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AHC Media

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Push is on to increase postpartum use of LARC

Your next patient is a young mother of two, and her youngest child is less than a year old. While she was using combined oral contraceptives (COCs) to prevent pregnancy, her busy schedule compromised compliance. The lab results are in: The pregnancy test is positive.

Such a scenario is a familiar one for family planning providers: 35% of pregnancies in the United States are conceived within 18 months of a previous birth.[1] Postpartum contraceptive provision is an important step in preventing short interpregnancy intervals and the associated risks of preterm birth, low birth weight, and preeclampsia.[1] Reducing the proportion of pregnancies conceived within 18 months of a previous birth is one of the objectives of the Department of Health and Human Services' Healthy People 2020, the national 10-year plan for health promotion and disease prevention. (Contraceptive Technology Update *reported on the charge to shorten intervals. See "Interpregnancy interval — You can help women," March 2014.)*

> "OFFERING WOMEN SUCH BIRTH CONTROL, WHILE THEY'RE STILL IN THE HOSPITAL, IS ... INCREDIBLY PATIENT-CENTERED ..."

The immediate postpartum period prior to hospital discharge can be an opportune time to offer contraception, because women might be more motivated to use contraception after giving birth and are known not to be pregnant. By inserting long-acting reversible contraceptive (LARC) methods, such as intrauterine devices

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(IUDs) and the contraceptive implant, immediately postpartum, providers are able to offer access to these methods for women who might not have insurance coverage after delivery or who might not attend their scheduled postpartum follow-up visit.

"Birth spacing, or taking sufficient time in between pregnancies, is vitally important for the health of both women and their babies, and LARC methods are the most effective forms of reversible contraception with the highest satisfaction rates," says **Katharine O'Connell White**, MD, MPH, director of the Fellowship in Family Planning program at Boston University/Boston Medical Center. "Offering women such birth control, while they're still in the hospital, is both incredibly patient-centered — she no longer has to worry about getting pregnant too soon — and cost-effective."

Consider the advantages

Results of a new study indicate that placement of implants and IUDs immediately postpartum can lead to high satisfaction with the methods.[2]

To perform the study, researchers enrolled 133 women in a prospective cohort study following immediate postpartum insertion of an implant or IUD at Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center, both in Baltimore, during eight months of 2011. Women in the study completed an enrollment survey during hospital admission and a follow-up telephone survey at six months and one year postpartum.

At six months postpartum, 72% of women provided follow-up information. Implant users were more likely to be using the originally placed device (40/41, 98% versus 45/55, 82%, p=0.02). Nine women reported IUD expulsions. Five of the nine women underwent IUD replacement following expulsion. When accounting for replacement of expelled IUDs, IUD continuation at six months was 89%, yielding similar continuation rates between groups (p=0.12). At one year postpartum, 51% provided follow-up information. Of those women, 82% still had a LARC method in place, with similar continuation by device type (84% for implants, 81% for IUDs, p=0.96). Among the women reached, no pregnancies were reported. Overall, satisfaction was similarly high in both groups, researchers note.[2]

For those who might not return for follow-up, the benefits of placing a LARC immediately postpartum greatly outweigh the risks of

EXECUTIVE SUMMARY

Postpartum contraceptive provision is an important step in preventing short interpregnancy intervals and the associated risks of preterm birth, low birth weight, and preeclampsia.

- Results of a new study indicate that placement of implants and intrauterine devices immediately postpartum can lead to high satisfaction with the methods.
- The American College of Obstetricians and Gynecologists recently strengthened its recommendation regarding use of long-acting reversible contraceptive methods as the most effective and safe form of reversible contraception, with information included on immediate postpartum use.

device expulsion or early removal, the researchers note. Immediate postpartum implant insertion might have the highest rate of continuation (up to three years) in the population who are most vulnerable to rapid repeat and unintended pregnancy, they state.[3]

There are several barriers to provision of LARC methods in the immediate postpartum setting, including lack of provider training, difficulty with stocking issues within the hospital setting, and challenges with obtaining a reimbursement, states the *Intrauterine Devices and Implants: A Guide to Reimbursement* website (http://bit.ly/1MhrmeA).

The website is a joint project of the Bixby Center and the American College of Obstetricians and Gynecologists National Family Planning and Reproductive Health Association, National Health Law Program, and the National Women's Law Center. *(To read more about the guide and website, see "Counseling on LARC methods cuts unintended pregnancy rates,"* Contraceptive Technology Update*, September 2015.)* Payment for delivery is often made using a "global fee" that does not specifically reimburse hospitals for the cost of LARC methods or the insertion procedure on a fee-for-service basis, the guide notes.

The ACOG LARC Program website (http://bit.ly/1N82hxZ) confirmed the following states and district have published final or proposed guidance regarding Medicaid reimbursement for postpartum LARC: Alabama, California, Colorado, District of Columbia, Georgia, Illinois, Indiana, Iowa, Louisiana, Maryland, Montana, New Mexico, New York, Ohio, Oklahoma, South Carolina, and Washington. *(The list is updated on a regular basis. Check it at http://bit.ly/1tlMUPw.)*

To help identify opportunities, challenges, and technical assistance needs to improve states' ability to promote LARCs during the immediate postpartum timeframe, the Association of State and Territorial Health Officials, which is based in Arlington, VA, has established a multistate LARC learning community. With support from the Centers for Disease Control and Prevention and partnerships with the Centers for Medicare and Medicaid Services and the Office of Population Affairs, the organization convened the learning community in August 2014 to help select six states (Colorado, Georgia, Iowa, Massachusetts, New Mexico, and South Carolina) that are establishing Medicaid payment policies or pilot programs to implement immediate postpartum LARC initiatives. Evaluation of the implementation of immediate postpartum LARC in the Learning Community states will be done by researchers at the University of Illinois at Chicago. *(You can obtain more information about the Learning Community at http://bit.ly/1SiJMi8.)*

Get up to speed

The *U.S. Medical Eligibility Criteria for Contraceptive Use (US MEC)* classifies immediate postpartum copper IUD insertion as Category 1 and immediate postpartum levonorgestrel intrauterine system insertion in nonbreastfeeding and breastfeeding women as Category 2.

Insertion of the implant is safe at any time in nonbreastfeeding women after childbirth (Category 1 rating). The *US MEC* classifies the placement of an implant in breastfeeding women less than four weeks after childbirth as Category 2 because of theoretic concerns regarding milk production and infant growth and development. Implants may be offered to women who are breastfeeding and more than four weeks after childbirth because the *US MEC* classifies delayed insertion as Category 1.[4]

The American College of Obstetricians and Gynecologists (ACOG) recently strengthened its recommendation regarding use of LARC methods as the most effective and safe forms of reversible contraception, with information included on immediate postpartum use.[5]

David Soper, MD, chair of the College's Gynecologic Practice Committee, says, "ACOG has long recommended LARC as the most effective reversible contraceptive option for most women, including those who have not given birth and adolescents who are sexually active. We continually see more and more data to support and strengthen our recommendations at the same time that more LARC options are becoming available."

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Could premenstrual syndrome be a flag for future risk of hypertension?

Results of a new study indicate that women with moderate-to-severe premenstrual syndrome (PMS) had a 40% higher risk of developing high blood pressure during the following 20 years compared to women experiencing few menstrual symptoms.[1]

Premenstrual syndrome is defined as recurrent moderate psychological and physical symptoms that occur during the luteal phase of menses and resolve with menstruation. The condition is estimated to affect 20-32% of premenopausal women.[2] Psychological symptoms associated with premenstrual syndrome might include irritability, depression, anxiety, mood swings, a flat mood (anhedonia), and lethargy. Physical symptoms might include breast tenderness, weight gain, bloating, muscle or joint pain, headache, and swelling of the extremities (hands and feet).[3]

To conduct the study, epidemiologist **Elizabeth Bertone-Johnson**, ScD, and colleagues in the School of Public Health and Health Sciences at the University of Massachusetts Amherst and the Harvard School of Public Health evaluated the relationship between PMS and blood pressure. The study included 1,257 women who developed clinically significant PMS between 1991 and 2005, and in 2,463 age-matched control participants with few menstrual symptoms. All participants were part of the Nurses' Health Study II, one of the largest, longest running investigations of women's health, overseen by researchers at Harvard School of Public Health and Brigham and Women's Hospital in Boston.

EXECUTIVE SUMMARY

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- Psychological symptoms associated with premenstrual syndrome might include irritability, depression, anxiety, mood swings, a flat mood (anhedonia), and lethargy. Physical symptoms might include breast tenderness, weight gain, bloating, muscle or joint pain, headache, and swelling of the extremities (hands and feet).

Researchers with the current study assessed PMS with a modified Calendar of Premenstrual Experiences, which includes such symptoms as palpitations, nausea, forgetfulness, dizziness, hot flashes, insomnia, depression, acne, and cramping. In their sub-study, scientists followed participants for new diagnoses of hypertension until 2011.

Data indicate that women with PMS had a hazard ratio for hypertension of 1.4 compared to women without PMS, a statistically significant increased risk of 40%. The risk associated with PMS was not impacted by oral contraceptive or antidepressant use; however, the higher risk was not present in women with high intakes of the B vitamins thiamine and riboflavin.

Bertone-Johnson and colleagues recently found that women with high dietary intake of the B vitamins thiamine and riboflavin had 25-35% lower risks of developing PMS.[4] Results from the present study are "consistent with these findings, and suggest that improving B vitamin status in women with PMS may both reduce menstrual symptom severity and lower hypertension risk," researchers note.

During the past 10 years, Bertone-Johnson's research group has evaluated a variety of behavioral and dietary risk factors for incident PMS. Bertone-Johnson says she has been "struck" by how similar the

risk factors her group has identified for PMS are to risk factors for cardiovascular disease (CVD) and hypertension.

"Some of these risk factors include smoking, high body mass index, low vitamin D and calcium intake, low B vitamin intake, and higher levels of inflammatory markers," notes Bertone-Johnson in an email interview with *Contraceptive Technology Update*. "The similarities of these risk factors, and potential similarities in the underlying mechanisms contributing to PMS and to CVD, raised the question of whether women with PMS would have higher risk of developing hypertension and CVD in later life (and thus whether PMS might be a sentinel of future CVD risk)."

What are options?

How can you help women with PMS? If symptoms are mild to moderate, they often can be relieved by changes in lifestyle or diet. When PMS symptoms begin to interfere with daily life, women might decide to seek medical treatment. Treatment will depend on the severity of symptoms; in more severe cases, medication might be indicated.

Regular aerobic exercise, such as brisk walking, running, cycling, and swimming, might help lessen PMS symptoms, thus reducing fatigue and depression. Encourage women to exercise regularly, not just during the days that they have symptoms. A good goal is at least 30 minutes of exercise most days of the week.

Relaxation methods also can help relieve PMS symptoms. Suggest relaxation therapy options such as breathing exercises, meditation, and yoga. Massage therapy also might be helpful. Some women find therapies such as biofeedback and self-hypnosis to be effective. Also discuss sleeping habits. Regular sleeping habits might help lessen moodiness and fatigue.

Simple changes in daily diet habits might help relieve PMS symptoms. Talk about following a diet rich in complex carbohydrates to reduce mood symptoms and food cravings. Complex carbohydrates are found in foods made with whole grains, such as whole wheat bread, pasta, and cereals; other examples include barley, brown rice, beans, and lentils. Suggest adding calcium-rich foods, such as yogurt and leafy green vegetables; counsel on reducing intake of fat, salt, and sugar. Discuss avoiding caffeine and alcohol.

By eating six small meals a day rather than three large ones, or eating slightly less at normal meals and adding three light snacks, women can keep their blood sugar level stable, helping to alleviate symptoms.

Can dietary supplements help? Taking 1,200 mg of calcium a day might help reduce the physical and mood symptoms that are associated with PMS. Use of magnesium supplements might help reduce water retention, breast tenderness, and mood symptoms.[5]

Providers might suggest use of extended cycles of combined oral contraceptives or the contraceptive vaginal ring, levonorgestrel intrauterine contraception, or the contraceptive injection for lessening dysmenorrhea associated with PMS.[6] However, not all might relieve the mood symptoms of PMS. It might be necessary to try more than one of these approaches before finding one that works.

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Antifungal drug tied to miscarriage risk

In a retrospective analysis of 1.4 million pregnancies in Denmark, use of the oral antifungal medication fluconazole during pregnancy was tied to a significantly increased risk of spontaneous abortion associated with fluconazole exposure (HR, 1.48; 95%CI, 1.23-1.77), compared with risk among unexposed women and women who used a topical antifungal during pregnancy. Until more data on the association are available, cautious prescribing of fluconazole in pregnancy might be advisable. Although the risk of stillbirth wasn't

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- Prevalence studies indicate that *Candida* species colonize the vagina in at least 20% of all women, rising to 30% in pregnancy. Most episodes of symptomatic vulvovaginal candidiasis occur during the second and third trimesters; the increased risk of candidiasis in pregnancy might be linked to pregnancy-related factors, such as immunologic alterations, increased estrogen levels, and increased vaginal glycogen production.
- Topical azole therapies, applied for seven days, are recommended for use among pregnant women.

significantly increased, this outcome should be investigated further.[1]

Prevalence studies indicate that *Candida* species colonize the vagina in at least 20% of all women and rises to 30% in pregnancy.[2] Most episodes of symptomatic vulvovaginal candidiasis (VVC) occur during the second and third trimesters; the increased risk of VVC in pregnancy might be linked to pregnancy-related factors, such as immunologic alterations, increased estrogen levels, and increased vaginal glycogen production.[1]

First-line treatment of such infection during pregnancy is topical antifungals via vaginal suppositories, observes **Ditte Mølgaard-Nielsen**, MSc, an epidemiology researcher at the Statens Serum Institut, Copenhagen, Denmark. However, a small number of pregnant women receive oral treatment with fluconazole despite limited safety information on spontaneous abortion and stillbirth, says Mølgaard-Nielsen, lead author of the current research.

To perform the current study, researchers evaluated the association between oral fluconazole exposure during pregnancy and the risk of spontaneous abortion and stillbirth. The study included 1.4 million pregnancies in Denmark from 1997-2013. From this group, oral fluconazole-exposed pregnancies were compared with up to four unexposed pregnancies, matched on maternal age, calendar year, and gestational age. Filled prescriptions for oral fluconazole were obtained from the National Prescription Register.

Among 3,315 women exposed to oral fluconazole from seven through 22 weeks' gestation, 147 experienced a spontaneous abortion, compared with 563 among 13,246 unexposed matched women. There was a significantly increased risk of spontaneous abortion associated with fluconazole exposure (hazard ratio [HR], 1.48; 95% confidence interval (CI), 1.23-1.77). Among 5,382 women exposed to fluconazole from gestational week seven to birth, 21 experienced a stillbirth, compared with 77 among 21,506 unexposed matched women. There was no significant association between fluconazole exposure and stillbirth (HR, 1.32 [95% CI, 0.82-2.14]), researchers note. Using topical azole exposure as the comparison, 130 of 2,823 women exposed to fluconazole versus 118 of 2,823 exposed to topical azoles had a spontaneous abortion (HR, 1.62 [95% CI, 1.26-2.07]. Twenty of 4,301 women exposed to fluconazole versus 22 of 4,301 exposed to topical azoles had a stillbirth (HR, 1.18 [95% CI, 0.64-2.16]).[1]

"Previous safety studies have focused on possible teratogenic effects associated with use of oral fluconazole in pregnancy (lower doses), because five case reports have linked long-term, high-dose fluconazole treatment in pregnant women to a distinct pattern of birth defect," states Mølgaard-Nielsen. "Until now there has only been two smaller observational studies investigating spontaneous abortion and stillbirth and with a total of 1,500 pregnant women treated with oral fluconazole."

Check the options

According to the Centers for Disease Control and Prevention's (CDC) 2015 *Sexually Transmitted Diseases Treatment Guidelines*, the diagnosis of *Candida* vaginitis is suggested clinically by the presence of external dysuria and vulvar pruritus, pain, swelling, and redness. Clinicians should look for such signs as vulvar edema, fissures, excoriations, and thick curdy vaginal discharge. Diagnosis can be made in a woman who has signs and symptoms of vaginitis in two ways:

- a wet preparation (saline, 10% potassium hydroxide [KOH]) or Gram stain of vaginal discharge that demonstrates budding yeasts, hyphae,

or pseudohyphae;

• a culture or other test that yields a positive result for a yeast species.[3]

According to the guidance from the CDC, only topical azole therapies, applied for seven days, are recommended for use among pregnant women.

Most organizations, such as the American College of Obstetricians and Gynecologists and the CDC, have advised against or caution with using fluconazole in pregnancy given concerns about adverse effects on the fetus, says **Jeanne Marrazzo**, MD, MPH, FACP, FIDSA, professor of medicine in the Division of Allergy and Infectious Diseases and adjunct professor in the Department of Global Health at the University of Washington. The Food and Drug Administration (FDA) warned in 2011 that chronic use of oral fluconazole in high doses (400-800 mg/day) during the first trimester of pregnancy might be associated with certain birth defects in infants. In issuing the warning, the FDA recommended that healthcare professionals counsel patients if the drug is used during pregnancy or if a patient becomes pregnant while taking the drug.

"We typically recommend topical (vaginal) clotrimazole or a similar agent in this setting," says Marrazzo, who also serves as medical director of the University of Washington STD Prevention Training Center.

There are no formal studies evaluating the use of long-term suppressive maintenance oral azoles in the treatment of recurrent vulvovaginal candidiasis in pregnancy. Most clinicians don't offer suppressive therapy in pregnancy and opt to treat individual symptomatic episodes only using a topical imidazole vaginally for seven days to minimize systemic exposure to medications.[1]

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Elevated testosterone levels might increase risk of uterine fibroids

Women who have high levels of both testosterone and estrogen in midlife might face a greater risk of developing benign uterine fibroids than women with low levels of the hormones, results of a new study indicate.[1]

Many women develop uterine fibroid tumors (leiomyomas) as they grow older. Research data indicate the prevalence of ultrasound-identified tumors as 33% in women 40 to 60 years of age, compared to 11-18% in women ages 30-40 and 4% in women ages 20-30.[2] The presence of uterine fibroid tumors is the most common indication cited for hysterectomy, representing more than 30% of such procedures.[3] Treatment options include watchful waiting; treatment with drugs or hormones, embolization, ultrasound thermal ablation; and invasive procedures such as partial or total hysterectomy.

The current 13-year longitudinal study looked at hormone levels and the incidence of uterine fibroids in women participating in the Study of Women's Health around the Nation (SWAN), a multi-site longitudinal, epidemiologic study designed to examine the health of women during

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- The presence of uterine fibroid tumors is the most common indication cited for hysterectomy and represents more than 30% of such procedures. Treatment options include watchful waiting; treatment with drugs or hormones, embolization, or ultrasound thermal ablation; and invasive procedures such as partial or total hysterectomy.

their middle years. Among the 3,240 women enrolled at the beginning of the study, 43.6% completed the follow-up visits. During their follow-up visits, participants had their blood tested for estrogen and androgen levels. In addition, enrollees were asked whether they had been diagnosed with or treated for uterine fibroids.

Among the study participants, 512 women reported having a single incidence of fibroids, and an additional 478 women had recurrent cases. Data indicate that participants who had high levels of testosterone in the blood were 1.33 times more likely to develop a single incidence of fibroids than women who had low levels of testosterone. Women who had high levels of testosterone and estrogen faced an even greater risk, researchers report. Although women with high levels of both hormones were more likely to report a single incidence of fibroids, they also were less likely to have a recurrence than women with low levels of the hormones, they note.[1]

The research suggests women undergoing the menopausal transition who have higher testosterone levels have an increased risk of developing fibroids, particularly if they also have higher estrogen levels, stated **Jason Wong**, ScD, a post-doctoral fellow in the Stanford University School of Medicine. The study represents the first longitudinal investigation of the relationship between androgen and estrogen levels and the development of uterine fibroids, said Wong in a release accompanying the paper.

The study's findings are particularly interesting because testosterone previously was unrecognized as a factor in the development of uterine fibroids, said **Jennifer Lee**, MD, PhD, associate professor at the Stanford University School of Medicine and a study co-author.

"The research opens up new lines of inquiry regarding how fibroids develop and how they are treated," noted Lee in a press statement. "Given that managing uterine fibroids costs an estimated $34.4 billion in annual medical expenditures nationwide, it is important to identify new ways to better treat this common condition."

What option is best?

The Duke Clinical Research Institute in Durham, NC, is working with nine centers across the United States in a five-year project to evaluate the effectiveness of different treatment strategies for women with uterine fibroids.

The project, a collaboration between the Patient-Centered Outcomes Research Institute and the Agency for Healthcare Research and Quality, is designed to help patients and clinicians make more informed choices about treatment options. (Contraceptive Technology Update *reported on the study kickoff; see "Duke Clinical Research Institute's initiative to look at options for uterine fibroids," December 2014.)*

The study is focused on developing a multi-center registry of women who have received surgical treatments for uterine fibroids. This registry, COMPARE-UF (Comparing Options for Management: Patient-centered REsults for Uterine Fibroids), will establish the infrastructure necessary to support patient-centered comparative clinical effectiveness research.

Therapies for isolated heavy menstrual bleeding associated with fibroids include tranexamic acid, an oral antifibrinolytic agent that is taken only on the days of heavy menstrual bleeding. This approach decreases bleeding and improves quality of life with minimal side effects.[4] Use of a levonorgestrel-releasing intrauterine device (IUD) or oral contraceptives can decrease menstrual bleeding and provides birth control.

Providers also might consider hysteroscopic myomectomy, an outpatient surgical procedure that allows women with submucosal fibroids to return to work within a few days. Another procedure is endometrial ablation, which uses heat, cold, or mechanical means to reduce menstrual bleeding.

In 2014, the Food and Drug Administration warned against the use of laparoscopic power morcellators in most women undergoing myomectomy or hysterectomy for treatment of fibroids. The FDA warned that uterine tissue might contain unsuspected cancer. The use of laparoscopic power morcellators during fibroid surgery might spread cancer, and it decreased the long-term survival of patients.

Therapies for women for whom the size of the fibroid(s) causes symptoms include gonadotropin-releasing hormone agonists, medications that turn off the ovaries' production of hormones, which reduces menstrual bleeding and causes considerable reduction in uterine volume. Uterine artery embolization, a minimally invasive interventional radiologic technique offers shorter hospital stays and less time to resumption of usual activities.

Providers also might look at MRI-guided focused ultrasound surgery, a fibroid-specific therapy that uses ultrasound thermal ablation to treat fibroids with no incisions and no hospital stay.

Radiofrequency ablation during laparoscopy is useful for destruction of fibroids during laparoscopy.[4]

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WASHINGTON WATCH

Supreme Court cases loom large in 2016

By ***Adam Sonfield***
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The most consequential reproductive health-related drama in Congress in 2016 most likely played out in January.

Conservative activists got their wish on Jan. 8, when President Obama was forced to veto legislation that would disqualify Planned Parenthood health centers from eligibility for federal funds, including Medicaid, for one year and that would repeal sweeping portions of the Affordable Care Act (ACA), including the major expansions of Medicaid adopted by 31 states and the District of Columbia and the federal subsidies intended to make private insurance affordable for low-income individuals and businesses.

The House had voted more than 50 times to repeal all or part of the ACA and had voted multiple times in 2015 to defund Planned Parenthood. By contrast, this legislation marked the first time the Senate has approved such provisions. The Senate used a special procedure that allowed for a simple majority vote, as opposed to the Senate's usual 60-vote supermajority.

Congressional leaders will have an override vote that is yet to be scheduled as of the time of this writing, but everyone involved understands that vote is certain to fail. Rather, conservatives will use the veto to rally voters for the 2016 elections, which will bring to power a new president — perhaps one who would sign a similar bill into law.

Congressional observers expect extensive posturing and rhetoric during the election year, but it is unlikely that any major reproductive health-related legislation will be enacted. Instead, all eyes are on the U.S. Supreme Court, which is hearing major cases this term related to abortion and contraception.

Abortion rights at risk

First up, with oral arguments scheduled for March 2, is the case of *Whole Woman's Health v. Cole*, which is potentially the most important case on abortion since 1992's landmark decision in *Planned Parenthood v. Casey*.

The case challenges the constitutionality of a Texas law designed to shut down access to abortion care in the state. The law does so by requiring that doctors who provide abortion services obtain admitting privileges at local hospitals and that healthcare facilities offering abortion care meet building specifications to essentially become mini-hospitals.

The plaintiffs in the case — along with their supporters, who filed 45 amicus briefs with the court[1] — argue that the law is based on a sham premise: that it is needed to protect women's health. Rather, as my Guttmacher Institute colleagues have argued, these types of restrictions actually harm women's health and are designed to cut off access to legal abortion care.[2]

The Guttmacher Institute joined one of the amicus briefs, along with dozens of social scientists who research abortion safety, incidence, and access in the United States.[3] Other briefs represent the perspectives of physicians, hospitals, public health specialists, constitutional scholars, abortion providers, individual women who have had abortions, business leaders, faith leaders, economists, historians, reproductive justice advocates, cities, states, 163 members of Congress, and the U.S. solicitor general on behalf of the federal government.

Guarantee debate

Later in its spring 2016 term, the Supreme Court will hear arguments on seven challenges, collectively referred to as *Zubik v. Burwell*, to the ACA's contraceptive coverage guarantee.

When the Obama administration implemented that provision of the ACA, it exempted houses of worship that object to sponsoring a health plan that includes contraceptive coverage. Furthermore, it set up an "accommodation" for nonprofit employers with religious objections, under which the employer does

not have to pay or arrange for contraceptive coverage, while an insurance company must separately provide the employees and dependents with that coverage at no additional cost.

The Supreme Court first addressed the issue in its 2014 decision in *Burwell v. Hobby Lobby Stores*, which effectively required the administration to extend its accommodation to certain for-profit companies.

In *Zubik*, the plaintiffs are challenging the accommodation itself and are arguing that the process, under which they must fill out a form to tell their insurance company or the federal government that they have a religious objection, makes them complicit in the coverage they find objectionable.

At stake might be contraceptive coverage for hundreds of thousands of U.S. women. According to a 2015 study from the Kaiser Family Foundation, an estimated 3% of nonprofits offering health insurance, and 10% of the largest such nonprofits, had taken up the accommodation.[4]

Decisions in both cases are likely to be issued in the waning days of June 2016. However the members of the Supreme Court rule in each of the cases, the decisions will affect access to abortion and contraceptive care nationwide and reverberate politically in the fall elections, as well as in Congress and state legislatures in the years to come.

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New option for vaginal discomfort after menopause

Results of a recent Phase III trial suggest that intravaginal dehydroepiandrosterone (DHEA) could provide women who cannot or do not wish to use intravaginal estrogen with an effective vaginal alternative for easing vaginal symptoms and pain with sex after menopause.[1] The drug, under development as Intrarosa by Endoceutics, a North American biopharma company, is under review by the Food and Drug Administration (FDA).

In menopause, vaginal tissues atrophy, the lining thins and secretes less and less fluid, and the pH becomes more alkaline, which leads to discomfort with sex, as well as increased susceptibility to vaginal infections and urinary problems for many women.[2] Providers offer moisturizers and lubricants as nonhormonal alternatives to intravaginal estrogen to temporarily ease pain with sex and provide moisture, but these treatments cannot correct the physical changes that produce the symptoms. These genitourinary syndromes of menopause can be problematic for many women. In a study of 94,000 postmenopausal women ages 50-79, 52% reported that they had been sexually active with a partner in the past year.[3]

The current study analyzed the local beneficial effects of Intrarosa, Endoceutics' DHEA product used intravaginally, on moderate to severe dyspareunia, the most frequent symptom of vulvovaginal atrophy due to menopause or genitourinary syndrome of menopause. In the prospective, randomized, double-

EXECUTIVE SUMMARY

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blind, and placebo-controlled study, the 325 women who used the daily 0.5% DHEA (6.5 mg) ovules enjoyed significant improvements after 12 weeks compared with the 157 women who used a placebo. Their scores on a scale of 0 to 3 for pain with sex dropped 0.36 points more than for the women who used the placebo.

Results suggest that women who used DHEA also had significantly less thinning of the vaginal lining, with them showing an 8.44% greater increase in lining cells called "superficial cells" and a 27.7% greater decrease in parabasal cells, the immature precursors of the superficial cells. The DHEA users' moderate to severe vaginal dryness also improved by 0.27 points more on a scale of 0 to 3. Researchers saw 86% to 121% better improvements in vaginal secretions, integrity of the vaginal lining, lining thickness, and tissue color in the women who used DHEA.[1]

Treatment of postmenopausal vaginal dryness is an important topic for providers who care for those in this patient population. Symptoms of vaginal dryness and atrophy can cause vulvar itching, painful sex, or increased risk of vaginal or bladder infections, says **JoAnn Pinkerton**, MD, NCMP, executive director of the North American Menopause Society in Cleveland.

"The good news is that we do have effective treatments," observes Pinkerton. "Over-the-counter lubricants and moisturizers, vaginal exercises, or dilators may make sex more comfortable, but don't 'fix' the problem of changes in the vaginal lining due to low estrogen levels."

Different forms of low-dose vaginal estrogen therapies include the following: Vagifem (vaginal tablet, Novo Nordisk, Plainsboro, NJ); Estrace (cream, Warner Chilcott, Rockaway, NJ); Premarin (cream, Pfizer, New York City,): Estring (low-dose vaginal ring, Pfizer); and an oral estrogen agonist/antagonist pill (ospemifene, Osphena, Shionogi, Florham Park, NJ).

However, not all women choose to take vaginal estrogen, sometimes out of fear raised by the boxed warning of risks from systemic hormones, which don't apply to the low-dose vaginal products, notes Pinkerton. Sometimes women can't take estrogen products and prefer not to take the new oral daily pill. These women need non-estrogen containing effective therapy, which "fixes" the problem more than just the improvement seen with vaginal moisturizers, she notes. The biggest need is in women with advanced estrogen-positive breast cancers, who are fearful of any type of estrogen, even low-dose vaginal therapies, says Pinkerton.

Vaginal DHEA suppositories are not yet approved by the FDA but are showing a positive effect in the vagina, she says. However, neither the new estrogen agonist/antagonist ospemifene (Osphena) nor the vaginal DHEA suppositories have been tested in women at high risk of breast cancer or with breast cancer, Pinkerton states. Anyone with an estrogen-sensitive cancer should discuss their problems with vaginal symptoms or painful sex with their gynecologist and their oncologist to determine what product is best and safest for them, says Pinkerton.

In a release accompanying the study results, **David Archer**, principle investigator of the Intrarosa trial and professor of obstetrics and gynecology and director of the Clinical Research Center at the Eastern Virginia Medical Center in Norfolk, said, "Having a new therapeutic option for menopausal women which is effective in treating painful sex without the possible safety concerns of traditional hormonal treatments should provide more women the ability to stop dealing with the issue on their own and give them a reason to reach out to their obstetrician-gynecologist or women's healthcare provider to get clinical support they need and discuss this novel solution."

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COMING IN FUTURE MONTHS

- Update on self-administered contraceptive injections
- New strategies examined to fight ovarian cancer
- Science looks at new estrogen for contraception
- Research advances on HIV vaccine

CONTRACEPTIVE TECHNOLOGY UPDATE®

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CNE/CME QUESTIONS

1. What classification does the *U.S. Medical Eligibility Criteria for Contraceptive Use* give immediate postpartum levonorgestrel intrauterine system insertion in both nonbreastfeeding and breastfeeding women?

A. Category 1
B. Category 2
C. Category 3
D. Category 4

2. What treatment does the Centers for Disease Control and Prevention advise for symptomatic vulvovaginal candidiasis treatment in pregnant women?

A. Topical azole therapies, applied for seven days
B. Fluconazole, 150 mg orally in single dose
C. Erythromycin base 500 mg orally three times a day for seven days
D. Ciprofloxacin 500 mg orally twice a day for three days

3. Presence of uterine fibroids represents approximately what pecent of hysterectomies?

A. 10%
B. 15%
C. 20%
D. 30%

4. What percentage of premenopausal women are estimated to experience premenstrual syndrome?

A. 10-15%
B. 15-20%
C. 20-32%
D. 33-45%

CNE/CME OBJECTIVES

After reading *Contraceptive Technology Update*, the participant will be able to:

1. identify clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services;
2. describe how those issues affect services and patient care;
3. integrate practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts;
4. provide practical information that is evidence-based to help clinicians deliver contraceptives sensitively and effectively.

STI QUARTERLY™

A SUPPLEMENT TO CONTRACEPTIVE TECHNOLOGY UPDATE

Snapshot from National HIV Prevention Conference: Strides have been made, yet hurdles remain

Annual HIV diagnoses in the United States dropped 19% from 2005-2014

The December 2015 National HIV Prevention Conference saw exciting developments announced by the Centers for Disease Control and Prevention (CDC) and partners, including new data on trends and disparities in the U.S. HIV epidemic. Data indicate annual HIV diagnoses in the United States dropped 19% from 2005 to 2014.[1] The decrease was driven by continuing declines among several populations, including heterosexuals, people who inject drugs, and African Americans, with the steepest declines seen among black women.[1]

For gay and bisexual men, trends over the decade have varied by race and ethnicity, research suggests.[1] Among white gay and bisexual men, diagnoses fell by 18%, while diagnoses among Latino gay and bisexual men continued to rise: up 24%. Diagnoses among black gay and bisexual men rose 22% between 2005 and 2014, but they leveled off after 2010. Public health officials note a similar trend in young black gay and bisexual men ages 13-24, who experienced an 87% increase in diagnoses from 2005 and 2014. However, between 2010 and 2014, the trend has leveled off at 85%.[1]

HIV testing has remained stable or increased among the groups experiencing declines in diagnoses in recent years. Researchers believe the decreases in diagnoses reflect a decline in new infections. Because HIV testing has remained stable among Latino gay and bisexual men during this period, the increases in HIV diagnoses suggest infections likely are increasing in this group, CDC officials note.

> "WE URGENTLY NEED TO ACCELERATE ACCESS TO TESTING, TREATMENT, AND NEW BIOMEDICAL PREVENTION STRATEGIES..."

The recent five-year trends coincide with the launch of the first National HIV/AIDS Strategy in 2010, said **Eugene McCray,** MD, director of CDC's Division of HIV/AIDS Prevention. Now that the investment in high-impact prevention approaches has increased, there is promise for further progress, he noted.

"We have the tools to stop HIV right now," said McCray in a statement accompanying the new date. "We urgently need to accelerate access to testing, treatment, and new biomedical prevention strategies so that everyone can protect themselves and their partners."

Check the numbers

What else does the new data reveal when it comes to HIV trends? Take a look at the statistics, which focused on trends in diagnoses over two time periods: 2005-2014 and 2010-2014. Among the findings:

- From 2005-2014, the annual number of HIV diagnoses in the United States fell 19% (from 48,795 to 39,718 per year), which was driven by declines among heterosexuals (down 35%) and people who inject drugs (down 63%).
- HIV diagnoses among black women dropped from 8,020 to 4,623 over the 2005-2014 period (down 42%), with continuing declines in recent years: 25% since 2010.

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EXECUTIVE SUMMARY

Data presented at the December 2015 National HIV Prevention Conference indicate annual HIV diagnoses in the United States dropped 19% from 2005 to 2014. It was driven by continuing declines among several populations, including heterosexuals, people who inject drugs, and African Americans, with the steepest declines seen among black women.

• For gay and bisexual men, trends over the decade have varied by race and ethnicity, research suggests.

• The CDC and its partners are taking steps to encourage further declines, with a new national HIV testing campaign and the beta version of an online tool to help individuals assess and reduce their risk of acquiring or transmitting HIV.

• Diagnoses among gay and bisexual men overall rose about 6% over the decade (from 25,155 to 26,612), but leveled off in more recent years.

• Among white gay and bisexual men, diagnoses dropped steadily, both over the decade (decreasing 18% from 9,966 to 8,207) and in more recent years (falling 6% from 8,766 to 8,207).

• Over the decade, diagnoses among black gay and bisexual men rose 22% (from 8,235 to 10,080), but stabilized in more recent years. While black gay and bisexual men ages 13-24 experienced a steep increase (87%, from 2,094 to 3,923) in diagnoses over the decade, diagnoses among young black gay and bisexual men actually declined by 2% (from 3,994 to 3,923) in the most recent years.

• Diagnoses continue to increase among Latino gay and bisexual men, both over the decade (by 24%, from 5,492 to 6,829) and in more recent years (by 13%, from 6,060 to 6,829).[1]

The CDC and its partners are taking steps to encourage further declines, with a new national HIV testing campaign and the beta version of an online tool to help individuals assess and reduce their risk of acquiring or transmitting HIV announced at the conference.

Jonathan Mermin, MD, director of CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, says, "The cornerstone of CDC's HIV prevention strategy is a high-impact approach that provides the right tools to the right people to achieve the greatest results. We will continue our high-impact approach to close gaps in HIV prevention and care, and accomplish the objectives that are essential to achieving further declines in diagnoses."

> "THE CORNERSTONE OF CDC'S HIV PREVENTION STRATEGY IS A HIGH-IMPACT APPROACH... TO ACHIEVE THE GREATEST RESULTS."

Data presented at the conference indicate that nationally, 87% of Americans knew their HIV status in 2012, but this percentage varied substantially across states, from a low of 77% in Louisiana to a high of 93% in New York and Hawaii.[1] Across the nation, just five states reached the national goal of 90% awareness: Hawaii, New York, Colorado, Connecticut, and Delaware. Seventy percent of the worst-performing states were in the South.

The "CDC is responding to the challenge of HIV in the South and nationwide by prioritizing the hardest-hit areas and populations and investing in the most effective strategies," said McCray. "These strategies include expanded testing for HIV, helping people living with HIV obtain ongoing care and treatment, and increasing awareness of and access to all effective prevention tools, including condoms, pre-exposure prophylaxis, or PrEP, and interventions to decrease risky behavior."

"Doing It" campaign

Conference attendees were given a first-hand look at the new national HIV testing campaign "Doing It," which features everyday people, community leaders, and celebrities emphasizing that HIV testing is a smart choice to stay healthy and protect people and their partners. Vignettes highlight people from a spectrum of communities, including gay, bisexual, heterosexual, African-American, Latino, white, male, female, and transgender people. *(Access information on "Doing It" at http://1.usa.gov/1PWhadW.)*

The bilingual HIV testing campaign within the Act Against AIDS portfolio emphasizes the importance of testing for all people ages 18-64. In addition to encouraging testing for all Americans, the campaign focuses on populations

who are most at risk for HIV.

What role can providers play in the "Doing It" campaign? More than 90% of new HIV infections in the United States could be prevented by testing and diagnosing people who have HIV and ensuring they receive prompt, ongoing care and treatment, notes Mermin. People with more than one sex partner, people with sexually transmitted infections (STIs), sexually active gay and bisexual men, and people who inject drugs are likely to be at high risk and should get tested at least once a year. Some sexually active gay and bisexual men might benefit from more frequent testing.

"Providers should be aware that CDC recommends everyone between the ages of 13 and 64 get tested for HIV at least once as part of routine healthcare," says Mermin. "They should also be aware that some people, like men who have sex with men, could benefit from more frequent testing."

The new comprehensive online HIV Risk Reduction Tool (http://1.usa.gov/1PkpeiY) allows people to obtain customized information on behaviors that place them at risk for HIV and to learn strategies that reduce their risk. The interactive tool allows users to compare the risks of different sexual activities and to see how one or a combination of prevention methods, such as condoms, PrEP, or HIV treatment for those living with HIV, could change their level of protection.

The CDC anticipates continued revision of the tool, as the agency pilots the tool with users and incorporates feedback and findings.

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Azithromycin remains effective in treatment of urogenital chlamydia, study data suggest

Results of a new study, conducted by researchers at the University of Alabama at Birmingham (UAB), the Los Angeles-based University of Southern California, and the Los Angeles County Department of Health Services, confirm that azithromycin remains effective in the treatment of urogenital chlamydia.[1]

To conduct the study, the research team compared two of the most commonly used medications for urogenital chlamydia: a single dose of azithromycin versus doxycycline given twice daily for seven days. Data indicate azithromycin had a cure rate of 97%, compared to a 100% cure rate for doxycycline.[1]

The goal of the trial was to look at the efficacies of azithromycin and doxycycline regimens for urogenital chlamydia treatment using a study design that could control for limitations of many of the chlamydia treatment randomized controlled trials (RCTs) held previously, says **William Geisler**, MD, professor in the Division of Infectious Diseases in the UAB Department of Medicine and principle investigator of the study. These limitations included difficulty controlling for re-exposure to chlamydia-infected partners, difficulty with treatment nonadherence, and using a less sensitive chlamydia test.

"The reason that azithromycin was the focus of evaluating for noninferiority compared with doxycycline was that there had been a few recent studies (with chlamydia treatment data) that have used a more sensitive chlamydia test than earlier chlamydia treatment RCTs and showed azithromycin cure rates to be lower than expected based on a meta-analysis of the earlier RCTs," Geisler stated in an email interview with *Contraceptive Technology Update*.

EXECUTIVE SUMMARY

Results of a new study, conducted by researchers at the University of Alabama at Birmingham, the University of Southern California, and the Los Angeles County Department of Health Services, confirm that azithromycin remains effective in the treatment of urogenital chlamydia.

- The Centers for Disease Control and Prevention recommends oral administration of 1 g of azithromycin in a single dose or 100 mg of doxycycline twice daily for seven days for the treatment of chlamydia infection.
- Azithromycin requires only one dose, while doxycycline requires patients to take multiple pills over seven days. Research indicates that patients are much more likely to adhere to therapy when taking a single dose compared to multiple doses over time.

The study was conducted among adolescents in youth correctional facilities to evaluate the noninferiority of azithromycin (1 g in one dose) compared to doxycycline (100 mg twice daily for seven days).

The study was designed with the primary endpoint as treatment failure at 28 days after treatment initiation, with treatment failure determined on the basis of nucleic acid amplification testing, sexual history, and outer membrane protein A genotyping of *C. trachomatis* strains. Data were collected by Los Angeles County study staff, managed by FHI 360, a Durham, NC-based nonprofit human development organization, and analyzed by co-authors from the University of Arkansas for Medical Sciences in Little Rock. The study was funded by the Division of Microbiology and Infectious Diseases of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

Among the 567 participants enrolled, 284 were randomly assigned to receive azithromycin, and 283 were randomly assigned to receive doxycycline. Analysis of the data indicates there were no treatment failures in the doxycycline group. In the azithromycin group, treatment failure occurred in five participants (3.2%; 95% confidence interval, 0.4 to 7.4%). The observed difference in failure rates between the treatment groups was 3.2 percentage points, with an upper boundary of the 90% confidence interval of 5.9 percentage points, which exceeded the prespecified absolute 5-percentage-point cutoff for establishing the noninferiority of azithromycin.[1]

Studies of sexually transmitted infections can be difficult to do, because medical providers often cannot monitor adherence to a drug regimen, the researchers note. Also, a successfully treated patient can become re-infected, often from the same partner, during therapy. The design of the current study allowed scientists to control for all the complicated variables that had hindered previous research projects of this nature, Geisler notes.

"Our study subjects were separated from previous partners and had limited sexual exposure," observed Geisler in a statement accompanying the study publication. "This approach allowed us to truly understand how well these drugs worked."

Check treatment options

The Centers for Disease Control and Prevention (CDC) recommends oral administration of 1 g of azithromycin in a single dose or 100 mg of doxycycline twice daily for seven days for the treatment of chlamydia infection.[2]

DATA INDICATE AZITHROMYCIN HAD A CURE RATE OF 97%, COMPARED TO A 100% CURE RATE FOR DOXYCYCLINE.

Nonadherence to doxycycline therapy can contribute to treatment failure. In one study, researchers reported no treatment failures among 58 participants who took 10-14 doses, as compared with treatment failure in four of 20 participants (20%) who took fewer than 10 doses.[3] In another study that evaluated doxycycline adherence among males with symptomatic chlamydia urethritis, data indicate treatment failure in one of 37 participants (3%) who took 14 doses, versus two of 10 participants (20%) who missed at least one dose.[4]

For providers, knowing whether azithromycin is an effective treatment option is important because patient adherence to therapy with doxycycline can be an issue, noted Geisler. Azithromycin requires only one dose, while doxycycline requires patients to take multiple pills over seven days. Studies have shown that patients are much more likely to adhere to therapy when taking a single dose compared to multiple doses over time.[5]

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