Dysmenorrhea
HELPING YOUR PATIENTS MANAGE

by KIMBERLY A. KHO, MD & JESSICA K. SHIELDS, DO
IF SHE’S GOING AROUND MORE THAN ONCE, IS IT TIME TO THINK TWICE ABOUT AZOLES?

For some patients, symptoms are not adequately addressed with 1 or 2 doses,2-4 and evidence suggests that broad and frequent use of azoles may be contributing to the increase in non-albicans Candida, and fluconazole-resistant Candida species.5-8

AS MANY AS 70% OF WOMEN HAVE BEEN PRESCRIBED FLUCONAZOLE BEYOND THE INDICATED 1-DOSE REGIMEN.1
IN THE TREATMENT OF VULVOVAGINAL CANDIDIASIS (VVC)

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For some patients, symptoms are not adequately addressed with 1 or 2 doses,²-⁴ and evidence suggests that broad and frequent use of azoles may be contributing to the increase in non-\textit{albicans Candida}, and fluconazole-resistant \textit{Candida} species.⁵-⁸

At SCYNEXIS, we’re exploring the potential for a novel, non-azole treatment in VVC. Find out more at www.RETHINKVVC.com


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On April 9, Contemporary OB/GYN® editorial board members met with the content team and several others from our corporate offices for the annual editorial board meeting. Like most meetings these days, it was virtual. But in 2 hours, the team reviewed content, talked strategies and goals, and enthusiastically discussed which topics might have the most meaning to the ob/gyn generalists who make up the core of this magazine’s audience.

It’s energizing to see the passion of 12 dedicated physicians who ensure that the latest research appears within these pages as peer-reviewed articles, and that we are meeting readers’ needs. You’ve seen some of that so far this year, including coverage on COVID-19, managing inflammatory bowel disease in pregnancy and post partum, and a myriad of other topics. In this issue, we continue to provide information with fresh approaches. On page 21, you will find a tear-out on maternal morbidity and mortality with information from Board Member Sarah J. Kilpatrick, MD, PHD.

Separately, Board Members Paula J. Adams Hillard, MD, and Ilana Cass, MD, tackle the topic of keeping politicians out of the exam room, in their column on page 6. They discuss legislation in 20 states, including New Hampshire and Arkansas, that could interfere in the physician-patient relationship. We are interested in your feedback on this topic. When it comes to government, how far is too far?

The cover story provides an approach for diagnosing and managing primary dysmenorrhea. And 2 physicians from The Ohio State University in Columbus share their expertise in “Diagnosis and Management of Gestational Diabetes,” which begins on page 10.

We trust you’ll stay tuned to these pages and our ever-evolving website, www.contemporaryobgyn.net, for the articles, videos, and podcasts that will come out of this very important meeting. We enjoy hearing from you about topics you would like to read about and receiving feedback on any content in these pages or online. Please send us an email at COGEditorial@mmhgroup.com.

As the pandemic continues, we also are pondering how health care might evolve to address patients’ needs. COVID-19 has permanently changed health care, and we will see those effects for years. The Los Angeles Times recently reported on the trend of urgent care ob/gyn clinics. These clinics are specifically focused on women’s care and help patients avoid what can be long wait times in traditional emergency departments (EDs). They also became a favorable option during the pandemic because people were afraid of contracting COVID-19 by going to an ED.

As always, thank you for reading, and let us know how we are doing.

Mike Hennessy Sr
Chairman and Founder, MJH Life Sciences™

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Behind The Scenes

Sexual health and wellness matters. That is why we’re addressing it with this Consortium. At each age and stage of your patients’ lives, sexual health and wellness should be considered as part of their overall health. As we ease out of the pandemic, the topic is even more important as some issues may have not been addressed during this time.

The Consortium features articles, podcasts, polls, and video interviews. We will highlight experts like Michael Krychman, MD, (left), as they provide practical advice to approach the topic with your patients. To hear Krychman’s perspective on sexual health and wellness, visit contemporaryobgyn.net/SHC-Krychman.
Obstetrics

10 Diabetes management in pregnancy
KARTIK K. VENKATESH, MD, PHD & MARK B. LONDON, MD

16 Enhanced recovery after cesarean section
OLUTOYI SI OGUNKA, MD & ELAINE L. DURYE, MD

20 Hypertensive disorders of pregnancy increase risk of premature death

21 What can you do to reduce maternal severe morbidity & mortality?
SARAH KILPATRICK, MD

CONTRACEPTION

32 Oral contraception and ovarian function

GYNECOLOGY

30 NASPAG 2021: Hillard’s Highlights
PAULA J. ADAMS HILLARD, MD

VULVOVAGINAL DISEASE

33 Transcutaneous temperature-controlled radiofrequency treatment

WELL WOMAN

34 Prevalence thresholds of screening tests

IN ADDITION

36 Legally Speaking

Helping Your Patients Manage Dysmenorrhea

by KIMBERLY A. KHO, MD & JESSICA K. SHIELDS, DO

IN THIS ISSUE

May 2021

EDITORIAL

6 Keeping politicians out of the exam room
PAULA J. ADAMS HILLARD, MD & ILANA CASS, MD

LIFE TRANSITIONS

8 Nocturia in menopause

OBSTETRICS

21 Oral contraception

NASPAG 2021: Hillard’s Highlights
PAULA J. ADAMS HILLARD, MD

CONTRACEPTION

32 Oral contraception and ovarian function

VULVOVAGINAL DISEASE

33 Transcutaneous temperature-controlled radiofrequency treatment

WELL WOMAN

34 Prevalence thresholds of screening tests

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Helping Your Patients Manage Dysmenorrhea

by KIMBERLY A. KHO, MD & JESSICA K. SHIELDS, DO
When your mission is to eradicate cervical cancer...

You partner with the ones that will get you there—sooner.

Innovators are always looking forward, ready to find new solutions to existing challenges. That’s why Hologic and Google Cloud have combined forces to transform cervical cancer screening using the best minds in science and technology.

Together, we aim to evolve digital cytology through the Genius™ Digital Diagnostics System and enhance its deep learning-based AI. As our collective expertise continues to shape the way we screen for cervical cancer, and explores the potential impact on ovarian and endometrial cancers, we do so with a common goal in mind—to save more women’s lives.

* Genius Digital Diagnostics is CE-marked for diagnostic use in Europe and is not currently available for sale in the U.S. May not be available in all markets. Contact your local Hologic representative for availability in your country.

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Keeping Politicians Out of the Exam Room

As ob/gyns, we care for patients with a variety of gynecologic and reproductive health issues that can be emotionally charged and intensely private. Although gynecologic health issues are medical issues as are headaches or sprained ankles, the extent to which individuals want to talk openly about them varies. In our offices, patients share their fears, their pains, and their hopes, and discuss their sexuality, their gender identity, and their sexual behaviors. We talk with preteens about puberty, with teens about their periods, with women who are excited to be pregnant, and with those who are not. We talk to women who have never told anyone about a past sexual assault. We talk with women who are facing infertility or the need for a hysterectomy. Our patients know we will listen to and treat them with dignity and provide accurate health education that enables them to be a partner in their health care decisions.

Three recent pieces of legislation highlight a threat to the physician-patient relationship. The proposal of laws that interfere with this complex and intimate relationship is a step too far. These pieces of legislation illustrate this overreach by the state: dictating medical care for transgender adolescents (Arkansas and 18 other states), mandating medically inaccurate information about abortion (18 states), and requiring resuscitation for newborns with fatal diagnoses (New Hampshire).

As Frank Bruni pointed out in his recent New York Times op-ed column, politicians are currently demonizing trans people in a new culture war, similar to the way in which they vilified gays and lesbians, charging that gay marriages would somehow undermine straight marriages. Politicians, including former President Donald Trump, assert that trans equality would “destroy women’s sports.” This is a political strategy that ignores the realities of the patients in our offices. It ignores the trans individual who has found puberty blockers to be immensely helpful or the trans persons who had previously been suicidal when attempting to fit in to a gender-binary world. It ignores the parents who have wrestled with their child’s affirmed gender identity, done extensive research and reading about the issue, and who love their child and support therapy and potentially medication to help alleviate their child’s gender dysphoria. It ignores our medical judgment and recommendations after we have listened to the patient and their parents. It ignores the expertise of our colleagues in endocrinology, psychology, adolescent medicine, adolescent gynecology, urology, and social work who work with transgender youth. As Bruni describes, these lawmakers are stunningly arrogant, and are “getting between physicians and patients.”

It is not controversial to agree that our obligation as physicians is to care for our patients in a way that best meets their needs. We should also agree that legislatures do not have a role in dictating specifics of medical care. The Coalition to Protect the Patient-Provider Relationship is comprised of nonpartisan, nonprofit organizations united in the “opposition to inappropriate interference in the relationship between a patient and health care provider.” Member organizations include the American College of Obstetricians and Gynecologists (ACOG), American Academy of Family Physicians, American Academy of Pediatrics, American College of Physicians, American Medical Association, American Medical Student Association, American Medical Women’s Association, American Nurses Association, American Osteopathic Association, American Public...
Health Association. The coalition states that “patients deserve accurate information, high-quality care, and the treatment options that best meet their needs. Physicians and other health care providers should be able to follow the best medical science and training based on available evidence, and adhere to their ethical obligations.”

It’s not just in areas of women’s health that we must protect that relationship. Other health and safety issues for which politicians are passing laws that stand between us and our patients include gun safety and environmental hazards. Resources for clinicians include a report, “Politics in the Exam Room: A Growing Threat,” by the National Partnerships for Women & Families, National Physicians Alliance, Natural Resources Defense Council, and Giffords Law Center to Prevent Gun Violence. According to ACOG’s policy statement on legislative interference with patient care, medical decisions, and the patient-physician relationship, “laws should not interfere with the ability of physicians to determine appropriate treatment options and have open, honest, and confidential communications with their patients. Nor should laws interfere with the patient’s right to be counseled by a physician according to the best currently available medical evidence and the physician’s professional medical judgment. ACOG strongly opposes any governmental interference that threatens communications between patients and their physicians or causes a physician to compromise his or her medical judgment about what information or treatment is in the best interest of the patient.”

When state legislators try to come between our patients and us, we must speak out strongly. We must not let politics trump science or interfere with our hallowed patient relationships. Our patients must be able to rely upon us to provide appropriate and confidential care, based on science and our medical judgment.

Hillard and Cass both are Editorial Advisory Board Members of Contemporary OB/GYN. You can let them know your thoughts on this topic by emailing COGeditorial@mmhgroup.com.

Gender Affirming Care For Minors Endorsed By Several Professional Organizations

As many state legislatures across the U.S. introduce or have in process bills that could directly impact the physician-patient relationship and how treatments are administered, several professional organizations issued position statements. In its statement, the North American Society of Adolescent and Pediatric Gynecology stated that it has nearly 470 members consisting of physicians, advanced practice providers, nurses, and professional health care trainees. “Our mission is to provide multidisciplinary leadership in education, research and gynecologic care to improve the reproductive health of all youth, inclusive of children and adolescents who are gender diverse. We advocate for the provision of unrestricted, unbiased and evidence-based practice of pediatric and adolescent gynecology. We stand with national medical organizations supporting comprehensive care of adolescents and the confidential relationship between patients and their physicians. We support the positions that physicians must be able to practice medicine that is informed by their years of medical education, training, experience, and the available evidence, freely and without threat of punishment. Patients, their families and caretakers in partnership with their physicians, not policymakers, should be the ones to make decisions about what care is best for them.”

The other organizations included the American College of Obstetricians and Gynecologists; the American Academy of Family Physicians; the American Academy of Pediatrics; the American Psychiatric Association; and the American Osteopathic Association.
Hormone Therapy For Postmenopausal Women With Nocturia

by BOB KRONEMYER

According to findings from a prospective observational study, hormone therapy resulted in a significant reduction in nocturia prevalence and bother in postmenopausal women with 2 nocturnal voids.

The investigators of the Belgium pilot study, whose findings were published in Menopause, concluded that the results were especially positive for both estrogen + progesterone (E + P) and tissue-selective estrogen complex (TSEC).

“Research group focuses on nocturia,” said coauthor Kim Pauwaert, MD, a urology resident at Ghent University Hospital in Belgium.

Previously, Pauwaert and her team conducted an exploratory study to observe the impact of nocturia among Belgian postmenopausal women.

In the current study, they observed whether hormonal treatment is effective in the same population.

All 245 postmenopausal women were recruited from the gynecological department of Ghent University Hospital between March 2018 and January 2020. They were divided into 4 groups, based on patient choice: E + P (n = 133), estrogen-only in patients with a prior hysterectomy (n = 47), TSEC (n = 33), and no treatment (n = 32).

The investigators observed nocturia and its causative factors using 2 standardized questionnaires before and after treatment: the International Consultation on Incontinence Questionnaire Nocturia Module and Targeting the individual’s Aetiology of Nocturia to Guide Outcomes.

These encouraging sleep results may reflect a change in hot flashes because perspiration and sweating during the night disturb sleep.

For the 3 treatment groups overall, there was a significant reduction in prevalence of nocturia twice per night, from 27.7% to 16.4%. The most pronounced reduction was noted in patients treated with either E + P or TSEC: \( p = .018 \) for both groups.

A significantly higher percentage of women reported either 1 nocturnal void or no nocturnal voids after 1 of the 3 treatments. This improvement from baseline was 45.1% to 51.2% for 1 void (\( p < .001 \)) and 27.2% to 32.4% for 2 voids (\( p < .001 \)).

At baseline, 45% of women who opted for hormonal therapy reported 1 nocturnal void. For 67.7% of these women, 6 months of treatment did not change nocturnal frequency, and in 8.3% there was an increase of nocturnal frequency to 2 voids per night.

On the other hand, 24% of women with 1 nocturnal void at baseline experienced a decline to no nocturnal voids after treatment (\( p < .001 \)). These improvements could be attributed to a significant reduction in the sleep sum score in patients treated with E + P or TSEC: \( p < .001 \) and \( p = .013 \), respectively.

These encouraging sleep results may reflect a change in hot flashes because perspiration and sweating during the night disturb sleep.

Estrogen-only therapy led to a significant reduction in the urinary tract sum score, which was the result of a decrease in urgency prevalence (\( p = .039 \)).

“We expected to achieve these results,” Pauwaert told Contemporary OB/GYN®. “However, we hoped to see an effect on renal and bladder functions.”

In Pauwaert’s opinion, postmenopausal women experiencing nocturia due to underlying sleep problems could benefit from hormonal treatment. The study supports testing in a future randomized study whether the different systemic and vaginal estrogens are more effective at reducing nocturia frequency than maintaining hormone depletion, according to Pauwaert.

She and her colleagues have planned a follow-up study to assess the effect of hormone therapy on kidney and bladder function.

DISCLOSURES Pauwaert received a research grant from Ferring Pharmaceuticals.

Bob Kronemyer is a freelance writer for Contemporary OB/GYN®.

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Nonmalignant gynecological conditions, such as chronic pelvic pain resulting from endometriosis and heavy menstrual bleeding resulting from uterine fibroids, can have a substantial impact on patient quality of life. It is important that providers understand the effects of these conditions and discuss treatment options with patients.

In a recent Contemporay OB/GYN® Viewpoints video series supported by AbbVie, Ayman Al-Hendy, MD, PhD, professor and director of translational research in the Department of Obstetrics and Gynecology at the University of Chicago in Illinois, led a discussion with thought leaders about the management of chronic pelvic pain and heavy menstrual bleeding. The panel also discussed ways to improve patient-provider communications and overcome the normalization associated with nonmalignant gynecological conditions. Ahead is a recap of clinical pearls and key takeaways from the discussion.

Chronic Pelvic Pain from Endometriosis: Diagnosis and Treatment Options

In the management of endometriosis, new developments are emerging regarding patient assessment, diagnosis, and treatment initiation via telehealth. Regarding imaging, Al-Hendy said that current tools for more generalized disease have limited utility and that the gold standard historically is laparoscopic diagnosis. There is usually a vast delay in diagnosis (eg, normalization of symptoms). Moreover, there are no reliable biomarkers for endometriosis, which remains an unmet need and should have further research in the field, Al-Hendy said.

In managing individualized treatment plans, Linda Bradley, MD, a professor of surgery at the Cleveland...
Clinic Lerner College of Medicine at Case Western Reserve University in Ohio, noted that there are new therapeutic opportunities and that treatment should be based on symptom burden, age, and pregnancy status. "I’m very liberal when it comes to any of these things because I think you get the best buy-in when [patients are] ready for treatment instead of us pushing treatment unless there’s something. Both ureters, they’ve got hydronephrosis. They’re not urinating. They [have] poor kidney function. Not all of us in this room have seen patients with that, but in our lifetime. Cumulatively, it’s a handful of patients. I’m probably a little more patient-centric in letting people do those things,” she said.

Stacey Missmer, ScD, a professor in the Department of Obstetrics, Gynecology, and Reproductive Biology at Michigan State University’s College of Human Medicine in East Lansing, added that there are no 1-size-fits-all treatments for patients with endometriosis. "There are treatments that are absolutely life changing [and] successful for patients, and there are patients with those exact treatments who have either no benefits or have [adverse] effects that further diminish quality of life… understanding going in that this requires a dialogue and an open discussion of those priorities, [in addition to selecting] treatments for those individuals, is really important."

When discussing treatment options with patients. Eric Surrey, MD, of the Colorado Center for Reproductive Medicine in Lone Tree, observed that it is crucial to know what a patient has been treated with before, as well as their concerns about treatment. "We have to tease out what the main goal of the patient is. I think perhaps the most important [thing] that Linda mentioned earlier is fertility versus [infertility] because the [treatment] of the patient who wants to conceive is completely different," he said. "They’re totally different evaluation and treatment paradigms. That’s critical. The other area is [if] there’s a specific problem besides, ‘I just want my pain to go away,’ to drill down. Tell me if you had to rank the most important parts. I think that could be very helpful [as well],” he said.

Not all treatments will be good or bad for all patients, Missmer noted. "[Although] patients’ stories are extremely important, definitely take into consideration that what works for 1 person may not be the best fit for you. What didn’t work for you may actually be very helpful for someone else. [Regarding] social media, a general respect for meeting people where they are and respecting their experiences is very important, as well."

When it comes to treatment options, Al-Hendy noted that first-line options have been well established. "Birth control pills [and] combination oral contraceptives traditionally have been advocated as a first-line of therapy in a cyclic fashion, or there’s some literature support with that to use it continuously.” Another agent worth pointing out is progestin, Al-Hendy noted. “We know from the basic science that endometriosis is a progesterone-resistant disease. It would make sense to, let’s say, oversaturate the system with progestin. Again, literature supports some utility and shows some benefit, at least in the short term,” Al-Hendy said.

A more recent mechanism that has been explored is gonadotropin-releasing hormone (GnRH), resulting in the development of GnRH agonists and antagonists. “For GnRH agonists, of course the mechanism of action is well known, and it would make sense to deprive endometriosis from estrogen and progestin, especially the estrogen component,” Al-Hendy said. However, long-term safety concerns limit their utility, he explained. “We cannot use them in the long term because of the severe [adverse] effects, such as bone mineral density loss and all the typical hyperestrogenic [adverse] effects.”

GnRH antagonists represent a new family of compounds in this area, and Al-Hendy noted that these agents have a rapid onset of action. “There’s no
flaring effect. It binds the receptor and starts inhibiting follicular genesis, ovarian estrogen, and progesterone production right away. You have to adjust the dose. They are available in different dose regimens, and at the high dose, you also get some of the same [adverse] effects I mentioned a second ago, the hyperestrogenic [adverse] effects.”

The role of surgery in patients with chronic pelvic pain resulting from endometriosis remains controversial, according to Surrey. In addition to the considerations of the need for surgical interventions, such as hysterectomy, Surrey noted that recurrence rates are worth thinking about. “Recurrence rates have been well described with hysterectomy, particularly when the ovaries are left in place,” he said. “I think if you do a hysterectomy and ignore additional endometriosis in the pelvis, it is maybe not the best operation. Just taking out the uterus and ignoring the rest of the disease, particularly if the ovaries are left in situ, may not be ideal.” Finally, he observed, “There are virtually no studies looking at recurrence rates for surgical versus medical therapy and even [fewer] looking at various medical therapeutic approaches.”

The Impact and Management of Uterine Fibroids

Heavy menstrual bleeding as a result of uterine fibroids can have a significant impact on patients’ lives, which, according to Missmer, should be a focus in clinician-patient dialogues. “A critical thing around these issues [is] making sure that we’re understanding, both in our families and communities, that life-impacting symptoms [such as] dysmenorrhea [are] preventing girls and women from conducting their lives as they wish; that is not normal,” Missmer said. “Uterine bleeding that is impacting the ability to go about one’s normal activities is not normal.” Particularly in adolescence, symptoms of uterine fibroids can be isolating, and patients may feel embarrassed to talk about it, according to Missmer.

Discussing the American College of Obstetricians and Gynecologists recommendations regarding the management of heavy menstrual bleeding with uterine fibroids, Bradley noted that history and physical exams are essential. “I think the guidelines [should] always start with our history. I think we need to look at what our best practice is, and I think physicians all over the country or all over the world have different tools that are available to them,” Dr. Bradley said. “Let’s just say that [history and physical exams are] done, and then we have imaging. Depending on size, I prefer, if it’s available, to do saline infusion sonogram,” she said. For larger uteruses, she noted, “we might want to do MRI to look at the intracavitary lesions. A CT scan, I think, has limited use,” Bradley explained.

In managing heavy menstrual bleeding with fibroids, Al-Hendy listed medical therapeutic options, such as tranexamic acid, oral contraceptives, progestin, GnRH agonists or analogues, and GnRH antagonists. He noted that tranexamic acid may be a “good option,” but current data show a focus on ovulatory bleeding with a limited group of fibroid patients. Aside from tranexamic acid, there are many hormonal options, and fibroids are estrogen dependent and incompatible with infertility. Al-Hendy observed that GnRH agonists cause severe hyperestrogenic status, causing the fibroid to shrink. However, he observed, serious adverse effects, such as irreversible bone loss, are possible, especially if these agents are used beyond 6 months and/or the patients has hyperestrogenic menopausal symptoms.

Surgical options should be considered for those who have failed therapy, according to Al-Hendy, and medical treatment should be tried before an invasive option. “I believe in the fibroid field, we tend to think of surgery as a first-line [therapy] because, traditionally, there [were] not a lot of good, durable, long-term treatment options,” he said.

Missmer provided an overview of the treatment algorithm based on patient choices and also discussed gaps in care for specific medical treatment. “The critical branching point is the patient’s intentions around childbearing and continued fertility. That is a definitive demarcation that sends clinicians on
The Role of Communication in the Management of Endometriosis and Uterine Fibroids

As treatment options for chronic pelvic pain and heavy menstrual bleeding continue to expand, the panelists noted that communication and building relationships with patients represent the foundation of effective care. In this regard, understanding the burden of these conditions is an essential first step. Missmer noted that embarrassment and anxiety about menstrual issues is common in individuals with these conditions, particularly in student athletes who may not want to be seen as a weak member of the team, for example. In addition to stigmas associated with these common nonmalignant gynecologic diseases, panelists explained that these conditions have an effect on social engagement and professional opportunities.

Given the difficulties regarding the stigmas of pelvic pain and heavy menstrual bleeding, the panelists noted the importance of active communication with patients and striving to understand the burden of these conditions. “We think one of the critical pieces here is to validate patients’ concerns,” Surrey said. Allowing patients to tell their story is essential, according to Bradley. “Storytelling in medicine is important, and, as we all learned in medical school, probably 70% to 80% of what we need to know, the patient tells us,” Bradley said.

According to Surrey, communication increases the likelihood of recognizing the condition and intervening earlier. “Clearly, with any medical condition, as soon as you can intervene, the less invasive [and less complicated] the treatment will be; it might even be very simple,” he noted. “On the clinician side, there has to be time taken to elicit the information [and] validate the patient’s concerns. Also, [in particular], it’s not just the adolescents who may not know that this isn’t normal,” Surrey said.

One element of effective communication with patients is establishing expectations, according to Missmer. “Is the problem because there hasn’t been any remediation or adequate remediation of the prioritized symptom that was the target of the change? Does the patient understand, and was there sufficient dialogue around the amount of time it would take?” Missmer asked. “[The problem may be that] because that primary symptom or set of symptoms this treatment was designed to tackle [has been treated], but now they’re experiencing a sense of fatigue, weight gain, weight loss, or other symptoms that weren’t necessarily part of that previous discussion. [There] hasn’t been a shift in importance for the patient in her quality of life.”

According to Surrey, setting appropriate expectations begins at the first visit. It involves conveying to patients that they should expect improvement, but that not everyone is the same. Surrey pointed out that addressing patient goals in a realistic matter is also critical. Establishing a relationship with patients based on trust is vital for success. “The beauty of our field is [that clinicians] have a lifelong relationship with patients, particularly those [who] are in general OB/GYN. The needs will change,” he said.

1 path or another that has been so nicely described already,” she said. “I think the critical thing around uterine preservation is that we still have emerging data in terms of short- and long-term consequences of hysterectomy and also of bilateral salpingo-oophorectomy.”

Missmer added that there are some long-term implications that fall under understanding the risks. “For example, it [has] been increasingly discussed and [is] perhaps becoming more normalized for ovary removal [in] women who [have] completed their desired childbearing when they had an endometrioma to remove the ovaries to prevent ovarian cancer. When you look at [these] data, women with endometriosis do have an increased risk of ovarian cancer, possibly driven primarily by endometriomas, [but] we don’t know that definitively yet. We know that, even with that increased risk, the lifetime risk of ovarian cancer is extremely small, but the lifetime risk of cardiovascular disease is large.
Introduction

Gestational diabetes mellitus (GDM) is the most common medical complication of pregnancy, and its rate has continued to increase in the United States. Currently, it affects approximately 1 in 10 or 380,000 pregnant women per year, and nearly 90% of cases of diabetes in pregnancy represent GDM. The prevalence of the condition has more than doubled among non-White, overweight, and low-income women in the last decade in an environment of increasing maternal age, obesity, and sedentary living. In this clinical review, we provide an overview of the epidemiology, screening, and clinical management of GDM.

GDM impact on adverse pregnancy outcomes, and treatment to reduce risk

GDM more than doubles the risk of perinatal morbidity and mortality, and this risk progressively increases with the severity of hyperglycemia and decreases with treatment, including both lifestyle changes and pharmacotherapy. For the infant, maternal hyperglycemia may cause fetal hyperinsulinemia, which results in excessive fetal growth (macrosomia, large for gestational age), birth trauma, neonatal hypoglycemia, delayed lung development, and fetal hypoxia. For the mother, GDM increases the risk of shoulder dystocia, cesarean delivery, and preeclampsia. Historically, the criteria employed to diagnose GDM were based on the likelihood of developing type 2 diabetes later in life rather than on identifying those at the highest risk of adverse perinatal outcomes due to glucose intolerance. The landmark Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study helped establish internationally agreed-upon diagnostic criteria for GDM among more than 25,000 pregnancies. This study demonstrated that increasing hyperglycemia defined by elevations in the 3 values of a 75-g, 2-hour oral glucose tolerance test (GTT) were associated with a progressively increasing risk of a large-for-gestation-age infant at birth, cesarean delivery, rising fetal C-peptide levels, and neonatal adiposity. HAPO’s results led the International Association of Diabetes and Pregnancy Study Groups (IADPSG) task force to recommend a 1-step test for GDM screening. However, after a systematic review of the findings, the National Institutes of Health Consensus Development Conference on diagnosing GDM found insufficient evidence of maternal or perinatal benefit to adopt 1-test screening and, rather, continued to endorse a 2-step approach to screening and diagnosis.

Diagnosis and Management of Gestational Diabetes

What every OB/GYN needs to know to manage this complication

by KARTIK K. VENKATESH, MD, PHD; AND MARK B. LANDON, MD

KARTIK K. VENKATESH, MD, PHD, is an assistant professor of obstetrics and gynecology in the Division of Maternal Fetal Medicine at The Ohio State University Wexner Medical Center and an assistant professor of epidemiology at the College of Public Health at The Ohio State University, both in Columbus.

MARK B. LANDON, MD, is the Richard L. Meiling Professor and chair of the Department of Obstetrics and Gynecology at The Ohio State University College of Medicine in Columbus.
When and how to screen for GDM

GDM is a state restricted to pregnant women whose impaired glucose intolerance is first discovered in pregnancy. Most of these women will have normal fasting glucose levels; hence, a glucose challenge is required to unmask this state. Historically, risk factors including a family history of diabetes, history of macrosomia or stillbirth, obesity, chronic hypertension, and maternal age were used to screen women at the highest risk of GDM. The problem is that more than half of women with an abnormal GTT lack any risk factors.

The American College of Obstetricians and Gynecologists (ACOG) recommends universal screening for all pregnant women. Screening generally is performed between 24 and 28 weeks when the “diabetogenic state” of pregnancy has been established. Two commonly used screening strategies include a 1-step test as endorsed by IADPSG versus a 2-step test as endorsed by ACOG (Table 1). A 1-step test includes a 75-g, 2-hour oral GTT in which a GDM diagnosis can be made when a single value was met or exceeded. A 2-step test involves an initial 50-g glucose challenge test followed by a 3-hour, 100-g oral GTT. The initial 50-g glucose challenge can be performed while fasting or after having eaten. A plasma value between 130 to 140 mg/dL is generally used as a threshold for performing a 3-hour oral GTT. To diagnose GDM based on the 3-hour GTT, ACOG endorses either the National Diabetes Data Group (NDDG) criteria or the less stringent Carpenter and Coustan criteria. Regardless of either set of criteria, if any 2 or more than 4 oral GTT values exceed established thresholds, the diagnosis of GDM is confirmed.

Results from multiple studies have demonstrated that although a larger number of women (nearly double) may be identified as having GDM using IADPSG 1-step criteria compared with 2-step criteria; importantly, this does not result in a decrease in adverse neonatal outcomes, including macrosomia. To summarize the current dilemma concerning these 2 screening strategies, the American Diabetes Association (ADA) concludes that (1) data are insufficient to demonstrate the superiority of one strategy over the other; (2) deciding which strategy to use in clinical practice may be affected by other factors, including cost-benefit, willingness to change practice, and cost and infrastructure considerations; and (3) further research is needed.

This year, Hillier et al reported the findings of a large, pragmatic trial comparing the single-step with the 2-step approach among nearly 24,000 pregnant women. Consistent with prior data using IADPSG criteria, the frequency of a GDM was double compared with the 2-step approach (17% vs 9%). However, the frequency of hypertensive disorders of pregnancy, primary cesarean delivery, and large-for-gestational-age infants, and the perinatal composite outcome were not different between the testing groups. The findings of this study highlight that whereas a 1-step screen may detect more women with GDM than a 2-step screen, there may be no apparent maternal or perinatal benefit overall to this approach.

Finally, ACOG recommends screening earlier in pregnancy for women with

<table>
<thead>
<tr>
<th>Table 1</th>
<th>IADPSG 1-step Versus 2-step Detection of GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 step¹</td>
</tr>
<tr>
<td></td>
<td>Screening 50 g, 1 hour</td>
</tr>
<tr>
<td>75-g GTT, 2 hours</td>
<td>100-g GTT, 3 hours</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>82 mg/dL</td>
</tr>
<tr>
<td>1-hour glucose</td>
<td>180 mg/dL</td>
</tr>
<tr>
<td>2-hour glucose</td>
<td>153 mg/dL</td>
</tr>
<tr>
<td>3-hour glucose</td>
<td>145 mg/dL</td>
</tr>
</tbody>
</table>

¹A 1-step diagnosis is made if 1 value is met or exceeded.
²A 2-step diagnosis is made when any 2 values of the GTT are met or exceeded.
GDM, gestational diabetes mellitus; GTT, glucose tolerance test; IADPSG, International Association of Diabetes and Pregnancy Study Groups; NDDG, National Diabetes Data Group.
Protect her possibilities with annual screening. Well woman exams have declined since the onset of the COVID-19 pandemic, and combined with the ongoing rise of STIs, this poses a serious threat to young women. Not only do women ages 15–24 account for 75% of chlamydia infections, but undiagnosed or untreated chlamydia and gonorrhea can lead to Pelvic Inflammatory Disease (PID) and cause infertility. So now is the time to protect her future.

Get her back to screening.

should undergo a diagnostic oral GTT, as between 5.7% and 6.4%, which is consistent with routine screening at 24 to 28 weeks. For those with an HbA1c level less than 5.7% but with risk factors, it is prudent to obtain a GCT as the HbA1c level may only be moderately predictive of early GDM compared with 2-step screening.  

**Firstline treatment for GDM: lifestyle intervention**  
The mainstays of GDM treatment begin with lifestyle interventions, including nutritional counseling, dietary changes, and daily exercise, with the goal of decreasing postprandial hyperglycemia (Table 2). Dietary and nutrition changes may include limiting carbohydrates to less than 40% of calories, increasing complex relative to simple carbohydrates. Recommended daily exercise includes 30 minutes of moderate-intensity aerobic exercise at least 5 days a week. Of note, a majority of women with GDM may be obese, and 2009 Institute of Medicine gestational weight gain recommendations do not make specific recommendations with regard to women with GDM.

Findings from 2 important trials over the last 20 years have shown that lifestyle interventions for GDM provide both maternal and infant benefits. The Australian Carbohydrate Intolerance Study in Pregnant Women was a multicenter, 10-year, randomized controlled trial (RCT) of 1000 women that demonstrated a significant reduction in the primary composite (perinatal death, shoulder dystocia, cesarean delivery, and hypertensive disorders of pregnancy). Taken together, these 2 studies demonstrate the benefit of treatment of even mild carbohydrate intolerance during pregnancy.

Once the patient commences an appropriate diet and exercise plan, close surveillance of blood glucose levels is necessary to ensure glycemic control is maintained. This is generally accomplished with patients performing daily self-monitored blood glucose checks, including a fasting level and 3 postprandial measurements 1 or 2 hours after each meal. The target glycemic thresholds of fasting glucose are less than 95 mg/dL, 1-hour postprandial glucose less than 140 mg/dL, and 2-hour postprandial glucose less than 120 mg/dL (Table 3). ACOG and ADA recommend the same thresholds for both GDM and pregestational diabetes. Once women achieve and maintain good glycemic control, the frequency of testing can be decreased. If these targets cannot be met and the majority of fasting and/or postprandial values are elevated, then pharmacotherapy is recommended.

Of note, for women with pregestational diabetes, glucose monitoring is increasingly being done using continuous glucose monitoring (CGM). This technology is currently not being widely used for GDM, though emerging data suggest that CGM can identify specific times of the day that are not identified with routine blood glucose monitoring, such as nocturnal hyperglycemia, which may be associated with an increased risk of adverse perinatal outcomes.
When to initiate pharmacotherapy and which medication to use

The challenge is that at least 1 in 4 women with GDM do not respond to lifestyle intervention, including diet and exercise, and require pharmacotherapy to achieve euglycemia. The optimum threshold for initiating pharmacologic therapy has not been established. Most clinicians initiate pharmacotherapy when 30% to 50% or more of finger-stick values are above the target range (fasting and 2-hour postprandial glucose ≥ 95 mg/dL and ≥ 120 mg/dL, respectively) in the past week. Both the ACOG and ADA recommend insulin as first-line therapy because it does not cross the placenta and improves perinatal outcomes.11,13 The Society for Maternal-Fetal Medicine recommends either metformin or insulin as reasonable first-line options.14 Although weight-based insulin regimens by trimester of pregnancy can be used, for which online calculators are readily available, a simpler approach for clinical practice is to initiate a single dose of long-acting neutral protamine Hagedorn (NPH) or insulin detemir at bedtime to treat fasting hyperglycemia. Shorter-acting insulin lispro or aspart can be used to target postprandial hyperglycemia. In our practice, we typically start with 12 to 20 U NPH insulin in the morning and 10 U NPH at bedtime. Then, 5 to 10 U of short-acting insulin lispro or aspart can be used to target postprandial hyperglycemia. In practice, women with fasting hyperglycemia (> 115 mg/dL) will generally fail to achieve adequate glycemic control with oral agents.

For a patient for whom fasting hypoglycemia (> 115 mg/dL) is the sole indication for pharmacotherapy, the authors start with a single injection of bedtime long-acting insulin.

Oral hypoglycemic agents including metformin and glyburide have increasingly become a popular alternative to injectable insulin over the past 2 decades.15 Historically, glyburide, a sulfonfonylurea, had been a frequently used oral agent for GDM. Metformin, a biguanide, lowers both basal and postprandial glucose, and is the preferred first-line agent to treat type 2 diabetes outside of pregnancy. An oral option may be preferable to frequent injections due to convenience, lower cost, ease of administration, and better adherence. Insurance coverage and cost of insulin have increasingly been problems, particularly for publicly insured patients. In many areas, this has restricted the available insulin formulary. Great controversy remains about the use of oral agents for GDM. Persistent concerns exist about the efficacy of oral agents for preventing adverse neonatal outcomes compared with insulin and the fact that oral agents (metformin and glyburide), unlike insulin, cross the placenta. We have found that, in practice, women with fasting hyperglycemia (> 115 mg/dL) will generally fail to achieve adequate glycemic control with oral agents.

In the landmark Metformin in Gestational Diabetes (MiG) trial, results of which were published in 2008, Rowan and colleagues randomized 761 women with GDM to either insulin or metformin. They noted that the risk of the composite outcome (neonatal hypoglycemia, respiratory distress, birth trauma, preterm birth, and need for phototherapy in the infant) was observed in about one-third of women in both groups.16 Of note, more than 40% of women receiving metformin required supplemental insulin to achieve adequate glycemic control. In 2018, Senat and colleagues randomized 914 women to either insulin or glyburide, and noted similar improvements in glycemia with each regimen. However, the frequency of macrosomia and neonatal hypoglycemia were similar between both groups.17 Several meta-analyses suggest that oral agents, particularly metformin,

<table>
<thead>
<tr>
<th>Time of day</th>
<th>Glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before breakfast “fasting”</td>
<td>60 to &lt; 95</td>
</tr>
<tr>
<td>Before lunch, dinner, and bedtime snack</td>
<td>60-105</td>
</tr>
<tr>
<td>1 hour after meals</td>
<td>&lt; 140</td>
</tr>
<tr>
<td>2 hours after meals</td>
<td>&lt; 120</td>
</tr>
<tr>
<td>2 AM to 6 AM</td>
<td>&gt; 60</td>
</tr>
</tbody>
</table>

Table 3: Target Plasma Glucose Levels in Pregnancy
are equivalent, if not superior, in preventing adverse neonatal outcomes. However, important limitations of the included studies are unclear diagnostic criteria and inability to adjust for impact of severity of hyperglycemia on treatment outcomes; poorly characterized heterogenous populations, often from low- and middle-income countries, unclear criteria for supplemental insulin, and small sample size.

Whether metformin places exposed children and mothers at higher risk of metabolic disease after delivery remains to be fully answered. In contrast to insulin, which does not cross the placenta, metformin poses a real concern due to the theoretic potential for developmental programming of metabolic dysfunction for children exposed in utero. MiG trial investigators reported that in a subset of children at a 5 to 7-year follow-up, those exposed to metformin had a higher body mass index (BMI; ie, were heavier) than those exposed to insulin. A recent meta-analysis affirmed that at 2 years, children exposed to metformin had higher BMIs compared with those exposed to insulin. Addressing the long-term safety of oral agents for GDM therefore remains an important research priority.

**Antepartum and delivery management**

Women with well-controlled GDM are at low risk of intrauterine fetal demise, and hence routine antepartum fetal testing is generally not initiated for uncomplicated diet-controlled class A1 GDM. But for women with a hypertensive disorder, prior stillbirth, or suspected macrosomia, fetal testing is undertaken. Additionally, women on pharmacotherapy with either insulin and/or oral agents (class A2) undergo at least weekly fetal testing beginning at 32 weeks’ gestation.

With regard to timing of delivery, many obstetricians have extrapolated the increased risk of stillbirth in women with type 1 and 2 diabetes to those with GDM; hence, women with GDM on pharmacotherapy are generally advised to undergo induction by week 39. The ACOG currently recommends that for women with well-controlled GDM with

### Table 4: Postpartum Screening Pathway for Women With GDM

<table>
<thead>
<tr>
<th>PREGNANCY COMPPLICATED BY GDM</th>
<th>Postpartum screening at 6-12 weeks (eg, 75-g OGTT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New diagnosis of diabetes mellitus</td>
<td>Referral to provider for diabetes management</td>
</tr>
<tr>
<td>Impaired fasting glucose, impaired glucose tolerance, or both</td>
<td>Referral for nutrition therapy and weight loss management</td>
</tr>
<tr>
<td>Normal</td>
<td>Continue screening every 3 years. Consider nutrition therapy and weight loss, as needed.</td>
</tr>
</tbody>
</table>

Modified from Gabbe’s Obstetrics: Normal and Problem Pregnancies, 8th ed. GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.
diet alone (class A1) delivery be considered at 39 + 0 to 40 + 6 weeks. For those patients receiving pharmacotherapy (class A2), delivery should be considered at 39 + 0 to 39 + 6 weeks. If glycemic control is suboptimal, then delivery should be considered at 37 + 0 to 38 + 6 weeks. As a guideline, for women with preexisting diabetes, scheduled cesarean delivery to prevent birth trauma is offered to those with suspected macrosomia (4500 g or greater at birth) or a history of prior shoulder dystocia.

**Postpartum screening for type 2 diabetes and effect of GDM on future health**

Women with GDM have a higher risk of developing glucose intolerance later in life, or an approximately 7-fold increased risk of developing type 2 diabetes compared with those without GDM. Among Hispanic women, nearly two-thirds may develop type 2 diabetes in 5 years after the index GDM pregnancy. By the time of postpartum testing between 6 and 12 weeks after delivery, about 1 in 3 women will receive a diagnosis of overt type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance. The risk of subsequent type 2 diabetes increases when diabetes is diagnosed earlier in pregnancy or when maternal fasting glucose levels are higher. Some of these women may represent cases of unidentified preexisting type 2 diabetes.

Both the ADA and ACOG recommend postpartum glucose testing using either a fasting plasma glucose or a 75-g, 2-hour oral GTT at 4 to 12 weeks after delivery for a pregnancy complicated by GDM (Table 4). And although thereafter the optimal testing frequency remains to be established, the ADA supports repeat testing every 3 years for women with prior GDM and normal postpartum screening results. The problem is that only about 1 in 5 women with GDM undergo postpartum screening, and innovative strategies are needed to increase its uptake.

Women should also be counseled about the risk of recurrence of GDM in a subsequent pregnancy, which may be as high as 40%. Important ways to decrease the risk of type 2 diabetes include breastfeeding, lifestyle changes, and pharmacotherapy with metformin. GDM may be associated with an increased risk of childhood obesity and subsequent metabolic dysfunction in the infant. The extent to which fetal programming of metabolic function in GDM has an intergenerational effect that can be modified by treatment remains to be answered.

**Conclusions**

GDM is one of the most common medical complications of pregnancy, and its frequency has nearly doubled in the last decade in an obesogenic environment. GDM doubles the risk of perinatal morbidity and mortality. All pregnant women should be screened for GDM, and currently a 2-step screening approach is most commonly used. First-line treatment includes lifestyle interventions, but nearly 1 in 4 women will require pharmacotherapy. Insulin is generally the preferred first-line pharmacotherapy.

**FIRST-LINE TREATMENT INCLUDES LIFESTYLE INTERVENTIONS, BUT NEARLY 1 in 4 WOMEN WILL REQUIRE PHARMACOTHERAPY.**

Insulin is generally the preferred first-line pharmacotherapy.

**CONFLICTS OF INTEREST:** The authors have no conflicts of interest to disclose.

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Enhanced Recovery After Cesarean Section

A case for adopting some ERAS principles for cesarean delivery

by OLUTOYOSI OGUNKUA, MD; AND ELAINE L. DURYEA, MD

Introduction
Enhanced Recovery After Surgery (ERAS) is an evidence-based, multidisciplinary approach to improving surgical care in the perioperative period. ERAS aims to minimize the physiologic response during surgery, optimizing patient outcomes without increasing postoperative complications. Enhanced Recovery After Cesarean (ERAC) expands ERAS principles to apply to obstetric-specific issues. This article aims to provide a brief history of ERAS, describe the core components of ERAC, and define the benefits of ERAC on patient outcomes.

History of ERAS
Early ERAS protocols focused on optimizing the experience of outpatient surgical patients. Improving pain control and decreasing postoperative nausea and vomiting were the initial areas of concentration. Early ambulation, immediate postoperative pain control, and tempering the nausea that is common after anesthetic medications allowed for a more rapid discharge home and decreased the length of hospital stay.

ERAC guidelines were introduced in 2018, long after the development of ERAS protocols in many other surgical specialties. ERAC was first developed for colorectal surgery. Treating preoperative risk factors helped decrease perioperative pathophysiologic responses and reduced morbidity. Preoperative care focused on treating preexisting diseases, improving nutrition, and monitoring for alcohol abuse. Intraoperative efforts were aimed at reducing surgical stress, preventing intraoperative hypothermia, and avoiding unnecessary blood use. The postoperative goals included managing pain, avoiding nausea or vomiting, and early refeeding to avoid ileus. Physicians also placed attention on treating hypoxemia and sleep disturbances. Other measures included limiting drains and nasogastric tubes and engaging patients in active rehabilitation to lessen muscle mass loss. Standardizing care through these protocols resulted in better patient outcomes. Over time, ERAS protocols were developed for many other surgical subspecialties.

Cesarean delivery remains the most common abdominal surgery in North America, and its rates have remained high despite efforts to prevent primary cesareans. ERAC guidelines were introduced in 2018, long after the development of ERAS protocols in many other surgical specialties. New mothers have

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to balance recovering from major abdominal surgery with caring for an infant. Breastfeeding, diaper changes, and the emotional toll of a potentially unplanned surgery take place in the postoperative period. For these reasons, the benefits of ERAC were not immediately apparent.

Core components of ERAC: Evidence-based practices

PREOPERATIVE CONSIDERATIONS

The guidelines for ERAC delivery differ slightly based upon scheduled versus unscheduled cesarean deliveries. The pathway begins at 10 to 20 weeks of gestational age for patients who will undergo scheduled cesarean deliveries. Comorbidities are optimized for delivery, including screening for and treatment of iron deficiency anemia and optimizing glycemic control for patients with diabetes (Table 1). The physician discusses ERAC goals with the patient for the preoperative, intraoperative, and postoperative periods. Reducing the period of fasting for women undergoing cesarean is emphasized, with a light meal being allowed up to 6 hours before surgery and clear liquids up until 2 hours before administration of anesthesia. For unscheduled or emergent cesarean deliveries, the preoperative pathway is compressed into a 30- to 60-minute window preceding delivery.

INTRAOPERATIVE CONSIDERATIONS

The intraoperative pathway minimizes surgical complications and prepares the patient for a safe postoperative course and successful discharge. Intravenous (IV) antibiotics should be administered within 60 minutes of surgical incision. First-generation cephalosporins are recommended for all women without allergies, with the addition of azithromycin in women with ruptured membranes. Skin cleansing should occur before incision with adequate drying time. Furthermore, patients should receive at least 2 prophylactic IV antiemetics with different mechanisms of action.

Regional anesthesia is preferred for cesarean delivery. Spinal anesthesia results in shorter block onset than epidurals, and intrathecal morphine helps with postoperative pain control. The guidelines suggest a transversus abdominis plane (TAP) block for patients who do not receive intrathecal or epidural morphine. The administration of ketorolac should occur after peritoneal closure, and scheduled nonopioid analgesia, such as acetaminophen, should be initiated.

The goal of multimodal anesthesia is to reduce postoperative opioid use. The use of prophylactic vasopressor infusion is recommended to prevent hypotension secondary to spinal anesthesia and maintain blood pressure at baseline. IV fluids should be limited to less than 3 L for routine cases to maintain euvolement. Published guidelines recommend that oxytocin administration be limited to the amount necessary to achieve and maintain adequate uterine tone.

In an effort to reduce intraoperative hypothermia, guidelines recommend the forced-air warming of the mother, warming IV fluids, and increasing the operating room temperature. Hypothermia can have adverse maternal effects, including coagulopathy, cardiac derangements, and higher infection risk. Additionally, neonatal hypothermia can result in adverse outcomes for the infant; therefore, the newborn should be dried and kept warm after delivery.

The ERAC guidelines also address immediate postdelivery infant care. Clamping of the umbilical cord for term infants should be delayed for at least 1 minute, whereas preterm infants should have the clamping delayed for 30 seconds. The ability to conduct neonatal resuscitation, if necessary, is vital for all cesarean deliveries. Avoid the routine use of oxygen supplementation and suctioning of the neonatal airway, except in cases of obstruction. Skin-to-skin contact is encouraged immediately after delivery to promote breastfeeding initiation within the first hour of life.

POSTOPERATIVE CONSIDERATIONS

Success during the postoperative pathway is dependent upon steps taken during the preoperative and intraoperative periods. The primary goal is ensuring patients return to baseline

THE PATHWAY BEGINS AT

10 to 20 weeks

of gestational age for patients who will undergo scheduled cesarean deliveries.
function and progress to successful discharge from the hospital. Early ambulation after resolution of neuraxial anesthetic is thought to decrease the risk of thromboembolic events and is one of the initial steps to return the patient to precesarean functional status.\(^6\) Additional, mechanic thromboembolism prophylaxis, such as pneumatic compression devices, is preferred for women not receiving pharmacologic thromboembolism prophylaxis for another indication.\(^12\)

Maintenance of euvoemia and appropriate intraoperative treatment of hypertension decreases the risk of postoperative nausea and vomiting. Early oral intake of ice chips and water should occur within 60 minutes of admission to the postanesthesia care unit.\(^8\) Patients are encouraged to resume a regular diet within 4 hours after surgery if there are no contraindications. Published guidelines recommend the discontinuation of Foley catheters for women who do not require ongoing urine output measurements.\(^3\) Early removal of the catheters is thought to facilitate ambulation, and theoretically also reduce the risk of symptomatic urinary tract infections.\(^8\)

Ideally, the multimodal pain regimen started in the operating room continues, or otherwise is initiated, upon reaching the postanesthesia care unit. A regimen emphasizing the use of acetaminophen and scheduled nonsteroidal anti-inflammatory drugs is favored.\(^12\) Prior to discharge, guidelines recommend monitoring the patient for anemia, with hemoglobin lab draws on postoperative day 1 or 2 for women with significant blood volume losses.\(^8\) Those found to have anemia should be treated appropriately. Lastly, mothers should receive breastfeeding support throughout the hospital stay with resources given for outpatient help at the time of discharge.

### Interventions and outcomes: Why adopt ERAC principles?

The mission of the ERAS Society is to improve recovery through use of the best available medical science. In most fields this equates to shorter recovery times, cost savings, and decreased rates of complications. Usually this is accomplished by minimizing surgical trauma and postoperative pain, which encourages rapid return to normal activities.

### LENGTH OF STAY

In other surgical specialties, instituting ERAS protocols has resulted in drastically decreased postoperative stays.\(^13\) The same has proved true for gynecologic surgery.\(^14\) However, surgical recovery is often not the rate-limiting factor for women undergoing cesarean delivery. Those who undergo cesarean delivery are also more likely to experience medical complications such as preeclampsia or intrauterine infections, which may dictate hospital length of stay regardless of surgical recovery trajectory. Additionally, many infants require 2 to 3 days of inpatient care after a cesarean delivery, and earlier discharge of the mother could decouple the mother-infant pair, which is unfavorable for many reasons. Earlier discharge of infants would likely require a greater number of follow-up visits for those infants, with the associated impact on neonatal outcomes unknown, and would likely require greater availability of outpatient lactation services as well.

### THROMBOEMBOLISM PROPHYLAXIS

Unfortunately, solid data on thromboembolism prophylaxis after cesarean delivery are limited given the rarity of the outcome. It is unclear at this time whether encouraging earlier ambulation per the guideline recommendations truly reduces the risk of venous thromboembolism over a short delay in ambulation with the use of pneumatic compression devices. Weighed against the possible increased risk of maternal falls and injuries with ambulation in the setting of waning neuraxial anesthesia,
aggressively promoting early ambulation after cesarean may in fact be harmful. If early ambulation is a part of an ERAC protocol, special attention should be paid to nursing protocols to ensure safety at the time of first ambulation.

**EARLY FOLEY CATHETER REMOVAL**
Currently, removal of Foley catheters immediately following cesarean delivery is recommended for women who do not require ongoing urine output measurements. This has created some controversy among leading experts. One concern is the lack of existing data on immediate Foley catheter removal in the setting of long-acting neuraxial opioids. This lack of data must be weighed against the unproven benefits of early ambulation. Additionally, one could assume that immediately removing the Foley catheter may increase the risk of unrecognized hypovolemia. Quantification of blood loss at the time of delivery, despite continued efforts to improve blood loss estimates and the use of quantitative blood loss measurements, is difficult. Often, decreased urine output may be an initial sign of hypovolemia requiring transfusion and is likely more difficult to detect with intermittent voiding.

**REDUCING OPIOID USE**
Multimodal pain regimens decrease the amount of opioids required by patients after cesarean delivery. However, the effect is diminished when other measures to control postoperative pain, such as TAP blocks and long-acting intrathecal morphine, are used concurrently. In fact, investigators of a number of studies examining opioid use with implementation of ERAC protocols have found no reduction in opioid use, though most of the studies included women receiving TAP block and/or intrathecal morphine. At our institution, where neither TAP block nor intrathecal morphine was routinely used, implementing a multimodal regimen resulted in a dramatic decrease in postoperative opioid use. Using nonopioid pain medications prevents the gastrointestinal adverse effects associated with opioids, such as nausea, vomiting, constipation, and decreased bowel motility. Less sedating pain medications also may promote ambulation and activities such as breastfeeding. Additionally, limiting opioid requirements during admission reduces the number of opioids needed for pain control at discharge. Opioid-naive women who receive frequent doses of opioids after cesarean delivery can become dependent after surgery.

**Conclusion**
Cesarean delivery is the most commonly performed surgery in the United States, with over 1 million infants delivered this way each year. Maternal morbidity and mortality rates in this country are higher than in other developed nations, and rates are higher still in women undergoing cesarean delivery. Therefore, it seems vital that any measure that improves outcomes should be adopted. However, more research is needed to understand which ERAS interventions are most useful in the setting of cesarean delivery. Some interventions, such as early Foley catheter removal, have proved useful in other surgical specialties but may not prove as useful in obstetrics. Additionally, other facets of ERAC may prove useful not for promoting early discharge, but for improving outcomes such as breastfeeding or reducing post-discharge opioid use. We owe it to pregnant women to find out and implement changes appropriately.

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**TAKEAWAYS**
- Enhanced recovery after cesarean (ERAC) applies evidence-based practices to improve patient outcomes.
- Practices can be implemented for both scheduled cesarean deliveries and unscheduled or emergent cases.
- ERAC incorporates interventions at every stage of the procedure: pre-, intra-, and postoperative phases.
- Decreased length of hospital stay is not the only possible benefit with ERAC. Women may also experience fewer complications, require fewer opioids, and be more successful with breastfeeding.
- Not all components of the ERAC protocol are based on high-level data, and implementation should take into account the specific needs of the patient.
Pregnancy Hypertensive Disorders Increase Risk of Premature Death

by SANDRA FYFE

Hypertensive disorders of pregnancy (HDPs), particularly gestational hypertension and preeclampsia, increase a woman’s risk of premature death, especially from cardiovascular disease (CVD), according to findings from a study in the *Journal of the American College of Cardiology*. The risk remains even for women with no diagnosis of chronic hypertension.

HDPs are one of the most frequent health challenges in pregnant women worldwide, occurring in about 10% of pregnancies. The 4 categories of disorders are gestational hypertension (GHTN), preeclampsia, chronic hypertension, and chronic hypertension with superimposed preeclampsia. Of these, preeclampsia and GHTN that occur at or after 20 weeks are leading causes of perinatal and maternal morbidity and mortality.

Jorge E. Chavarro, MD, ScD, an associate professor of medicine at Harvard Medical School and associate professor of medicine at Harvard T.H. Chan School of Public Health, in Boston, Massachusetts, served as lead author. He and colleagues performed the study to examine the association between HDPs, particularly GHTN and preeclampsia, and a subsequent link to chronic hypertension and risk of premature death.

They examined data from 88,395 parous nurses between the ages of 25 and 42 who participated in the Nurse’s Health Study II between 1989 and 2017. Investigators of this study had collected data about lifestyle, health conditions, and reproductive characteristics over a period of nearly 30 years, and focused on HDPs, particularly gestational hypertension and preeclampsia. They used Cox proportional hazards models adjusted for relevant confounders to estimate confidence intervals and hazard ratios for connections between premature mortality and HDPs.

Using the Nurse’s Health Study II, they divided the women into 4 groups: no HDPs and chronic hypertension, HDPs only, chronic hypertension only, or both HDPs and subsequent chronic hypertension. Investigators said 14% of women (12,405) had HDPs in at least 1 pregnancy. Of the 88,395 women in the study, 2387 (2.7%) died before age 70 in 28 years of follow-up. Cancer accounted for 1141 deaths, whereas CVD accounted for 212 deaths. According to the authors, during follow-up of HDPs, either preeclampsia or GHTN was associated with a 1.31 hazard ratio for early death (95% CI, 1.18-1.46) and a 42% increase in premature death. The association remained even after adjusting for cofounders and for reproductive characteristics, diet, and lifestyle post pregnancy. Women with preeclampsia and/or GHTN had a higher baseline body mass index, chronic hypertension, gestational diabetes, and a parental history of myocardial infarction or stroke.

“Relations were strongest for CVD-related mortality (HR, 2.26; 95% CI, 1.67 to 3.07). The association between HDPs and all-cause premature death persisted, regardless of the subsequent development of chronic hypertension (HR, 1.20 [95% CI, 1.02 to 1.40] for HDPs only and HR, 2.02 [95% CI, 1.75 to 2.33] for both HDPs and subsequent chronic hypertension),” the investigators reported.1

Patients with HDP had more than twice the risk of premature CVD mortality. Regarding the development of chronic hypertension, investigators saw a higher risk of all-cause premature CVD mortality in patients with HDPs alone, those with chronic hypertension alone, and those with both HDPs and subsequent chronic hypertension.

“Our results suggest that HDPs, either GHTN or preeclampsia, were associated with a greater risk of premature mortality, especially CVD-related deaths, even in the absence of chronic hypertension,” Chavarro said.2 “Our results highlight the need for clinicians to screen for the history of HDPs when evaluating CVD morbidity and mortality risk of their patients.”

HDPs are one of the most frequent health challenges in pregnant women worldwide.

Investigators of another study, for which results were published in the *Journal of the American College of Cardiology*, found increased rates of cardiac complications in women with obesity versus women of normal weight.3 Study coauthor Candice K. Silversides, MD, of the Division of Cardiology at the University of Toronto and the Pregnancy and Heart Disease Program at Mount Sinai and Toronto General Hospitals in Ontario, said that pregnant women with heart disease and obesity should be educated about these risks.

Sandra Fyfe is a freelance writer for Contemporary OB/GYN®.

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chronic hypertension)" the investigators reported.1

Patients with HDP had more than twice the risk of premature CVD mortality. Regarding the development of chronic hypertension, investigators saw a higher risk of all-cause premature CVD mortality in patients with HDPs alone, those with chronic hypertension alone, and those with both HDPs and subsequent chronic hypertension.

“Our results suggest that HDPs, either GHTN or preeclampsia, [were] associated with a greater risk of premature mortality, especially CVD-related deaths, even in the absence of chronic hypertension,” Chavarro said.2 “Our results highlight the need for clinicians to screen for the history of HDPs when evaluating CVD morbidity and mortality risk of their patients.”

HDPs are one of the most frequent health challenges in pregnant women worldwide.

Investigators of another study, for which results were published in the *Journal of the American College of Cardiology*, found increased rates of cardiac complications in women with obesity versus women of normal weight.3 Study coauthor Candice K. Silversides, MD, of the Division of Cardiology at the University of Toronto and the Pregnancy and Heart Disease Program at Mount Sinai and Toronto General Hospitals in Ontario, said that pregnant women with heart disease and obesity should be educated about these risks.1
WHAT CAN YOU DO to Reduce Maternal Severe Morbidity & Mortality

by SARAH J. KILPATRICK, MD, PHD

- Review all maternal deaths at your institution.
- Participate in Levels of Maternal Care designation.
- Implement bundles: hemorrhage, hypertension, etc.
- Have perinatal staff take implicit bias training.
- Have clear severe hypertension treatment guidelines posted and treat acute severe hypertension within 30 minutes.
- Debrief after each adverse event.
- Have a massive transfusion protocol and hemorrhage kit on L+D.
- Participate in multidisciplinary simulations in the L+D unit and in testing areas.
- Expand community outreach for better access for Medicaid and others.
- Screen for VTE risk and treat appropriately.
- Utilize toolkits.
- Review all cases of severe maternal morbidity (ICU admissions and/or transfusions of 4 or more units of red blood cells).
What Can You Do to Reduce Maternal Severe Morbidity & Mortality

REFERENCES
In the evaluation of uterine conditions

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Primary dysmenorrhea is defined as painful menstruation in the absence of an identifiable cause. Characterized by recurrent, crampy lower abdominal pain occurring during menstruation, dysmenorrhea is the most common gynecologic complaint and affects 50% to 90% of women. For half of women, the pain experienced is at least moderate to severe. Secondary dysmenorrhea refers to the same clinical features of pain during menstruation, but is attributable to pelvic pathology such as endometriosis, fibroids, adenomyosis, and congenital anatomic abnormalities (Figure 1). The management of primary dysmenorrhea is directed toward diagnosing other causes of symptoms and identifying medical therapies that satisfactorily control the patient’s symptoms. Despite its high prevalence, dysmenorrhea is often underdiagnosed, inadequately treated, and normalized even by patients themselves, who may accept the symptoms as an inevitable response to menstruation. This frequent normalization and minimization of menstrual pain leads many patients to dismiss their own symptoms and can lead to the assumption that treatment is neither warranted nor available. All clinicians, and specifically gynecologists, should proactively inquire about the impact of menstrual-related symptoms on quality of life.
Primary dysmenorrhea generally begins in adolescence, once ovulatory cycles are established. The associated pain arises from the release of excess prostanoids, including prostaglandins at the time of endometrial sloughing. Prostanoids are derived from the cyclooxygenase pathway, which is initiated by phospholipase A2. This enzyme is released when the destabilization and breakdown of cellular lysosomes occurs as a result of declining progesterone levels at the end of the luteal phase. High levels of progesterone, as occur after ovulation, stabilize these lysosomes. The rise and fall of progesterone, as controlled by ovulation, and its influence on phospholipase A2 explains why primary dysmenorrhea does not occur at the very beginning of menarche, when cycles are anovulatory. Compared with asymptomatic women, those with dysmenorrhea have higher levels of prostaglandins in endometrial tissue and menstrual fluid. The increased level of prostaglandins at the time of menstruation is theorized to cause myometrial hypercontractility, resulting in hypoxia and ischemia of uterine muscle and the perception of pain, as well as systemic symptoms often associated with dysmenorrhea such as nausea and diarrhea.

The physical, social, emotional, and economic impact of dysmenorrhea is substantial. A population-based survey of women older than 18 years with primary dysmenorrhea reported that more than half described symptoms that limited their activities and 17% missed school or work as a result. Dysmenorrhea is the most common cause of short-term absence from school in adolescent girls, and 1 in 8 adolescents and women aged 14 to 20 report missing school or work as a result of the condition. Other cross-sectional studies including thousands of women worldwide have demonstrated similar findings of primary dysmenorrhea that affect relationships, functioning, and productivity, and contribute to absenteeism. In the United States, an estimated $2 billion is lost annually due to missed work and productivity. Despite the significant effects on quality of life, the prevalence of primary dysmenorrhea is considered to be underestimated — women frequently do not seek medical treatment because of the commonly held belief that pain is an expected part of menstruation.

**Diagnosis**

Evaluating and diagnosing primary dysmenorrhea (Figure 2) does not require specialization in women’s health or pelvic pain, and initial complaints frequently are presented to pediatricians and primary care physicians. Gynecologists serve an important role in raising awareness of the condition and are a resource for treatment options and further evaluation.
If empiric therapy fails, a diagnosis can often be reached by obtaining a detailed medical, family, psychosocial, and gynecologic (including menstrual and sexual) history. A complete menstrual history includes age at menarche, duration of bleeding, intervals between menses, and assessment of menstrual flow; associated symptoms such as pain, nausea, diarrhea, and fatigue; and the timing of onset, severity of pain, and effect on daily activities. The onset of primary dysmenorrhea typically begins 6 to 24 months after menarche. Pelvic pain that starts with menarche, or quickly thereafter, may be associated with obstructive genital tract malformations and should prompt further evaluation. Pain is primarily midline and is often described as cramping in the lower abdomen or suprapubic region. Patients may describe pain that radiates around the abdomen and into the lumbar area or along the anterior or medial thigh. Persistent unilateral symptoms may suggest anatomic abnormalities as the cause of pain. Generally, symptoms begin a few hours before or after menstrual blood flow, peak at the time of heaviest blood flow, and resolve on cycle day 2 or 3. The timing, quality, duration, and location of pain associated with primary dysmenorrhea is consistent from one menstrual cycle to the next and does not progressively worsen with time. Progressive worsening or pain that persists after menses concludes is not characteristic of primary dysmenorrhea and may be related to endometriosis and other secondary causes. Symptoms frequently associated with dysmenorrhea include nausea, vomiting, diarrhea, headaches, muscle cramps, and poor sleep quality, though these can also be found with secondary causes such as endometriosis. Additional patient factors that suggest secondary causes of dysmenorrhea include mid-cycle or acyclic pain, abnormal uterine bleeding, and infertility.

A pelvic examination is recommended in adult women presenting for the first time with dysmenorrhea because the likelihood of secondary causes is much higher in this population. However, a pelvic exam is not necessary in non-sexually active patients—specifically adolescents—if the elicited history is descriptive of primary dysmenorrhea, and in the absence of other symptoms such as infection or abnormal bleeding. The pelvic exam should be normal in patients with primary dysmenorrhea when not menstruating. Localized pain or physical findings such as uterine enlargement, pelvic mass, displacement or deviation of the cervix, nodularity in the rectovaginal septum, or uterine or cervical tenderness not associated with menstruation point to secondary causes. Sexually transmitted infections should be ruled out with appropriate testing as a potential cause of dysmenorrhea in all sexually active patients.

Transvaginal ultrasonography is the preferred method for the initial evaluation of pelvic organs. In non-sexually active adolescents and young women, a transabdominal pelvic ultrasound is preferable to accommodate patient comfort. Dysmenorrhea associated with adnexal pathology or uterine abnormalities (such as leiomyoma, adenomyosis, and some Müllerian anomalies) can be diagnosed with ultrasound. Although endometriosis is a common cause of secondary dysmenorrhea, routine pelvic ultrasound is frequently unremarkable in affected patients unless there is anatomic distortion, endometrioma, or evidence of deep infiltrative endometriosis. Advances in imaging have enabled clinicians to better evaluate deep infiltrating endometriosis on pelvic MRI, but this modality is not.

<table>
<thead>
<tr>
<th>Diagnosis of Dysmenorrhea</th>
<th>Symptoms suggesting secondary cause</th>
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<tbody>
<tr>
<td>Symptoms highly suggestive of primary dysmenorrhea</td>
<td>Symptoms suggesting secondary cause</td>
</tr>
<tr>
<td>▪ Symptom onset &gt; 6 months, but &lt; 24 months of menarche</td>
<td>▪ Dyschezia</td>
</tr>
<tr>
<td>▪ Pain starting a few hours before or at time of bleeding</td>
<td>▪ Dyspareunia</td>
</tr>
<tr>
<td>▪ Pain stopping before or with conclusion of bleeding</td>
<td>▪ Cyclic hematocrit</td>
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<tr>
<td>▪ Midline pain; can radiate to back or thighs</td>
<td>▪ Intramenstrual bleeding</td>
</tr>
<tr>
<td>▪ Pain characteristics are consistent and predictable from one cycle to the next</td>
<td>▪ Progressively worsening dysmenorrhea</td>
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<td>▪ Noncyclic pelvic pain</td>
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<td>▪ Onset with menarche</td>
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<td>▪ Unilateral pain</td>
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<td></td>
<td>▪ Abnormal bleeding</td>
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**SHARED SYMPTOMATOLOGY**
- Gastrointestinal: nausea, vomiting, diarrhea
- Neurologic: headaches, dizziness
- Muscle cramps
- Fatigue
- Poor sleep quality
generally recommended as an initial step in evaluating dysmenorrhea unless clinical presentation suggests a secondary cause.

Treatment

Delays in diagnosis and treatment are common and should be avoided. The goals of treatment are to provide satisfactory pain and symptom relief and reduce the disturbance in daily activities. Adolescents and young women who are not sexually active and report history and symptoms typical for primary dysmenorrhea should be started on empiric treatment without necessitating the completion of a pelvic exam or radiologic studies. However, if symptoms persist despite treatment for 3 months, further evaluation with an exam and imaging are warranted to evaluate for secondary causes. Adult patients whose history indicates primary dysmenorrhea and in whom pelvic exam findings are negative and infectious diseases have been ruled out can also be offered empiric therapy prior to further investigation with imaging. Therapeutic options should take into account a patient’s contraceptive needs, as both nonsteroidal anti-inflammatory drugs (NSAIDs) and hormonal contraceptives are considered first-line agents, either separately or in combination. Hormonal contraceptives effective in the treatment of dysmenorrhea include combined oral contraceptive (COC) pills, the vaginal ring, and the transdermal patch. Long-acting reversible contraceptives (LARCs) such as levonorgestrel-releasing intrauterine devices (LNG-IUDs) and etonogestrel-releasing implantable rods are also effective. NSAIDs effectively treat dysmenorrhea by decreasing prostaglandin levels via the inhibition of cyclo-oxygenase–mediated production. Randomized, placebo-controlled trials support the efficacy of NSAIDs in the treatment of primary dysmenorrhea. However, there is limited evidence suggesting that one NSAID is more effective than another. OTC options, such as naproxen and ibuprofen, are easily accessible and affordable for most patients. Specific instructions on optimal dosage, frequency, and duration of cyclic NSAID use should be given to patients. This is especially important for the adolescent population, in which underdosing and subtherapeutic treatment is common and thereby can lead to what is perceived to be treatment failure. Therapy should be initiated at symptom or bleeding onset, based on a scheduled basis, and continued until cycle day 2 or 3; for moderate to severe pain, therapy can be started 1 to 2 days before symptom onset (Figure 3). It should be noted that 18% of patients with no apparent secondary etiologies for dysmenorrhea are resistant to NSAID therapy despite adherence to recommended treatment regimens.

Endometrial ablation does improve dysmenorrhea associated with heavy menstrual bleeding in women no longer desiring future fertility.

The most widely studied hormonal agents, estrogen-progestin COCs, inhibit proliferation of the endometrial lining, thereby decreasing prostaglandin production within the uterus. They have been demonstrated as effective in treating dysmenorrhea in several randomized controlled trials. Relief of symptoms has been shown with all formulations of COCs, including low-dose pills (20 μg ethinyl estradiol). Progestin-only methods, LNG-IUDs, and implantable rods have also demonstrated efficacy in reducing dysmenorrhea; even adolescents and women who have never been sexually active should consider these LARCs. Continuous norethindrone acetate 5 mg is equally effective to COC, but is not approved for contraception in the United States. Patients are encouraged to continue first-line therapy for 3 to 6 months, and their response to therapy should be monitored 2 to 3 months after its initiation. If adequate relief of symptoms is not achieved, further evaluation or referral to gynecologic specialists is recommended. Notably, up to 70% of adolescents who fail initial therapy will have endometriosis, and this prevalent condition should remain on the differential diagnosis if symptoms progress or are suboptimally controlled with empiric therapy.

Alternative therapies, such as heat, exercise, and dietary and behavioral interventions, are frequently employed by patients. Most therapies are low risk and may provide individual patients with improved symptom control. Promising data, though limited, support the use of exercise, and high-frequency transcutaneous electrical nerve stimulation and topical heat have demonstrated the most favorable results. Limited and contradictory data exist regarding the efficacy of dietary modifications and herbal supplements in the treatment of dysmenorrhea. These alternatives may be useful as adjunctive therapies or in patients who are unable to take or are disinterested in pharmaceutical treatments.

Nerve transection procedures such
### Figure 3: Treatment Recommendations

| NSAID | Target: Decrease prostaglandin production  
|-------|-----------------------------------------------  
|       | Considerations: No data favor one NSAID over another; consider cost and availability.  
|       | • Ibuprofen 600 mg every 6 hours  
|       | • Naproxen sodium 550 mg every 6 hours  
|       | • Start 1-2 days before symptom onset or at time of symptom onset; continue until day 2 or 3 of menses.  
|       | • May alternate/supplement with acetaminophen 650 mg every 6 hours  

| HORMONAL | Target: Interrupt ovulation and reduce endometrial proliferation  
|---------|---------------------------------------------------------------  
|         | Considerations: Does the patient have any contraindications to estrogen therapy?  
|         | • All estrogen-containing contraceptives are effective for treatment of dysmenorrhea.  
|         | • Progesterone-only methods are likely effective but less well studied. Irregular bleeding is common, but often not associated with pain.  

| Limited data to support use | • High-frequency transcutaneous nerve stimulation  
|                            | • Heat (caution patients regarding excessive/chronic use, which can lead to burns or skin changes)  
|                            | • Yoga/exercise*  
|                            | • Magnesium (dosing recommendations unknown)  
|                            | • Vitamin E 200-400 IU daily  
|                            | • Ginger 750-2000 mg twice daily  

| No data to support use, but minimal risk of harm associated with use | • Rose tea, sweet fennel seed extract, fish oil, krill oil, omega 3 fatty acids, fenugreek, valerian, Zataria, zinc sulphate, fish oil, vitamin B1  
|                                                                     | • Acupuncture/acupressure  

*Although the data supporting the use of exercise to manage menstrual pain are of low quality, exercise is an important component of promoting a healthy lifestyle and can reduce stress. Exercise should be encouraged, especially in young women as they begin to develop healthy habits.*

| Patient RESPONDS to therapy | • Continue current therapy.  
|                            | • Primary dysmenorrhea is the likely diagnosis.  

| Patient DOES NOT respond to therapy | • Evaluate treatment adherence.  
|                                      | • Combine NSAID and hormonal therapy if not already using both.  
|                                      | • Consider continuous oral contraceptive pill if not already using this method.  
|                                      | • Consider causes for secondary dysmenorrhea.  
|                                      | • Pelvic examination  
|                                      | • Pelvic ultrasound  

| Fertility sparing | Diagnostic laparoscopy, excision of endometriosis if present  

| Non–fertility sparing | • Hysterectomy  
|                      | • Endometrial ablations with Mirena IUD insertion  

| Treatments of last resort | • Uterine nerve ablation  
|                           | • Presacral neurectomy  
|                           | • Calcium channel blockers  
|                           | • Glyceryl nitrate  

Although these procedures relieve pain, relief may be temporary due to nerve regeneration. The risks and adverse effects (constipation, urinary dysfunction) may outweigh the benefit.  

Undesirable adverse effect profile

(DMPA, depo-medroxyprogesterone acetate; IUD, intrauterine device; NSAID, non-steroidal anti-inflammatory drug.)
as laparoscopic uterine nerve ablation and presacral neurectomy may be considered in patients not treated with the therapies above, and in whom other secondary causes are not identified. However, there is insufficient evidence to recommend their use for primary dysmenorrhea, and the potential benefits must be weighed against the risks. Endometrial ablation does improve dysmenorrhea associated with heavy menstrual bleeding in women no longer desiring future fertility. In a retrospective study of 144 patients, up to 50% reported resolution of menstrual pain when menstrual flow was diminished by ablation. Finally, hysterectomy may be considered in patients who have completed childbearing or who do not desire uterine preservation and have had an inadequate response to other therapies.

**Further Evaluation**

Although the majority of women will improve with these first-line medical therapies, particularly if amenorrhea is achieved, those who do not improve warrant further evaluation. Scheduled follow-up after initial treatment is important to avoid delays in diagnosis as many patients seeking attention for dysmenorrhea will have already experienced diagnostic and treatment delays. Frequently, concurrent diagnoses of various sources of pelvic pain such as vulvodynia, pelvic floor dysfunction, and painful bladder syndrome can occur along with dysmenorrhea. Endometriosis should be high on the differential diagnosis even during the initial evaluation, regardless of patient age. If a 3- to 6-month trial of empiric medical management does not control symptoms and evaluation does not suggest other causes, such as congenital anomaly or infection, laparoscopy with a plan for concurrent surgical management should be pursued. Endometriotic lesions may not present as classical “powder burn” lesions, especially in younger women, and surgeons offering diagnostic laparoscopy should be trained and equipped to diagnose atypical lesions and resect abnormal appearing tissue for both pathologic diagnosis and therapeutic ends.

**Primary dysmenorrhea is a chronic pain condition, and, as seen in similar pain conditions ... the processing of stimuli via the peripheral and central nervous system is altered.**

**Future Directions**

As with other “benign” gynecologic conditions, despite the high prevalence of primary dysmenorrhea, research funding has been limited. Early studies implicate prostanoids as an underlying mechanism, yet there is still much to be understood mechanistically. NSAID therapy fails to satisfactorily improve menstrual pain in 18% of women, suggesting that prostanoids may not account for all symptomatology. Primary dysmenorrhea is a chronic pain condition and, as seen in similar pain conditions (eg, irritable bowel syndrome, bladder pain syndrome, fibromyalgia), the processing of stimuli via the peripheral and central nervous system is altered. Findings from several neuroimaging studies have demonstrated differences in metabolic activity in areas of the brain related to pain perception and in the cerebral structure in key brain regions in women with dysmenorrhea compared with controls. These central changes may underlie the findings by Hellman et al in which they observed that one-fifth of patients with moderate to severe dysmenorrhea also demonstrated hypersensitivities to passive bladder filling despite no prior complaint of bladder pain syndrome. Whether these functional MRI findings represent cause or effect of primary dysmenorrhea has yet to be determined, but they offer opportunities for translational research and the potential for targeted therapy.

**Conclusions**

Primary dysmenorrhea is a prevalent, underdiagnosed, but treatable condition. Unfortunately, normalization of the association between menstrual cycles and pain leads to delays in evaluation and diagnosis for women of all ages. Inquiry into the severity of symptoms frequently reveals a significant negative impact on quality of life with potentially far-reaching consequences. Gynecologists play an important role in building patient and community awareness of the condition, and in its diagnosis and management. Progressive worsening of symptoms or suboptimal symptom control with first-line agents warrants further evaluation for secondary causes, including endometriosis. Women with menstrual pain should not be dismissed and their symptoms should not be considered inevitable and thereby acceptable.
NASPAG 2021: Hillard’s Highlights

Contemporary OB/GYN® Editorial Board Member Paula J. Adams Hillard, MD, reports on the Annual Clinical & Research Meeting (ACRM) of the North American Society for Pediatric and Adolescent Gynecology (NASPAG), which was held virtually on March 18 to 21. The meeting drew gynecologists who specialize in pediatric and adolescent gynecology (PAG) and pediatricians who practice adolescent medicine, nursing and advanced practice nursing professionals, and various other clinicians who take care of girls and adolescents with gynecologic problems.

Via Zoom, participants viewed plenary sessions that profiled some of the most topical issues in treating this patient population. The topics included a focus on telehealth in PAG with Veronica E. Issac, MD; the latest research in our surgical field from Peter C. Minneci, MD; and an update on COVID-19 with Denise J. Jamieson, MD, MPH. Tanya L. Kowalczyk Mullins, MD, MS, presented on pre-exposure prophylaxis (PrEP) for the prevention of HIV among adolescents and young adults. Ted L. Anderson, MD, PHD, provided an overview of adnexal masses in the PAG population; Jennifer E. Dietrich, MD, MSc, reviewed Müllerian anomalies and their management nationally and internationally; and Sophie Soares and Lisa Polen of the Population Council presented on “Intentional Design: Employing a Global Evidence Base to Promote the Space, Access, and Agency of Adolescent Girls and Young Women.”

Open discussions with our LGBTQ patients remain more vital than ever, especially as overreaching state governments are passing laws that affect how practitioners can care for these patients. One of the most notable workshops was titled “LGBT Health: The Need for Sexual and Mental Health Screening.” M. Brett Cooper, MD, and May Lau, MD, talked about the risks for sexually transmitted diseases, as sexual minority individuals who have sex with different and same-sex partners have higher odds of sexual risk-taking behaviors. Both transgender males and females were noted to have risks related to engaging in condomless sex. According to the presenters, the Youth Risk Behavior Survey (YRBS) revealed we are not appropriately testing sexual and gender minority youths for HIV and other sexually transmitted infections (STIs). The American College of Obstetricians and Gynecologists, the US Preventive Services Task Force, and the Centers for Disease Control and Prevention all recommend gonorrhea and chlamydia testing annually for sexually active females and from adolescence through the mid-20s for those possessing a vagina. The presenters also emphasized that anxiety and depression screening is critical among transgender and gender nonconforming youth, as the 2019 YRBS found that more than two-thirds of LGBT students felt sad or hopeless most days, about 47% reported that they had considered attempting suicide, and 23% actually had attempted suicide.

Another valuable workshop addressed how to incorporate trauma-informed care (TIC) into a clinical setting, and was presented by Heather C. Millar, MD, with Sharon Lorber, LCSW, and Heather Farina, NP. Our understanding of childhood abuse and trauma comes from a seminal report of abuse, neglect, and household dysfunction that described adverse childhood experiences (ACEs). These have subsequently been found to be highly correlated with such conditions as depression, early sexual activity, IV drug use, smoking, and an increased risk of having an adolescent pregnancy. Within our field of gynecology, ACEs and childhood trauma are associated with an increased risk of chronic pelvic pain, dysmenorrhea, dyspareunia, STIs, pelvic inflammatory disease, and supportive environment in caring for adolescents and youth include asking patients their preferred name and pronouns, making sure to spend time alone with the adolescent, providing assurances of confidentiality (within the legal confines of each state), avoiding heteronormative questions, normalizing behaviors, and asking patients to clarify if they used terms the clinician didn’t understand. The presenters also emphasized that anxiety and depression screening is critical among transgender and gender nonconforming youth, as the 2019 YRBS found that more than two-thirds of LGBT students felt sad or hopeless most days, about 47% reported that they had considered attempting suicide, and 23% actually had attempted suicide.

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premenstrual syndrome or premenstrual dysphoric disorder. Thus, we will all see patients with a history of trauma, emphasizing the need for TIC in our practices. TIC has been associated with increased adherence to medications, reduced substance use, improved physical health outcomes, and decreased burnout for staff. Trauma memories can be triggered by a number of components of our gynecologic practices, including vaginal exams and childbirth. But they can also be triggered by seemingly innocuous medical exams such as blood pressure evaluation and measurement of height and weight.

The workshop presenters’ recommendations for a TIC approach to clinical care included: acknowledging the trauma, giving the patient choice and control in their care, building a relationship with the patient, avoiding having the patient retell their story, and providing coping strategies (including a focus on grounding and distraction techniques, referral for mental health services, and exploring models of peer support).

Quick take-home messages from a sampling of oral abstracts included the following:

1. At least 30% of females with unilateral renal agenesis or dysgenesis also have a Müllerian anomaly. Thus, screening is justified in this population (and also in those with a prenatal diagnosis of renal anomalies), with screening ultrasound around the expected time of menarche.

2. The average delay in diagnosis of endometriosis is greater among adolescents than among adult women. A confirmatory diagnosis with laparoscopy could be performed earlier in adolescents with chronic pelvic pain to diagnose the condition.

3. Lichen sclerosus occurs in premenarchal girls and is frequently misdiagnosed, with a delay of 1 to 2 years prior to appropriate diagnosis. SWIFT (Soreness/pain, Whitening, urinary Incontinence, Fissures, and clitoral hood Thickening) symptoms and findings on examination are predictive of this diagnosis; interestingly, the addition of pruritis symptoms does not improve the predictive value.

4. Among adolescent girls presenting to the emergency department for an evaluation of heavy menstrual bleeding, the American Academy of Pediatrics’ recommendation that they be screened for iron deficiency is infrequently followed. In addition, few of these girls are discharged home on oral iron, representing missed opportunities for both the diagnosis and treatment of iron deficiency.

Ob/gyns who are interested in learning more about the gynecologic care of girls and adolescents may wish to save the date for next year’s NASPAG ACRM—April 7 to 9, 2022, in Chicago. I anticipate that it will be another wonderful opportunity to take a deeper dive into the topic of PAG.
In a prospective study to assess the effects of an oral contraceptive containing estetrol and drospirenone on ovarian function, investigators found that treatment achieved complete ovulation inhibition in patients.

The European prospective study, the results of which were published in the journal *Contraception*, compared estetrol 15 mg/drospirenone 3 mg (E4/DRSP) with ethinylestradiol 20 µg/drospirenone 3 mg (EE/DRSP) in a 24/4-day regimen for 3 consecutive cycles. Interestingly, complete ovulation inhibition occurred with E4/DRSP, despite the oral contraception exhibiting less suppression of the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH) than EE/DRSP.

The single-center, randomized, open-label, parallel study in healthy young women with proven ovulatory cycles was conducted at Dinox Female Health Care in Groningen, the Netherlands, between February 2017 and June 2018. Participants received either E4/DRSP (n = 41) or EE/DRSP (n = 41). Follicular size and endometrial thickness were measured by transvaginal ultrasound every 3 days in cycles 1 and 3, and blood was sampled for hormone analysis.

Ovarian function expressed as Hoogland score was based on follicular size and serum estradiol (E2) and progesterone (P) concentrations. Ovulation was defined as a ruptured follicle-like structure (FLS) greater than 13 mm with serum E2 concentrations greater than 27 pg/mL and serum P concentrations greater than 1.57 ng/mL.

The investigators evaluated return of ovulation after treatment cessation, as well as safety throughout the study. None of the women ovulated with E4/DRSP treatment; however, during EE/DRSP therapy, 1 woman ovulated once and 1 woman ovulated twice.

Most participants had a Hoogland score of 1 (no ovarian activity) in cycle 1: 85.0% of the E4/DRSP group and 82.9% of the EE/DRSP group. In cycle 3, a Hoogland score of 1 was attained by 65.8% of women in the E4/DRSP group vs 83.8% in the EE/DRSP group.

Suppression of FSH and LH concentrations was less pronounced with E4/DRSP than with EE/DRSP. "The reduced pituitary suppression with E4/DRSP probably caused the minor differences in ovarian suppression in cycle 3," wrote the authors.

More women developed an active FLS during treatment with E4/DRSP than with EE/DRSP: 21.1% vs 5.4%. This resulted in a slightly larger mean FLS diameter and associated higher Hoogland 4 scores.

According to the authors, these small differences have no clinical significance. In addition, both treatments comparably suppressed E2 and P and endometrial thickness.

In the E4/DRSP group, ovulation occurred on average 15.5 days (range, 10-22) after the last placebo tablet, whereas in the EE/DRSP group it was 18.1 days (range, 6-25) after the last placebo tablet.

Reported treatment-related adverse events that occurred in greater than 5% of the entire cohort included breast pain, breast enlargement, headache, emotional lability, nausea, lower abdominal pain, and acne. A similar frequency of these events occurred in both groups, except for breast pain, which was reported by 11 women receiving E4/DRSP and 4 women receiving EE/DRSP.

Most treatment-related adverse events were of mild or moderate intensity. However, 3 women in the E4/DRSP group reported an adverse event of severe intensity: gastroenteritis, emotional lability, and stress. This compared with 2 women in the EE/DRSP group, who reported emotional lability and depressed mood. Other safety assessments did not show significant abnormalities.

"If it becomes commercially available, E4/DRSP, containing a naturally occurring estrogen, should be as effective as EE/DRSP," wrote the authors.
TTCRF Greatly Improves SUI, Sexual Dysfunction, and Genital Appearance

by SANDRA FYFE

Women who received transcutaneous temperature-controlled radiofrequency treatment (TTCRF) saw substantial improvement in stress urinary incontinence (SUI), sexual dysfunction (SD), and female genital appearance. The findings of a recent study were published in *Aesthetic Surgery Journal*.

Sejal Ajmera Desai, MD, MBBS, a consultant ob/gyn at the Indian Academy of Vaginal Aesthetics in Mumbai, India, and colleagues examined TTCRF’s use in 78 patients, 41 of whom had SD and 37 of whom had SUI. TTCRF involves the use of safe RF and additional controls that monitor tissue temperature with thermistors and thermocouples, the authors explained. The procedure is effective at improving lax skin. “Energy-based devices such as TTCRF enhance vulvovaginal rejuvenation by inducing thermal-dependent matrix remodeling, which involves neocollagenesis and neoelastogenesis. They have been shown to increase type I collagen production in the extracellular matrix via stimulation of fibroblasts,” the authors said. They reported that neovascularization is increased, which improves lubrication. TTCRF also “increases glycogen content and small nerve fiber density in the papillary dermis,” and it restores vaginal milieu and flora, which improves mucosal hydration.

According to the authors, most patients had 3 or fewer TTCRF treatment sessions. Photographs prior to and 6 weeks after the procedure were used to track results in a blinded method. Before the procedure, patients with SD were given the Female Sexual Function Index (FSFI) questionnaire, and patients with SUI were given the International Consultation on Incontinence Questionnaire—Short Form (ICIQ-UI-SF). A paired t-test was used to compare pre- and postprocedure results.

All patients saw improvement following TTCRF. Those with SD had a mean FSFI score of 21.77 before the procedure, which increased to 25.79 ($P < .00001$) post procedure, with significant improvements in sexual desire, arousal, orgasm, pain, and satisfaction.1 For patients with SUI, the mean ICIQ-UI-SF score decreased from 10.10 before the procedure to 4.81 post procedure ($P < .00001$).1 In addition, the investigators reported improvements in wrinkles, quality of skin, and tumescence of labia majora in all the patients. Study coauthor George Kroumpouzos, MD, PhD, FAAD, medical director at GK Dermatology and a clinical associate professor at Brown University in Providence, Rhode Island, said that the most significant takeaway from this study for providers is that TTCRF is safe and effective. “TTCRF has not only aesthetic but also functional benefits as evidenced by improvements in sexual function and SUI,” he said. This study is “the first that showed substantial efficacy of TTCRF with validated instruments, including the FSFI questionnaire and the ICIQ-UI-SF.” Kroumpouzos said larger, controlled studies that require more effective patient recruitment are needed: “Several publications have indicated that a substantial percentage of patients do not seek treatment of vaginal laxity and sexual dysfunction and fail to discuss such problems with their gynecologist. Barriers of communication on issues regarding SD and SUI have not been broken.” The impact of the number of TTCRF sessions on efficacy should be studied, he said, to help evaluate the cost-effectiveness of the procedure and compare it with the cost of other noninvasive modalities such as lasers. “Almost all participants [95%] were satisfied with the results in our TTCRF study. However, further studies are needed to compare TTCRF with other noninvasive modalities for feminine rejuvenation such as fractional carbon dioxide laser, photobiomodulation, carboxytherapy [topical carbon dioxide gel], platelet-rich plasma, and fillers. This will determine the comparative efficacy, cost-effectiveness, and long-term safety of such procedures. Such studies can help determine how TTCRF can be combined with other noninvasive treatments for additional benefit,” he said.

Sandra Fyfe is a freelance writer for Contemporary OB/GYN®.

FOR REFERENCES VISIT contemporaryobgyn.net/TTCRF.
Findings from a literature review show that the prevalence thresholds of various screening tests used in ob/gyn health care settings are significantly higher than the estimated disease prevalence. As a result, the authors of the review, published in the *European Journal of Obstetrics & Gynecology and Reproductive Biology*, surmise that for population-level screening, a notable proportion of positive screening tests are likely false-positives.

“There are a significant number of false-positive screening tests we see clinically on a regular basis,” said primary investigator Jacques Balayla, MD, MPH, an Osler Fellow in the Department of Obstetrics and Gynecology at McGill University in Montreal, Canada. “The implications for patient counseling and resource allocation that a false-positive result may carry are consequential, yet rarely addressed in modern medicine.”

The authors searched Medline, Embase, Google Scholar, Scopus, Web of Science, Cochrane database, and PubMed to obtain the sensitivity and specificity estimates for 10 screening tests. They then used those estimates to calculate disease-specific prevalence thresholds and compare them with the actual estimates of disease prevalence.

The prevalence thresholds and average estimates of disease prevalence (shown in parentheses) were as follows:

- 31% (6%) for 50-g oral glucose tolerance test, 7% (0.2%) for noninvasive prenatal testing, 19.5% (0.2%) for combined first trimester screening, 18% (15% to 45%) for vaginal-rectal swab for group B streptococcus in pregnancy, 21% (0.2%) for cervical cytology (Papanicolaou) testing, 27% (0.2%) for human papillomavirus testing, 25% (12.5%) for mammography, 25% (12.5%) for manual breast exam, 6% to 13% (4.2% -4.7%) for cervical-vaginal swab testing for gonorrhea and chlamydia and 32% (10%) for testing serum anti-Müllerian hormone levels for polycystic ovary syndrome.

“We were surprised how poor the predictive value of most tests for ob/gyn actually is, particularly when carrying out universal screening programs,” Balayla said. “More disturbing perhaps is the significant discrepancy between the prevalence threshold — the prevalence level above which the screening test yields the most reliable results — and the actual prevalence of disease. Such a large difference may explain why we observe false-positive results at the bedside so frequently.”

A number of guidelines have begun to transition to a risk-based approach to the diagnosis and management of certain conditions in ob/gyn, Balayla said.

“In the meantime, having an understanding of Bayes theorem and the prevalence threshold can aid the clinical counseling of patients,” he said. He developed the prevalence threshold statistic for the study. “If an individual’s risk is below the threshold, such as amongst patients with no symptoms or risk factors, a patient’s results may not be reliable; therefore, counseling should reflect this fact to avoid undue stress, until diagnostic testing can be conducted,” he said.

For women whose risk lies above the threshold, “resource allocation and ease of access to the health care system should be prioritized,” Balayla said.

Developing new tests and screening technologies with sensitivity and specificity parameters that improve upon current standards is one strategy to reduce the rate of false-positives.

Balayla reports no relevant financial disclosures.

Bob Kronemyer is a freelance writer for *Contemporary OB/GYN*.

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2. Internal data

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Methotrexate in an Intrauterine Pregnancy—An Interesting Twist

What was to blame for this fetal demise?

The patient in this case was a 36-year-old G3P2002, who presented to the emergency department (ED) on May 30 with complaints of lower abdominal pain (8 out of 10) and prior vaginal spotting. A urine pregnancy test was positive, with a subsequent quantitative human chorionic gonadotropin (hCG) level of 209 mIU/mL. Her vital signs were stable, with hemoglobin and hematocrit (H/H) levels of 12.7 g/dL and 35.9%, respectively. An ultrasound revealed an endometrium that was 11 mm thick, with no visualized intrauterine gestational sac. There were no adnexal masses or fluid in the cul-de-sac. A right ovarian cyst measuring 1.5 cm was seen. The report noted no intrauterine gestational sac and the right ovarian cyst and gave a differential diagnosis of an early intrauterine pregnancy, ectopic pregnancy, or abortion. Correlation with hCG levels and a possible follow-up ultrasound were recommended.

The patient was seen in the same ED 5 days later, on June 4, with complaints of abdominal and right lower quadrant pain. She had an hCG level of 2,399 mIU/mL, with H/H levels of 12.6 g/dL and 36%. An ultrasound on this date revealed a small fluid collection within the endometrial cavity.

Three days later, on June 7, the patient was seen in the physician’s office. The note documented that the patient was seen in the ED for pain, with the last hCG level being 2,399 mIU/mL. The note also stated that a right ovarian cyst was seen, with no free fluid. An ultrasound in the physician’s office was interpreted as showing a double ring-like structure in the right adnexa less than 2 cm in diameter. The assessment was an ectopic pregnancy. The plan was to obtain an hCG level and administer methotrexate. Methotrexate was administered prior to the return of the hCG level.
hCG level, which was 6484 mIU/mL. A repeat hCG level reading 4 days later was 13,232 mIU/mL. The patient was seen in the physician’s office 7 days later, on June 14, with an ultrasound interpreted as showing normal ovaries bilaterally and a right 3-cm adnexal cyst. On June 17, 3 days later, the patient was seen in the ED with an hCG level of 10,409 mIU/mL and H/H levels of 12.8 g/dL and 35.9%. An abdominal ultrasound performed in the radiology department revealed an intrauterine pregnancy, with a crown rump length of 2.8 mm, with no cardiac activity identified. A resolving corpus luteum in the right ovary was noted. The patient was advised in the ED to follow up with her physician for obstetrical care and genetic counseling due to the previously administered methotrexate.

The patient was seen in the physician’s office on June 19, where a repeat ultrasound revealed a crown rump length of 4.7 mm, with no cardiac activity visualized. The diagnosis was a fetal demise, with a dropping hCG level. Subsequently, a dilation and curettage were performed.

The patient ultimately sued the physician for an incorrect diagnosis of an ectopic pregnancy and the negligent use of methotrexate in an intrauterine pregnancy. At the trial, the plaintiff’s witnesses testified that the ultrasound on June 7, although of poor quality, was sufficient to identify an intrauterine gestational sac. In addition, the right ovarian “double ring” structure, interpreted to be an ectopic pregnancy, was actually the previously visualized right ovarian cyst, most likely a corpus luteum. Had the physician reviewed the prior studies, this would

LEARNING POINTS

1. **Juries often find for the physician**
   The use of methotrexate in an early intrauterine pregnancy is a current and ongoing concern. In this case, despite the weight of the evidence, the jury rendered a defense verdict, highlighting the fact that juries often find for physicians in malpractice cases. This was a fortunate outcome. However, the defense had to address several issues that made the case more difficult to defend.

2. **Issues regarding hCG levels**
   In a stable patient, the physician is advised not to treat a suspected ectopic pregnancy with methotrexate based on a single hCG level, unless the ultrasound is definitive in the diagnosis. This patient had serial hCG levels that were rising appropriately. Although an appropriate increase in hCG level does not preclude the diagnosis of an ectopic pregnancy, it should cause the physician to reevaluate the diagnosis and treatment plan. For several reasons, the physician should know the hCG level results before administering methotrexate. An appropriate increase, as in this case, should prompt a reassessment of the patient. In addition, the hCG may be at such a level that, even in the case of a definite ectopic pregnancy, methotrexate may have a higher failure rate. Thus, surgical treatment may be more appropriate for the patient.

3. **Issues regarding the ultrasound studies**
   Physicians should review prior imaging studies and compare the findings with current studies. Electronic health records, which often allow remote access to staff physicians, have facilitated this. A review of prior ultrasound findings, including the images if available, is helpful in constructing a timeline and arriving at the appropriate diagnosis.

4. **Ultrasound quality**
   Ultrasounds were performed in the physician’s office with several different machines. The images were of relatively poor quality, likely related to the age of the ultrasound machines. Contemporary ultrasound machines should be used to acquire appropriate images. In addition, machines should undergo preventive maintenance on an annual basis to assure ongoing quality imaging.
have been obvious. Methotrexate was administered prior to the return of the hCG level, which increased appropriately to 6484 mIU/mL. The experts opined that this was a further breach of the standard of care. Had the physician waited for the hCG level to return, methotrexate administration would have been delayed until the clinical situation was clearer. Thus, the correct diagnosis of an intrauterine pregnancy would have been made. In addition, there was no need to intervene on June 7, as the patient was clinically stable. The plaintiff’s experts further testified that the administration of methotrexate likely led to the early embryonic demise.

The defense experts stated that the patient had 2 ultrasounds, on May 30 and June 4, which did not confirm an intrauterine pregnancy. Further, on June 4, when the hCG level was more than 2000 mIU/mL (actual level, 2399 mIU/mL), an ultrasound should have revealed an intrauterine pregnancy if it was developing normally. Otherwise, a nonviable intrauterine pregnancy or ectopic pregnancy must be considered. The defense further claimed that with the patient’s history of vaginal bleeding and continued abdominal pain, an ectopic pregnancy must be considered. The physician claimed that the ultrasound on June 7 was properly interpreted, with no visualized intrauterine gestational sac and a double ring–like structure in the right adnexa, consistent with an ectopic pregnancy. As such, the administration of methotrexate was appropriate.

After 4 hours of deliberation, the jury returned a defense verdict.

The ultrasound images and interpretation did not meet applicable guidelines. Guidelines from the American Institute of Ultrasound in Medicine for appropriate imaging for both obstetrics and gynecology are available at www.aium.org/resources/guidelines.aspx. Documentation guidelines are also available at www.aium.org/resources/guidelines/documentation.pdf. If one adheres to such guidelines, a case is more defensible.

The right ovarian “double ring” structure, interpreted to be an ectopic pregnancy, was actually the previously visualized right ovarian cyst, most likely a corpus luteum.

Had the physician reviewed the prior studies, this would have been obvious.

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Although it’s predominantly administered to children and adolescents, the 9-valent human papillomavirus (9vHPV) vaccine is recommended for people aged 11 to 26 years and was recently expanded to be administered to women up to age 45 years. This age range means that it’s possible for a woman to be given the vaccine during pregnancy and research on the impact of an inadvertent 9vHPV vaccine exposure in pregnancy is limited. A study in JAMA Network Open offers some much needed information on whether exposure is linked to adverse birth outcomes.1

The investigators used data from 7 health systems in the Vaccine Safety Datalink, which included pregnancies among girls and women who were aged 12 to 28 years that ended between October 2015 and November 2018. They included all singleton pregnancies that ended in a live birth, stillbirth, or spontaneous abortion. Vaccine exposures were distal (9vHPV or 4-valent HPV [4vHPV] vaccine administered from 22 to 16 weeks before last menstrual period [LMP]), peripregnancy (9vHPV vaccine administered from 42 days before LMP until LMP), and during pregnancy (9vHPV vaccine administered from LMP to 19 completed weeks’ gestation).

The study included 1493 pregnancies; in the cohort, there were 445 9vHPV vaccine exposures during pregnancy, 496 peripregnancy 9vHPV vaccine exposures; and 552 4vHPV or 9vHPV distal vaccine exposures. The investigators found that administering the 9vHPV vaccine during pregnancy was not linked to an increased risk of spontaneous abortion (HR, 1.12; 95% CI, 0.66-1.93) compared with a distal vaccine exposure. Similar findings were found with peripregnancy 9vHPV vaccine exposures (relative risk [RR], 0.72; 95% CI, 0.42-1.24). When looking at the live births (n = 1409), exposure to 9vHPV vaccine during pregnancy was not linked to preterm birth (RR, 0.73; 95% CI, 0.44-1.20) or small for gestational age birth (RR, 1.31; 95% CI, 0.78-2.20) and similar results were seen in peripregnancy exposures among small for gestational age birth (RR, 1.10; 95% CI, 0.65-1.88) and preterm births (RR, 0.72; 95% CI, 0.45-1.17). Across all exposure groups, birth defects were rare and happened in about 1% of live births.

The investigators concluded that exposure to the 9vHPV vaccine either during or around pregnancy is not a common occurrence and that when exposure does happen, is not linked to either spontaneous abortions or select adverse birth outcomes. Clinicians should use the findings to advise how they discuss inadvertent 9vHPV vaccine exposures.

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