all practices find it beneficial to outsource RCM.

Associated Physicians is a 20-doctor independent practice in Madison, Wis., that offers comprehensive primary care services, including physical therapy, nutrition counseling, and diabetes education while operating its own lab.

The accompanying volume and complexity of paperwork, reporting, and regulations would push some practices to outsource their RCM, but Associated Physicians does nearly everything with its own employees. “We want to remain independent. Part of that independence is wanting to do as much inside as possible,” says Executive Director Terri Carrufel-Wert, RN, MHA.

The practice employs 11 back office personnel, including coders and billing and payment specialists. While that’s substantial overhead, Carrufel-Wert and Business Operations Manager Margaret Wilkinson, CMC, say the team saves money by performing at a very high level.

Communication and coordination are key, Carrufel-Wert says. Everyone, from physicians to billing clerks, works from the same guidelines, and new providers are quickly trained on office procedures. The coders are so well-versed in regulations that they seldom make billing errors and even occasionally correct private payers, she adds.

Employees are cross-trained on jobs so there’s no drop-off in performance during someone’s absence. The staff analyzes potential new practice offerings and equipment to determine if reimbursement will make them profitable.

The practice is proactive with patients as well. Whenever possible, it obtains payment upfront and frequently has to educate patients about what their insurance covers and how much it pays.

The hard work pays off. The average time between billing and reimbursement from payers and patients is 22 days, which Wilkinson says is much shorter than average.

“We had to do a lot of training and educating, but we are now able to deliver quality care at an affordable price,” Wilkinson adds.

A personal touch
Newton Family Physicians has done its own RCM for all 37 years of its existence and expects to continue to do so, says practice administrator Melissa White.

“We find it just works better for us,” says White. The Newton, N.C., practice has six physicians and four nurse practitioners. Doing its own RCM requires three full-time-equivalent employees doing coding, billing, and other back office tasks, while White and a part-time employee handle collections.

The practice has considered using a vendor for RCM and probably would save money by doing so, White says, but worries that introducing a third party would hurt long-standing patient relationships in the rural communities it serves.

For example, the practice knows when a patient has lost a job or been sick and will take that into consideration during billing, White says. It also offers no-interest payment plans.

“It’s not always about saving two cents,” she says. “From a community perspective, we just have better reception.” While the practice will use a collection agency for some unpaid debts, it prefers to rely on the personal touch, White says, adding, “We found that it works better for us because when you call someone and they know you they’re more likely to deal with you than they are with a collection agency.”
Their personal, in-house approach works, she says, adding that Newton has a reimbursement rate of 97% to 99%.

**RCM patterns**

As part of his RCM, Jeffrey Kagan, MD meets with his accountant annually to project income and expenses for his two-physician practice in Newington, Conn.

The accuracy of those predictions determines whether the practice is profitable or if Kagan must tap into a line of credit to pay himself and employees. After 25 years in practice, he has identified reimbursement patterns, such as slower and fewer patient payments in the first half of the year because people have not yet met their insurance deductibles.

This trend has gotten worse as more employers switch to high-deductible plans, he says.

The practice uses an outside vendor for billing and occasionally hires a collection agency, but performs other functions itself. Kagan does everything he can to get patients to pay their co-pays and other costs at the time of their appointment. “If I can get my money in 3 months, I’m thrilled,” he says. “There are some who take longer, but none of my expenses get held up for 3 months.”

He takes payments via credit cards, accepting the service fee if it means getting paid faster. He also has had to get stricter with non-paying patients, either dropping the worst offenders or refusing to schedule new appointments until their debts are settled.

His staff also knows to verify insurance eligibility at the beginning of an appointment. “It only takes a few minutes to do that in the beginning, but it probably takes an hour to fix it later,” he says.

Choosing an RCM vendor

Using an RCM vendor does not have to be an all-or-nothing proposition. Many independent physicians, like Melissa Lucarelli, MD, a solo practitioner in Randolph, Wis., choose to outsource some functions and keep others.

She recommends developing policies and processes for each phase of RCM, from preauthorization to collections, then scrutinizing them to determine if it makes financial sense to outsource that phase. That self-examination led her from doing virtually everything in-house to outsourcing most of the work.

**GUIDELINES FOR SELECTING AN RCM VENDOR**

Whether outsourcing all RCM functions or only some services, here are some guidelines for selecting a vendor from industry sources:

1. **CHOOSE A REPUTABLE AND EXPERIENCED VENDOR.** Ask about qualifications, certifications, and association memberships. Check references.

2. **KNOW WHAT YOU’RE PAYING FOR.** Vendors offer a variety of services and packages and comparison shopping can be confusing. Make sure you get what you need and aren’t paying for services you don’t need. Ask an experienced attorney to review the contract.

3. **MAKE SURE THE VENDOR PROVIDES A CUSTOMIZABLE AND USABLE DASHBOARD.** This is a practice’s interface with RCM and if it’s hard to use or difficult to read the operation will suffer.

4. **GET ANALYTICS.** A good RCM vendor will not only handle coding and billing, but offer real-time analytics tools that filter data, generate the necessary reports, and make it easy to identify problem areas that should be addressed.

5. **MAKE SURE THE VENDOR PROVIDES REGULAR UPDATES.** Reimbursement is constantly changing, and RCM software must be current to avoid problems with denials and failure to meet reporting and performance standards.

6. **CHECK THE VENDOR’S CUSTOMER SERVICE RECORD AND REFERENCES** and know exactly what type and how much help your contract stipulates.

7. **MAKE SURE IT’S COMPATIBLE WITH YOUR EHR SYSTEM** and that you will be able to run your own reports.

8. **SET AGREED-UPON PERFORMANCE GOALS.** You’re hiring a vendor to improve RCM and having benchmarks in place will let you know if that’s being accomplished.

James F. Sweeney is a freelance writer in Cleveland. He is a former newspaper and magazine reporter and editor.

**DISCLOSURE** The author reports no potential conflicts of interest with regard to this article.

**FROM THE PAGES OF**

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When patients hit ‘record’ at the doctor’s office

In the age of social media, what is an ob/gyn’s legal liability when a patient records everything?

by ERICKA L. ADLER

I was recently at my physician’s office and observed a patient recording herself and a family member in the waiting room. She continued recording as she walked down the practice hallway and entered the examination room. It was clear that the patient had not only recorded herself, but also had captured other patients in the room and patient names being called out. She even potentially captured conversation between patients and health care providers. Yet, no one from the practice told her to stop filming, questioned her activities, or otherwise reacted. Has this happened in your practice? If it did, how would you react?

The above scenario is hardly surprising in the age of social media. While most healthcare providers and medical practices are aware of the significant limitations the Health Insurance Portability and Accountability Act of 1996 (HIPAA) places on their activities, it is less clear how to react when it’s the patient who wants to record the physician and could potentially expose protected health information of other patients.

Practices should address the issue of patients recording themselves and others by planning ahead. A practice should develop a policy for handling such activity and prepare the necessary paperwork for patients to acknowledge the policy put in place. If a practice chooses to allow such recordings, then the policy must set the appropriate parameters for recording at the practice, such as where filming can occur, whether permission must be requested, and other necessary requirements.

Sometimes patients ask their physicians directly to record an encounter for arguably legitimate reasons, such as to help remember medical information or instructions or share the details of the visit with caretakers or loved ones. A practice should have a separate approach for physician recordings and should tailor it to physician preferences.

What happens if a patient does not ask permission and records the physician without his or her knowledge? While this may violate the practice’s policies, such activity can also expose the practice to liability and impact its reputation. What information was in plain sight and recorded that presented a HIPAA issue? Could the practice be liable for anything else related to the recording? How did the staff behave? Practices should be aware at all times that recordings may take place without their knowledge, so appropriate HIPAA precautions and patient interactions should be the norm through training and preparation.

Finally, practices should be aware that patients have the right in most states to record interactions with third parties where the law only requires one party to consent to the recording. This means a patient does not need to inform the physician that she is recording at all. Other states require that both parties are aware of the recording. In these states, this means that a patient who records a physician or staff interaction without permission has actually violated the law.

I recommend exploring these issues with legal counsel in order to assure that your practice is properly protected, and that any plan is tailored specifically to your practice’s needs. For example, the approach may be different for an obstetric practice compared to one that focuses on cancer or gynecologic conditions. Knowledgeable legal counsel can assist in understanding your practice’s legal risks and potential vulnerabilities.

Ericka L. Adler has practiced in the area of regulatory and transactional healthcare law for more than 20 years. She represents physicians and other healthcare providers across the country in their day-to-day legal needs, as well as a wide variety of compliance issues.

DISCLOSURE The author reports no potential conflicts of interest with regard to this article.
# Edinburgh Postnatal Depression Scale

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt in the past 7 days, not just how you feel today. Here is an example, already completed.

**Q**: I have felt happy:
- [ ] Yes, all the time
- [ ] Yes, most of the time
- [ ] No, not very often
- [ ] No, not at all

This would mean: “I have felt happy most of the time” during the past week.

Please complete the other questions in the same way.

## IN THE PAST 7 DAYS:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>I have been able to laugh and see the funny side of things</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>As much as I always could</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not quite so much now</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Definitely not so much now</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not at all</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>I have looked forward with enjoyment to things</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>As much as I ever did</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rather less than I used to</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Definitely less than I used to</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hardly at all</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>I have blamed myself unnecessarily when things went wrong*</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Yes, most of the time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, some of the time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not very often</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No, never</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>I have been anxious or worried for no good reason</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>No, not at all</td>
<td></td>
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<tr>
<td></td>
<td>Hardly ever</td>
<td></td>
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<td></td>
<td>Yes, sometimes</td>
<td></td>
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<tr>
<td></td>
<td>Yes, very often</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>I have been so unhappy that I have been crying*</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Yes, most of the time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, quite often</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Only occasionally</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No, never</td>
<td></td>
</tr>
</tbody>
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Download a PDF of the patient education handout and scoring information at [ContemporaryObGyn.net/PostnatalDepression](http://ContemporaryObGyn.net/PostnatalDepression)
Rectocele repair necessary?

CONTINUED FROM PAGE 56

of pain with walking and sitting (the latter requiring use of a hollow pillow) in addition to dyspareunia. Her exam revealed a tight fourchette, perineal tenderness, and posterior vaginal wall firmness. The diagnosis was pudendal neuralgia, with tightness related to the permanent suture used for the posterior repair. A recommendation was made for rectocele revision and consideration of a pudendal block. An additional exam by a pain specialist at the institution revealed an introitus of average diameter, thinning of the posterior fourchette, and pain with direct palpation in the area of the pudendal nerve. A recommendation was made for referral to a urologist specializing in treatment of pudendal neuralgia.

The patient elected to have rectocele revision, which was performed approximately 12½ weeks after her original surgery. The surgery included removal of two of eight permanent sutures and introital closure to functionally widen the introitus. She was seen 1 week after surgical revision with 10/10 perineal pain. Exam revealed some sutures coming out, thus several knots were removed. One week later, the patient had decreased discomfort and swelling in the perineal area. She was using a nonsteroidal anti-inflammatory drug (NSAID) for pain control.

Three weeks postoperatively, she had improved pain and was able to sit comfortably for a short time. Consideration was again given to pudendal nerve blocks if necessary. Eight weeks postoperatively the patient’s discomfort was improved, as was defecation. She was able to have intercourse without significant pain. She had mildlevator muscle spasm and a recommendation was made for physical therapy and estrogen cream.

Twelve weeks after the surgical revision, despite a reduction in pain of almost 50%, the patient was seen with a request to remove the remainder of the permanent sutures. The urogynecologist did not recommend this, but rather, recommended psychiatric evaluation. That consultation revealed that the patient was developing borderline chronic pain syndrome and she was treated with a tricyclic antidepressant (TCA).

Three weeks after that appointment, the patient self-referred to a third urogynecologist in the Midwest for evaluation. That exam revealed an anatomically normal vagina and introitus. No sutures were evident along the posterior vaginal wall or on rectovaginal exam. There was somelevator tenderness and the diagnosis confirmed pelvic floor tension myalgia.

This evaluation also identified possible pudendal nerve entrapment and recommendations were made for electromyelography (EMG), an antidepressant (apparently the patient had stopped taking her TCA), physical therapy, pudendal nerve injections, and possible unroofing of the pudendal nerve. Seven weeks later, the patient’s EMG revealed increased pudendal motor terminal latency, consistent with right pudendal neuropathy. It was felt the pudendal nerve may have been placed on stretch at the first surgery. The third urogynecologist performed a pudendal nerve block and was able to achieve perineal anesthesia. The patient was also placed on gabapentin. Although the patient seemingly improved physically, she contacted her psychiatrist concerned that a local physician she saw told her, during a pelvic exam, that the surgical repair made her look “vaginal.” She verbalized diminished trust in her caregivers.

Nine weeks after the pudendal block, when the third urogynecologist followed up with the patient by phone, he found that she was improved. A recommendation was made for continued pelvic floor therapy and right pudendal nerve release, with the possible addition of acupuncture. The woman’s gabapentin dose was increased. She requested a narcotic for pain relief and was referred to her local physician for a prescription, if necessary.

Six weeks after that, the patient self-referred to another local gynecologist for continued pain and possible surgical evaluation of persistent or residual endometriosis. That physician made a referral to a urologist for cystoscopy for evaluation for...
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interstitial cystitis; it was normal. The patient then underwent diagnostic laparoscopy, now slightly more than a year after the original surgery. That revealed essentially no adhesions and only “superficial endometriosis” of the anterior and posterior cul-de-sacs. However, pathology revealed iron deposition, with no definite endometrial glands or stroma identified. The patient was encouraged to continue with physical therapy, which she did for the next 2 months. Of note, 2 days after this third surgery, record requests were received from a plaintiff’s attorney.

Eight months after the third surgery, the patient was seen for a well-woman visit by a third gynecologist, with complaints of painful intercourse. Her exam revealed a tender perineum. She was prescribed gabapentin, narcotics, and estrogen cream. Two months later, she was referred to a pain specialist who recommended botulinum toxin or sacral nerve stimulation. Her evaluation continued at the time of trial. Of note, the patient remained on disability throughout this entire time.

At trial, the plaintiff’s experts emphasized the lack of an indication for the rectocele repair, with a lack of documented symptoms related to the rectocele. There were no abnormalities related to the patient’s bowel function or difficulty with defecation. During four annual exams preceding surgery, no bowel-related symptoms were documented and the patient’s physical exams consistently documented, “Rectum: normal.” There were discrepancies noted in the patient’s exam, with a first-degree rectocele documented at her annual exam, and a first- to second-degree rectocele documented in her preop history and physical, dated 5 weeks later. Finally, there was no attempt to institute stool softeners or attempt more conservative measures prior to surgical treatment. These experts opined that repair of the rectocele should not have been performed. In addition, use of permanent sutures for rectocele repair was a breach of the standard of care. They had no significant criticisms of the care rendered by the multiple physicians who cared for the patient after her original surgery.

The defense experts, both with excellent academic credentials, testified that adequate symptoms were documented. They also testified that use of permanent sutures for closure of the rectocele, although not common, was not a breach of the standard of care. Further, care of the patient was difficult due to her numerous self-referrals to multiple physicians throughout the country. The primary gynecologist was not even aware of the patient’s pursuit of other physicians’ care.

Ultimately, the jury found for the plaintiff for a sum of $750,000. In polling jurors after the verdict, the defense counsel found that the jurors felt the rectocele repair was not necessary. A consistent comment from the jurors was that the defense experts, although highly qualified, did not relate well with the jury. Conversely, the expert witnesses were down to earth and believable.

Learning points
Surgical treatment of an asymptomatic rectocele is not recommended.
If symptoms are present, careful documentation is critical. Further, attempts at more conservative treatments prior to surgery are warranted in most cases.

Communication with patients is critical. The patient sought second opinions regarding her care within 8 weeks of the original surgery. If a provider senses that a patient is dissatisfied with outcomes, initiating a discussion and offering additional opinions may avert the need for multiple self-referrals.

The defense attorney raised concerns, in retrospect, about the defense experts’ inability to connect with the jury. Although immensely qualified, they appeared aloof and argumentative at trial. Hence, selection of a quality expert extends beyond the curriculum vitae. It entails selection of individuals who can communicate well with the jury, bringing complicated concepts down to a level understandable to the panel.

Did traumatic vacuum extraction cause this infant’s delays? Plaintiff alleged that excessive force from implementing the vacuum resulted in intracranial hemorrhage.

Vesicovaginal fistula after laparoscopic hysterectomy Patient communication and preoperative consent are the main focuses of this case.

contemporaryobgyn.net/vacuum-extraction

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Was this rectocele repair necessary?

Treatment should follow a conservative approach – especially when the patient is asymptomatic.

A 40-year-old G2P202 was seen for her well-woman visit with complaints of heavy menstrual bleeding, "symptoms of a rectocele," and her uterus falling lower and lower. No specific symptoms related to the rectocele were documented. There was right lower quadrant pain on the abdominal exam. The woman’s pelvic exam revealed first- to second-degree uterine prolapse, a first-degree cystocele, and a first-degree rectocele. Pelvic ultrasound identified a solid, right adnexal mass measuring 5 x 7 x 7 cm. The patient was scheduled for possible laparoscopy and/or laparotomy with total abdominal hysterectomy, right salpingo-oophorectomy, possible bladder repair, and possible posterior repair. She underwent a cystometry (CMG), due to complaints of occasional urine leakage during prior well-woman visits, and the results were normal.

The woman’s pelvic exam revealed first- to second-degree uterine prolapse, a first-degree cystocele and a first-degree rectocele.

The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, and posterior repair, with surgical findings of extensive endometriosis and a right endometrioma. Technically, the rectocele repair included tying the uterosacral ligaments together, reducing the rectocele with three concentric sutures with a delayed-absorbable suture, and further closure with eight interrupted sutures with permanent, monofilament suture. The patient’s hospital course was uncomplicated, with no pain or immobility following surgery.

The patient’s post-op appointment 6 weeks after surgery was normal, with the exam documenting a normal perineum and vagina. One week later, she complained of vaginal pain and pressure. Her exam was normal, with the exception of slight vaginal thinning. The physician treated her with estrogen cream.

Two weeks after the last appointment, the patient self-referred to a urogynecologist who specializes in pelvic pain, for significant dyspareunia, inability to have sex due to pelvic pain, and loss of urine x 1. The patient’s exam was normal, with no evidence of suture erosion or fistula. There was levator hypertonicity bilaterally. With a diagnosis of levator spasm, the patient was referred for pelvic floor physiotherapy, given a central muscle relaxant, and offered analgesic injections. Over the next week she was able to have intercourse two times and was doing better overall. Her exam remained normal. The analgesic injections were not required at this time. The patient continued with her physical therapy on a weekly basis.

About 3 weeks later—now 12 weeks after the original surgery—the patient self-referred to another urogynecologist at a prominent academic institution in the southwest. She complained of pelvic pain, dyspareunia, inability to have sex due to pelvic pain, and loss of urine x 1. The patient’s exam was normal, with no evidence of suture erosion or fistula. There was levator hypertonicity bilaterally. With a diagnosis of levator spasm, the patient was referred for pelvic floor physiotherapy, given a central muscle relaxant, and offered analgesic injections. Over the next week she was able to have intercourse two times and was doing better overall. Her exam remained normal. The analgesic injections were not required at this time. The patient continued with her physical therapy on a weekly basis.

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Dr. Shwayder is professor of obstetrics and gynecology and former Chair at the University of Mississippi Medical Center. He is a graduate of the University of Denver College of Law and is a nationally and internationally recognized expert in gynecologic ultrasound and minimally invasive surgery. He actively consults on legal matters in medicine, including liability in ultrasound and gynecologic surgery, as well as issues surrounding privileging and insurance fraud.
BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR ParaGard® T 380A Intrauterine Copper Contraceptive

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE
ParaGard® is indicated for intrauterine contraception for up to 10 years. The pregnancy rate in clinical studies has been less than 1 pregnancy per 100 women each year.

CONTRAINDICATIONS
ParaGard® should not be placed when one or more of the following conditions exist:
1. Pregnancy or suspicion of pregnancy
2. Abnormalities of the uterus resulting in distortion of the uterine cavity
3. Acute pelvic inflammatory disease, or current behavior suggesting a high risk for pelvic inflammatory disease
4. Postpartum endometritis or postabortal endometritis in the past 3 months
5. Known or suspected uterine or cervical malignancy
6. Genital bleeding of unknown etiology
7. Mucopurulent cervicitis
8. Wilson’s disease
9. Allergy to any component of ParaGard®
10. A previously placed IUD that has not been removed

WARNINGS
1. Intrauterine Pregnancy
If intrauterine pregnancy occurs with ParaGard® in place and the string is visible, ParaGard® should be removed because of the risk of spontaneous abortion, premature delivery, sepsis, septic shock, and, rarely, death. Removal may be followed by premature labor and delivery.

If the string is not visible, and the woman decides to continue her pregnancy, check if the ParaGard® is in her uterus (for example, by ultrasound). If ParaGard® is in her uterus, warn her that there is an increased risk of spontaneous abortion and sepsis, septic shock, and, rarely, death. In addition, the risk of premature labor and delivery is increased.

Human data about risk of birth defects from copper exposure are limited. However, studies have not detected a pattern of abnormalities, and published reports do not suggest a risk that is higher than the baseline risk for birth defects.

2. Ectopic Pregnancy
Women who become pregnant while using ParaGard® should be evaluated for ectopic pregnancy. A pregnancy that occurs with ParaGard® in place is more likely to be ectopic than a pregnancy in the general population. However, because ParaGard® prevents most pregnancies, women who use ParaGard® have a lower risk of an ectopic pregnancy than sexually active women who do not use any contraception.

3. Pelvic Infection
Although pelvic inflammatory disease (PID) in women using IUDs is uncommon, IUDs may be associated with an increased relative risk of PID compared to other forms of contraception and to no contraception. The highest incidence of PID occurs within 20 days after insertion. Therefore, the visit following the first post-insertion menstrual period is an opportunity to assess the patient for infection, as well as to check that the IUD is in place. Since pelvic infection is most frequently associated with sexually transmitted organisms, IUDs are not recommended for women at high risk for sexual infection. Prophylactic antibiotics at the time of insertion do not appear to lower the incidence of PID.

PID can have serious consequences, such as tubal damage (leading to ectopic pregnancy or infertility), hysteroscetomy, sepsis, and, rarely, death. It is therefore important to promptly assess and treat any woman who develops signs or symptoms of PID.

Guidelines for treatment of PID are available from the Centers for Disease Control and Prevention (CDC), Atlanta, GA at www.cdc.gov or 1-800-311-3435. Antibiotics are the mainstay of therapy. Most healthcare professionals also remove the IUD.

The significance of actinomyces-like organisms on Papanicolaou smear in an asymptomatic IUD user is unknown, and so this finding alone does not always require IUD removal and treatment. However, because pelvic actinomyosis is a serious infection, a woman who has symptoms of pelvic infection possibly due to actinomyces should be treated and have her IUD removed.

4. Immunocompromise
Women with AIDS should not have IUDs inserted unless they are clinically stable on antiretroviral therapy. Limited data suggest that asymptomatic women infected with human immunodeficiency virus may use intrauterine devices. Little is known about the use of IUDs in women who have illnesses causing serious immunocompromise. Therefore these women should be carefully monitored for infection if they choose to use an IUD. The risk of pregnancy should be weighed against the theoretical risk of infection.

5. Embedment
Partial penetration or embedment of ParaGard® in the myometrium can make removal difficult. In some cases, surgical removal may be necessary.

6. Perforation
Partial or total perforation of the uterine wall or cervix may occur rarely during placement, although it may not be detected until later. Spontaneous migration has also been reported. If perforation does occur, remove ParaGard® promptly, since the copper can lead to intraperitoneal adhesions. Intestinal penetration, intestinal obstruction, and/or damage to adjacent organs may result if an IUD is left in the peritoneal cavity. Pre-operative imaging followed by laparoscopy or laparotomy is often required to remove an IUD from the peritoneal cavity.

7. Expulsion
Expulsion can occur, usually during the menses and usually in the first few months after insertion. There is an increased risk of expulsion in the nulliparous patient. If unnoticed, an unintended pregnancy could occur.

ParaGard® T 380A Intrauterine Copper Contraceptive

8. Wilson’s Disease
Theoretically, ParaGard® can exacerbate Wilson’s disease, a rare genetic disease affecting copper excretion.

PRECAUTIONS
Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

1. Information for patients
Before inserting ParaGard® discuss the Patient Package Insert with the patient, and give her time to read the information. Discuss any questions she may have concerning ParaGard® as well as other methods of contraception. Instruct her to promptly report symptoms of infection, pregnancy, or missing strings.

2. Insertion precautions, continuing care, and removal.
3. Vascular bleeding
In the largest clinical trials with ParaGard®, menstrual changes were the most common medical reason for discontinuation of ParaGard®. Discontinuation rates for pain and bleeding combined are highest in the first year of use and diminish thereafter. The percentage of women who discontinued ParaGard® because of bleeding problems or pain during these studies ranged from 11.9% in the first year to 2.2% in year 9. Women complaining of heavy vaginal bleeding should be evaluated and treated, and may need to discontinue ParaGard®.

4. Vasovagal reactions, including fainting
Some women have vasovagal reactions immediately after insertion. Hence, patients should remain supine until feeling well and should be cautious when getting up.

5. Expulsion following placement after a birth or abortion
ParaGard® has been placed immediately after delivery, although risk of expulsion may be higher than when ParaGard® is placed at times unrelated to delivery. However, unless done immediately postpartum, insertion should be delayed to the second postpartum month because insertion during the first postpartum month (except for immediately after delivery) has been associated with increased risk of perforation. ParaGard® can be placed immediately after abortion, although immediate placement may result in a slightly higher risk of expulsion than placement at other times. Placement after second trimester abortion is associated with a higher risk of expulsion than placement after the first trimester abortion.

6. Magnetic resonance imaging (MRI)
Limited data suggest that MRI at the level of 1.5 Tesla is acceptable in women using ParaGard®. One study examined the effect of MRI on the Cu-7™ Intrauterine Copper Contraceptive and Lippes Loop™ intrauterine devices. Neither device moved under the influence of the magnetic field or heated during the spin-echo sequences usually employed for pelvic imaging. An in vitro study did not detect movement or temperature change when ParaGard® was subjected to MRI.

7. Medical diathermy
Theoretically, medical (non-surgical) diathermy (short-wave and microwave heat therapy) in a patient with a metal-containing IUD may cause heat injury to the surrounding tissue. However, a small study of eight women did not detect a significant elevation of intrauterine temperature when diathermy was performed in the presence of a copper IUD.

8. Pregnancy
ParaGard® is contraindicated during pregnancy.

9. Nursing mothers
Nursing mothers may use ParaGard®. No difference has been detected in concentration of copper in human milk before and after insertion of copper IUD. The literature is conflicting, but limited data suggest that there may be an increased risk of performation and expulsion if a woman is lactating.

10. Pediatric use
ParaGard® is not indicated before menarche. Safety and efficacy have been established in women over 16 years old.

ADVERSE REACTIONS
The most serious adverse events associated with intrauterine contraception are discussed in WARNINGS and PRECAUTIONS. These include:

- Intrauterine pregnancy
- Septic abortion
- Ectopic pregnancy
- Pelvic infection
- Perforation
- Embedment

The following adverse events have also been observed. These are listed alphabetically and not by order of frequency or severity.

- Anemia
- Backache
- Dysmenorrhea
- Dyspareunia
- Expulsion, complete or partial
- Leukorrhea
- Menstrual flow, prolonged
- Menstrual spotting
- Pain and cramping
- Urticular allergic skin reaction
- Vaginitis

CooperSurgical, Inc
95 Corporate Drive
Trumbull, CT 06611

This brief summary is based on the ParaGard full prescribing information dated September 2014.

PAR-41287 01/18
The only one for almost everyone™

Only Paragard® IUD, with 1 hormone-free active ingredient (copper), delivers the strongest combination of benefits for the widest range of women1,2*

The Paragard Promise:
- Proven >99% efficacy
- 100% hormone free
- Pregnancy prevention for up to 10 years
- Immediately reversible whenever she decides

Satisfy more patients with Paragard—the only highly effective, reversible birth control that is completely hormone free. Learn more at hcp.paragard.com or call 1-877-PARAGARD.

Indication
Paragard is intended for intrauterine contraception for up to 10 years.

Important Safety Information
- Paragard must not be used by women who have acute pelvic inflammatory disease (PID); have had a postpregnancy or postabortion uterine infection in the past 3 months; have cancer of the uterus or cervix; have an infection of the cervix; have an allergy to any component; or have Wilson’s disease.
- If a woman misses her period, she must be promptly evaluated for pregnancy.
- Possible serious complications that have been associated with intrauterine contraceptives are PID, embedment, perforation of the uterus, and expulsion.
- Paragard must not be used by women who are pregnant as this can be life threatening and may result in loss of pregnancy or infertility.
- The most common side effects of Paragard are bleeding and spotting; for most women, these typically subside after 2 to 3 months.
- Paragard does not protect against HIV or other sexually transmitted infections (STI).

Please see the following page for a brief summary of full Prescribing Information.

References:

*According to the Centers for Disease Control and Prevention (CDC), Paragard is one of the least restrictive birth control options across all patient types compared to other IUDs.