MDEDGE.COM/OBGMANAGEMENT | VOL 30, NO 1 | JANUARY 2018

OBG MANAGEMENT

30th ANNIVERSARY

30 years in service to you
Robert L. Barbieri, MD

Mannitol's usefulness in evaluating ureteral patency

8 common questions about newborn circumcision
Henry Lerner, MD

Ovarian cancer

An expert panel provides guidance on risk-based assessment and management

In collaboration with ACOG
Value-based payment: What does it mean, and how can you get ahead?

Does maternal sleep position affect risk of stillbirth?
Only at mdedge.com/obgmanagement

Managing opioid use during pregnancy
p. 11

Follow us on Facebook and Twitter

NOW AVAILABLE

DEMONSTRATED TO SIGNIFICANTLY DECREASE MODERATE TO SEVERE **DYSPAREUNIA DUE TO MENOPAUSE**[1]

Not actual size.

NON-ESTROGEN BASED, CONVERTS TO ESTROGENS AND ANDROGENS*

Prasterone is a precursor that is locally converted to estrogens and androgens with minimal systemic exposure.[1,2] *The mechanism of action of INTRAROSA is not fully established[1]

ONCE-DAILY TREATMENT

Individually wrapped vaginal inserts with disposable applicators[1]

NO FDA BOXED WARNING[2]

No restrictions on duration of use[2,3]

To order samples and learn more about INTRAROSA, including our patient savings program, visit IntrarosaHCP.com

Indication

INTRAROSA is a steroid indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

Important Safety Information

INTRAROSA is contraindicated in women with undiagnosed abnormal genital bleeding. Estrogen is a metabolite of prasterone. Use of exogenous estrogen is contraindicated in women with a known or suspected history of breast cancer. INTRAROSA has not been studied in women with a history of breast cancer.

In four 12-week randomized, placebo-controlled clinical trials, the most common adverse reaction with an incidence ≥2 percent was vaginal discharge. In one 52-week open-label clinical trial, the most common adverse reactions with an incidence ≥2 percent were vaginal discharge and abnormal Pap smear.

Brief Summary: Consult full Prescribing Information for complete product information.

CONTRAINDICATIONS

Undiagnosed abnormal genital bleeding: Any postmenopausal woman with undiagnosed, persistent or recurring genital bleeding should be evaluated to determine the cause of the bleeding before consideration of treatment with INTRAROSA.

WARNINGS AND PRECAUTIONS Current or Past History of Breast Cancer

Estrogen is a metabolite of prasterone. Use of exogenous estrogen is contraindicated in women with a known or suspected history of breast cancer. INTRAROSA has not been studied in women with a history of breast cancer.

ADVERSE REACTIONS Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In four (4) placebo-controlled, 12-week clinical trials [91% - White Caucasian non-Hispanic women, 7% - Black or African American women, and 2% - "Other" women, average age 58.8 years of age (range 40 to 80 years of age)], vaginal discharge is the most frequently reported treatment-emergent adverse reaction in the INTRAROSA treatment group with an incidence of ≥2 percent and greater than reported in the placebo treatment group. There were 38 cases in 665 participating postmenopausal women (5.71 percent) in the INTRAROSA treatment group compared to 17 cases in 464 participating postmenopausal women (3.66 percent) in the placebo treatment group.

In a 52-week non-comparative clinical trial [92% - White Caucasian non-Hispanic women, 6% - Black or African American women, and 2% - "Other" women, average age 57.9 years of age (range 43 to 75 years of age)], vaginal discharge and abnormal Pap smear at 52 weeks were the most frequently reported treatment-emergent adverse reactions in women receiving INTRAROSA with an incidence of ≥2 percent. There were 74 cases of vaginal discharge (14.2 percent) and 11 cases of abnormal Pap smear (2.1 percent) in 521 participating postmenopausal women. The eleven (11) cases of abnormal Pap smear at 52 weeks include one (1) case of low-grade squamous intraepithelial lesion (LSIL), and ten (10) cases of atypical squamous cells of undetermined significance (ASCUS).

References: 1. Intrarosa [package insert]. Waltham, MA: AMAG Pharmaceuticals, Inc.; 2017. **2.** Archer DF, Labrie F, Bouchard C, et al; VVA Prasterone Group. *Menopause*. 2015;22(9):950-963. **3.** Labrie F, Archer DF, Koltun W, et al; VVA Prasterone Research Group. *Menopause*. 2016;23(3):243-256.

Intrarosa™ Prasterone VAGINAL INSERTS

amag PHARMACEUTICALS

#1 IN READERSHIP!*

OBG MANAGEMENT
mdedge.com/obgmanagement

Enhancing the quality of women's health care and the professional development of ObGyns and all women's health care clinicians

*Source: Kantar Media, Medical Surgical Study December 2017, Obstetrics/Gynecology Combined Office & Hospital Readers.

JANUARY 2018 | VOL 30, NO 1

OBG MANAGEMENT

SS7 Roundtable

Optimal risk assessment and management of the potential ovarian cancer case

Expert guidance on individualizing an assessment approach for the patient at risk for ovarian cancer

EXPERT PANEL FEATURING NEAL M. LONKY, MD, MPH, MODERATOR; WITH LESLIE M. RANDALL, MD; DEVANSU TEWARI, MD; AND JASON D. WRIGHT, MD

11 Update

Obstetrics

JAIMEY M. PAULI, MD

A maternal-fetal medicine physician tackles 3 high-priority obstetric topics: managing opioid use disorders in pregnant women, protocols for postpartum hemorrhage, and new carrier screening recommendations

17 Value-based payment: What does it mean, and how can ObGyns get out ahead?

ELIZABETH WIEAND, MSPH; DAVID C. LAGREW JR, MD

SS1 SPECIAL SECTION

Patient-centered risk assessment for ovarian cancer: Individualizing your approach

NEAL M. LONKY, MD, MPH; JEANINE M. GENKINGER, PHD, MHS; LESLIE M. RANDALL, MD; DEVANSU TEWARI, MD; AND JASON D. WRIGHT, MD

Follow us on Facebook and on Twitter @obgmanagement

27 8 common questions about newborn circumcision

HENRY MICHAEL LERNER, MD

38 Examining the Evidence

Is mannitol a good alternative agent for evaluating ureteral patency after gynecologic surgery?

CHERYL B. IGLESIA, MD

5 EDITORIAL

30 years in service to you, our community of women's health clinicians

ROBERT L. BARBIERI, MD

10 COMMENT & CONTROVERSY

Questions value of ACOG/SMFM guidelines

32 MEDICAL VERDICTS

Unnecessary laparotomy: $625,000 award

34 PRODUCT UPDATE

MyoSure MANUAL; Rivanna's Accuro 3D; PeriGen; Instavit

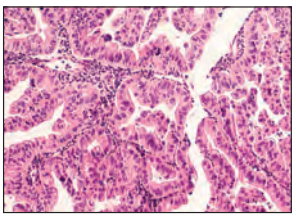
35 OBG MARKETPLACE

The official job board of OBG MANAGEMENT

36 INDEX OF ADVERTISERS

See what's ON THE WEB! page 4

APM Framework
17



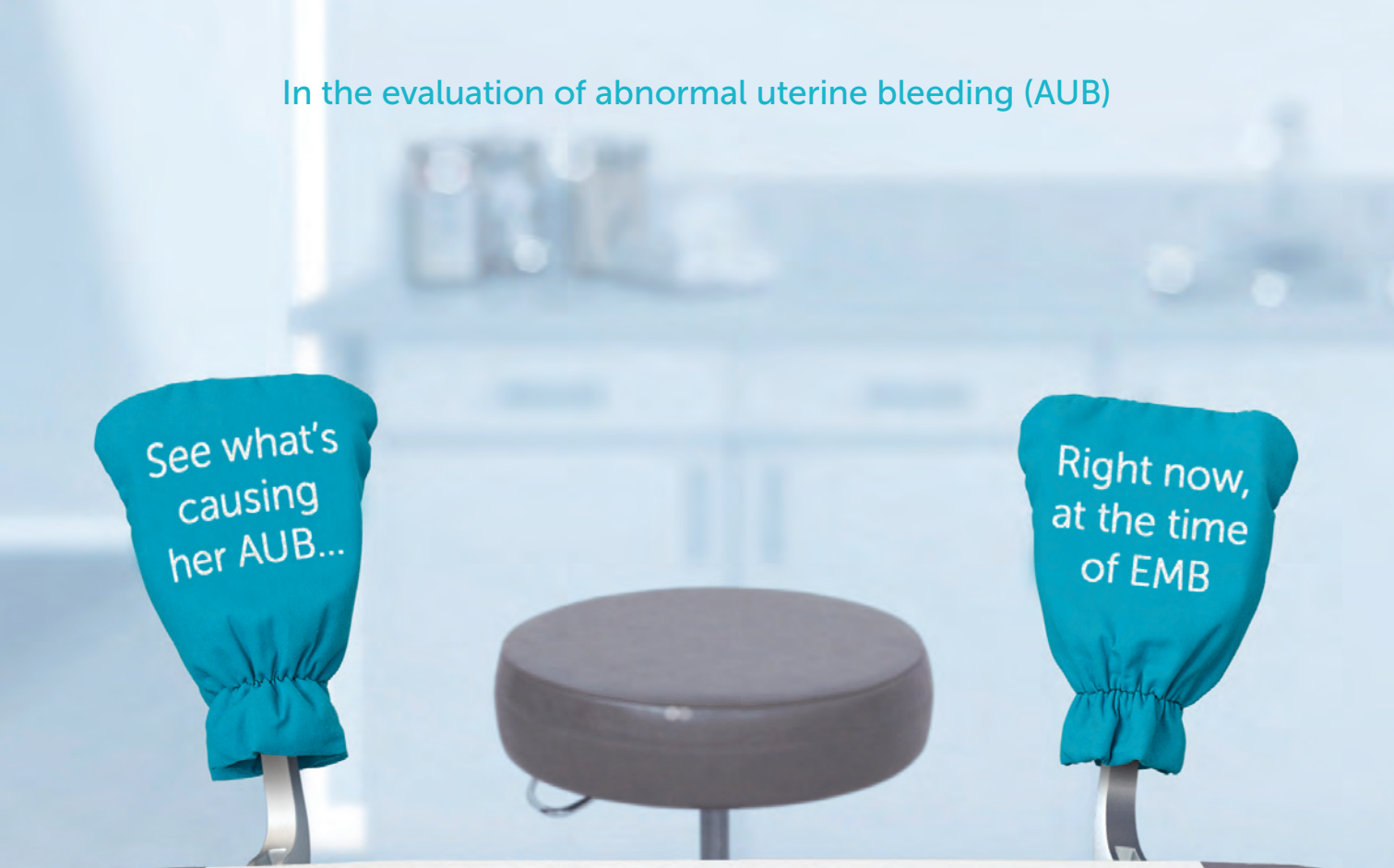
Ovarian cancer
SS1

FAST TRACK **FAST TRACK** is a system to enable you as a reader to move quickly through each issue of **OBG MANAGEMENT**, identifying articles or sections of articles to read in depth.

OBG MANAGEMENT (ISSN 1044-307x) is published monthly by Frontline Medical Communications Inc, 7 Century Drive, Suite 302, Parsippany, New Jersey 07054. The contents of this publication may not be reproduced in whole or part without the written consent of the owner. 2018 subscription rates (includes full-text access to mdedge.com/obgmanagement): United States: $158.00; elsewhere: $205.00. Single copy orders must be prepaid: United States: $27.00; Canada/Mexico: $33.00; other: $38.00. Periodicals postage paid at Parsippany, NJ, and additional mailing offices. Orders and Claims: OBG Management Subscription Service, 151 Fairchild Avenue, Suite 2, Plainview, New York 11803-1709, phone (800) 480-4851, or e-mail quadrantobgm@emscirc.com. POSTMASTER: Please send address changes to OBG Management Subscription Service, 151 Fairchild Avenue, Suite 2, Plainview, New York 11803-1709.

COVER IMAGE: KIMBERLY MARTENS

In the evaluation of abnormal uterine bleeding (AUB)



Make direct visualization with Endosee® part of your first step in diagnosing AUB

- Gives you point-of-care visualization in just seconds—at a patient's first visit, or any time endometrial biopsy is considered
- Allows you to identify uterine focal pathology more accurately than endometrial biopsy alone,[1] transvaginal ultrasound, or saline infusion sonohysterography[2]
- Handheld, portable, cordless system is quick to set up in any room at any time. Average procedure time is less than 3 minutes.

www.endosee.com
800.243.2974
203.601.5200

CooperSurgical

References: 1. Garcia, A. *OBG Manage.* 2013;25:44-48.
2. Grimbizis GF, Tsolakidis D, Mikos T, et al. *Fertil Steril.* 2010;94:2721-2725.

endosee®
office hysteroscopy

ON THE WEB
at obgmanagement.com

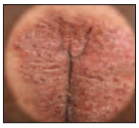
WEB EXCLUSIVES

Are these the right metrics to measure episiotomy rates?
MYRON R. KANOFSKY, MD

Contraceptive considerations for women with headache and migraine
RONALD T. BURKMAN, MD

Visit us online for daily news

VIDEO LIBRARY



Common skin diseases of the vulva: Red down there
NANCY FANG, MD; TYLER M. MUFFLY, MD; AND MISHA MILLER, MD

Brought to you by the Society of Gynecologic Surgeons
See QR code on page 7

Does maternal sleep position affect risk of stillbirth?
JOHN T. REPKE, MD

How do you assess a patient for a bisphosphonate drug holiday?
MICHAEL MCCLUNG, MD

Watch these, and more, expert surgical technique and commentary videos in the EXPLORE: Multimedia section online

AUDIO LIBRARY

What to do about the problem of non-FDA approved compounded bioidentical hormones
CYNTHIA STUENKEL, MD

Listen to this, and more, audio interviews with the experts in the EXPLORE: Multimedia section online

FRONTLINE MEDICAL COMMUNICATIONS
7 Century Drive, Suite 302
Parsippany, NJ 07054-4609
www.frontlinemedcom.com

30 years in service to you, our community of women's health clinicians

It is all about your professional development and well-being, as well as your patients' health and well-being

Robert L. Barbieri, MD
Editor in Chief, OBG MANAGEMENT
Chair, Obstetrics and Gynecology
Brigham and Women's Hospital, Boston, Massachuetts
Kate Macy Ladd Professor of Obstetrics,
Gynecology and Reproductive Biology
Harvard Medical School, Boston

The mission of OBG MANAGEMENT is to enhance the quality of women's health care and the professional development of obstetrician-gynecologists and all women's health care clinicians. As we celebrate the beginning of our 30th anniversary year, we recommit to our mission by providing the highest quality of health information through both print and electronic portals.

OBG MANAGEMENT: Print and electronic portals for knowledge acquisition

Experienced clinicians acquire new knowledge and refresh established concepts through discussions with trusted colleagues and by reading journals and books that contain information relevant to their practice. A continuing trend in professional development is the accelerating transition from a reliance on print media (print journals and books) to electronic information delivery. Many clinicians continue to enjoy reading medical journals and magazines. ObGyns are no different; 96% report reading the print edition of medical journals.[1] At OBG MANAGEMENT we are committed to continue to mail you a monthly copy of our journal.

However, in the time-pressured setting of office- and hospital-based patient care, critical information is now frequently accessed through an electronic portal that is web based and focused on immediately answering a high priority question necessary for optimal patient care. OBG MANAGEMENT provides our community with rapid access to electronic versions of the journal and all previously published editorial material. Many web exclusives are found online as well, including audio and video techniques and commentary. The OBG MANAGEMENT website has a powerful search engine, which permits our readers to rapidly and conveniently access all previously published articles. In addition, our community members that have provided us with electronic contact information receive regular electronic communications about recently published literature (Clinical Edge), highly read articles and topical alerts from the journal, and MD-IQ quizzes to help review recent research and guidelines in an interactive medium.

The information base needed to practice medicine is massive and continues to grow rapidly. No single print textbook or journal can cover this vast information base. Libraries of print material are cumbersome to use and

Thanks to our distinguished Editorial Board

Board members not only contribute guidance and leadership but they also contribute their clinical and practice management expertise through articles, columns, commentary, and techniques throughout the publication year.

Arnold P. Advincula, MD
2017 Update on minimally invasive gynecologic surgery

Andrew M. Kaunitz, MD
Did long-term follow-up of WHI participants reveal any mortality increase among women who received HT?

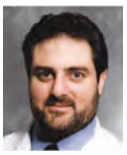
John T. Repke, MD
What is the optimal opioid prescription length after women's health surgical procedures?

Linda D. Bradley, MD
The importance of weight management and exercise—Practical advice for your patients

David G. Mutch, MD
Does laparoscopic versus open abdominal surgery for stage I endometrial cancer affect oncologic outcomes?

Joseph S. Sanfilippo, MD, MBA
Reengineering your office to be perfect for your patients

Steven R. Goldstein, MD
2017 Update on bone health



Errol R. Norwitz, MD, PhD, MBA
STOP using instruments to assist with delivery of the head at cesarean

James A. Simon, MD
Flibanserin is poised for FDA approval. But why this drug? And why now?

Cheryl B. Iglesia, MD
Is mannitol a good alternative agent for evaluating ureteral patency after gynecologic surgery?

JoAnn V. Pinkerton, MD
2017 Update on menopause

ordinarily not accessible at the site of patient care. Electronic portals are the only means of providing immediate access to all medical knowledge. Electronic technology enables the aggregation of vast amounts of information in a database that is rapidly accessible from anywhere, and new search technology is making it easier to quickly locate the information you need.

The next frontier in medical information exchange is the application of artificial intelligence to cull "answers" from the vast aggregation of data. By combining all available medical information and artificial intelligence processes, in the near future, clinicians will be able to instantaneously get an answer to a question they have about how to care for a specific patient. A decade ago, when a question was entered into an Internet search engine, the response was typically a list of potential websites where the answer might be located. In the past few years, with the integration of huge databases and artificial intelligence, some advanced search engines now provide a specific answer to a question, followed by a list of relevant websites. For example, if you enter this question: "What countries have the greatest number of people?" into the Google search tool, in less than 1 second a direct answer is provided: "China has the world's largest population (1.4 billion), followed by India (1.3 billion). The next most populous nations—the United States, Indonesia, Brazil and Pakistan—combined have less than 1 billion people." The next step in medical information communication will be the deployment of artificial intelligence systems that can directly answer a query from a clinician about a specific patient.

Our distinguished Editorial Board and authors—the heart and mind of OBG Management

The editorial team at OBG MANAGEMENT is proud to work with

CONTINUED ON PAGE 8

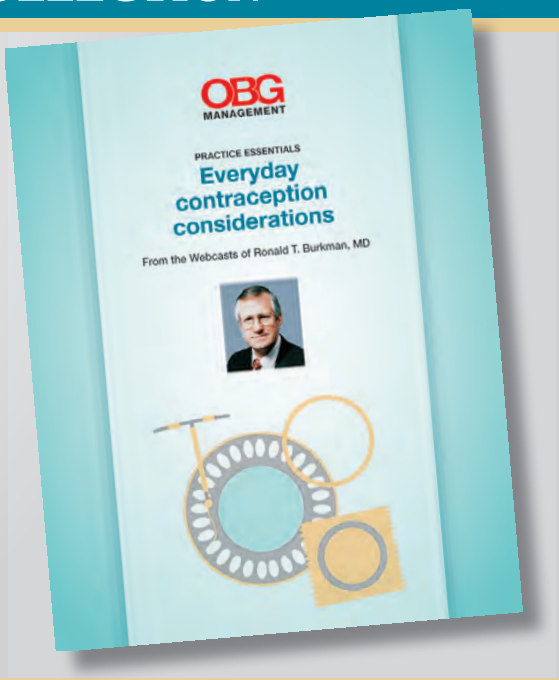
EXCLUSIVE MULTIMEDIA COLLECTION

PRACTICE ESSENTIALS

Everyday contraception considerations

Dr. Ronald T. Burkman provides insights on using the CDC's tools to solve complex contraception cases, obesity and contraceptive efficacy, the risk of venous thromboembolism with hormonal contraception, considerations for women with headache and migraine, choosing emergency contraception for your patient, and more. Use this e-collection of articles and webcasts as a resource for your practice.

Find this exclusive collection only at
mdedge.com/obgmanagement



SGS video series!

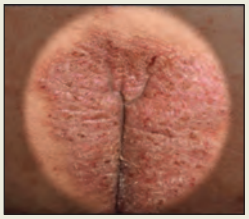
SGS SOCIETY OF GYNECOLOGIC SURGEONS

View this new video at
obgmanagement.com
Brought to you by the Society of Gynecologic Surgeons

OBG MANAGEMENT

Common skin diseases of the vulva: Red down there

NANCY FANG, MD; TYLER M. MUFFLY, MD; AND MISHA MILLER, MD



In this video, the authors review normal vulvar anatomy and describe the diagnosis and management of common benign dermatologic conditions of the vulva, including lichen simplex chronicus, lichen sclerosus, and lichen planus. They discuss the comorbidities of each of these dermatoses and review techniques for vulvar biopsy.

Copyright Society of Gynecologic Surgeons

◀ Use this QR code* to view the video at **mdedge.com/obgmanagement**

*Free QR readers are available for smartphones at the iPhone App Store, Android Market, and BlackBerry App World.

CONTINUED FROM PAGE 6

The gratitude exercise

Showing more gratitude to those who have been most meaningful in your life may increase your wellness. Try the gratitude exercise outlined below.

To prepare for the exercise you will need about 15 minutes of uninterrupted time, a quiet room, and a method for recording your thoughts (pen/paper, electronic word processor, voice recorder).

Sit quietly and close your eyes. Spend 5 minutes thinking about the people in your life whose contributions have had the greatest positive impact on your development. Think deeply about the importance of their role in your life. Select one of those important people.

Open your eyes and spend 10 minutes expressing in writing your thoughts and feelings about that person. Once you have completed expressing yourself in writing, commit to reading your words, verbatim, to the person within the following 48 hours. This could be done by voice communication, video conferencing, or in-person.

View the "Gratitude Experiment" on YouTube to see a video summary of reactions to participating in a gratitude experiment (https://www.youtube.com/watch?v=oHv6vTKD6lg).

the distinguished medical leaders who write our articles and serve on our Editorial Board. The guidance we receive from our Board and the expert editorial material generated by our authors is critical to advancing the quality of OBG MANAGEMENT. Our Board members and authors care deeply about improving women's health and closing gaps between current and optimal practice. Our Board members and authors are truly expert clinicians with vast experience. Our readers can have great confidence in their recommendations.

Improving clinician wellness and resilience and reducing burnout

Clinicians throughout the world are reporting decreased levels of professional fulfillment and increased levels of burnout.[2–4] This epidemic is likely caused by many factors, including the deployment of poorly designed electronic health systems, the administrative guidance for clinicians to work faster with fewer support staff, increasing administrative and secretarial burden on clinicians, and institutional constraints on clinician autonomy. Many of these problems only can be addressed at the level of the health system, but some are in the control of individual clinicians.

In the upcoming years, OBG MANAGEMENT will prioritize deepening the knowledge about the factors that support clinician wellness and share approaches that may help you to improve your wellness and resilience and reduce your experience of burnout. Recent research reports that increasing your focus on showing gratitude to other important people in your life will enhance your wellness. In a study completed in a health care setting, 102 clinicians were randomly assigned to 1 of 3 groups: 1) write about gratitude and work, 2) write about hassles and work, or 3) do not write about work. Those assigned to the 2 writing groups were instructed to write on their topic twice weekly for 4 weeks. At the end of the study the clinicians assigned to the gratitude writing assignment reported less stress and fewer depressive symptoms than the clinicians assigned to the other 2 groups.[5] The investigators concluded that among clinicians a structured exercise to focus thoughts and feelings on expressions of gratitude is an effective approach to reduce stress and depressive symptoms. I recommend that you complete "the gratitude exercise" (see box on this page).

The future of obstetrics and gynecology is bright

Medical students are electing to pursue a career in obstetrics and gynecology in record numbers. The students entering the field and the residents currently in training are superbly prepared and have demonstrated their commitment to advancing reproductive health by experiences in advocacy, research, and community service. We need to ensure that these super-star young physicians are able to have a 40-year career that is productive and fulfilling. ●

RBARBIERI@FRONTLINEMEDCOM.COM

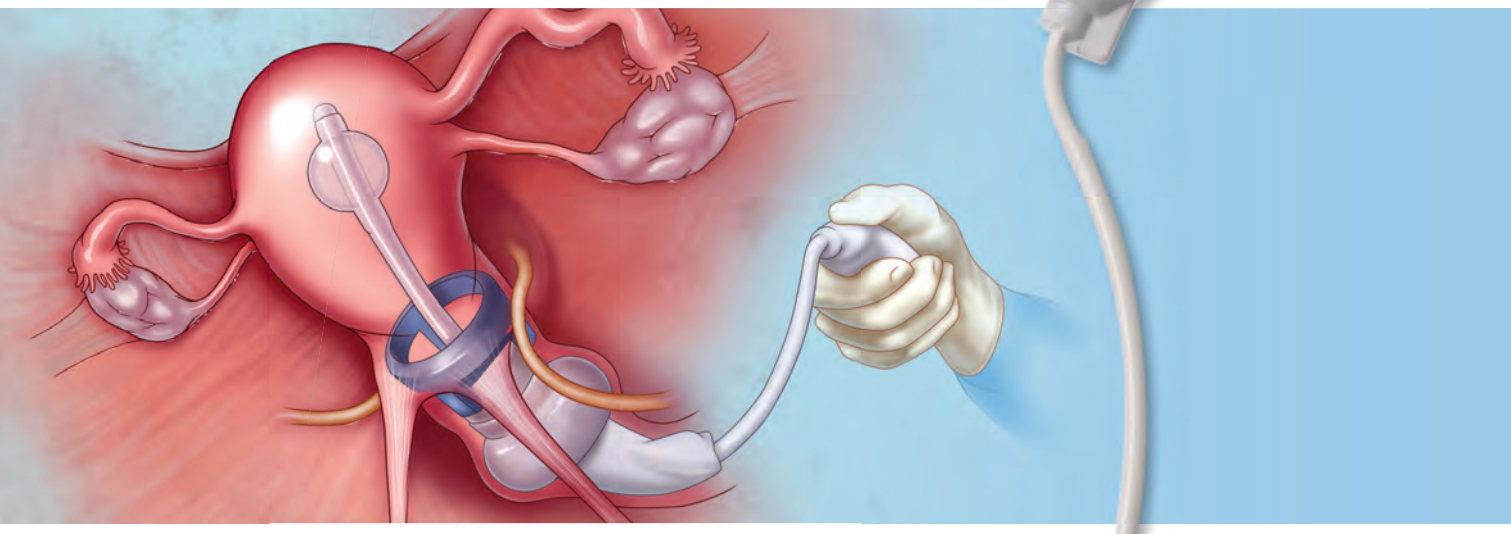
Dr. Barbieri reports no financial relationships relevant to this article.

References

1. Kantar Media. Sources and Interactions. Medical/Surgical Edition. Kantar Media; New York, New York; 2017.
2. Dyrbye LN, West CP, Satele D, et al. Burnout among U.S. medical students, residents and early career physicians relative to the general U.S. population. Acad Med. 2014;89(3):443–451.
3. Vandenbroeck S, Van Gerven E, De Witte H, Vanhaecht K, Godderis L. Burnout in Belgian physicians and nurses. Occup Med (London). 2017;67(7):546–554.
4. Siu C, Yuen SK, Cheung A. Burnout among public doctors in Hong Kong: cross-sectional survey. Hong Kong Med J. 2012;18(3):186–192.
5. Cheng ST, Tsui PK, Lam JH. Improving mental health in health care practitioners: randomized controlled trial of a gratitude intervention. J Consult Clin Psychol. 2015;83(1):177–186.

The Advincula Delineator™

Exceptional Strength. Single-use Convenience.



The Advincula Delineator is engineered to combine exceptional strength and safety with the ease and convenience of a disposable uterine manipulator. The shaft and Koh-Efficient® colpotomy system are fully integrated, providing unprecedented access, visualization and safety during TLH, LSH and LAVH procedures.

- Rigid colpotomy cup clearly delineates vaginal fornices with proper cephalad pressure.
- Best in class pneumo occluder balloon is built into the Koh-Efficient.
- Exceptional control and strength.
- No assembly required.

Advincula
DELINEATOR™
with Koh-Efficient® Technology

CooperSurgical

To place an order, or to learn more, contact your CooperSurgical representative, visit CooperSurgical.com, or call 800.243.2974 or 203.601.5200.

82612 Rev. 9/15

COMMENT & CONTROVERSY

FOR THE MANAGEMENT OF LABOR, PATIENCE IS A VIRTUE
ROBERT L. BARBIERI, MD
(EDITORIAL; AUGUST 2017)

Questions value of ACOG/ SMFM guidelines

The labor management guidelines recommended by the American College of Obstetricians and Gynecologists (ACOG) and the Society of Maternal-Fetal Medicine (SMFM) are terrible. Now retired, I trained in 1959–1963. In my career as an obstetrician, my primary cesarean delivery rate was 10% or less, and part of that was external pressure from people who did not know how to deliver a baby. Persistent occiput posterior position is a problem of inadequate flexion of the head, often due to ineffective contractions earlier. In such a situation, "pit" early! Rotate the head if you must, and teach residents how, please. The guidelines do not discuss the exhausted mother who goes home after a long labor or hours of pushing. I have interviewed new obstetricians in my community as early as 1980 who did not know what deep transverse arrest was. There, I am done voicing my disgust with obstetrics as it is practiced today.

James Honig, MD
Merritt Island, Florida

Managing difficult labor scenarios

I concur with Dr. Barbieri's views on labor management that watchful waiting and giving the patient adequate time to progress naturally is the key to increase the chances of vaginal delivery. After all, labor is a physiologic process and should progress naturally. Having said that, I would like to know Dr. Barbieri's views on handling certain circumstances in which patients these days land in the labor room, including 1) postdated

DECEMBER 2017

pregnancy with reduced fetal movements and not in labor; 2) full-term/ postterm pregnancy with free-floating head and poor Bishop score; 3) full-term pregnancy with niggling pains for more than 1 week; and many such conditions that place you in the dilemma of whether to induce, knowing that chances of failure are high.

Manju Hotchandani, MD
New Delhi, India

Midwives always use patience to guide labor

As a Certified Nurse-Midwife since 1985 (now retired), "patience" in managing labor has always been my guide, as it has been for my midwifery colleagues. This is another example of ACOG finally acknowledging the truths we women have always known, without crediting the wisdom of midwives over the centuries. Lamaze International's 6 Healthy Birth Practices also must have been their guide. "Evolving concepts of normal labor progress," as though this was new information, would be humorous if it were not so frustrating!

Marsha Kelly, CNM
Charlotte, North Carolina

Dr. Barbieri responds

The readers of OBG MANAGEMENT have vast clinical experience, and we can all learn from their insights and guidance. On behalf of all our readers, I thank Drs. Honig and Hotchandani and Ms. Kelly for taking the time to share their expert advice.

Every clinician involved in the birth process is deeply committed to a safe delivery for both mother and baby. Clinicians guide the birth process based on the unique characteristics and needs of each woman. Dr. Honig advocates for the active management of the labor process, while Ms. Kelly advocates for less intervention. Both approaches to labor management may be optimal depending on the unique clinical needs of each woman. Dr. Hotchandani inquires about managing common obstetric presentations. In my practice, induction is recommended for all women postterm who report consistently reduced fetal movement with the goal of reducing the risk of sudden intrauterine fetal demise. For healthy women at term with painful contractions and reassuring fetal status, but no cervical change, we support and counsel the patient and offer therapeutic rest with morphine. For women at term with a floating head and poor Bishop score, we would not intervene, until 41 weeks' gestation when we would initiate gentle cervical ripening with mechanical or pharmacologic treatment.

WE WANT TO HEAR FROM YOU!

›› Contact us at **rbarbieri@frontlinemedcom.com**

Please include the city and state in which you practice.

Jaimey M. Pauli, MD
Dr. Pauli is Associate Professor and Attending Perinatologist, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Penn State Health, Milton S. Hershey Medical Center, Hershey, Pennsylvania.

The author reports no financial relationships relevant to this article.

A maternal-fetal medicine physician tackles 3 high-priority obstetric topics: managing opioid use disorders in pregnant women, protocols for postpartum hemorrhage, and new carrier screening recommendations

The past year brought new information and guidance from the American College of Obstetricians and Gynecologists (ACOG) on many relevant obstetric topics, making it difficult to choose just a few for this Update. Opioid use in pregnancy was an obvious choice given the national media attention and the potential opportunity for intervention in pregnancy for both the mother and the fetus/newborn. Postpartum hemorrhage, an "oldie but goodie," was chosen for several reasons: It got a new definition, a new focus on multidisciplinary care, and an exciting novel tool for the treatment toolbox. Finally, given the rapidly changing technology, new screening recommendations, and the complexity of counseling, carrier screening was chosen as a genetic hot topic for this year.

IN THIS ARTICLE

Opioid screening
page 12

PPH action plan
page 13

Carrier screening guidance
page 14

Opioids, obstetrics, and opportunities

Reddy UM, Davis JM, Ren Z, Greene MF; Opioid Use in Pregnancy, Neonatal Abstinence Syndrome, and Childhood Outcomes Workshop Invited Speakers. Opioid use in pregnancy, neonatal abstinence syndrome, and childhood outcomes: Executive summary of a joint workshop. Obstet Gynecol. 2017;130(1):10–28.

ACOG Committee on Obstetric Practice. ACOG committee opinion No. 711: Opioid use and opioid use disorder in pregnancy. Obstet Gynecol. 2017;130(2):e81–e94.

The term "opioid epidemic" is omnipresent in both the lay media and the medical literature. In the past decade, the United States has had a huge increase in the number of opioid prescriptions, the rate of admissions and deaths due to prescription opioid misuse and abuse, and an increased rate of heroin use attributed to prior prescription opioid use.

Obstetrics is unique in that opioid use and abuse disorders affect 2 patients simultaneously (the mother and fetus), and the treatment options are somewhat at odds in that they need to balance a stable maternal status and intrauterine environment with the risk of neonatal abstinence syndrome (NAS). Additionally, pregnancy is an opportunity for a woman with opioid use disorder to have access to medical care (possibly for the first time) leading to the diagnosis and treatment of her disease. As the clinicians on the front line, obstetricians therefore require education and guidance on best practice for management of opioid use in pregnancy.

In 2017, Reddy and colleagues, as part of

a joint workshop on opioid use in pregnancy, and a committee opinion from ACOG provided the following recommendations.

Screening

Universally screen for substance use, starting at the first prenatal visit; this is recommended over risk factor–based screening.

Use a validated screening tool. A tool such as a questionnaire is recommended as the first-line screening test (for example, the 4Ps screen, the National Institute on Drug Abuse Quick Screen, and the CRAFFT Screening Interview).

Do not universally screen urine and hair for drugs. This type of screening has many limitations, such as the limited number of substances tested, false-positive results, and inaccurate determination of the frequency or timing of drug use. Information regarding the consequences of the test must be provided, and patient consent must be obtained prior to performing the test.

FAST TRACK

Medication-assisted treatment prevents withdrawal symptoms and cravings, decreases relapse risk, improves compliance, and leads to better obstetric outcomes

Treatment

Use medication-assisted treatment with buprenorphine or methadone, which is preferred to medically supervised withdrawal. Medication-assisted treatment prevents withdrawal symptoms and cravings, decreases the risk of relapse, improves compliance with prenatal care and addiction treatment programs, and leads to better obstetric outcomes (higher birth weight, lower rate of preterm birth, lower perinatal mortality).

Know that buprenorphine has several advantages over methadone, including the convenience of an outpatient prescription, a lower risk of overdose, and improved neonatal outcomes (higher birth weight, lower doses of morphine to treat NAS, shorter treatment duration).

Prioritize methadone as the preferred option for pregnant women who are already receiving methadone treatment (changing to buprenorphine may precipitate withdrawal), those with a long-standing history of or multi-substance abuse, and those who have failed other treatment programs.

Prenatal care

Screen for comorbid conditions such as sexually transmitted infections, other medications or substance use, social conditions, and mental health disorders.

Perform ultrasonography serially to monitor fetal growth because of the increased risk of fetal growth restriction.

Consult with anesthesiology for pain control recommendations for labor and delivery and with neonatalogy/pediatrics for NAS counseling.

Intrapartum/postpartum care

Recognize heightened pain. Women with opioid use disorder have increased sensitivity to painful stimuli.

Continue the maintenance dose of methadone or buprenorphine throughout hospitalization, with short-acting opioids added for a brief period for postoperative pain.

Prioritize regional anesthesia for pain control in labor or for cesarean delivery.

Consider alternative therapies such as regional blocks, nonopioid medications (nonsteroidal anti-inflammatory drugs, acetaminophen), or relaxation/mindfulness training.

Avoid mixed antagonist and agonist narcotics (butorphanol, nalbuphine, pentazocine) as they may cause acute withdrawal.

Encourage breastfeeding to decrease the severity of NAS and maternal stress and increase maternal-child bonding and maternal confidence.

Offer contraceptive counseling and services immediately postpartum in the hospital, with strong consideration for long-acting reversible contraception.

Opioid prescribing practices

Opioids are prescribed in excess post–cesarean delivery. Several recent studies have demonstrated that most women are prescribed opioids post–cesarean delivery in excess of the amount they use (median 30–40 tablets prescribed, median 20 tablets used).[1,2] The leftover opioid medication

usually is not discarded and therefore is at risk for diversion or misuse. A small subset of patients will use all the opioids prescribed and feel as though they have not received enough medication.

Prescribe post–cesarean delivery opioids more appropriately by considering individual inpatient opioid requirements or a shared decision-making model.[3]

Prioritize acetaminophen and ibuprofen during breastfeeding. In a recent editorial in OBG Management, Robert L. Barbieri, MD, recommended that whenever possible, acetaminophen and ibuprofen should be the first-line treatment for breastfeeding women, and narcotics that are metabolized by CYP2D6 should be avoided to reduce the risk to the newborn.[4]

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Universal screening for substance use should be performed in all pregnant women, and clinicians should offer medication-assisted treatment in conjunction with prenatal care and other supportive services as the standard therapy for opioid use disorder. More selective, patient-specific opioid prescribing practices should be applied in the obstetric population.

Postpartum hemorrhage: New definitions and new strategies for stemming the flow

ACOG Committee on Practice Bulletins—Obstetrics. ACOG practice bulletin No. 183: Postpartum hemorrhage. Obstet Gynecol. 2017;130(4):e168–e186.

From the very first sentence of the new ACOG practice bulletin, postpartum hemorrhage (PPH) is redefined as "cumulative blood loss greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process (includes intrapartum loss) regardless of route of delivery." Although this does not seem to be a huge change from the traditional teaching of a 500-mL blood loss at vaginal delivery and a 1,000-mL loss at cesarean delivery, it reflects a shift in focus from simply responding to a certain amount of bleeding to using a multidisciplinary action plan for treating this leading cause of maternal mortality worldwide.

Focus on developing a PPH action plan

As part of the shift toward a multidisciplinary action plan for PPH, all obstetric team members should be aware of the following:

- For most postpartum women, by the time they begin to show signs of hemodynamic compromise, the amount of blood loss approaches 25% of their total blood volume (1,500 mL). Lactic acidosis, systemic inflammation, and a consumptive coagulopathy result.
- Risk stratification prior to delivery, recognition and identification of the source of bleeding, and aggressive early resuscitation to prevent hypovolemia are paramount. Experience gleaned from trauma massive transfusion protocols suggests that judicious transfusion of packed red blood cells, fresh frozen plasma, and platelets in a 1:1:1 ratio is appropriate for obstetric patients. Additionally, patients with low fibrinogen levels should be treated with cryoprecipitate.
- The use of fixed transfusion ratios and standardized protocols for recognition and management of PPH has been demonstrated to increase earlier intervention

FAST TRACK

ACOG's new PPH definition reflects a shift in focus from simply responding to a certain amount of bleeding to using a multidisciplinary action plan for treatment

TABLE Facts about tranexamic acid

- The dose is 1 g IV; it may be repeated once in 24 hours
- Half-life is 2 hours
- Clearance is renal—so do *not* use in patients with renal impairment
- Antifibrinolytic activity usually lasts 7 to 8 hours
- Tranexamic acid is contraindicated in patients with a history of thromboembolism in pregnancy
- The drug is believed to be compatible with breastfeeding

and resolution of hemorrhage at an earlier stage, although the maternal outcomes results have been mixed.

- Multidisciplinary team drills and simulation exercises also should be considered to help solidify training of an institution's teams responsible for PPH response.

Novel management option: Tranexamic acid

In addition to these strategies, there is a new recommendation for managing refractory PPH: tranexamic acid, which works by binding to lysine receptors on plasminogen and plasmin, inhibiting plasmin-mediated fibrin degradation.[5] Previously, tranexamic acid was known to be effective in trauma, heart surgery, and in patients with thrombophilias. Pacheco and colleagues recently demonstrated reduced mortality from obstetric bleeding if tranexamic acid was given within 3 hours of delivery, without increased thrombotic complications.[5] ACOG recommends its use if initial medical therapy fails, while the World Health Organization strongly recommends that tranexamic acid be part of a standard PPH package for all cases of PPH (**TABLE**).[6]

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Postpartum hemorrhage requires early, aggressive, and multidisciplinary coordination to ensure that 1) patients at risk for hemorrhage are identified for preventive measures; 2) existing hemorrhage is recognized and quickly treated, first with noninvasive methods and then with more definitive surgical treatments; and 3) blood product replacement follows an evidence-based standardized protocol. Tranexamic acid is recommended as an adjunct treatment for PPH (of any cause) and should be used within 3 hours of delivery.

FAST TRACK

Tranexamic acid was shown to reduce mortality from obstetric bleeding when given within 3 hours of delivery

Carrier screening—choose something

ACOG Committee on Genetics. Committee opinion No. 690: Carrier screening in the age of genomic medicine. Obstet Gynecol. 2017;129(3):e35–e40.

ACOG Committee on Genetics. Committee opinion No. 691: Carrier screening for genetic conditions. Obstet Gynecol. 2017;129(3):e41–e55.

Ideally, carrier screening should be offered prior to pregnancy to fully inform couples of their reproductive risks and options for pregnancy. If not performed in the preconception period, carrier screening should be offered to all pregnant women. If a patient chooses screening and screens positive for a particular disorder, her reproductive partner should then be offered screening so that the risk of having an affected child can be determined.

New ACOG guidance on prepregnancy and prenatal screening

Carrier screening recommendations have evolved as the technology available has expanded. All 3 of the following strategies now are considered "acceptable" according to 2 recently published ACOG committee opinions.

Traditional *ethnic-specific* carrier screening, previously ACOG's sole recommendation, involves offering specific genetic

CONTINUED ON PAGE 16

The **#1 brand** of absorbable hemostats[1]

Now in powder form

SURGICEL® Powder Absorbable Hemostat

Built to stop continuous, broad-surface oozing — fast.

- Unique structure penetrates through blood to stop bleeding at the source[2]
- SURGICEL Powder has been demonstrated to sustain hemostasis even when it is irrigated[3]*
- Device delivers consistent expression of powder regardless of orientation[4]

Discover the benefits of SURGICEL Powder at ethicon.com/trysurgicelpowder

*Based on a preclinical animal study

ETHICON
PART OF THE Johnson & Johnson FAMILY OF COMPANIES

Shaping the future of surgery

References: 1. US Market Share Report, December 2016. Ethicon, Inc. **2.** Surface energy/tension analysis among ORC Aggregate, ORC Fine Fiber, and Arista. Ethicon, Inc. **3.** SURGICEL® Powder versus ARISTA™ AH and PerClot in a Swine Acute Liver Biopsy Model. Final Report, PSE Accession No. 15-0120, Project No. 16438. Ethicon, Inc. **4.** Expression testing- ADAPTIV Document 100293850-1. Ethicon, Inc.

COMING SOON...

- **Postsurgical recovery: Optimizing pain relief, minimizing opioids**
  Mikio Nihira, MD, MPH, and Adam C. Steinberg, DO
- **3 cases of chronic pelvic pain solved with nonsurgical, nonopioid therapies**
  Sara Till, MD, and Suzie As-Sanie, MD
- **Enhanced recovery for the chronic pain patient**
  Janelle Moulder, MD, MSCR
- **2018 Update on fertility**
  G. David Adamson, MD
- **Is HPV cotesting (vs HPV alone) necessary?**
  Mark Einstein, MD
- **2018 Update on cancer**
  Jason Wright, MD
- **How to avoid and manage complications when placing ports and docking**
  John P. Lenihan Jr, MD
- **2018 Update on genetic testing**
  Mary Norton, MD
- **CPT and Medicare coding changes for 2018**
  Melanie Witt
- **Optimal management of stage 3 and 4 pelvic organ prolapse**
  Vincent Lucente, MD; Rebecca Rogers, MD; and Patrick Culligan, MD
- **How to optimize the patient, and physician, experience in a patient-centric world**
  James Merlino, MD

Value-based medicine: A series in collaboration with ACOG

The American College of Obstetricians and Gynecologists

- **Value-based payment: What does it mean and how can ObGyns get out ahead?**
  Elizabeth Wieand, MSPH, and David Lagrew, MD (see page 17)
- **Quality measurements: How are they determined?**
  Steve Hasley, MD
- **The role of patient reported outcomes in women's health**
  Kimberly D. Gregory, MD, MPH; Lisa M. Korst MD, PhD; Samia Saeb, MPH; and Moshe Fridman, PhD
- **Training: How can we educate residents and students on how much things cost?**
  Mark Woodland, MD, MPH
- **Trends in the use of value-based payment in health care: The current climate in Washington**
  Lucia DiVenere, MA

OBG MANAGEMENT

CONTINUED FROM PAGE 14

WHAT THIS EVIDENCE MEANS FOR PRACTICE

All pregnant patients or patients considering pregnancy should be offered carrier screening as standard reproductive care, including screening for cystic fibrosis, hemoglobinopathies, and spinal muscular atrophy. Ethnic, panethnic, or expanded carrier screening (and patient-requested specific screening) all are acceptable options, and a standard screening and counseling protocol should be determined by the ObGyn or practice.

screening to patients from populations with a high prevalence for certain conditions. One such example is Tay-Sachs disease screening in Ashkenazi Jewish patients.

***Panethnic* screening,** which takes into account mixed or uncertain backgrounds, involves screening for a certain panel of disorders and is available to all patients regardless of their background (for example, cystic fibrosis screening offered to all pregnant patients).

***Expanded* carrier screening** is when a large number of disorders can be screened for simultaneously for a lower cost than previous testing strategies. Expanded carrier screening panels vary in number and which conditions are tested by the laboratory. An ideal expanded carrier screening panel has been debated in the literature but not agreed on.[7]

ObGyns and practices therefore are encouraged to develop a standard counseling and screening protocol to offer to all their patients while being flexible to make available any patient-requested screening that is outside their protocol. Pretest and posttest counseling, including a thorough family history, is essential (as with any genetic testing) and should include residual risk after testing, potential need for specific familial mutation testing instead of general carrier screening, and issues with consanguinity.

FAST TRACK

All pregnant women should be offered screening for cystic fibrosis, hemoglobinopathies, and spinal muscular atrophy

Three essential screens

Regardless of the screening strategy chosen from the above options, 3 screening tests should be offered to all pregnant women or couples considering pregnancy (either individually or in the context of an expanded screening panel):

- **Cystic fibrosis.** At the least, a panel of the 23 most common mutations should be used. More expanded panels, which include hundreds of mutations, increase detection in non-Caucasian populations and for milder forms of the disease or infertility-related mutations.
- **Hemoglobinopathies (sickle cell, α- and β-thalassemia).** Complete blood count and red blood indices are recommended for all, with hemoglobin electrophoresis recommended for patients of African, Middle Eastern, Mediterranean, or West Indian descent or if mean corpuscular volume is low.
- **Spinal muscular atrophy (SMA).** The most recent addition to ACOG's recommendations for general carrier screening due to the relatively high carrier frequency (1-in-40 to 1-in-60) and the severity of the disease, SMA causes degeneration of the spinal cord neurons, skeletal muscular atrophy, and overall weakness. Screening is via polymerase chain reaction for *SMN1* copy number: 2 copies are normal, and 1 copy indicates a carrier of the *SMN1* deletion. About 3% to 4% of patients will screen negative but still will be "carriers" due to having 2 copies of the *SMN1* gene on 1 chromosome and no copies on the other chromosome. ●

References

1. Bateman BT, Cole NM, Maeda A, et al. Patterns of opioid prescription and use after cesarean delivery. Obstet Gynecol. 2017;130(1):29–35.
2. Osmundson SS, Schornack LA, Grasch JL, Zuckerwise LC, Young JL, Richardson MD. Postdischarge opioid use after cesarean delivery. Obstet Gynecol. 2017;130(1):36–41.
3. Prabhu M, McQuaid-Hanson E, Hopp S, et al. A shared decision-making intervention to guide opioid prescribing after cesarean delivery. Obstet Gynecol. 2017;130(1):42–46.
4. Barbieri RL. Stop using codeine, oxycodone, hydrocodone, tramadol, and aspirin in women who are breastfeeding. OBG Manag. 2017;29(10):8–12.
5. Pacheco LD, Hankins GD, Saad AF, Costantine MM, Chiossi G, Saade GR. Tranexamic acid for the management of obstetric hemorrhage. Obstet Gynecol. 2017;130(4);765–769.
6. WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage. Geneva, Switzerland: World Health Organization; 2017.
7. Stevens B, Krstic N, Jones M, Murphy L, Hoskovec J. Finding middle ground in constructing a clinically useful expanded carrier screening panel. Obstet Gynecol. 2017;130(2):279–284.

VALUE-BASED MEDICINE: PART 1

Value-based payment: What does it mean, and how can ObGyns get out ahead?

Paying for value seems to be all the rage in health care right now. But what does this term really mean? And what is behind this move toward incentivizing value?

Elizabeth Wieand, MSPH, and David C. Lagrew Jr, MD

For ObGyns to be successful, understanding the basics of quality and cost measurement is essential, along with devoting more attention to what they are being evaluated on and held accountable for. But how will ObGyns be impacted by the push to incentivize them for delivering value in their work?

Although much of health care policy has become politically divisive lately, one area of agreement is that, in the United States, we have unsustainable health costs and the exorbitant amount our country pays for health care does not translate to improved outcomes. The United States spends more than most other developed nations on health care (roughly, $9,403 per capita in 2014) but has some of the lowest life expectancies, along with the highest maternal and infant mortality rates, compared with peer nations.[1–4]

One of the key culprits in our health system's inefficiencies is the fee-for-service payment model. Fee-for-service incentivizes the delivery of a high volume of care without any way to determine whether that care is achieving the desired outcomes of improved health and quality of life. Not only does fee-for-service drive up the volume of care but it also rewards the delivery of high-cost services, regardless of whether those services provide what is best for the patient.

During the previous administration, Secretary of Health and Human Services Sylvia Mathews Burwell set goals for moving away from fee-for-service in Medicare and in the health system more broadly. Congress also passed legislation that provides incentives for Medicare providers to transition away from fee-for-service with the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). While fee-for-service remains the predominant form of payment for many physicians, value-based payment arrangements are gaining a toehold. In 2014, 86% of physicians

Ms. Wieand is Program Director, Payment and Delivery System Policy, American College of Obstetricians and Gynecologists, Washington, DC.

Dr. Lagrew is Executive Medical Director of Women's Services, St. Joseph–Hoag Health Region of Providence Healthcare, Irvine, California.

The authors report no financial relationships relevant to this article.

Developed in collaboration with the American College of Obstetricians and Gynecologists

IN THIS ARTICLE

Assessing value in health care
page 18

Alternative payment models
page 19

How can ObGyns succeed?
page 25

reported working in a practice receiving fee-for-service. Those fees accounted for nearly 72% of revenue.[5] This percentage likely will continue to decrease over the next few years as government and private payers seek to promote value-based payment systems.

Assessing quality

"Value" in the context of health care is often defined as quality or outcomes relative to costs.[6] Before payers can reward value, there must be measurement of performance to determine the quality of care being delivered. Quality measures are tools to help quantify access to care, processes, outcomes, patient experience, and organizational structure within the health care system. ObGyns likely encounter process, outcome, and patient experience measures most frequently in their practice.

Although outcome measures are generally held as the gold standard for quality measurement, they are often hard to obtain—either because of issues of temporality and rarity of events or because the data are hard to capture through existing formats. In lieu of measuring outcomes, process measures are often used to determine whether certain services that are known to be tied to desired health outcomes were delivered. Patient experience measures are also rising in popularity and are seen as a critical tool to ensuring that care that purports to be patient-centered actually is so.

FAST TRACK

In lieu of outcome measures for quality measurement, process, and increasingly patient experience, measures are often used

Measures are specified to different levels of accountability, ranging from the individual physician all the way to the population. Some measures also can be specified at multiple levels. One major concern is the problem of attribution—that is, the difficulty of assigning who is primarily responsible for a specific quality metric result. Because obstetrics and gynecology is an increasingly team-based specialty, the American College of Obstetricians and Gynecologists (ACOG) recommends that measures that are used to reward or penalize providers should reflect performance at the care team or practice level, not at the individual physician or health care provider level.[7] As consolidation of providers continues, it is expected that team-based care will increase and that the use of advanced practice providers will increase.[8]

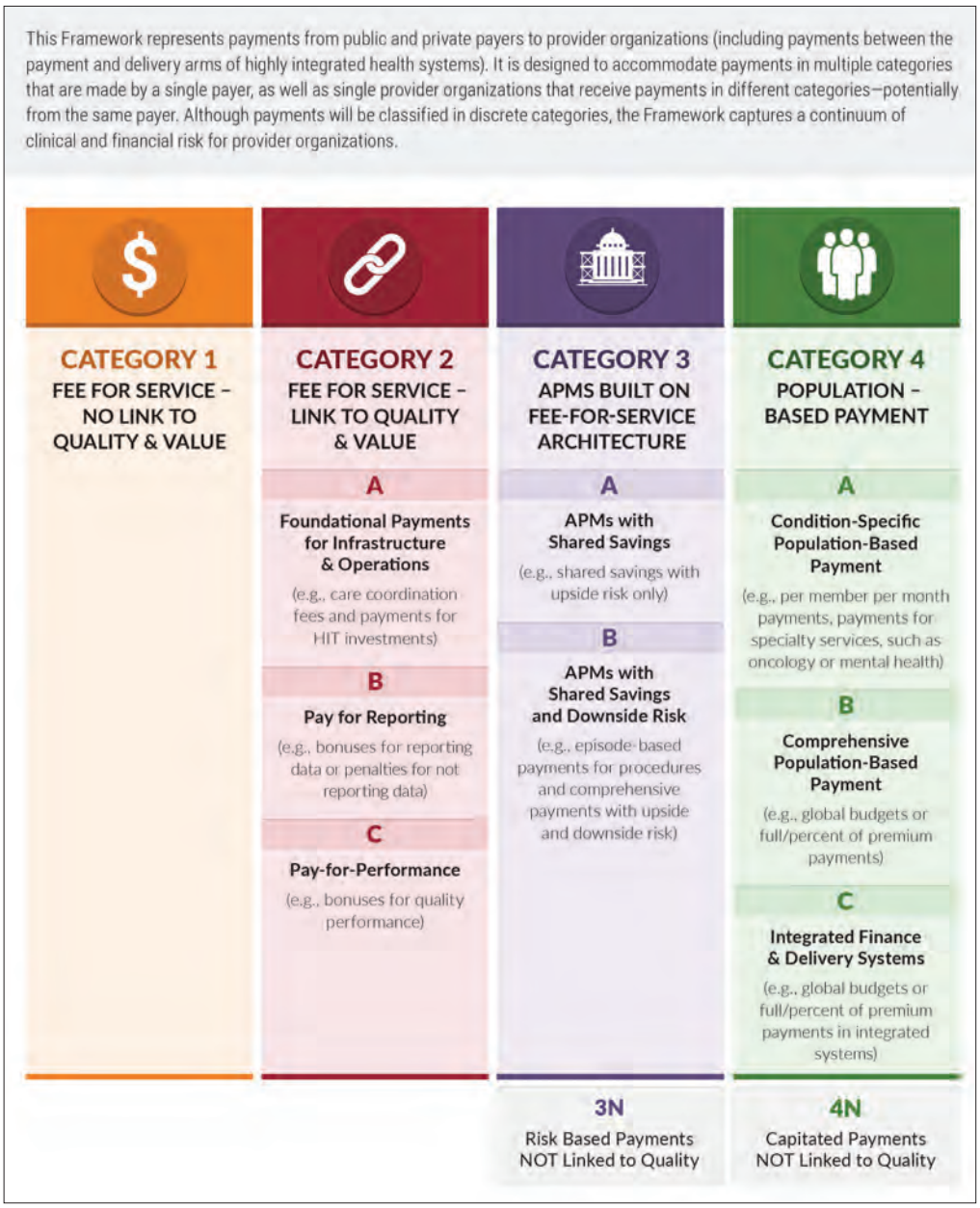
Data to determine performance can come from a variety of sources, including claims, electronic health records (EHRs), paper medical record abstraction, birth certificates, registries, surveys, and separate reporting mechanisms. There are pros and cons of these various sources. Because administrative claims data are so easily obtainable, many measures have been developed based on this data source, but there are significant limitations to assessments made with such data. These limitations include inherent problems with translating clinical diagnoses into specific codes and inadequate documentation to support particular diagnoses and procedure codes.[9] Claims data are limited by what physicians and other health care providers code for in their claims, making proper coding an essential skill for ObGyns to master.

Although there has been an increase in measures that rely on clinical data found in EHRs and registries—which are more robust and capture a wider breadth of indicators—claims-based measures still form the basis for many reporting programs because of standardization and ease of access to data. Data quality will become increasingly more important in a value-based payment world because completeness, risk adjustment, and specificity will be determined by the data recorded. This need for data quality will require that improvements be made in the user interface of EHRs and that providers pay specific attention to making sure their documentation is complete. New designs for EHRs should assist in that task, and data extraction should become a by-product of documentation.[10]

Paying for value

In an attempt to move away from fee-for-service medicine, payers and employers are adopting alternative payment models (APMs) that are intended to reward physicians and other health care providers for delivering value. Although APMs can be a catchall term, the Health Care Payment Learning and Action Network (LAN), a multi-stakeholder

FIGURE Alternative payment models: The APM Framework[11]



collaborative convened by the US Centers for Medicare & Medicaid Services, has laid out a framework for the different types of APMs[11] (**FIGURE**). This framework provides a common reference point for concepts related to value-based care.

Although ACOG does not endorse all the concepts and principles included in the LAN white paper, it does support moving away from fee-for-service payments that lack any link to quality or outcomes. Originally, the LAN envisioned that all physicians, providers, and hospital systems would move in the direction of adopting Category 4 APMs, but in the recent "refresh" of the LAN's white paper, the authors recognized that not all entities will be able to move toward population-based payments—nor will it be beneficial for all providers to do so. ACOG agrees that not all ObGyns will be able to thrive under

FAST TRACK

There are 4 categories of alternative payment models; ACOG supports those categories that move away from fee-for-service payments that lack any link to quality or outcomes

CONTINUED ON PAGE 25

Are your adult patients with iron deficiency anemia (IDA) getting what they need from oral iron therapy?

Typical oral iron dose*

Ferrous sulfate tablets 325 mg, taken 3x daily for 30 days (dose may vary depending on patient condition)[1,2]

*Not intended to represent all possible oral iron regimens.

Typical oral iron absorption

Even in healthy subjects, less than 10% of oral iron is absorbed[3]

INDICATIONS

Injectafer® (ferric carboxymaltose injection) is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in adult patients who have intolerance to oral iron or have had unsatisfactory response to oral iron, and in adult patients with non-dialysis dependent chronic kidney disease.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its inactive components.

WARNINGS AND PRECAUTIONS

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Injectafer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but were not limited to, pruritus, rash, urticaria, wheezing, or hypotension were reported in 1.5% (26/1775) of these subjects.

In clinical studies, hypertension was reported in 3.8% (67/1775) of subjects. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea were observed in 6% (106/1775) of subjects. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Injectafer administration.

In the 24 hours following administration of Injectafer, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Injectafer.

ADVERSE REACTIONS

In two randomized clinical studies, a total of 1775 patients were exposed to Injectafer, 15 mg/kg of body weight, up to a single maximum dose of 750 mg of iron on two occasions, separated by at least 7 days, up to a cumulative dose of 1500 mg of iron. Adverse reactions reported by ≥2% of Injectafer-treated patients were nausea (7.2%); hypertension (3.8%); flushing/hot flush (3.6%); blood phosphorus decrease (2.1%); and dizziness (2.0%).

The following serious adverse reactions have been most commonly reported from the post-marketing spontaneous reports: urticaria, dyspnea, pruritus, tachycardia, erythema, pyrexia, chest discomfort, chills, angioedema, back pain, arthralgia, and syncope.

To report adverse events, please contact American Regent† at 1-800-734-9236. You may also contact the FDA at www.fda.gov/medwatch or 1-800-FDA-1088.

Please see brief summary of Full Prescribing Information on the following pages.

Help your patients access the iron they need‡
www.injectafercopay.com
Restrictions apply§

INJECTAFER SAVINGS

Injectafer provides up to 1500 mg of iron in just 2 administrations separated by at least 7 days[4]

Up to 750 mg in a single dose‖¶ + **Up to 750 mg** in a single dose‖¶ = Total cumulative dose **up to 1500 mg** per course

At least 7 days apart

IV infusion over at least 15 minutes or Slow IV push over 7.5 minutes

injectafer®
ferric carboxymaltose injection

Many IDA patients have iron deficits of approximately 1500 mg[5#]

Monitor your patients. When oral fails, it's time to consider Injectafer.

To learn more, visit **www.injectaferHCP.com**

Injectafer has not been studied in pregnant women. Injectafer should be prescribed during pregnancy only if the potential benefit justifies the potential risk to the fetus.

†American Regent® is a registered trademark of Luitpold Pharmaceuticals, Inc.

‡For appropriate adult IDA patients (see INDICATIONS). Not all patients need 1500 mg of iron. The amount of iron needed for each patient must be determined by the prescribing clinician.

§The Injectafer Savings Program is only available for adults 18 years or older who are commercially insured or cash-paying patients. It provides up to a maximum savings limit of $500 per dose and a $1000 program limit for coverage up to 2 doses. Insurance out of pocket must be over $50. Additional restrictions may apply. Please see full Terms and Conditions.

‖For adult patients weighing less than 50 kg (110 lb), give each dose as 15 mg/kg body weight for a total cumulative dose not to exceed 1500 mg of iron per course of treatment.

¶When administered via IV infusion, dilute up to 750 mg of iron in no more than 250 mL of sterile 0.9% sodium chloride injection, USP, such that the concentration of the infusion is not <2 mg of iron per mL and administer over at least 15 minutes. When administered as a slow IV push, give at the rate of approximately 100 mg (2 mL) per minute.

#Calculated iron deficit based on the modified Ganzoni formula: Subject weight in kg x (15 - current hemoglobin g/dL) x 2.4 + 500. If subject TSAT >20% and ferritin >50 ng/mL, the 500-mg constant is not needed.

References: 1. FERROUS SULFATE—ferrous sulfate tablet. DailyMed website. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f886cb50-3791-4c36-ac0d-2c327cd9e3ea#modal-label-archives. Accessed November 21, 2016. **2.** FERROUS SULFATE—ferrous sulfate, dried tablet, film coated. DailyMed website. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=292ab31a-4857-4960-995d-e80f09106e28. Accessed November 21, 2016. **3.** Zhu A, Kaneshiro M, Kaunitz JD. Evaluation and treatment of iron deficiency anemia: a gastroenterological perspective. *Dig Dis Sci.* 2010;55(3):548-559. **4.** Injectafer® [package insert]. Shirley, NY: American Regent, Inc.; 2013. **5.** Koch TA, Myers J, Goodnough LT. Intravenous iron therapy in patients with iron deficiency anemia: dosing considerations. *Anemia.* 2015:763576. doi:10.1155/2015/763576.

Daiichi-Sankyo

Printed in USA PP-US-IN-0348 09/17

BRIEF SUMMARY OF PRESCRIBING INFORMATION **Rx Only**
INJECTAFER® (ferric carboxymaltose injection)
Please see package insert for Full Prescribing Information

INDICATIONS AND USAGE: Injectafer is an iron replacement product indicated for the treatment of iron deficiency anemia in adult patients:

- who have intolerance to oral iron or have had unsatisfactory response to oral iron;
- who have non–dialysis-dependent chronic kidney disease.

DOSAGE AND ADMINISTRATION: For patients weighing 50 kg (110 lb) or more: Give Injectafer in two doses separated by at least 7 days. Give each dose as 750 mg for a total cumulative dose not to exceed 1500 mg of iron per course.

For patients weighing less than 50 kg (110 lb): Give Injectafer in two doses separated by at least 7 days. Give each dose as 15 mg/kg body weight for a total cumulative dose not to exceed 1500 mg of iron per course.

The dosage of Injectafer is expressed in mg of elemental iron. Each mL of Injectafer contains 50 mg of elemental iron. Injectafer treatment may be repeated if iron deficiency anemia reoccurs.

Administer Injectafer intravenously, either as an undiluted slow intravenous push or by infusion. When administering as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. When administered via infusion, dilute up to 750 mg of iron in no more than 250 mL of sterile 0.9% sodium chloride injection, USP, such that the concentration of the infusion is not less than 2 mg of iron per mL and administer over at least 15 minutes.

When added to an infusion bag containing 0.9% sodium chloride injection, USP, at concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

Inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-use only. Any unused drug remaining after injection must be discarded.

Avoid extravasation of Injectafer since brown discoloration of the extravasation site may be long lasting. Monitor for extravasation. If extravasation occurs, discontinue the Injectafer administration at that site.

DOSAGE FORMS AND STRENGTHS: 750 mg iron / 15 mL single-use vial

CONTRAINDICATIONS: Hypersensitivity to Injectafer or any of its components.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions: Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Injectafer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but not limited to, pruritus, rash, urticaria, wheezing, or hypotension were reported in 1.5% (26/1775) of these subjects.

Hypertension: In clinical studies, hypertension was reported in 3.8% (67/1,775) of subjects in clinical trials 1 and 2. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea were observed in 6% (106/1,775) of subjects in these two clinical trials. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Injectafer administration.

Laboratory Test Alterations: In the 24 hours following administration of Injectafer, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Injectafer.

ADVERSE REACTIONS

Adverse Reactions in Clinical Trials: Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in clinical practice.

In two randomized clinical studies [Studies 1 and 2, *See Clinical Studies*], a total of 1,775 patients were exposed to Injectafer 15 mg/kg body weight up to a maximum single dose of 750 mg of iron on two occasions separated by at least 7 days up to a cumulative dose of 1500 mg of iron.

Adverse reactions reported by ≥1% of treated patients are shown in the following table.

Table 1. Adverse reactions reported in ≥1% of Study Patients in Clinical Trials 1 and 2

Term	Injectafer (N=1775) %	Pooled Comparators[a] (N=1783) %	Oral iron (N=253) %
Nausea	7.2	1.8	1.2
Hypertension	3.8	1.9	0.4
Flushing/Hot Flush	3.6	0.2	0.0
Blood Phosphorus Decrease	2.1	0.1	0.0
Dizziness	2.0	1.2	0.0
Vomiting	1.7	0.5	0.4
Injection Site Discoloration	1.4	0.3	0.0
Headache	1.2	0.9	0.0
Alanine Aminotransferase Increase	1.1	0.2	0.0
Dysgeusia	1.1	2.1	0.0
Hypotension	1.0	1.9	0.0
Constipation	0.5	0.9	3.2

[a]Includes oral iron and all formulations of IV iron other than Injectafer

Other adverse reactions reported by ≥0.5% of treated patients include abdominal pain, diarrhea, gamma glutamyl transferase increased, injection site pain/irritation, rash, paraesthesia, sneezing. Transient decreases in laboratory blood phosphorus levels (<2 mg/dL) have been observed in 27% (440/1638) patients in clinical trials.

Post-marketing Experience: Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following serious adverse reactions have been most commonly reported from the post-marketing spontaneous reports with Injectafer: urticaria, dyspnea, pruritus, tachycardia, erythema, pyrexia, chest discomfort, chills, angioedema, back pain, arthralgia, and syncope. One case of hypophosphatemic osteomalacia was reported in a subject who received 500 mg of Injectafer every 2 weeks for a total of 16 weeks. Partial recovery followed discontinuation of Injectafer.

DRUG INTERACTIONS: Formal drug interaction studies have not been performed with Injectafer.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C.

Risk Summary

Adequate and well controlled studies in pregnant women have not been conducted. However, animal reproduction studies have been conducted with ferric carboxymaltose. In these studies, administration of ferric carboxymaltose to rabbits during the period of organogenesis caused fetal malformations and increased implantation loss at maternally toxic doses of approximately 12% to 23% of the human weekly dose of 750 mg (based on body surface area). The incidence of major malformations in human pregnancies has not been established for Injectafer. However, all pregnancies, regardless of exposure to any drug, has a background rate of 2 to 4% for major malformations, and 15 to 20% for pregnancy loss. Injectafer should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

Administration of ferric carboxymaltose to rats as a one-hour intravenous infusion up to 30 mg/kg/day iron on gestation days 6 to 17 did not result in adverse embryofetal findings. This daily dose in rats is approximately 40% of the human weekly dose of 750 mg based on body surface area. In rabbits, ferric carboxymaltose was administered as a one-hour infusion on gestation days 6 to 19 at iron doses of 4.5, 9, 13.5, and 18 mg/kg/day. Malformations were seen starting at the daily dose of 9 mg/kg (23% of the human weekly dose of 750 mg). Spontaneous abortions occurred starting at the daily iron dose of 4.5 mg/kg (12% of the human weekly dose based on body surface area). Pre-implantation loss was at the highest dose. Adverse embryofetal effects were observed in the presence of maternal toxicity.

A pre- and post-natal development study was conducted in rats at intravenous doses up to 18 mg/kg/day of iron (approximately 23% of the weekly human dose of 750 mg on a body surface area basis). There were no adverse effects on survival of offspring, their behavior, sexual maturation or reproductive parameters.

Nursing Mothers: A study to determine iron concentrations in breast milk after administration of Injectafer (n=11) or oral ferrous sulfate (n=14) was conducted in 25 lactating women with postpartum iron deficiency anemia. Mean breast milk iron levels were higher in lactating women receiving Injectafer than in lactating women receiving oral ferrous sulfate.

Pediatric Use: Safety and effectiveness have not been established in pediatric patients.

Geriatric Use: Of the 1775 subjects in clinical studies of Injectafer, 50% were 65 years and over, while 25% were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

OVERDOSAGE: Excessive dosages of Injectafer may lead to accumulation of iron in storage sites potentially leading to hemosiderosis. A patient who received Injectafer 18,000 mg over 6 months developed hemosiderosis with multiple joint disorder, walking disability and asthenia. Hypophosphatemic osteomalacia was reported in a patient who received Injectafer 4000 mg over 4 months. Partial recovery followed discontinuation of Injectafer.

DESCRIPTION: Ferric carboxymaltose, an iron replacement product, is an iron carbohydrate complex with the chemical name of polynuclear iron (III) hydroxide 4(R)-(poly-(1→4)-*O*-α-D-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate. It has a relative molecular weight of approximately 150,000 Da corresponding to the following empirical formula:

$[FeO_x(OH)_y(H_2O)_z]_n\ [\{(C_6H_{10}O_5)_m\ (C_6H_{12}O_7)\}_l]_k$,

where $n \approx 10^3$, $m \approx 8$, $l \approx 11$, and $k \approx 4$

(l represents the mean branching degree of the ligand).

Injectafer (ferric carboxymaltose injection) is a dark brown, sterile, aqueous, isotonic colloidal solution for intravenous injection. Each mL contains 50 mg iron as ferric carboxymaltose in water for injection. Injectafer is available in 15 mL single-use vials. Sodium hydroxide and/or hydrochloric acid may have been added to adjust the pH to 5.0-7.0.

Vial closure is not made with natural rubber latex.

CLINICAL PHARMACOLOGY

Mechanism of Action: Ferric carboxymaltose is a colloidal iron (III) hydroxide in complex with carboxymaltose, a carbohydrate polymer that releases iron.

Pharmacodynamics: Using positron emission tomography (PET) it was demonstrated that red cell uptake of ^{59}Fe and ^{52}Fe from Injectafer ranged from 61% to 99%. In patients with iron deficiency, red cell uptake of radio-labeled iron ranged from 91% to 99% at 24 days after Injectafer dose. In patients with renal anemia red cell uptake of radio-labeled iron ranged from 61% to 84% after 24 days Injectafer dose.

Pharmacokinetics: After administration of a single dose of Injectafer of 100 to 1000 mg of iron in iron deficient patients, maximum iron levels of 37 µg/mL to 333 µg/mL were obtained respectively after 15 minutes to 1.21 hours post dose. The volume of distribution was estimated to be 3 L.

The iron injected or infused was rapidly cleared from the plasma, the terminal half-life ranged from 7 to 12 hours. Renal elimination of iron was negligible.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity studies have not been performed with ferric carboxymaltose.

Ferric carboxymaltose was not genotoxic in the following genetic toxicology studies: *in vitro* microbial mutagenesis (Ames) assay, *in vitro* chromosome aberration test in human lymphocytes, *in vitro* mammalian cell mutation assay in mouse lymphoma L5178Y/TK+/- cells, *in vivo* mouse micronucleus test at single intravenous doses up to 500 mg/kg.

In a combined male and female fertility study, ferric carboxymaltose was administered intravenously over one hour to male and female rats at iron doses of up to 30 mg/kg. Animals were dosed 3 times per week (on Days 0, 3, and 7). There was no effect on mating function, fertility or early embryonic development. The dose of 30 mg/kg in animals is approximately 40% of the human dose of 750 mg based on body surface area.

CLINICAL STUDIES: The safety and efficacy of Injectafer for treatment of iron deficiency anemia were evaluated in two randomized, open-label, controlled clinical trials (Trial 1 and Trial 2). In these two trials, Injectafer was administered at a dose of 15 mg/kg body weight up to a maximum single dose of 750 mg of iron on two occasions separated by at least 7 days up to a cumulative dose of 1500 mg of iron.

Trial 1: Iron Deficiency Anemia in Patients Who Are Intolerant to Oral Iron or Have Had Unsatisfactory Response to Oral Iron

Trial 1 was a randomized, open-label, controlled clinical study in patients with iron deficiency anemia who had an unsatisfactory response to oral iron (Cohort 1) or who were intolerant to oral iron (Cohort 2) during the 14 day oral iron run-in period. Inclusion criteria prior to randomization included hemoglobin (Hb) <12 g/dL, ferritin ≤100 ng/mL or ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%. Cohort 1 subjects were randomized to Injectafer or oral iron for 14 more days. Cohort 2 subjects were randomized to Injectafer or another IV iron per standard of care [90% of subjects received iron sucrose]. The mean age of study patients was 43 years (range, 18 to 94); 94% were female; 42% were Caucasian, 32% were African American, 24% were Hispanic, and 2% were other races. The primary etiologies of iron deficiency anemia were heavy uterine bleeding (47%) and gastrointestinal disorders (17%).

Table 2 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 35 or time of intervention.

Table 2. Mean Change in Hemoglobin From Baseline to the Highest Value Between Day 35 or Time of Intervention (Modified Intent-to-Treat Population)

	Cohort 1		Cohort 2	
Hemoglobin (g/dL) Mean (SD)	**Injectafer (N=244)**	**Oral Iron (N=251)**	**Injectafer (N=245)**	**IV SC[a] (N=237)**
Baseline	10.6 (1.0)	10.6 (1.0)	9.1 (1.6)	9.0 (1.5)
Highest Value	12.2 (1.1)	11.4 (1.2)	12.0 (1.2)	11.2 (1.3)
Change (from baseline to highest value)	1.6 (1.2)	0.8 (0.8)	2.9 (1.6)	2.2 (1.3)
p-value	0.001		0.001	

SD=standard deviation; [a]:Intravenous iron per standard of care

Increases from baseline in mean ferritin (264.2 ± 224.2 ng/mL in Cohort 1 and 218.2 ± 211.4 ng/mL in Cohort 2), and transferrin saturation (13 ± 16% in Cohort 1 and 20 ± 15% in Cohort 2) were observed at Day 35 in Injectafer-treated patients.

Trial 2: Iron Deficiency Anemia in Patients with Non–Dialysis-Dependent Chronic Kidney Disease

Trial 2 was a randomized, open-label, controlled clinical study in patients with non–dialysis-dependent chronic kidney disease. Inclusion criteria included hemoglobin (Hb) ≤11.5 g/dL, ferritin ≤100 ng/mL or ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%. Study patients were randomized to either Injectafer or Venofer. The mean age of study patients was 67 years (range, 19 to 96); 64% were female; 54% were Caucasian, 26% were African American, 18% Hispanics, and 2% were other races.

Table 3 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 56 or time of intervention.

Table 3. Mean Change in Hemoglobin From Baseline to the Highest Value Between Baseline and Day 56 or Time of Intervention (Modified Intent-to-Treat Population)

Hemoglobin (g/dL) Mean (SD)	**Injectafer (N=1249)**	**Venofer (N=1244)**
Baseline	10.3 (0.8)	10.3 (0.8)
Highest Value	11.4 (1.2)	11.3 (1.1)
Change (from baseline to highest value)	1.1 (1.0)	0.9 (0.92)
Treatment Difference (95% CI)	0.21 (0.13, 0.28)	

Increases from baseline in mean ferritin (734.7 ± 337.8 ng/mL), and transferrin saturation (30 ± 17%) were observed at Day 56 in Injectafer-treated patients.

PATIENT COUNSELING INFORMATION

- Question patients regarding any prior history of reactions to parenteral iron products.
- Advise patients of the risks associated with Injectafer.
- Advise patients to report any signs and symptoms of hypersensitivity that may develop during and following Injectafer administration, such as rash, itching, dizziness, lightheadedness, swelling and breathing problems.

Daiichi-Sankyo

This is not all the risk information for Injectafer.
Please see www.injectafer.com for Full Prescribing Information.

MOD-US-IN-0002
7/17

CONTINUED FROM PAGE 19

population-based payments, so we must lead the way in developing models and measures that appropriately assess value in the care that ObGyns provide.

ACOG has undertaken its first foray into value-based payments by developing an "episode group" related to benign hysterectomy, with attendant quality measures. (An episode group is a collection of services associated with treating a condition or performing a procedure that are both clinically and temporally related.) The goal in creating episode groups is to create alignment across payers so that ObGyns are not faced with multitudinous payer-specific metrics and reporting requirements. As the benign hysterectomy episode group is refined and adopted by payers, ACOG plans to expand to other treatments and, eventually, develop condition-based episode groups that incentivize the most appropriate treatment options for patients.

Current forms of APMs are mostly Category 2 and 3 models. Rates of proper screening for cervical and breast cancer have been used as performance metrics for bonus payments. Major payers have pushed specific metrics as cutoffs for limiting narrow networks.[12] For example, Covered California, the state health care exchange, has set a nulliparous term singleton vertex cesarean rate of 23.9% by 2018 as a necessary standard for inclusion of a hospital's entire services (obstetric and nonobstetric) in their network. Episode group payments for total obstetric care included in the episode routine services, such as ultrasonography, have been previously utilized to discourage overutilization.

Such payment incentives can lead to underutilization of resources, however, which might lead to poorer outcomes and therefore result in overall greater cost. For example, poor screening for fetal anomalies or poorly managed medical conditions such as diabetes can lead to markedly increased costs in neonatal management. Therefore, some authorities have proposed tying incentives for obstetric care to performance outcome measures in neonatal care as a method of finding "sweet spots" for utilization of complex services and episode groups. Such models will depend on more robust clinical information sources and standardization.[8]

How can ObGyns succeed?

So what does success look like under these value-based payments for ObGyns? This is new territory, in a rapidly changing environment in which providers who flourished under the fee-for-service system will only survive under the new system if they become knowledgeable about the nuances of the new payment methods. Providers should understand that success is going to be defined as reaching the "Triple Aim"[13] of improving the health of the population, containing costs, and improving the experience of health care.

Practice patient-centered care. One way to better position yourself is to focus on delivering patient-centered care and improving customer service in your practice. By implementing patient satisfaction surveys, you can identify where you are most vulnerable. One option is to utilize the Consumer Assessment of Healthcare Providers and Systems Clinician and Group Survey, developed by the US Department of Health and Human Services' Agency for Healthcare Research & Quality. However, there are other assessment tools available, and you should investigate what works best for your practice.

Code properly. Another key to making sure you are in an optimal position is to properly document and code the services you deliver. Accurately capturing the clinical complexity of your patients will help down the road with risk adjustment and risk stratification for cost and quality measures. Many payment models, including episode groups, are built on the fee-for-service system, so coding for services is still important in the transition to alternative models. Modern EHRs are building new tools to assist clinician documentation, such as tools that aid coding. Carefully groomed and up-to-date problem lists can help providers keep track of appropriate testing and screening by enabling decision support tools that are imbedded in the systems. Although upgrading can be expensive, especially for small group practices, the development of

FAST TRACK

ObGyns will need to become knowledgeable about nuances of new payment methods and understand that success will be defined as improving the health of the population, containing costs, and improving the experience of health care

"software as a service" or cloud-based EHRs will likely drive individual costs down.[10]

One example of point-of-care decision support that ACOG is spearheading to support our Fellows is the ACOG Prenatal Record (APR) by Dorsata.[14] The APR is an application designed by ObGyns to work seamlessly with an existing EHR system to improve clinical workflow, save time, and help ObGyns support high-quality prenatal outcomes. The APR uses the same simplicity, flexibility, and familiarity of the original paper-based flowsheet, but in an electronic format to integrate ACOG guidance, which provides a more robust solution. The APR uses information such as gestational age, pregnancy history, the problem list, and other risk factors to provide patient and visit-specific care plans based on ACOG clinical practice guidelines. It was designed to help reduce physician burden by creating an easy-to-navigate electronic flowsheet that provides everything ObGyns need to know about each patient, succinctly captured in a single view.

ACOG also offers comprehensive coding workshops across the country and webinars on special coding topics to help Fellows learn to properly code their services. Availing yourself of these educational opportunities now so that you are better prepared to transition to value-based payment is a great way to ensure success in the future.

Chances are that some of your payers are already requiring you to report on metrics or tracking your performance using claims data. Pay attention to the performance measures that you are being held accountable for by payers when you review your payer contracts. Make sure you understand how your patients may fall into and out of the measure numerators and denominators. Ask yourself whether these metrics are ones that you can reasonably influence and that are within your control.

Of course, you can also reach out to ACOG for help. We are here to educate, inform, and guide you on these changes and provide assistance to ensure your success. Send inquiries to: practicemanagement@acog.org. ●

FAST TRACK

When reviewing payor contracts, understand the performance measures you are being held accountable for, how your patients may affect the measures, and whether the measures are within your control

References

1. The World Bank. Health expenditure per capita (current US $). 2017. http://data.worldbank.org/indicator/SH.XPD.PCAP?year_high_desc=true. Accessed December 4, 2017.
2. Gonzales S, Sawyer B. How does U.S. life expectancy compare to other countries? Peterson Center on Healthcare and the Kaiser Family Foundation. 2017. http://www.healthsystemtracker.org/chart-collection/u-s-life-expectancy-compare-countries/?_sf_s=life#item-start. Accessed December 4, 2017.
3. World Health Organization. Trends in maternal mortality: 1990 to 2015: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. http://apps.who.int/iris/bitstream/10665/194254/1/9789241565141_eng.pdf?ua=1. Accessed December 4, 2017.
4. MacDorman MF, Mathews TJ, Mohangoo AD, Zeitlin J. International comparisons of infant mortality and related factors: United States and Europe, 2010. Natl Vital Stat Rep. 2014;63(5):1–6.
5. Kane, CK. American Medical Association Policy Research Perspectives. Payment and delivery in 2014: The prevalence of new models reported by physicians. 2015. https://www.ama-assn.org/sites/default/files/media-browser/member/health-policy/practicepay-prp2015_0.pdf. Accessed December 4, 2017.
6. Porter ME. What is value in health care? N Engl J Med. 2010;363(26):2477–2481.
7. Task Force on Collaborative Practice. Collaboration in practice: Implementing team-based care. Washington, DC: American College of Obstetricians and Gynecologists. 2016. https://www.acog.org/Resources-And-Publications/Task-Force-and-Work-Group-Reports/Collaboration-in-Practice-Implementing-Team-Based-Care. Accessed December 4, 2017.
8. Lagrew DC Jr, Jenkins TR. The future of obstetrics/gynecology in 2020: a clearer vision: finding true north and the forces of change. Am J Obstet Gynecol. 2014;211(6):617–622.
9. Riley GF. Administrative and claims records as sources of health care cost data. Med Care. 2009;47(7 suppl 1):S51–S55.
10. Lagrew DC Jr, Jenkins TR. The future of obstetrics/gynecology in 2020: a clearer vision. Transformational forces and thriving in the new system. Am J Obstet Gynecol. 2015;212(1):28–33.
11. US Centers for Medicare & Medicaid Services. Health Care Payment Learning and Action Network. Alternative Payment Models (APM) Framework. 2017. https://innovation.cms.gov/initiatives/Health-Care-Payment-Learning-and-Action-Network/. Accessed December 4, 2017.
12. Morse S. Covered California will exclude hospitals with high rates of C-sections. Healthcare Finance. 2016. http://www.healthcarefinancenews.com/news/covered-california-will-exclude-hospitals-high-rates-c-sections. Accessed December 4, 2017.
13. Institute for Healthcare Improvement. The IHI Triple Aim. 2017. http://www.ihi.org/engage/initiatives/TripleAim/Pages/default.aspx. Accessed December 4, 2017.
14. A pregnancy app for your EHR. 2017. https://www.dorsata.com/. Accessed December 4, 2017.

OBG MANAGEMENT

SPECIAL SECTION

PATIENT-CENTERED RISK ASSESSMENT FOR OVARIAN CANCER: INDIVIDUALIZING YOUR APPROACH

Neal M. Lonky, MD, MPH
Clinical Professor
Department of Obstetrics and Gynecology
University of California, Irvine
Physician Lead, Strategic EMR Documentation and Analysis
Department of Obstetrics and Gynecology
Member, Board of Directors
Southern California Permanente Medical Group
Kaiser Permanente
OBG MANAGEMENT Contributing Editor

Jeanine M. Genkinger, PhD, MHS
Associate Professor
Department of Epidemiology
Columbia University Mailman School of Public Health
New York, New York

Leslie M. Randall, MD
Associate Professor
Division of Gynecologic Oncology
University of California, Irvine, School of Medicine

Devansu Tewari, MD
Division Director, Gynecologic Oncology
Department of Obstetrics and Gynecology
Kaiser Permanente Orange County
Women's Health Services
Associate Clinical Professor
University of California, Irvine, School of Medicine

Jason D. Wright, MD
Sol Goldman Associate Professor and Chief, Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
Columbia University College of Physicians and Surgeons
New York, New York

Ovarian cancer: Risk assessment and patient management in the prevention of morbidity and mortality

Until screening approaches with good predictive values for ovarian cancer in average-risk women are developed, clinicians must rely on risk evaluation and watch for relevant signs and symptoms that require strategic follow-up testing

Neal M. Lonky, MD, MPH

In medicine, specifically gynecology, we are accustomed to a "screen, triage, and treat" secondary cancer prevention approach. The advent of the Pap smear, the subsequent discovery of the role of human papilloma virus (HPV) (and importantly its often-treatable precursors) testing in assessing risk for cervical cancer, health care access improvements (due to the myriad of insurance vehicles), and acceptable therapies for precursors and cancer have led to a dramatic reduction in cervical cancer incidence and mortality in industrialized countries.[1] Begun in the mid-20th century, this progress continues today.

HPV vaccine: A quantum leap in cancer prevention

HPV vaccination as primary prevention is a major breakthrough. With vaccination, a viral precursor can be immunologically blocked from causing carcinogenesis for the most prevalent HPV strains. This reduces not only cancer but also precursors and benign condyloma, which drain the health care economy for access to diagnosis and therapy in what I call the "revolving door of lower genital tract precursor emergence and regression."

HPV vaccination has not reached a desired rate in the United States due to social mores and other barriers to acceptance that deserve attention in a separate article. Where does that leave us when women present with concerning symptoms or family history and want impactful care that could potentially save their life? We should refocus our mind-set from screening, triage, and treatment to risk assessment and reduction of cancer sequelae. More importantly, we must educate women that the efforts that work for one cancer do not work for another cancer.

Dr. Lonky reports that he has received grant or research support from Merck & Co.

The conundrum of ovarian cancer detection

The American College of Obstetricians and Gynecologists' patient education page on ovarian cancer states that unlike the Pap test for cervical cancer and colonoscopy for colon cancer, there currently is no screening test to detect ovarian cancer in asymptomatic women.[2]

Ideally, a screening test should be able to detect ovarian cancer in, preferably, an early treatable stage. In fact, however, when average-risk women undergo screening—such as with transvaginal ultrasonography or a cancer antigen 125 (CA 125) test—many of those with abnormal results may undergo unnecessary surgery and experience resultant potential harm.[3] The potential harm outweighs the preventive utility in average-risk women.

This leaves the gynecologist to detect cancer at an early treatable stage or to tertiary prevention of mortality (not the cancer itself) from ovarian cancer. Beginning with clinical history and physical examination findings, some cases receive relevant triage ultrasonography and serum-based surveillance tests.

CONTINUED ON PAGE SS4

Ob.Gyn. News®

STAY TUNED

for on-site coverage of the San Antonio Breast Cancer Symposium and the Society for Maternal-Fetal Medicine annual meeting

DON'T MISS

our exclusive columns

- > Drugs, Pregnancy, & Lactation
- > Gynecologic Oncology Consult
- > Master Class

GET BREAKING NEWS

on the web at **obgynnews.com**

CONTINUED FROM PAGE SS2

With the advent of biomarkers revealing genetic risk factors, patients identified with mutations such as the *BRCA* gene or Lynch syndrome are offered adjunct surveillance with ultrasonography and other modalities to amplify the screening predictive value, because the disease prevalence in these groups improves the overall value of interventions.[4] This is where confusion may occur: the use of testing in screening versus in triage following a clinically identified relevant risk factor.

Fine-tuning ovarian cancer risk assessment

Sadly, since we do not have a primary prevention modality, like a vaccine, for ovarian cancer, we are left to find this cancer early instead of at a treatable precancerous stage. It is possible that, soon, we may have more powerful screening tests (high *negative* predictive value) and triage tools (high *positive* predictive value) to identify women at risk and avoid unnecessary surgeries.

We evaluate the challenges and opportunities of assessing risk for ovarian cancer in various patient scenarios in the roundtable discussion on page SS7, featuring Drs. Leslie Randall, Jason Wright, and Devansu Tewari. In addition, on page SS5, Dr. Jeanine Genkinger describes the epidemiology of ovarian cancer and explores the risks associated with gene mutations and risk assessment models. ■

References

1. Lonky NM, Penner KR, Diedrich JT. Current aims and challenges associated with cervical cancer prevention. Clin Obstet Gynecol. 2014;57(2):241–255.
2. American College of Obstetricians and Gynecologists. Frequently asked questions (FAQ096): gynecologic problems—ovarian cancer. https://www.acog.org/Patients/FAQs/Ovarian-Cancer. Published July 2017. Accessed December 4, 2017.
3. Committee on Gynecologic Practice, Society of Gynecologic Oncology. Committee Opinion No. 716: The role of the obstetrician-gynecologist in the early detection of epithelial ovarian cancer in women at average risk. Obstet Gynecol. 2017;130(3):e146–e149.
4. Committee on Practice Bulletins–Gynecology, Committee on Genetics, Society of Gynecologic Oncology. Practice bulletin No. 182: Hereditary breast and ovarian cancer syndrome. Obstet Gynecol. 2017;130(3):e110–e126.

Ovarian cancer epidemiology for the practicing gynecologist

A targeted, 2-tiered approach to identify and monitor women at high risk for ovarian cancer holds promise for reducing false-positive results and improving mortality

Jeanine M. Genkinger, PhD, MHS

Ovarian cancer is considered a rare, but highly fatal, cancer unless it is detected early. In 2017, an estimated 22,440 cases of ovarian cancer occurred in the United States.[1] The most common (60%) and aggressive type of epithelial ovarian cancer is the high-grade serous type.[2] Overall, only 44% of women diagnosed with ovarian cancer survive more than 5 years post-diagnosis.[3,4] Yet, when ovarian cancer is detected at a localized stage (15% of cases), the 5-year survival rate is 94%.[3,4]

A number of reasons exist for the late diagnosis and high fatality rate, including few known modifiable risk factors, no effective screening tools, and lack of early diagnostic symptoms unique to ovarian cancer. Thus, approaches to prevent disease or identify it at earlier stages are critical to reduce the morbidity and mortality of this deadly disease.

Genetic and reproductive risk factors

Identifying known risk factors for ovarian cancer is crucial for early detection and risk assessment. Women with mutations in the *BRCA1* or *BRCA2* gene are at a much higher risk for developing ovarian cancer (16%–68% for *BRCA1* and 11%–27% for *BRCA2*).[5–16] Yet, a continuum of risk exists even for women with the same mutation, which contributes to difficulty in clinical decision making.

Women with a family history only have a much higher risk of ovarian cancer than the general population[17] such that having 1 affected first-degree relative increases a woman's risk 3-fold, and having multiple affected relatives increases a woman's risk 11-fold.[18]

The author reports no financial relationships relevant to this article.

However, family history and/or genetic predisposition[19] accounts only for 5% to 10% of cases.[19,20] The majority of other risk factors for ovarian cancer are reproductive: older age at menarche, menopausal hormone use, and endometriosis.[21,22] By contrast, tubal ligation and oral contraceptive (OC) use are estimated to lower ovarian cancer risk by 30% to 50%, and parity, breastfeeding, and hysterectomy are additional known or suspected preventive factors.[23–28]

Risk assessment model utility

Currently, validated risk assessment models that integrate established risk factors exist for primary prevention. The Rosner model includes age at menopause, age at menarche, OC use, and tubal ligation; the concordance statistic (area under the receiver operator curve [AUC]) is 0.60.[29] The Pfeiffer model includes OC use, menopausal hormone therapy use, and family history of breast or ovarian cancer, with a discriminatory power of 0.59.[30] The Ovarian Cancer Association Consortium model includes 17 risk factors and 17 genome-wide significant single nucleotide polymorphisms (*BRCA1* and *BRCA2* mutations were not included); the AUC increased only to 0.66.[31] Due to their modest discriminatory power, these models have limited screening potential.[30]

Screening provides no mortality benefit

Currently, the US Preventive Services Task Force does not recommend screening for ovarian cancer.[32] Findings from recent large clinical trials of serum cancer antigen 125 (CA 125) and transvaginal ultrasonography demonstrated that these screening

modalities do not confer a benefit for mortality.[33–35] In fact, in the intervention arm participants had increased false-positive results, with at least 1 serious complication and/or adverse event.[33–35]

The major concern regarding CA 125 is that it may not be specific enough to ovarian cancer; in fact, CA 125 is elevated in benign conditions, such as pregnancy and menstruation, and is expressed in only about half of early-stage ovarian cancers.[36,37]

Targeted screening in high-risk patients has potential

These previous studies examining screening approaches were employed in average-risk women and may not represent the findings from a targeted approach in high-risk women. In the future, one suggestion for improved screening is a 2-tiered approach in which risk assessment models are used to identify high-risk women, who are then targeted for screening with a panel of markers that represent pathways to disease. This combined approach may reduce false-positives and improve mortality compared with using risk assessment or screening alone. Recent modeling supports this approach as effective for other diseases, such as breast cancer.[38–40] ■

References

1. American Cancer Society. Cancer Facts & Figures 2017. Atlanta, GA: American Cancer Society; 2017.
2. Jones PM, Drapkin R. Modeling high-grade serous carcinoma: how converging insights into pathogenesis and genetics are driving better experimental platforms. Front Oncol. 2013;3:217.
3. American Cancer Society. Cancer Facts & Figures 2013. Atlanta, GA: American Cancer Society; 2013.
4. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58(2):71–96.
5. Ramus SJ, Antoniou AC, Kuchenbaecker KB, et al; Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Ovarian cancer susceptibility alleles and risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers. Hum Mutat. 2012;33(4):690–702.
6. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet. 2003;72(5):1117–1130.
7. Antoniou AC, Spurdle AB, Sinilnikova OM, et al. Common breast cancer-predisposition alleles are associated with breast cancer risk in BRCA1 and BRCA2 mutation carriers. Am J Hum Genet. 2008;82(4):937–948.
8. Begg CB, Haile RW, Borg A, et al. Variation of breast cancer risk among BRCA1/2 carriers. JAMA. 2008;299(2):194–201.
9. Chen S, Iversen ES, Friebel T, et al. Characterization of BRCA1 and BRCA2 mutations in a large United States sample. J Clin Oncol. 2006;24(6):863–871.
10. Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. Am J Hum Genet. 1998;62(3):676–689.
11. Hopper JL, Southey MC, Dite GS, et al. Population-based estimate of the average age-specific cumulative risk of breast cancer for a defined set of protein-truncating mutations in BRCA1 and BRCA2. Australian Breast Cancer Family Study. Cancer Epidemiol Biomarkers Prev. 1999;8(9):741–747.
12. Milne RL, Osorio A, Cajal TR, et al. The average cumulative risks of breast and ovarian cancer for carriers of mutations in BRCA1 and BRCA2 attending genetic counseling units in Spain. Clin Cancer Res. 2008;14(9):2861–2869.
13. Simchoni S, Friedman E, Kaufman B, et al. Familial clustering of site-specific cancer risks associated with BRCA1 and BRCA2 mutations in the Ashkenazi Jewish population. Proc Natl Acad Sci U S A. 2006;103(10):3770–3774.
14. Struewing JP, Hartge P, Wacholder S, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. N Engl J Med. 1997;336(20):1401–1408.
15. Thompson D, Easton D, Breast Cancer Linkage Consortium. Variation in cancer risks, by mutation position, in BRCA2 mutation carriers. Am J Hum Genet. 2001;68(2):410–419.
16. Thompson D, Easton D, Breast Cancer Linkage Consortium. Variation in BRCA1 cancer risks by mutation position. Cancer Epidemiol Biomarkers Prev. 2002;11(4):329–336.
17. Metcalfe KA, Finch A, Poll A, et al. Breast cancer risks in women with a family history of breast or ovarian cancer who have tested negative for a BRCA1 or BRCA2 mutation. Br J Cancer. 2009;100(2):421–425.
18. Stratton JF, Pharoah P, Smith SK, Easton D, Ponder BA. A systematic review and meta-analysis of family history and risk of ovarian cancer. Br J Obstet Gynaecol. 1998;105(5):493–499.
19. Pearce CL, Rossing MA, Lee AW, et al. Combined and interactive effects of environmental and GWAS-identified risk factors in ovarian cancer. Cancer Epidemiol Biomarkers Prev. 2013;22(5):880–890.
20. Bougie O, Weberpals JI. Clinical considerations of BRCA1- and BRCA2-mutation carriers: a review. Int J Surg Oncol. 2011;2011:374012.
21. Risch HA. Hormonal etiology of epithelial ovarian cancer, with a hypothesis concerning the role of androgens and progesterone. J Natl Cancer Inst. 1998;90(23):1774–1786.
22. Holschneider CH, Berek JS. Ovarian cancer: epidemiology, biology, and prognostic factors. Semin Surg Oncol. 2000;19(1):3–10.
23. Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial ovarian cancers in white women. Collaborative Ovarian Cancer Group. Am J Epidemiol. 1992;136(10):1184–1203.
24. Risch HA, Marrett LD, Howe GR. Parity, contraception, infertility, and the risk of epithelial ovarian cancer. Am J Epidemiol. 1994;140(7):585–597.
25. Franceschi S, Parazzini F, Negri E, et al. Pooled analysis of 3 European case-control studies of epithelial ovarian cancer: III. Oral contraceptive use. Int J Cancer. 1991;49(1):61–65.
26. Vessey M, Painter R. Oral contraceptive use and cancer. Findings in a large cohort study, 1968–2004. Br J Cancer. 2006;95(3):385–389.
27. Rosenberg L, Palmer JR, Zauber AG, et al. A case-control study of oral contraceptive use and invasive epithelial ovarian cancer. Am J Epidemiol. 1994;139(7):654–661.
28. Cibula D, Widschwendter M, Majek O, Dusek L. Tubal ligation and the risk of ovarian cancer: review and meta-analysis. Hum Reprod Update. 2011;17(1):55–67.
29. Rosner BA, Colditz GA, Webb PM, Hankinson SE. Mathematical models of ovarian cancer incidence. Epidemiology. 2005;16(4):508–515.
30. Pfeiffer RM, Park Y, Kreimer AR, et al. Risk prediction for breast, endometrial, and ovarian cancer in white women aged 50 y or older: derivation and validation from population-based cohort studies. PLoS Med. 2013;10(7):e1001492.
31. Clyde MA, Palmieri Weber R, Iversen ES, et al; on behalf of the Ovarian Cancer Assosciation Consortium. Risk prediction for epithelial ovarian cancer in 11 United States–based case-control studies: incorporation of epidemiologic risk factors and 17 confirmed genetic loci. Am J Epidemiol. 2016;184(8):579–589.
32. Barton MB, Lin K. Screening for ovarian cancer: evidence update for the US Preventive Services Task Force reaffirmation recommendation statement. AHRQ publication No. 12-05165-EF3. Rockville, MD: Agency for Healthcare Research and Quality; 2012.
33. Buys SS, Partridge E, Black A, et al. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian

CONTINUED ON PAGE SS14

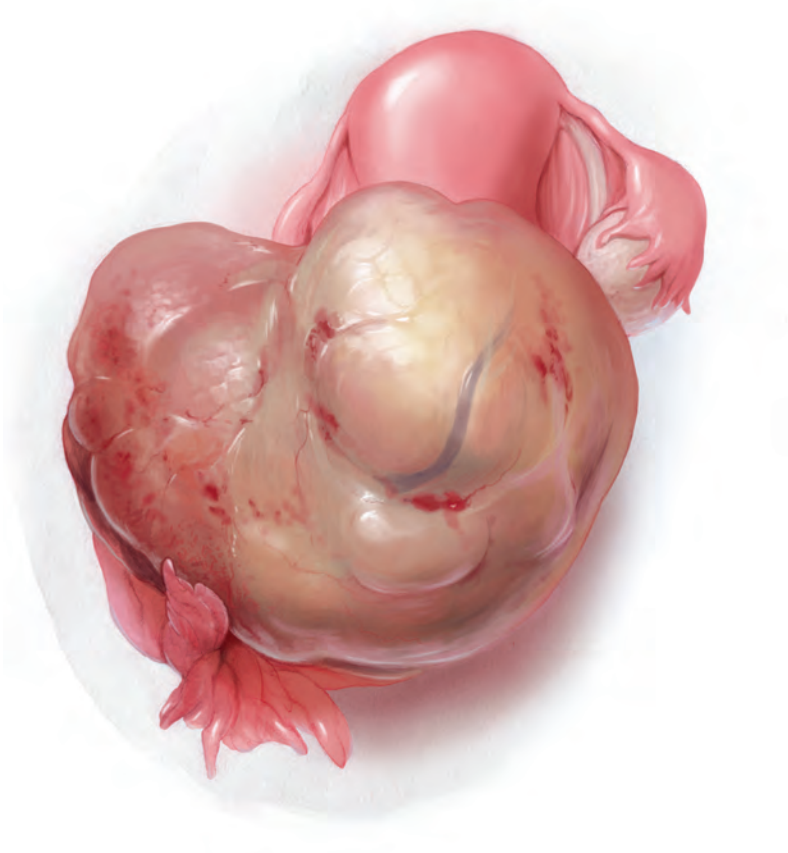
ROUNDTABLE

Optimal risk assessment and management of the potential ovarian cancer case

Expert guidance on individualizing an assessment approach for the patient at risk for ovarian cancer

Expert panel featuring Neal M. Lonky, MD, MPH, moderator; with Leslie M. Randall, MD; Devansu Tewari, MD; and Jason D. Wright, MD

In this roundtable discussion moderated by OBG Management Contributing Editor Neal M. Lonky, MD, MPH, 3 leading gynecologic oncologists use a case-based approach to discuss their strategies for assessing patients at risk for ovarian cancer. Considerations include patient age, history, genetic profile, and symptoms.



Assessing the premenopausal high-risk patient with positive family history, genetic concerns

Neal M. Lonky, MD, MPH: Your patient is at high risk for ovarian cancer due to a strong family history or genomic concerns. She is premenopausal and has no symptoms. What overall management approach would you take for this patient?

Leslie M. Randall, MD: For women with true genomic concerns, prevention is far preferred to surveillance. The specific high-risk genes are *BRCA1, BRCA2, RAD51C, RAD51D*, and *BRIP1,* plus Lynch syndrome (*MLH1, MSH2, MSH6, PMS1*, and *EpCAM*), and the minimum surgery for these women is a risk-reducing salpingo-oophorectomy (RRSO). RRSO is recommended between 30 and 35 years of age for *BRCA1* mutation carriers, and between 40 and 45 years for carriers of the other mutations listed, regardless of menopausal status. This is true for all age groups and in both symptomatic and asymptomatic patients.

If women have undiagnosed but suspected genetic mutations, they should be referred for genetic counseling and possible testing based on established criteria. Until better screening modalities are available, identifying these women for RRSO is our best method for improving ovarian cancer

Dr. Lonky reports that he has received grant or research support from Merck & Co.

Dr. Wright reports that he has served as a consultant to Clovis Oncology and Tesaro Inc.

Dr. Randall and Dr. Tewari report no financial relationships relevant to this article.

ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

mortality. Screening, however, can be considered for mutation carriers who do not meet these age criteria, desire future childbearing, or are not yet willing to undergo RRSO, as well as for women with a strong family history who test negative for mutations in these genes.

There is no current standard recommendation for screening, but clinicians can start by educating patients regarding the symptoms of ovarian cancer and performing an annual pelvic examination. Further testing protocols include at least a yearly transvaginal ultrasound scan and a serum cancer antigen 125 (CA 125) test. This approach was not successful in the general population as reported by the Prostate, Lung, Colorectal and Ovarian (PLCO) screening project.[1] Screen-detected cancers in the PLCO were predominantly diagnosed in stages III or IV, and at the expense of false-positive results attributable to ultrasound findings that prompted unnecessary surgeries and subsequent complications.

An alternative strategy of reserving ultrasonography for women with a rising annual CA 125 level (termed "multimodal screening") was studied in the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKTOCS).[2] While multimodal screening was associated with less unnecessary surgery, cancers were still diagnosed at an advanced stage. There was a trend for mortality reduction, however, for women who had normal screening for the initial 7 to 14 years of monitoring.

Finally, a third approach, the Risk of Ovarian Cancer Algorithm (ROCA), also employs a mathematical CA 125 trend model with increased frequency (measurement of CA 125 every 3 months).[3] In the high-risk, genomic concern population, this strategy showed improved sensitivity for early stage disease compared with historical methods, even before the CA 125 level was greater than 35 U/mL. The ROCA, however, requires further study in a larger cohort before it can be accepted as standard of care.

Jason D. Wright, MD: Appropriate risk assessment typically is the first step when considering screening for ovarian cancer. Women with a personal or family history of breast and ovarian cancer should undergo genetic counseling. For those who meet the criteria for genetic testing, testing for deleterious mutations of the *BRCA1* and *BRCA2* genes can be performed. Women with a *BRCA* mutation are considered at high risk and warrant heightened surveillance and consideration of risk-reducing surgery.

Many commercially available genetic tests now evaluate a panel of genes in addition to *BRCA1* and *BRCA2*. While those genes are associated with ovarian cancer, the risk is generally lower than that associated with *BRCA1* and *BRCA2*. Data on how best to manage patients with abnormalities in these lower-penetrance genes are more limited.

For a premenopausal woman who has not completed childbearing, transvaginal ultrasonography with serum CA 125 testing can be considered. The National Comprehensive Cancer Network currently endorses such screening in women with a *BRCA1* or *BRCA2* mutation starting at age 30 to 35 years.[4] It should be noted that the benefit of such screening is uncertain, and screening has not been shown to reduce mortality in these women. The frequency of screening is at the discretion of the clinician, but it is often performed at an interval of every 6 months.

Devansu Tewari, MD: The most important thing always to consider in someone presumed to have a high risk of ovarian cancer is the accuracy of their family history. Clearly a first-degree relative, such as a mother, daughter, or sister with ovarian cancer, or someone who has tested positive for a genetic mutation needs to be confirmed.

If the patient is considered at high risk based on family history alone, a referral to a geneticist is warranted to determine if testing is needed. Unfortunately, screening opportunities—other than routine gynecologic examinations—outside of a clinical trial are limited.

The postmenopausal high-risk patient with no symptoms of ovarian cancer

Dr. Lonky: What is your approach for a postmenopausal patient who has no symptoms?

Dr. Randall: My approach in the asymptomatic, postmenopausal patient is much like that for the premenopausal one: RRSO for known genetic mutation carriers, genetic testing for potential carriers, and the option to use ultrasound and CA 125 monitoring in the rest.

In women with significant family history (ovarian cancer in more than 1 first-degree relative), RRSO might be considered in those who are medically fit for surgery. Hysterectomy could be

CONTINUED ON PAGE SS10

OVA1, combined with clinical assessment, has a 98% NPV providing a better pathway for managing potential malignancy in pelvic masses[1]

1. Bristow RE, Smith A, Zhang Z, et al. Ovarian malignancy risk stratification of the adnexal mass using a multivariate index assay. Gynecol Oncol. 2013;128(2):252-259.
2. Ovarian Cancer Screening Tests: Safety Communication - FDA Recommends Against Use. U.S. Food & Drug Administration. September 2016.

Pelvic Mass on Ultrasound

Indicates Malignant

Cyst >10cm, papillary or solid components, irregularity, presence of ascites, high color Doppler flow.

Get CA-125 and refer to Gyn Onc immediately

Not Clear

Everything else (3-10cm) not thin walled, >1 septation, small nodules.

OVA1 gets you a clear picture when managing pelvic masses with a 96-98% NPV[1]

⇨ Elevated risk of malignancy

- Refer GynOnc
- GynOnc consults

Low risk of malignancy ⇦

- OB/GYN Treats
- No Further Imaging

Indicates Benign

Simple appearance, smooth, thin walls, absence of solid components or septations, generally <10cm, but even above 10cm if cyst is simple risk of malignancy is <1%.

Watchful waiting + management of symptoms

Choose the only FDA-approved and ACOG Level B test that works better for women.[2]

ASPiRA LABS A VERMILLION COMPANY

Learn more at **vermillion.com** | 1-844-ASPiRA1

CONTINUED FROM PAGE SS8

considered for women with indications such as high-grade cervical dysplasia, postmenopausal bleeding, or the need for tamoxifen therapy.[5] In addition, women with *BRCA1* mutations might be at higher risk for serous uterine cancers, and this should be discussed during surgical planning for RRSO.[6] Hysterectomy increases the risks of surgery, but these risks can be minimized by using a minimally invasive surgical approach.

Dr. Wright: Postmenopausal women with a *BRCA* mutation who have not undergone oophorectomy should strongly consider prophylactic RRSO. RRSO typically is recommended between the ages of 35 and 40 after the completion of childbearing. Since women with *BRCA2* mutations have later onset of ovarian cancer, RRSO can be delayed until 40 to 45 years of age in these patients.

Dr. Tewari: An asymptomatic patient without a genetic mutation should undergo routine annual gynecologic examinations. Screening outside of a clinical trial is not recommended. Women carrying a known genetic mutation, such as a *BRCA1* or *BRCA2* mutation, should have undergone risk-reducing surgery to remove the tubes and ovaries; those who have not already had RRSO should be counseled to do so. The issue related to hysterectomy needs to be discussed with these patients, given studies showing increased rates of uterine papillary serous cancers,[6] and if a personal history of breast cancer exists this may need to be factored in as well.

Suspicious symptoms in a premenopausal high-risk patient

Dr. Lonky: Please describe your management approach for a premenopausal patient who has current symptoms.

Dr. Randall: According to Goff and colleagues, symptoms that are concerning for ovarian cancer include pelvic and abdominal pain, urinary urgency and/or frequency, increased abdominal size and bloating, and early satiety present for less than 1 year and occurring more than 12 days per month.[7] Although not always specific to ovarian cancer, the presence of these symptoms increases the performance of diagnostic testing.

Dr. Wright: Yes, clinicians should have a heightened suspicion in women who have persistent symptoms that have been associated with ovarian cancer. This is particularly true for high-risk women with a *BRCA* mutation or those with a family history of ovarian cancer. These patients should undergo pelvic examination, transvaginal ultrasonography, and assessment of serum CA 125.

Dr. Randall: For these women, I start with abdominal and pelvic examinations, followed by abdominal and vaginal ultrasound with serum markers based on the presence and appearance of a pelvic mass. If the mass is large (>10 cm) and/or complex, in this age group I consider tumors of both epithelial and nonepithelial ovarian origin, in addition to colorectal cancer, and perform tests for CA 125, carcinoembryonic antigen (CEA), germ cell markers (lactate dehydrogenase [LDH], human chorionic gonadotropin [hCG], alpha-fetoprotein [AFP]), and sex cord/stromal markers (inhibin B and testosterone).

Large masses will need to be managed surgically, and unless they appear purely simple on ultrasound and all serum markers are normal, these should be managed by a gynecologic oncologist, especially in the setting of genomic concerns. If imaging shows a smaller mass or ascites alone, CA 125 and CEA typically are adequate markers, and the patient should be referred for gynecologic oncology evaluation and consideration for surgery. Benign diagnoses, such as endometriosis, pelvic abscess, and ectopic pregnancy, should not be excluded in this age group for fear of cancer.

Dr. Tewari: Any symptoms such as worsening abdominal or pelvic pain, bloating, urinary frequency, or gastrointestinal changes that do not improve should trigger a gynecologic examination followed by a transvaginal ultrasound to rule out a pelvic mass. If the patient carries a genetic mutation, I would include a CA 125 test to correlate with the imaging findings.

For known *BRCA1* and *BRCA2* genetic carriers, I would recommend prophylactic removal of both the tubes and the ovaries if childbearing has been completed (ages 35 to 40 years), and I would consider extending the age limit into the mid-40s for *BRCA2* carriers, given the later age of presentation.

Suspicious symptoms in a postmenopausal high-risk patient

Dr. Lonky: And how would you manage a postmenopausal patient who reports having current symptoms?

Dr. Tewari: I would follow the same approach for a symptomatic postmenopausal patient as for a premenopausal patient.

Dr. Wright: I agree. As with symptomatic premenopausal patients, we should be suspicious of ovarian cancer–related persistent symptoms in postmenopausal women, especially high-risk women who have a *BRCA* mutation or family history of ovarian cancer. Pelvic examination, transvaginal ultrasonography, and assessment of serum CA 125 are warranted.

Dr. Randall: I would mention that, in postmenopausal women, the risk of malignancy is greater for epithelial ovarian and nongynecologic primaries, such as colon and breast cancer. In addition, the risk for germ cell tumors is much lower than in premenopausal women, and that for sex cord stromal tumors is somewhat equivocal. Therefore, patients should have up-to-date breast and colon screening, and serum studies can be limited to CA 125 and CEA. In these patients, the threshold for gynecologic oncology referral and surgical evaluation should be low.

The premenopausal average-risk woman with symptoms

Dr. Lonky: Consider a woman at average risk for ovarian cancer who is premenopausal and has current symptoms. Please describe your management approach for this patient.

Dr. Wright: While ovarian cancer is often considered the "silent killer," some symptoms have been associated with ovarian cancer. As mentioned, women with ovarian cancer frequently describe symptoms of abdominal and pelvic pain, early satiety, bloating, and urinary urgency and frequency. Although these symptoms are common in the general population, women with ovarian cancer tend to experience them more frequently as well as persistently. An ovarian cancer symptom index has been developed; it includes pelvic and abdominal pain, urinary urgency and frequency, increased abdominal size, bloating, and difficulty eating or feeling full, with symptoms present for less than 1 year and for more than 12 days per month. While some studies have found that these symptoms are useful in detecting ovarian cancer, others have questioned the overall value of symptomatology.

Patients and clinicians should have a heightened suspicion for ovarian cancer when these symptoms are noted. When they do occur, evaluation can include pelvic and rectovaginal examination along with transvaginal ultrasound and measurement of serum CA 125. CA 125 is a nonspecific marker and is often elevated, particularly in premenopausal women. If the results of these tests raise concern for ovarian cancer, patients should be referred to a gynecologic oncologist or a physician with expertise in the diagnosis and management of ovarian cancer.

Dr. Randall: In this age group, other markers, such as human epididymis protein 4 (HE4) and a multivariate index assay (OVA1), might be helpful. HE4 is especially helpful when an elevated CA 125 is likely due to benign disease, such as endometriosis, adenomyosis, or leiomyomata. In these cases, HE4 is much less likely to be falsely elevated, and the Risk of Malignancy Algorithm (ROMA) can be used to calculate risk, but the HE4 level alone is sufficient to triage benign from malignant masses in low-risk patients.[8,9] OVA1 can be used to assist in the triage of pelvic masses planned for surgery due to size or symptomatology to benign gynecologic or gynecologic oncology surgeons. Of note, if the CA 125 is elevated, OVA1 also will be elevated and therefore less helpful than in cases where the CA 125 is normal.

Dr. Tewari: Without an abnormal finding on imaging, I would not order a CA 125 test given the high false-positive rate. If a mass is identified, its clinical features would determine if a CA 125 test is warranted as well as the next steps in surgical management.

Dr. Randall: Fortunately, premenopausal women at average risk for ovarian cancer typically have benign diagnoses, even when they are symptomatic. I would perform the same evaluation as in the high-risk patient, but I would have a higher threshold to suspect cancer, to refer to oncology, and to recommend or perform immediate surgical intervention.

The postmenopausal average-risk woman with symptoms

Dr. Lonky: Your average-risk patient is postmenopausal and has current symptoms. What is your management approach?

Dr. Randall: The approach in this age group is the same as that for the average-risk premenopausal

patient with symptoms, but cancer diagnoses including ovarian, endometrial, colon, or metastatic breast cancer are higher on the differential. Again, up-to-date breast and colon screening, endometrial biopsy for postmenopausal bleeding and abnormal uterine lining thickness, ultrasonography, and serum markers are the mainstays for evaluation.

Pre- and postmenopausal average-risk patients with no symptoms

Dr. Lonky: What is your approach for women who are at average risk for ovarian cancer and have no symptoms—whether they are premenopausal or postmenopausal?

Dr. Wright: Among average-risk women—whether they are premenopausal or postmenopausal—routine screening for ovarian cancer is not recommended. Overall, the prevalence of ovarian cancer in the general population is low. Therefore, even screening tests with a high specificity have a low predictive value for the detection of ovarian cancer, and they require evaluating a large number of women without cancer. This is problematic for ovarian cancer—which requires that women undergo surgery to diagnose a cancer.

Two large screening trials, one in the United States and one in the United Kingdom, evaluated the utility of screening average-risk women with CA 125 and transvaginal ultrasonography for the detection of ovarian cancer.[1,2] Neither trial was able to demonstrate a reduction in mortality with screening. Both trials noted that a significant number of women require surgical intervention to detect 1 case of ovarian cancer, and that surgery was associated with significant morbidity. Based on these data, the US Preventive Services Task Force considers the harms of screening to outweigh the benefits and classifies ovarian cancer screening as category D.

Dr. Randall: I agree, as shown in the PLCO and UKTOCS trials, the harms of screening currently outweigh any benefit.[1,2] Therefore, aside from screening for indications for genetic testing, I do not recommend any special testing in these age groups.

Dr. Tewari: The annual gynecologic examination gives ObGyns an opportunity to ask about symptoms that may be suggestive of ovarian cancer.

Other considerations

Dr. Lonky: Are there any other special case concerns to discuss?

Dr. Tewari: A lot of focus has centered around screening, which ignores the evidence for warranting increased symptom awareness. We need to convey to women the need to be aware of ovarian cancer symptoms, especially those listed in the ovarian cancer symptom index. Use of the symptom index has been associated with identifying the disease at earlier stages, which is important because that is when response and cure rates are higher.

Dr. Randall: I would like to mention additional imaging. Computerized tomography (CT) and magnetic resonance imaging (MRI) should be reserved for cases with abnormal ultrasound findings. CT with intravenous contrast has poor sensitivity for soft-tissue definition and is best employed to detect ascites, retroperitoneal lymphadenopathy, peritoneal carcinomatosis, and gastrointestinal or urinary tract obstruction. T2-weighted MRI with gadolinium contrast has excellent soft-tissue resolution and can be particularly helpful to differentiate ovarian and uterine masses in premenopausal women faced with surgery who desire to retain fertility.

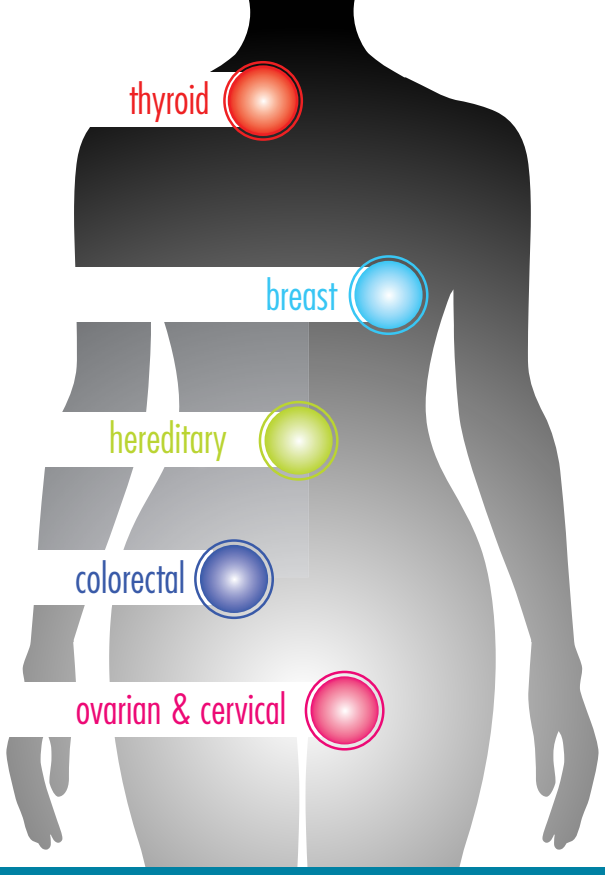
Advanced imaging techniques, such as positron emission tomography (PET), increase costs significantly and often do not change management beyond that derived from CT or MRI studies. Therefore, PET should not be used routinely in the workup of these women.

Dr. Wright: Similar to liquid biopsies, there is interest in detecting ovarian cancer cells that are exfoliated through the lower genital tract. These cells could be obtained in a manner that is similar to collecting a specimen for a Pap test. A technology currently being developed by PapGene Inc uses cells collected from the cervix and examines them for molecular abnormalities. A pilot study found that the test identified 9 of 22 (41%) ovarian cancers. These types of tests are currently being evaluated as a potential modality to aid in the detection of ovarian cancer.

Dr. Lonky: Please explain what liquid biopsies are and how can they be used in gynecology.

Dr. Wright: Liquid biopsy is a test in which a blood sample is collected and analyzed to look for tumor cells. The hope with liquid biopsies is that ovarian cancer could be detected at an earlier

CONTINUED ON PAGE SS14



Everything **she** needs

with the services **you** expect.

LabCorp offers a comprehensive test menu that supports the continuum of care. From screening to diagnosis, treatment decisions, and surveillance, LabCorp is a one-source laboratory provider. LabCorp's advanced technologies enable clinicians to detect and define the disease more accurately for informed treatment decisions.

Tests **She** Needs - cancer prevention, detection, and management

- Breast Cancer
- Cervical Cancer
- Colorectal Cancer
- Hereditary Cancers
- Ovarian Cancer
- Thyroid Cancer

Services **You** Expect - from patient encounter to follow-up

- Scientific expertise
- Genetic counselors
- Patient information and counseling reports
- Patient portal
- Online appointments for blood draws at LabCorp collection sites
- EMR interface solutions
- Monthly cytology summary reports

LabCorp

For more information about LabCorp tests and services, visit www.labcorp.com.

CONTINUED FROM PAGE SS12

stage. Liquid biopsy requires that tumor cells are present in the bloodstream and that these cells have molecular abnormalities that can be used to distinguish the tumor cells from normal cells. There currently are several promising technologies available, and many are undergoing testing and evaluation. At present, this is not a test that is used routinely in practice.

Dr. Tewari: Yes, they are the newest wave in next-generation sequencing. With no effective screening strategies for ovarian cancer to date, liquid biopsies serve as a potential future option. Although the technology of next-generation sequencing is improving by the minute, its role in gynecologic cancers at this time is more one of potential and promise than widespread acceptance. However, that day may not be far off as more and more studies are showing successful comparisons.

Dr. Randall: Liquid biopsies are attractive because not only do they save the patient the inconvenience, risk, and cost of a surgical or CT-guided percutaneous biopsy but also they are associated with a very quick turnaround time (days versus 3 to 4 weeks for tissue biopsy) for timely clinical decision making. If better markers of early stage gynecologic cancers of all types are validated, this technique has significant potential for screening, diagnosis, and monitoring of response to therapy. ■

References

1. Buys SS, Partridge E, Black A, et al; PLCO Project Team. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. JAMA. 2011;305(22):2295–2303.
2. Jacobs IJ, Menon U, Ryan A, et al. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet. 2016;387(10022):945–956.
3. Skates SJ, Greene MH, Buys SS, et al. Early detection of ovarian cancer using the Risk of Ovarian Cancer Algorithm with frequent CA125 testing in women at increased familial risk—combined results from two screening trials. Clin Cancer Res. 2017;23(14):3628–3637.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Genetic/familial high-risk assessment: breast and ovarian. Version 1.2018—October 3, 2017.
5. Lu KH, Kauff ND. Does a BRCA mutation plus tamoxifen equal hysterectomy? Gynecol Oncol. 2007;104(1):3–4.
6. Shu CA, Pike MC, Jotwani AR, et al. Uterine cancer after risk-reducing salpingo-oophorectomy without hysterectomy in women with BRCA mutations. JAMA Oncol. 2016;2(11):1434–1440.
7. Goff BA, Mandel LS, Drescher CW, et al. Development of an ovarian cancer symptom index: possibilities for earlier detection. Cancer. 2007;109(2):221–227.
8. Moore RG, Miller MC, Disilvestro P, et al. Evaluation of the diagnostic accuracy of the risk of ovarian malignancy algorithm in women with a pelvic mass. Obstet Gynecol. 2011;118(2 pt 1):280–288.
9. Anton C, Carvalho FM, Oliveira EI, Maciel GA, Baracat EC, Carvalho JP. A comparison of CA125, HE4, risk ovarian malignancy algorithm (ROMA), and risk malignancy index (RMI) for the classification of ovarian masses. Clinics (Sao Paolo). 2012;67(5):437–441.

CONTINUED FROM PAGE SS6

(PLCO) cancer screening randomized controlled trial. JAMA. 2011;305(22):2295–2303.
34. Menon U, Ryan A, Kalsi J, et al. Risk algorithm using serial biomarker measurements doubles the number of screen-detected cancers compared with a single-threshold rule in the United Kingdom Collaborative Trial of Ovarian Cancer Screening. J Clin Oncol. 2015;33(18):2062–2071.
35. Jacobs IJ, Menon U, Ryan A, et al. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet. 2016;387(10022):945–956.
36. Wittenberger T, Sleigh S, Reisel D, et al. DNA methylation markers for early detection of women's cancer: promise and challenges. Epigenomics. 2014;6(3):311–327.
37. Jacobs I, Bast RC Jr. The CA 125 tumour-associated antigen: a review of the literature. Hum Reprod. 1989;4(1):1–12.
38. Munoz D, Near AM, van Ravesteyn NT, et al. Effects of screening and systemic adjuvant therapy on ER-specific US breast cancer mortality. J Natl Cancer Inst. 2014;106(11).
39. Usher-Smith JA, Emery J, Kassianos AP, Walter FM. Risk prediction models for melanoma: a systematic review. Cancer Epidemiol Biomarkers Prev. 2014;23(8):1450–1463.
40. Wang X, Oldani MJ, Zhao X, Huang X, Qian D. A review of cancer risk prediction models with genetic variants. Cancer Inform. 2014;13(suppl 2):19–28.

8 common questions about newborn circumcision

As the medical benefits of male circumcision become more widely known, it is important to dispel the myths and describe the evidence surrounding this traditional surgical practice

Henry Michael Lerner, MD

In the United States, circumcision is the fourth most common surgical procedure—behind cataract removal, cesarean delivery, and joint replacement.[1] This operation, which dates to ancient times, is chosen for medical, personal, or religious reasons. It is performed on 77% of males born in the United States and on 42% of those born elsewhere who are living in this country.[2] Whether it is performed depends not only on the parents' race, ethnic background, and religion but also on region: US circumcision rates range from 74% in the Midwest to 30% in the West, and in between are the Northeast (67%) and the South (61%).[3]

Circumcision is not without controversy. Some claim that it is unnecessary cosmetic surgery, that it is genital mutilation, that the patient cannot choose it or object to it, or that it decreases sexual satisfaction.

In this article, I review 8 common questions about circumcision and provide data-based answers to them.

Dr. Lerner is Assistant Clinical Professor, Department of Obstetrics and Gynecology, Harvard Medical School, Boston, Massachusetts.

The author reports no financial relationships relevant to this article.

1. Should a newborn be circumcised?

For many years, the medical benefits of circumcision were scientifically ambiguous. With no clear answers, some thought that parents should base their decision for or against circumcision not on any potential medical benefit but rather on their family or religious tradition, or on a social standard, that is, what the majority of families in their community do.

Over the past 20 years, a growing body of evidence has demonstrated real medical benefits of circumcision. In 2012, the American Academy of Pediatrics (AAP), which previously had been neutral on the subject, issued a task force report concluding that the health benefits of circumcision outweigh its risks and justify access to the procedure.[3,4] However, the report stopped short of recommending circumcision.

Opponents have expressed several concerns about circumcision. First, they say, it is painful and unnecessary, and performing it when life has just begun takes the decision away from the adult-to-be, who may want to be uncircumcised as an adult but will have no recourse. Second, they say circumcision will diminish the adult's sexual pleasure. However, there is no proof this occurs, and it is unclear how the claim could be adequately verified.[5]

CONTINUED ON PAGE 28

IN THIS ARTICLE

Health benefits of circumcision page 28

Steps to ensure the best outcome page 29

Who should perform circumcisions? page 30

CONTINUED FROM PAGE 27

Health benefits of circumcision[3]

- Prevention of phimosis and balanoposthitis (inflammation of glans and foreskin), penile retraction disorders, and penile cancer.
- Fewer infant urinary tract infections.
- Decreased spread of human papillomavirus–related disease, including cervical cancer and its precursors, to sexual partners.
- Lower risk of acquiring, harboring, and spreading human immunodeficiency virus infection, herpes virus infection, and other sexually transmitted diseases.
- Easier genital hygiene.
- No need for circumcision later in life, when the procedure is more involved.

FAST TRACK

Epinephrine should never be used with local analgesia for penile infiltration

2. What is the best analgesia for circumcision?

Although in decades past circumcision was often performed without any analgesia, in the United States analgesia is now standard of care. The AAP Task Force on Circumcision formalized this standard in a 2012 policy statement.[4] For newborn circumcision, analgesia can be given in the form of analgesic cream, penile ring block, or dorsal nerve block.

Analgesic EMLA cream (a mixture of local anesthetics such as lidocaine 2.5%/prilocaine 2.5%) is easy to use but is minimally effective in relieving circumcision pain,[6] although some investigators have reported it is efficacious compared with placebo.[7] When used, the analgesic cream is applied 30 to 60 minutes before circumcision.

Both penile ring block and dorsal nerve block with 1% lidocaine are easy to administer and are very effective.[8,9] They are best used with buffered lidocaine, which partially relieves the burning that occurs with injection. With both methods, the smaller the needle used (preferably 30 gauge), the better.

These 2 block methods have different injection sites. For the ring block, small amounts of lidocaine (1.0 to 1.5 mL) are given in a series of injections around the entire circumference of the base of the penis. The dorsal block targets the 2 dorsal nerves located at 10 o'clock and 2 o'clock at the base of the penis. Epinephrine, given its vasoconstrictive properties and the potential for necrosis, should never be used with local analgesia for penile infiltration.

Analgesia can be supplemented with comfort measures, such as a pacifier, sugar water, gentle rubbing on the forehead, and soothing speech.[10]

3. What conditions are required for safe circumcision?

As circumcision is not medically required and need not occur in the days immediately after birth, it should be performed only when conditions are optimal:

- A pediatrician or other practitioner must first examine the newborn.
- The newborn must be full-term, healthy, and stable.
  - —The best time to circumcise a baby born prematurely is right before discharge from the intensive care nursery.
- The penis must be of normal size and without anatomical defect—no micropenis, hypospadias, or penoscrotal webbing.
- The lower abdominal fat pad must not be so large that it will cause the shaft's skin to cover the exposed penile head.
- If there is a family history of a bleeding disorder, the newborn must be evaluated for the disorder before the circumcision.
- The newborn must have received his vitamin K shot.

4. What is the best circumcision method?

Circumcision can be performed with the Gomco circumcision clamp, the Mogen circumcision clamp, or the PlastiBell circumcision device. Each device works well, provides excellent results, and has its pluses and minuses. Practitioners should use the device with which they are most familiar and comfortable, which likely will be the device they used in training.

In the United States, the Gomco clamp is perhaps the most commonly used device. It provides good cosmetic results, and its metal "bell" protects the entire head of the penis. Of the 3 methods, however, it is the most difficult—

the partially cut foreskin must be threaded between the bell and the clamp frame before the clamp is tightened. In many cases, too, there is bleeding at the penile frenulum.

The Mogen clamp, another commonly used device, also is used in traditional Jewish circumcisions. Of the 3 methods, it is the quickest, produces the best hemostasis, and is associated with the least discomfort.[10] To those unfamiliar with the method, there may seem to be a potential for amputation of the head of the penis, but actually there virtually is no risk, as an indentation on the penile side of the clamp protects the penile head.

The PlastiBell device is very easy to use but must stay on until the foreskin becomes necrotic and the bell and foreskin fall off on their own—a process that takes 7 to 10 days. Many parents dislike this method because its final result is not immediate and they have to contend with a medical implement during their newborn's first week home.

Electrocautery is not recommended. Some clinicians, especially urologists, use electrocautery as the cutting mechanism for circumcision. A review of the literature, however, reveals that electrocautery has not been studied head-to-head against traditional techniques, and that various significant complications—transected penile head, severe burns, meatal stenosis—have been reported.[11,12] It is certainly not a mainstream procedure for neonatal circumcision.

Evaluate penile anatomy for abnormalities

Before performing any circumcision, the head of the penis should be examined to rule out hypospadias or other penile abnormalities. This is because the foreskin is utilized in certain penile repair procedures. The pediatrician should perform an initial examination of the penis at the formal newborn physical within 24 hours of delivery. The clinician performing the circumcision should re-examine the penis just before the procedure is begun—by pushing back the foreskin as much as possible—as well as during the procedure, once the foreskin is lifted off the penile head but before the foreskin is excised.

Take steps to ensure the best circumcision outcome

- Just before the procedure, have a face-to-face discussion with the parents. Confirm that they want the circumcision done, explain exactly what it entails, and let them know they will receive complete aftercare instructions.
- Make sure one of the parents signs the consent form.
- Circumcise the right baby! Check the identification bracelet and confirm that the newborn's hospital and chart numbers match.
- Prevent excessive hip movement by securing the baby's legs. The usual solution is a specially designed plastic restraint board with Velcro straps for the legs.
- Examine the infant's penile anatomy prior to the procedure to make certain it is normal.
- For pain relief, administer enough analgesia, as either dorsal nerve block or penile ring block (the best methods). Before injection, draw the plunger of the syringe back to make certain that the needle is not in a blood vessel.
- During the procedure, make sure the entire membranous layer of foreskin covering the head of the penis is separated from the glans.
- Watch the penis for several minutes after the circumcision to make sure there is no bleeding.

5. When is the best time to perform a circumcision?

The medical literature provides no firm answer to this question. The younger the baby, the easier it is to perform a circumcision as a simple procedure with local anesthesia. The older the baby, the larger the penis and the more aware the baby will be of his surroundings. Both these factors will make the procedure more difficult.

Most clinicians would be reluctant to perform a circumcision in the office or clinic after the baby is 6 to 8 weeks old. If a family desires their son to be circumcised after that time—or a medical condition precludes earlier circumcision—the procedure is best performed by a pediatric urologist in the operating room.

6. What are the potential complications of circumcision?

The rate of circumcision complications is very low at 0.2%.[13] That being said, the 3 most common types of complications are

postoperative bleeding, infection, and damage to the penis.

Far and away the most common complication is postoperative **bleeding**, usually at the frenulum of the head of the penis (the 6 o'clock position). In most cases, the bleeding is light to moderate. It is controlled with direct pressure applied for several minutes, the use of processed gelatin (Gelfoam) or cellulose (Surgicel), sparing use of silver nitrate, or placement of a polyglycolic acid (Vicryl) 5-0 suture.

Infection, an unusual occurrence, is seen within 24 to 72 hours after circumcision. It is marked by swelling, redness, and a foul-smelling mucus discharge. This discharge must be differentiated from dried fibrin, which is commonly seen on the head of the penis in the days after circumcision but has no odor or association with erythema, fever, or infant fussiness. True infection should be treated, in collaboration with the child's pediatrician, with a staphylococcal-sensitive penicillin (such as dicloxacillin).

More serious is **damage to the penis**, which ranges from accidental dilation of the meatus to partial amputation of the penile glans. Any such injury should immediately prompt a consultation with a pediatric urologist.

More of a nuisance than a complication is the **sliding of the penile shaft's skin** up and over the glans. This is a relatively frequent occurrence after normal, successful circumcisions. Parents of an affected newborn should be instructed to gently slide the skin back until the head of the penis is completely exposed again. After several days, the skin will adhere to its proper position on the shaft.

FAST TRACK

Potential complications include postoperative bleeding, infection, penile damage, and sliding of the penile shaft's skin up and over the glans

7. What is a Jewish ritual circumcision?

For their newborn's circumcision, Jewish parents may choose a bris ceremony, formally called a brit milah, in fulfillment of religious tradition. The ceremony involves a brief religious service, circumcision with the traditional Mogen clamp, a special blessing, and an official religious naming rite. The bris traditionally is performed by a mohel, a rabbi or other religious official trained in circumcision. Many parents have the bris done by a mohel who is a medical doctor. In the United States, the availability of both types of mohels varies.

8. Who should perform circumcisions—obstetricians or pediatricians?

The answer to this question depends on where you practice. In some communities or hospitals, the obstetrician performs newborn circumcision, while in other places the pediatrician does. In addition, depending on local circumstances or the specific population involved, circumcisions may be performed by a pediatric urologist, nurse practitioner, or even out of hospital by a trained religiously affiliated practitioner.

Obstetricians began doing circumcisions for 2 reasons. First, obstetricians are surgically trained whereas pediatricians are not. It was therefore thought to be more appropriate for obstetricians to do this minor surgical procedure. Second, circumcisions used to be done right in the delivery room shortly after delivery. It was thought that the crying induced by performing the circumcision helped clear the baby's lungs and invigorated sluggish babies. Now, however, in-hospital circumcisions are usually done in the days following delivery, after the baby has had the opportunity to undergo his first physical examination to make sure that all is well and that the penile anatomy is normal.

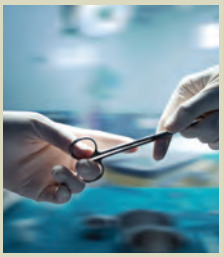
Clinician experience, proper protocol contribute to a safe procedure

In the United States, a large percentage of male infants are circumcised. Although circumcision has known medical benefits, the procedure generally is performed for family, religious, or cultural reasons. Circumcision is a safe and straightforward procedure but has its risks and potential complications. As with most surgeries, the best outcomes are achieved by practitioners who are well

trained, who perform the procedure under supervision until their experience is sufficient, and who follow correct protocol during the entire operation. ●

References

1. Dallas ME. The 10 most common surgeries in the US. Healthgrades website. https://www.healthgrades.com/explore/the-10-most-common-surgeries-in-the-us. Reviewed August 15, 2017. Accessed October 2, 2017.
2. Laumann EO, Masi CM, Zuckerman EW. Circumcision in the United States: prevalence, prophylactic effects, and sexual practice. JAMA. 1997;277(13):1052–1057.
3. American Academy of Pediatrics Task Force on Circumcision. Male circumcision. Pediatrics. 2012;130(3):e756–e785.
4. American Academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. Pediatrics. 2012;130(3):585–586.
5. Morris BJ, Krieger JN. Does male circumcision affect sexual function, sensitivity, or satisfaction? A systematic review. J Sex Med. 2013;10(11):2644–2657.
6. Howard FM, Howard CR, Fortune K, Generelli P, Zolnoun D, tenHoopen C. A randomized, placebo-controlled comparison of EMLA and dorsal penile nerve block for pain relief during neonatal circumcision. Prim Care Update Ob Gyns. 1998;5(4):196.
7. Taddio A, Stevens B, Craig K, et al. Efficacy and safety of lidocaine-prilocaine cream for pain during circumcision. N Engl J Med. 1997;336(17):1197–1201.
8. Lander J, Brady-Fryer B, Metcalfe JB, Nazarali S, Muttitt S. Comparison of ring block, dorsal penile nerve block, and topical anesthesia for neonatal circumcision: a randomized controlled trial. JAMA. 1997;278(24):2157–2162.
9. Hardwick-Smith S, Mastrobattista JM, Wallace PA, Ritchey ML. Ring block for neonatal circumcision. Obstet Gynecol. 1998;91(6):930–934.
10. Kaufman GE, Cimo S, Miller LW, Blass EM. An evaluation of the effects of sucrose on neonatal pain with 2 commonly used circumcision methods. Am J Obstet Gynecol. 2002;186(3):564–568.
11. Tucker SC, Cerqueiro J, Sterne GD, Bracka A. Circumcision: a refined technique and 5 year review. Ann R Coll Surg Engl. 2001;83(2):121–125.
12. Fraser ID, Tjoe J. Circumcision using bipolar scissors can be a safe and simple operation. Ann R Coll Surg Engl. 2000;82(3):190–191.
13. Wiswell TE, Geschke DW. Risks from circumcision during the first month of life compared with those for uncircumcised boys. Pediatrics. 1989;83(6):1011–1015.



Unnecessary laparotomy: $625,000 award

A WOMAN IN HER 20S reported cramping and rectal bleeding to her ObGyn. Pelvic and rectal examinations were normal. Her family physician's exam and a gastroenterologist's rectal exam and colonoscopy were all normal. A radiologist (Dr. A) identified a 3-cm by 6-cm mass on transvaginal ultrasonography. A computed tomography (CT) scan read by another radiologist (Dr. B) confirmed the mass. After receiving the radiologists' reports, the ObGyn told the patient that she had a small tumor that needed immediate removal. No mass was found during exploratory laparotomy.

Three years postsurgery, after trying to conceive, the patient underwent exploratory laparoscopy to evaluate her fallopian tubes. A surgeon found significant pelvic adhesions occluding the left fallopian tube. He lysed the adhesions and resected the left fallopian tube.

PATIENT'S CLAIM: The patient sued the ObGyn and both radiologists, alleging that the unnecessary surgeries resulted in reduced fertility.

Postoperatively, the ObGyn told the patient that the surgery, performed for "nothing," was the radiologists' fault, and that she would have no trouble conceiving. He later blamed her fallopian tube damage on a diagnosis of chlamydia that was successfully treated years earlier with no evidence of reinfection.

The ObGyn disregarded Dr. A's recommendation for a CT scan with rectal contrast; instead he ordered oral contrast. The ObGyn also ignored Dr. B's recommendation for magnetic resonance imaging (MRI).

The mass misidentified by the radiologists was described in 2 different places on the anterior wall of the bowel, both outside the purview of a gynecologist. Given the uncertain diagnosis, referral to a general surgeon was mandated; exploratory laparotomy was not indicated. The ObGyn never referred the patient to a general surgeon for evaluation or sent records or films to the surgeon whom he claimed to have consulted before surgery. The general surgeon denied that any such discussion occurred. The surgeon's first contact with the patient occurred when he was called into the operating room because the ObGyn could not find a mass; the patient was under anesthesia and her abdomen was open.

DEFENDANTS' DEFENSE: The ObGyn claimed that he had developed a plan with the general surgeon before surgery: if the mass was a uterine fibroid, he would remove it, but if the mass was mesenteric, the surgeon would operate.

The ObGyn was justified in performing surgery based on the patient's complaints and the radiologists' findings.

The radiologists contended that, since neither of them expressed certainty, both requested further studies, and neither suggested surgery, their treatment was consistent with the standard of care.

VERDICT: A $625,000 Pennsylvania verdict was returned, finding the ObGyn 100% liable.

Brachial plexus injury: permanent disability

AFTER CONCERNING TEST RESULTS, a woman went to the hospital for induction of labor. During vaginal delivery, a shoulder dystocia was encountered. The baby was born within 60 seconds using the McRoberts maneuver and suprapubic pressure. The ObGyn charted mild shoulder dystocia.

The child has decreased mobility of his left arm. MRI studies and surgical findings confirmed brachial plexus rupture and avulsion at C5–C7. Despite nerve grafting, the child has a significant disability to his left arm and shoulder.

PARENT'S CLAIM: The ObGyn negligently applied excessive lateral traction, improperly used lateral traction as a maneuver, and instructed the mother to continuously push.

PHYSICIAN'S DEFENSE: Shoulder dystocia was properly diagnosed and resolved using standard maneuvers. Traction and pushing are needed during shoulder dystocia management to determine whether the maneuvers are successful. Brachial plexus injuries can occur because of the normal forces of labor and delivery.

VERDICT: An Illinois defense verdict was returned.

Both ureters injured during TAH

A 49-YEAR-OLD WOMAN UNDERWENT total abdominal hysterectomy (TAH)

These cases were selected by the editors of OBG Management *from* Medical Malpractice Verdicts, Settlements, & Experts, *with permission of the editor, Lewis Laska (www.verdictslaska.com). The information available to the editors about the cases presented here is sometimes incomplete. Moreover, the cases may or may not have merit. Nevertheless, these cases represent the types of clinical situations that typically result in litigation and are meant to illustrate nationwide variation in jury verdicts and awards.*

PHOTO: ISTOCK

for removal of a uterine fibroid performed by her gynecologist and a surgical assistant. The patient had limited urine output immediately after surgery, no urinary output overnight, and abdominal pain. The gynecologist ordered a urology consultation. A CT scan showed bilateral ureteral obstruction; an interventional radiology study confirmed a blockage due to severance of both ureters. A nephrostomy was performed and, 6 weeks later, the ureters were reimplanted.

PATIENT'S CLAIM: The severing of both ureters was a negligent surgical error. While the risk of injuring a single ureter is a recognized complication of TAH, it is unacceptable that both ureters were severed.

DEFENDANTS' CLAIM: Standard of care was met: bilateral ureteral injury is a known risk of TAH. Before surgery, the patient was fully informed of the risks and signed a consent agreement. There was no intraoperative evidence that the ureters had been damaged. The injuries were detected as soon as medically possible and timely and successfully treated.

VERDICT: An Illinois defense verdict was returned.

Failure to detect breast cancer: $21.9M verdict against radiologist

A WOMAN WENT to a diagnostic imaging service for ultrasonography (US) after an earlier US was suspicious for a breast mass. She had a history of left breast pain and swelling that had been treated with antibiotics. The radiologist interpreted the second ultrasound as showing no masses; he noted skin thickening and a lymph node abnormality.

Nine months after initial US, the patient had a breast biopsy performed in another state. She was diagnosed with stage 3 breast cancer.

PATIENT'S CLAIM: The radiologist failed to properly interpret the findings of the second ultrasound.

PHYSICIAN'S DEFENSE: The radiologist contended that he was not liable because the technologist failed to place the transducer over the breast lump. The first US films were not provided for comparison.

VERDICT: A $21.9 million Florida verdict was returned.

Mother claims PTSD after twin's stillbirth

EXPECTING TWINS, a 23-year-old woman at 33.5 weeks' gestation reported pain. The ObGyn noted that her cervix was 4-cm dilated, 1 twin was in breech position, and that labor had begun. He recommended that the patient go to the hospital for cesarean delivery but told her that she could go home, shower, and gather her belongings first. When the mother arrived at the hospital 2.5 hours later, the fetal heart-rate (FHR) monitor indicated that one twin's heart was not active. An emergency cesarean delivery was performed. One twin was safely born, but the other died.

PARENT'S CLAIM: The ObGyn failed to properly address the onset of labor. The twin died because of compression of the umbilical cord. If the mother had gone directly to the hospital, FHR abnormalities would have been apparent and timely intervention could have been taken.

The stillbirth caused the onset of severe emotional distress in the mother leading to posttraumatic stress disorder (PTSD). She had extensive counseling. Her psychologist reported that the patient also suffered from complex grief disorder.

PHYSICIAN'S DEFENSE: The ObGyn's actions did not cause the injury. The twins' hearts were monitored at the last prenatal examination and were normal. It was appropriate for the ObGyn to allow the patient to return home before going to the hospital; the situation was urgent but not emergent. The stillbirth resulted from chorioamnionitis, a microscopic condition that is difficult to detect. A pathologist confirmed the diagnosis after examining the placenta.

The extent of the patient's grief was contested. An expert psychiatrist reported that complex grief disorder is not a recognized medical condition, and that, upon his examination, the patient did not exhibit PTSD symptoms.

VERDICT: A New York defense verdict was returned.

Vesicovaginal fistula after hysterectomy

A 39-YEAR-OLD WOMAN with a history of 4 cesarean deliveries and an enlarged fibroid uterus underwent TAH. She subsequently developed urinary incontinence.

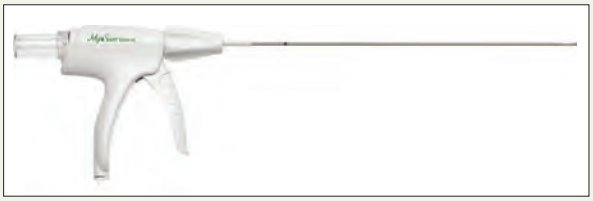
PATIENT'S CLAIM: The ObGyn used an inappropriate dissection technique to remove the uterus, causing a bladder injury. He also sutured the vaginal cuff to the bladder, causing the formation of a vesicovaginal fistula. Repair surgeries were unsuccessful and the patient now is permanently incontinent.

PHYSICIAN'S DEFENSE: The standard of care was met. The patient had a preexisting bladder weakness due to the size of her uterus and prior surgeries. The bladder injury is a known complication of the surgery. The vaginal cuff adhered to the bladder due to postsurgical scarring or fibrosis.

VERDICT: A Michigan defense verdict was returned. ●

PRODUCT Update

HYSTEROSCOPY TISSUE REMOVAL DEVICE



Hologic, Inc, has introduced the **MyoSure® MANUAL Tissue Removal Device** for resecting and removing tissue during in-office hysteroscopic intrauterine procedures. When used with the **MyoSure** hysteroscope, the **MyoSure MANUAL** device has a fully integrated vacuum that does not require external suction and can be operated using a 1-L saline bag. The clear tissue trap allows for visual confirmation of removed tissue, holds up to 4 g of tissue, and detaches to send the specimen to pathology. **Hologic** says that the **MyoSure MANUAL** gives physicians multifunction control of the 360° blade for removal of tissue, including fibroids and polyps. The **MyoSure Manual** is a sterile, nonpowered, hand-actuated, single-use device.

This new **Hologic** product joins the **MyoSure** suite of gynecologic surgical products that includes the MyoSure, MyoSure REACH, MyoSure XL, and MyoSure LITE devices.

FOR MORE INFORMATION, VISIT: http://myosure.com/

SPINAL NAVIGATION TECHNOLOGY FOR EPIDURAL ANESTHESIA

The **Accuro® 3D** image-guided spinal navigation technology by **Rivanna Medical®** is a handheld, lightweight, untethered ultrasound-based system designed to help apply spinal and epidural anesthesia. Ultrasonography is the imaging modality of choice for epidurals in expectant mothers who must avoid the radiation involved in other imaging procedures, according to **Rivanna Medical**.

In a recent trial, **Accuro** identified the appropriate epidural injection sites along the lower spine and calculated the depth to the epidural space. Actual epidural depth was confirmed by measuring needle penetration during successful epidural delivery by anesthesia providers. **Accuro** predicted this depth within an average of 0.61 cm, reports **Rivanna Medical**. In addition, **Accuro** identified the appropriate spinal interspace for needle insertion in 94% of patients and enabled 87% success in first-attempt epidural administration.

FOR MORE INFORMATION, VISIT: https://rivannamedical.com/

SOFTWARE AND HUB HELP IDENTIFY CRITICALLY ILL L&D PATIENTS

PeriGen, Inc, a software-solutions company, has launched **PeriWatch™ HUB™**, new perinatal software and a dashboard for labor and delivery (L&D) units.

PeriGen says that its **PeriWatch** modules provide state-of-the-art L&D documentation and fetal surveillance coupled with analytics and an electronic critical-condition dashboard for hospital maternity units.

HUB is an intelligent perinatal dashboard designed to facilitate the timely recognition of maternity patients who develop critical illness. Using **PeriGen**'s proprietary algorithms, it prioritizes patients based on physician-chosen threshold settings for vital signs, labor progress, and fetal heart rate patterns, and consolidates that data into an easy-to-read interactive dashboard.

FOR MORE INFORMATION, VISIT: http://perigen.com/

ORAL SPRAY VITAMINS: ALTERNATIVE TO PILLS

Instavit® Spray Vitamins offer an alternative to patients who have difficulty swallowing pills. **Instavit** says that its oral vitamins, sprayed directly into the mouth, are sugar-free, tasty, gluten-free, and contain zero calories. The sprays are manufactured to the highest standard in cGMP, FDA approved facilities in the United States. Each **Instavit** spray provides an exact and measured amount of liquid, allowing for correct dosing and also permitting individualization of intake. A 14-oz spray bottle contains about 28 doses.

The **Instavit** line includes: "Prenatal Care," "Vitamin B12," "Instant Energy," "Vitamin D," "Daily Health," "Sweet Dreams," "Immune Strength," "Clearer Thinking," and "Instavit for Kids." **Instavit** products are available in retail stores in North America.

FOR MORE INFORMATION, VISIT: http://www.instavit.com/

WE WANT TO HEAR FROM YOU!

›› Contact us at **rbarbieri@frontlinemedcom.com**

Please include the city and state in which you practice.

INDEX OF ADVERTISERS

AMAG Pharmaceuticals
HSDD Condition Awareness C4
Intrarosa C2

Aspira Labs
Ova1 . . . . . P SS9

CooperSurgical
Delineator . . . . . P 9
Endosee . . . . . P 3

Daiichi-Sankyo
Injectafer . . . . . PP 20–24

Ethicon
Surgicel . . . . . P 15*

LabCorp
Cancer Prevention, Detection, and Management for Women's Health . . . . . P SS13

*Demographic advertisement

CONTINUED FROM PAGE 38

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This study showed that surgeon satisfaction was greatest with the use of mannitol as a distending medium for intraoperative evaluation of ureteral patency compared with oral phenazopyridine, intravenous sodium fluorescein, and normal saline distention. However, time to surgeon confidence of ureteral patency was similar with all 4 methods. More data are needed related to UTIs and the cost of mannitol compared with the other 3 methods.

CHERYL B. IGLESIA, MD

sodium fluorescein or normal saline distention. The median (range) visual analog scores for ureteral patency were phenazopyridine, 48 (0–83); sodium fluorescein 20 (0–82); mannitol, 0 (0–44); and normal saline, 23 (3–96) (P<.001).

There was no difference across the 4 groups in the timing to surgeon confidence of ureteral patency, length of cystoscopy (on average, 3 minutes), and development of postoperative urinary tract infections (UTIs).

Most dissatisfaction related to phenazopyridine is the fact that the resulting orange-stained urine can obscure the bladder mucosa.

One significant adverse event was a protocol deviation in which 1 patient received an incorrect dose of IV sodium fluorescein (500 mg) instead of the recommended 25-mg dose.

Study strengths and weaknesses

The strength of this study is in its randomized design and power. Its major weakness is surgeon bias, since the surgeons could not possibly be blinded to the method used.

The study confirms the problem that phenazopyridine makes the urine so orange that bladder mucosal lesions and de novo hematuria could be difficult to detect. Recommending mannitol as a hypertonic distending medium (as it is used in hysteroscopy procedures), however, may be premature. Prior studies have shown increased postoperative UTIs when 50% and 10% dextrose was used versus normal saline for cystoscopy.[1,2] Since the Grimes study protocol did not include postoperative urine collection for cultures, more research on UTIs after mannitol use would be needed before surgeons confidently could use it routinely.

In our practice, surgeons prefer that intravenous sodium fluorescein be administered just prior to cystoscopy and oral phenazopyridine en route to the operating room. I agree that a major disadvantage to phenazopyridine is the heavy orange staining that obscures visualization.

Finally, this study did not account for cost of the various methods; standard normal saline would be cheapest, followed by phenazopyridine. ●

FAST TRACK

There was no difference across the 4 groups in the timing to surgeon confidence of ureteral patency, length of cystoscopy, and development of postoperative UTIs

References

1. Narasimhulu DM, Prabakar C, Tang N, Bral P. 50% dextrose versus normal saline as distention media during cystoscopy for assessment of ureteric patency. Eur J Obstet Gynecol Reprod Biol. 2016;199:38–41.
2. Siff LN, Unger CA, Jelovsek JE, Paraiso MF, Ridgeway BM, Barber MD. Assessing ureteral patency using 10% dextrose cystoscopy fluid: evaluation of urinary tract infection rates. Am J Obstet Gynecol. 2016;215(1):74.e1–e6.

Did you see these related articles and videos?

» **Alternative options for visualizing ureteral patency during intraoperative cystoscopy**
Paola A. Rosa, DO, Capt, MC, USAF; Scott Kambiss, DO, Col, MC, USAF; and Raul Yordan-Jovet, MD
From the Society of Gynecologic Surgeons

» **Sodium fluorescein as an alternative to indigo carmine during intraoperative cystoscopy**
Paula J. Doyle, MD; Erin E. Duecy, MD; and Ronald W. Wood, PhD
From the Society of Gynecologic Surgeons

» **Farewell to indigo carmine**
Robert L. Barbieri, MD

They're available in the archive at **mdedge.com/obgmanagement**

OBG MANAGEMENT

Is mannitol a good alternative agent for evaluating ureteral patency after gynecologic surgery?

Maybe, but we need more data. There was a significant difference in surgeon satisfaction with the use of mannitol as a bladder distention medium during intraoperative cystoscopy compared with normal saline infusion, oral phenazopyridine, or intravenous sodium fluorescein in an unblinded randomized trial of 130 women who underwent gynecologic surgery at a single institution.

FAST TRACK

Physician satisfaction was statistically significant with the use of mannitol as a bladder distention medium over oral phenazopyridine, and satisfaction was better compared with use of IV sodium fluorescein or normal saline distention

Grimes CL, Patankar S, Ryntz R, et al. Evaluating ureteral patency in the post-indigo carmine era: a randomized controlled trial. Am J Obstet Gynecol. 2017;217(5):601.e1–e10.

EXPERT COMMENTARY
Cheryl B. Iglesia, MD, is Director, Section of Female Pelvic Medicine and Reconstructive Surgery, MedStar Washington Hospital Center, and Professor, Departments of ObGyn and Urology, Georgetown University School of Medicine, Washington, DC. Dr. Iglesia is a member of the OBG MANAGEMENT Board of Editors.

Although the incidence of lower urinary tract and ureteral injury following gynecologic surgery is low, intraoperative identification of ureteral patency can prevent serious long-term sequelae. Since the indigo carmine shortage in 2014, US surgeons have searched for multiple alternative agents. Intravenous methylene blue is suboptimal due to its systemic adverse effects and the length of time for dye excretion in the urine.

Grimes and colleagues conducted a study to determine if there was any significant difference in surgeon satisfaction among 4 different alternatives to indigo carmine for intraoperative ureteral patency evaluation.

The author reports no financial relationships relevant to this article.

Details of the study

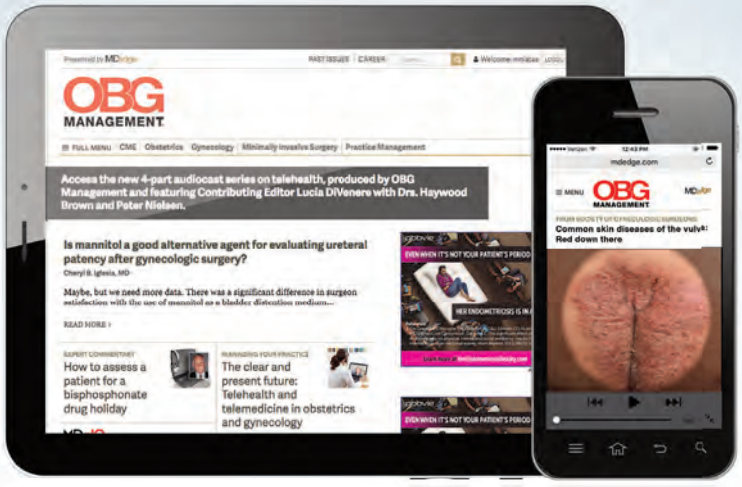
The investigators conducted a randomized clinical trial of 130 women undergoing benign gynecologic or pelvic reconstructive surgery. Four different regimens were used for intraoperative ureteral evaluation: 1) oral phenazopyridine 200 mg, 2) intravenous sodium fluorescein 25 mg, 3) mannitol bladder distention, and 4) normal saline bladder distention.

Study outcomes. The primary outcome was surgeon satisfaction based on a 0 to 100 point visual analog scale rating (with 0 indicating strong agreement, 100 indicating disagreement). Secondary outcomes included ease of ureteral jet visualization, time to surgeon confidence of ureteral patency, and occurrence of adverse events over 6 weeks.

Surgeon satisfaction rating. The investigators found statistically significant physician satisfaction with the use of mannitol as a bladder distention medium over oral phenazopyridine, and slightly better satisfaction compared with the use of intravenous

CONTINUED ON PAGE 37

Have you visited **mdedge.com/obgmanagement** this week?



Look at all the Web exclusive content!

Common skin diseases of the vulva: Red down there
Nancy Fang, MD; Tyler M. Muffly, MD; and Misha Miller, MD
Brought to you by the Society of Gynecologic Surgeons

Are these the right metrics to measure episiotomy rates?
Myron R. Kanofsky, MD

Does maternal sleep position affect risk of stillbirth?
John T. Repke, MD

How to assess a patient for a bisphosphonate drug holiday
Michael R. McClung, MD

Technique for apical suspension at the time of total laparoscopic hysterectomy
Allan Adajar, MD; Lourdes Juarez, MD; James S. Nitti, MD; and Andrea Padilla, MD
Brought to you by the Society of Gynecologic Surgeons

What is the optimal opioid prescription length after women's health surgical procedures?
John T. Repke, MD

Career (of your dreams) advice for young MIGS surgeons
Hye-Chun Hur, MD

Laparoscopic management of chronic pelvic pain due to pelvic adhesions and uterine attachment to abdominal wall mesh utlitizing J-Plasma
Craig E. McCoy, DO

Chlamydia infection: Common, and consequential to women's health
Kathy Christie, Senior Editor, and Tyler Mundhenk, Web and Multimedia Editor

Hypoactive sexual desire disorder: The ideal patient for treatment with flibanserin
Sheryl Kingsberg, MD

Your patient has a large symptomatic fibroid: Tools for decision making
Arnold P. Advincula, MD

Researchers say there is room for improvement in ObGyn opioid prescribing practices
Lila O'Connor, Editor

Clinical implications of cesarean-induced isthmoceles
Deborah Reale, Managing Editor

Plus, visit us online for daily news!

OBG MANAGEMENT

Of course, current and past articles are still there for you—in full text and as convenient, downloadable PDF files. And you'll find an easy way to contact us.

LET'S TALK ABOUT hypoactive SEXual desire disorder

Sex, brain, body: Make the connection™

Hypoactive sexual desire disorder (HSDD) is the most prevalent female sexual dysfunction, affecting approximately 1 in 10 premenopausal women in the United States.[1,2] Its primary symptom is the persistent or recurrent deficiency or absence of sexual or erotic thoughts or fantasies and desire for sexual activity.[3]

Many women suffer in silence.[4,5] Patient understanding of HSDD remains low, and they aren't actively seeking the help they need.[6]

References: 1. Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol.* 2008;112(5):970-978. **2.** Goldstein I, Kim NN, Clayton AH, et al. Hypoactive sexual desire disorder: International Society for the Study of Women's Sexual Health (ISSWSH) expert consensus panel review. *Mayo Clin Proc.* 2017;92(1):114-128. **3.** McCabe MP, Sharlip ID, Atalla E, et al. Definitions of sexual dysfunctions in women and men: A consensus statement from the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med.* 2016;13(2):135-143. **4.** Maserejian NN, Parish S, Shifren JL, Huang L, Gerstenberger E, Rosen RC. Healthcare utilization in women diagnosed with hypoactive sexual desire disorder: interim baseline results from the HSDD registry for women. *J Womens Health.* 2010;19(11):2001-2009. **5.** Data on file. AMAG Pharmaceuticals, Inc. **6.** Shifren JL, Johannes CB, Monz BU, Russo PA, Bennett L, Rosen R. Help-seeking behavior of women with self-reported distressing sexual problems. *J Womens Health.* 2009;18(4):461-468.

amag PHARMACEUTICALS