CONTEMPORARY OB/GYN SEPTEMBER 2013, Vol. 58, No. 9

UMBILICAL CORD PROLAPSE ■ IVF AND TWINS ■ REDUCING INFANT MORTALITY ■ EHR BENEFITS AND COSTS

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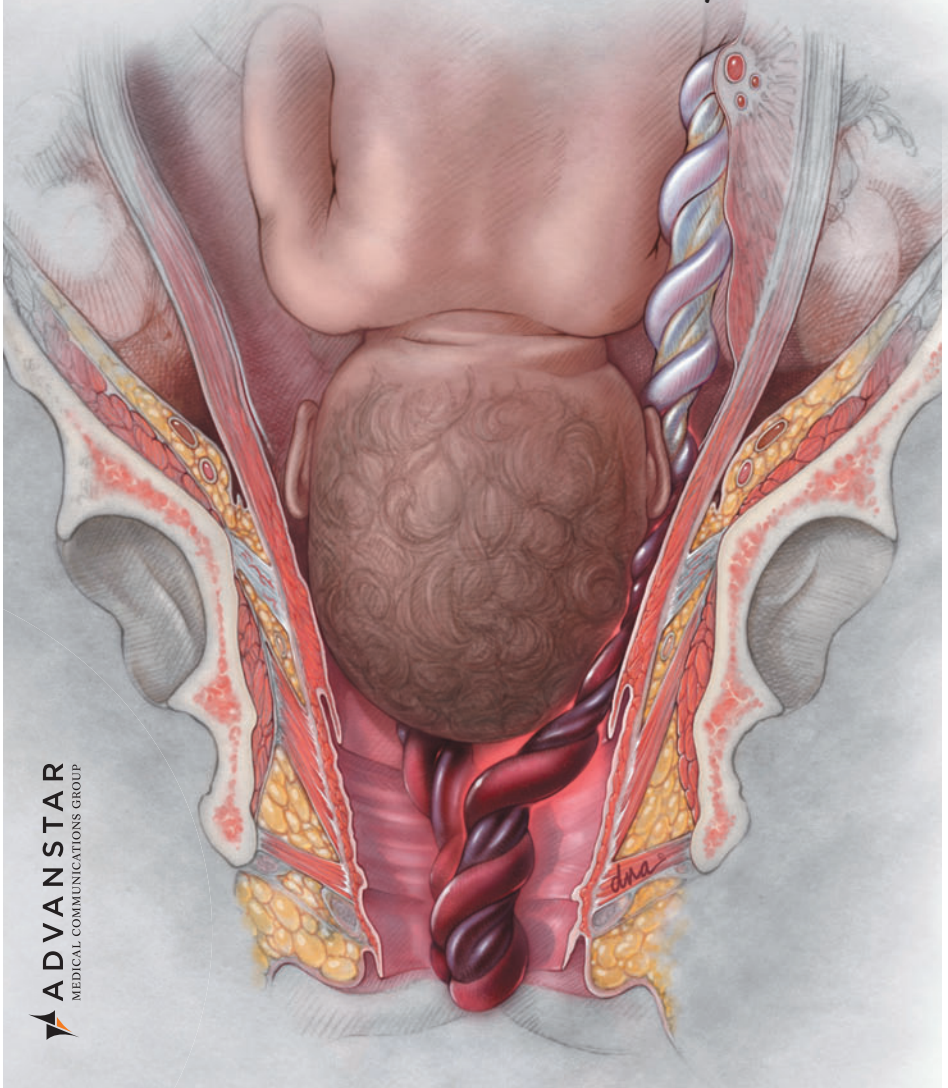

DR. LOCKWOOD ON ICD-10 and the ob/gyn

IVF: Why not twins?

Norbert Gleicher, MD

LEGALLY SPEAKING

Excision without patient consent

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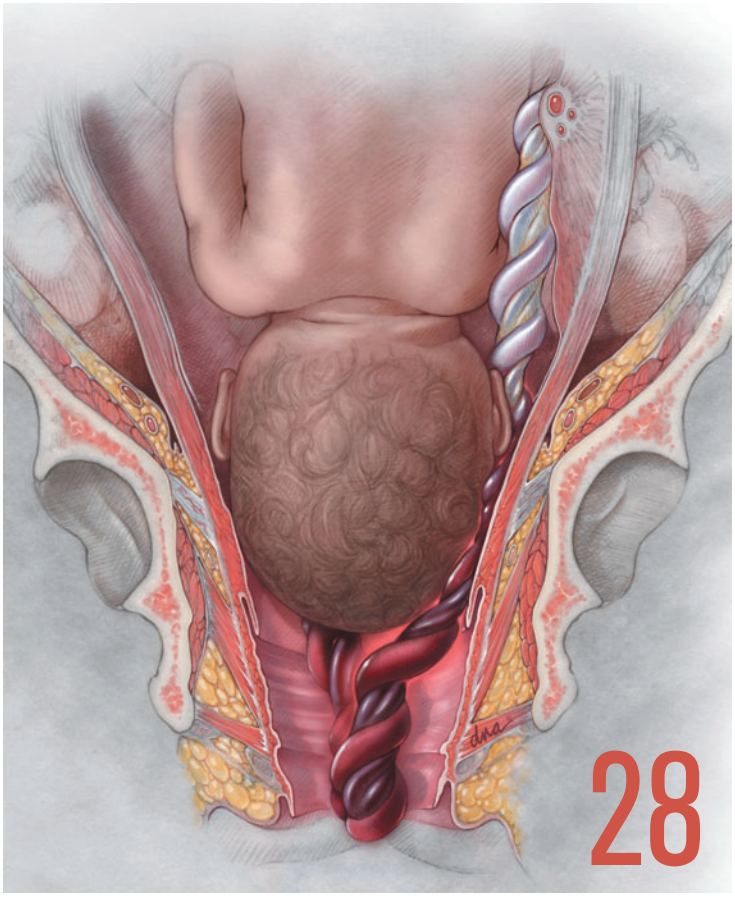

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BY **CHARLES J. LOCKWOOD, MD, MHCM**

ICD-10 and the ob/gyn

If you're getting bored with implementing all the changes in health care wrought by the Affordable Care Act, federal electronic medical record (EMR) mandates, value-based purchasing penalties, increased Medicare audits, unannounced visits from the Joint Commission, and escalating scrutiny from your state's department of health, you are in luck. In about a year, on October 1, 2014, the nation will switch from ICD-9 to ICD-10 codes. This transition will likely be expensive and will certainly be stressful for both you and your office staff.

My advice is to prepare now.

A brief history of the ICD classification system

In 1948 the newly formed World Health Organization (WHO) sought to establish a worldwide system to classify illnesses to promote better measurement of public health outcomes across countries. The resultant lists became the International Classification of Diseases (ICD). Its ninth iteration was released by the WHO in 1977 but it took the United States another 6 years to adopt a clinically modified version (ICD-9-CM), primarily to facilitate Medicare billing.[1]

We have been using various modifications of this system for the past 30 years. The ICD-9-CM codes consist of 3 volumes. The first 2 volumes deal with disease diagnoses and the third, unique to the United States, addresses inpatient procedures.

The federal government contends that the now-36-year-old classification system is simply too old, too unsophisticated, and too limited to justify continued use. Indeed, many classification categories have no additional "space" to permit cataloging of newly discovered disease variants and new procedures.

Moreover, the government also argues that ICD-9 lacks the level of detail needed to facilitate accurate billing, track public health outcomes, and identify emerging pandemics, as well as support health systems' quality improvement and resource utilization efforts.

Ironically, the United States is introducing the ICD-10 classification system nearly 20 years after it was implemented in most other WHO countries, and at a time when the rest of the world is gearing up for ICD-11. Then again, we still measure distance in inches and miles in this country.

How will ICD-10 work and how does it differ from ICD-9?

The ICD-10 system has 2 different components. The first, ICD-10-CM, is based upon the 1990 WHO ICD-10 as modified by the Centers for Disease Control and Prevention and the National Center for Health Statistics. The ICD-10-CM system focuses on disease classification and increases by nearly 5-fold the number of diagnostic codes in ICD-9-CM, from about 14,000 to 68,000.[2]

The second component is the ICD-10-PCS (procedure classification system), which increases the number of procedure codes nearly 20-fold compared with the old ICD-9-CM (volume 3) procedure set, from around 4,000 to 87,000.[3] The ICD-10-PCS system was developed by the Centers for Medicare and Medicaid Services (CMS) aided by 3M Health Information Management, and is for use only in United States inpatient settings.[3] It should not be confused with, and is not meant to replace, the American Medical Association's CPT (Current Procedural Terminology) codes, which are designed to characterize services rendered by providers in both outpatient and inpatient settings (eg, CPT 59400 – antepartum care, delivery and postpartum care).[4]

As noted above, the federal government contends that ICD-10 will improve everything from billing access to our ability to detect impending pandemics. Indeed, it is true

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FIGURE ICD-10-PCS coding format

that ICD-10 codes add a great deal more relevant clinical information. For example, the ICD-9 system does not address laterality (ie, it doesn't distinguish among left, right, and bilateral lesions) nor the episode of care (ie, whether a presentation is initial or subsequent).

The ICD-9 system also lacks any real clinical specificity. For example, where there was one ICD-9 code for a closed fracture of the femur (821.01) there now will be at least 24 codes dealing with such fractures (eg, ICD-10 code S72325G is for "Nondisplaced transverse fractures of the shaft of the left femur, subsequent encounter for closed fracture with delayed healing").

The ICD-10 codes are structurally more complex than the ICD-9 codes. Each ICD-10 code can have 3 to 7 alphanumeric characters instead of ICD-9's 3 or 4 (see Figure). The ICD-10-CM codes have 3 to 7 alphanumeric characters, with the first character always being a letter, the second always a number, and the remaining 5 characters either letters or numbers. All letters are used except U. A decimal point is placed after the first 3 characters. Laterality can be noted in the 5th or 6th digit (1=right; 2=left; and 3=bilateral).[2]

Certain CM code categories, including certain obstetrical ones, always require a 7th character that reflects either the encounter type (usually used with injuries, e.g., A=initial; D=subsequent or S=sequelae), or the identity of the fetus in a multi-fetus pregnancy.

If there are fewer than 6 other characters used for a CM code in which a 7th character is required, the dummy placeholder "x" must be used to present all 7 values (eg, O69.0xx3 labor and delivery complicated by prolapse of cord, fetus # 3). The ICD-10-CM codes are contained in 21 chapters, including Chapter 2, Neoplasms (C00-D48); Chapter 14, Diseases of the genitourinary system (N00-N99), which includes N70-N77-Inflammatory diseases of female pelvic organs and N80-N98-Noninflammatory diseases of female pelvic organs; and Chapter 15, Pregnancy, childbirth and the puerperium (O00-O99).

The ICD-10-PCS codes use all 7 characters without a decimal point. Each character can be either a number or a letter, creating 34 possible values (10 numbers from 0 to 9 plus 24 letters). Thus, there is plenty of "room to grow" to accommodate new procedures. The letters O and I are not used to avoid confusion with the numbers 0 and 1.

All the ICD-10-PCS codes can be derived from the 16 separate sections delineated by the first character in the 7-digit sequence (eg, 0 for medical and surgical procedures, including gynecological surgery, 1 for obstetrical procedures, B for imaging, G for mental health, etc.). That is, the first digit defines the broad procedure category in which a given code can be located.

Changes relevant to ob/gyn

There are twice as many obstetrical codes in ICD-10-CM (2,155) as in ICD-9 (1,104).[5] These new codes add specificity to the characterization of obstetrical conditions. As noted, the ICD-10-CM obstetric codes are listed in Chapter 15. These codes have sequencing priority over those from other chapters and start with the letter "O," not the number zero.

Unlike the ICD-9 codes, ICD-10-CM obstetrical codes are not divided by antepartum, delivery, and postpartum status, but most new codes indicate the trimester of pregnancy in their final character.[6] An additional code from category Z3A should be used to define specific weeks of gestation (eg, Z3A.42 would indicate 42 weeks' gestation). The Z codes connote reasons for encounters in the ICD-10 system.

There are now more codes to describe the nature of medical complications in pregnancy. For example, when diabetes complicates pregnancy it can be further classified as pre-existing (type 1 or 2) and by the trimester in which the encounter occurred (e.g., O24.011 defines "Pre-existing diabetes mellitus, type 1, in pregnancy, first trimester"). Alternatively, gestational diabetes can be described along with its treatment (O24.011 defines "Gestational diabetes mellitus in pregnancy, diet controlled").

Conversely, routine office visits during uncomplicated pregnancies require a code from category Z34 ("Encounter for supervision of normal pregnancy") as the first-listed diagnosis, but no codes from Chapter 15.[7] When a patient has had a full-term uncomplicated delivery of a healthy

ICD-10 transition will require less training, more planning for physicians

BY ALISON RITCHIE

Physicians who fear that they will need to memorize 68,000 new medical codes beginning next year can set their minds at ease.

In a recent *Medical Economics* webinar, "ICD-10 Expert Views on Preparation," 3 panelists discussed some of the major implementation concerns for physicians and offered advice to help them get started.

Rhonda Buckholtz, AACP's vice president of ICD-10 education and training, said physicians should have staff trained incrementally.

"We suggest that you do some rounds of readiness audits," said Buckholtz. "Talk to your vendors. Find out what their timelines are. We have to make sure that everybody works together in the industry, so we don't fail when this comes out."

But physicians may not require as much training as they might think. Buckholtz said physicians in small-to-midsize practices may require only 3 to 6 hours of code training. That's because physicians should think less about the numbers and more about the documentation content that ties into them.

"If you break ICD-10 down, there's actually about 22 unique documentation concepts," said Buckholtz. "For example, if you're talking about a headache, there could be 80-some codes for a headache or migraine. But the documentation concepts break down to about 6.

"So when you teach [physicians] these documentation concepts, this makes it much more manageable for them and puts it in a way that's much more meaningful," Buckholtz added. "We're not saying it's not going to take that much time. But I can't image a physician sitting in one of my 16-hour coding courses. They don't need that same level of training."

Coders, however, will require 20 to 40 hours of training, depending on their specialty and skill level.

Rosemarie Nelson, principal consultant for MGMA Health Care Consulting Group, said that for small-practice physicians who operate with solely a biller, it's time to invest in staff. She suggested getting key staff members ICD-10 code-certified.

"Now people will think, 'Gee, this is going to cost me more.' But when the impact is on all of your financials, there may not be a better alternative," Nelson said. "It would be foolhardy to think that we're going to get physicians trained to understand all of these codes. We need to think about the solutions a little differently."

singleton fetus following an uncomplicated pregnancy and postpartum course, code O80 is used and no others from chapter 15. This code should be accompanied by Z37.0 (Single live birth) as the only outcome-of-delivery code.

The ICD-10-CM codes for elective abortion are contained in Chapter 21 (Factors Influencing Health Status and Contact with Health Services). As noted, Chapter 14 (N00-N99) itemizes diseases of the genitourinary system, which include diagnoses related to the female reproductive and urinary tracts.

As noted above, in ICD-10-PCS, obstetrical procedure codes are designated by the number 1 in the first character of the code, as opposed to medical and surgical procedures, which are designated by the number 0 (zero). For obstetrical procedures, the second character is 0 (zero), connoting pregnancy, and procedures are further characterized by the remaining 5 digits.

Conversely, gynecological surgery is listed under the medical and surgical first character 0 (zero), and then by second character U indicating the female reproductive body system (ie, 0U) and further defined by the other 5 digits (note that while U is not used in ICD-10-CM codes, it is used for PCS codes).

Preparing for ICD-10

Implementation of ICD-10 will require extensive preparation by physicians and their office staff. Billing software will need to be updated, forms changed, and staff trained in the new codes. ICD-10 implementation will also require that coders have a greater knowledge of anatomy, physiology, and medical terminology.[2]

For physicians, implementation will require far more elaborate documentation, because a much higher level of detail is needed to support the more specific ICD-10 codes. Courses and checklists can help. For practices with compatible EMRs, new computer-assisted coding (CAC) programs may also be worth the investment. These programs abstract data using natural language processing and generate suggested ICD-10 codes based on the text words entered.

Expect a productivity decline as you implement ICD-10

BY ERLINE C. FRANKS, CCS-P, CMRS

The major impact from ICD-10 you can expect to see in your practice is a drop in productivity.

The code sets associated with ICD-10 are not a simple update. Rather, they adopt changes in structure and concepts that differentiate them greatly from ICD-9.

Mastering the new code set will take even seasoned coders longer than it took to conquer ICD-9. Don't expect efficiency to normalize immediately following ICD-10 implementation.

Productivity will be affected for all participants in the healthcare system:

- Physicians will be required to provide more detailed documentation related to disease etiology, anatomic site, and severity; healing stages; weeks in pregnancy; and episodes of care.
- Practice managers will have to establish a budget, create initial and ongoing training agendas, and review contracts to determine the impact of ICD-10.
- Nurses and laboratory staff will need to deal with revised forms, provide increased documentation, and revised authorization policies.
- Billing, coding, and front-desk personnel will be confronted with a new advanced beneficiary notice based on local and national coverage determinations; the need for updated and more complex super bills and encounter forms; and the increase in the number of codes.

Although the changes are extensive, the government believes this approach ultimately will lower costs and improve healthcare quality.

An organized approach to implementation is necessary, starting with an impact assessment and a careful inventory of all the office practice changes required to permit the ICD-10 roll-out.[2] Planning should include a timeline of requisite steps. Coordination with payors and testing of systems will also be necessary. However, even with these steps, there is evidence that use of ICD-10 is associated with increased coding time and delays in accounts receivable.[2]

Implementation also will not be cheap. One estimate of the cost for a 3-person practice is around $83,000, rising to $285,000 for a larger 9- to 10-physician practice.[8] These figures are likely to be lower for ob/gyn offices because of the smaller number of new codes used on a regular basis.

Take-home message

Like it or not, ICD-10 is coming. It holds the promise of improved public health, hospital quality assurance, patient safety, and resource utilization, and may reduce CMS fraud and abuse. On the other hand, it will certainly increase practice costs and the workload of all physicians and their office staff. However, use of CAC and more advanced EMRs may mitigate some of the workload and expense.

Finally, because the United States is the last developed nation on the planet not to embrace the ICD-10 system, its time has certainly come. COG

DR LOCKWOOD, editor in chief, is Dean of the College of Medicine and Vice President for Health Sciences at The Ohio State University, Columbus, Ohio.

REFERENCES

1. Mitchell M. The history of ICD 9 coding. http://www.ehow.com/about_5389427_history-icd-coding.html. Accessed August 20, 2013.

2. AAPC. ICD-10: The history, the impact and the keys to success. http://aapcmarketing.s3.amazonaws.com/documents/AAPC_ICD-10_white_paper.pdf. Accessed August 20, 2013.

3. ICD-10 coding: ICD-10-CM vs. ICD-10-PCS. http://www.icd10codesearch.com/coding.php. Accessed August 20, 2013.

4. HealthCare Information Management, Inc. What is the difference between ICD-10-CM and ICD-10-PCS? http://www.hcim.com/2010/04/what-is-the-difference-between-icd-10-cm-and-icd-10-pcs/. Accessed August 20, 2013.

5. Carmichael A. Exploring ICD-10-CM's Chapter 15: pregnancy, childbirth & the puerperium. http://www.icd10monitor.com/index.php?option=com_content&id=415:exploring-icd-10-cms-chapter-15-pregnancy-childbirth-a-the-puerperium&Itemid=106. Accessed August 20, 2013.

6. AAPC. Ob/gyn quick reference for ICD-10-CM. http://cloud.aapc.com/documents/OB-GYN-Quick-Reference_ICD-10-CM.pdf. Accessed August 20, 2013.

7. ICD-10 coding fact sheet: obstetrics and gynecology. http://www.gkcmma.com/sites/www.gkcmma.com/files/resources/ICD-10_OBGYN_Fact_Sheet.pdf. Accessed August 20, 2013.

8. Meyer H. Coding complexity: US health care gets ready for the coming of ICD-10. *Health Aff.* 2011;30(5):968-974.

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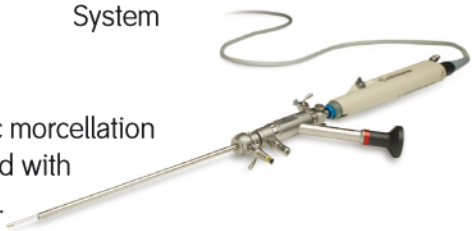

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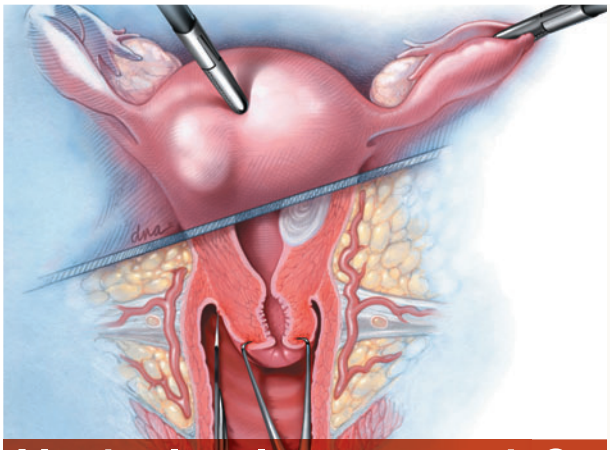

Vaginal or laparoscopic?

A map for hysterectomy success

contemporaryobgyn.net/selecting_hysterectomy_route

A guide to selecting appropriate candidates and the best route for the procedure for benign conditions. Authors Bethany D. Skinner, MD, and John O.L. DeLancey, MD, outline a structured approach to lead to the best outcomes for your patients.

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Google Glass is being tested by surgeons at Ohio State University, where our editor in chief, Charles J. Lockwood, practices. Thanks, Dr. Lockwood, for sharing this cool clip of the technology in use, from CBS News.

Google Glass: The new surgical assistant?
www.cbsnews.com
Google Glass is being touted as a game changer for surgeons and their patients. The camera embedded in the doctors' glasses can livestream what they see and

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Editorial Board Member Joshua Copel is reporting and tweeting live this weekend from the 22nd Annual Ob-Gyn Ultrasound Update for Clinical Practice. Here, over 50 residents listen to John Hobbins on 1st tri dating.

Watch this space and follow @contempobgyn on Twitter for updates on the conference, via hashtag #gohonyc

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Survey finds women misinformed about mesh surgery

A single-institution survey of women at urogynecology and female urology clinics finds them misinformed about vaginal mesh surgery and reluctant to undergo the procedure in the future. The results, reported by *Contemporary OB/GYN* Editorial Board member John O.L. DeLancey, MD, and colleagues, were reported in *Female Pelvic Medicine and Reconstructive Surgery*.

The anonymous questionnaire was completed between April and June 2012 by a convenience sample of women chosen by researchers in the Department of Obstetrics and Gynecology at the University of Michigan. Patient demographics, information sources, and the women's beliefs and concerns about mesh surgery were assessed on the survey. Fisher's exact test was used to identify predictors of patients' beliefs about mesh. Logistic and linear regressions were used to identify predictors of aversion to surgery and higher concern regarding future surgery.

The women's most common source of information about mesh was television commercials (57.8%)

Of the 164 women who completed the survey, 62.2% said they had knowledge about mesh surgery for prolapse and/or incontinence and were included in subsequent analyses. The mean age of the subjects was 58 ±12.5 years and 24.5% of them had previous mesh surgery.

The women's most common source of information about mesh was television commercials (57.8%) and only 23.5% of them said they received information from a medical professional. When asked about mesh, 54% of the women said they had heard about a class-action lawsuit in progress, 47.1% had heard that mesh causes pain, 34.3% about the possibility of bleeding, 29.4% about bleeding and vaginal exposure of mesh, and 27.5% had heard that mesh should be removed because of a recall. Of the women surveyed, 22.1% said they would not consider mesh surgery.

Level of concern, information from friends/family, and knowledge of a class-action lawsuit all were predictive of aversion to mesh surgery on multivariate logistic regression.

Brown LK, Fenner DE, Berger MB, Delancey JO, Morgan DM, Patel DA, Schimpf MO. Defining patients' knowledge and perceptions of vaginal mesh surgery. *Female Pelvic Med Reconstr Surg.* 2013;19(5):282-287.

Mesh complications and miscommunications

A review of pathology evaluations of explanted vaginal mesh specimens highlights a need for greater communication between surgeons and pathologists, says a team of researchers including John O.L. DeLancey, MD, a member of the *Contemporary OB/GYN* editorial board. Better communication will help to ensure accurate documentation, diagnosis, and opportunity for study of the pathophysiology of mesh complications, they claim.

"We recommend improved communication between surgeon and pathologist first and foremost through more complete documentation to aid the pathologist's examination and enable understanding of the pathophysiology of mesh complications," the authors write in the July-August issue of *Female Pelvic Medicine & Reconstructive Surgery*. "This is particularly germane as this subject is 'under the microscope,' as it were, by health care providers, regulatory bodies, the legal system and patients."

The researchers, of the Division of Female Pelvic Medicine and Reconstructive Surgery, Department of Obstetrics and Gynecology, University of Michigan Health System, Ann Arbor, studied the process by which specimens from vaginal mesh removal operations are submitted to pathology departments for evaluation.

Their most striking finding was of limited surgical team documentation of mesh product type or material type on pathology requisition forms. While such requisition details might seem trivial, the authors note, these details help guide the pathologic exam. Explants containing metal or other nonbiological material generally cannot be submitted for standard tissue processing and sectioning. This is because metal and other foreign materials may not be sectioned and made into slides by standard means.

"No history was provided to the pathologist in 24.5% and the mesh type or product name was indicated on only

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Boxed WARNING: Endometrial Cancer and Cardiovascular Disorders

Osphena is an estrogen agonist/antagonist with tissue selective effects. In the endometrium Osphena has estrogen agonistic effects. There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogen therapy. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.

The Women's Health Initiative (WHI) estrogen-alone substudy reported an increased risk of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE) [0.625 mg], relative to placebo. Osphena 60 mg had thromboembolic and hemorrhagic stroke incidence rates of 0.72 and 1.45 per thousand women vs. 1.04 and 0 per thousand women for placebo and a DVT incidence rate of 1.45 vs. 1.04 per thousand women for placebo. Osphena should be prescribed for the shortest duration consistent with treatment goals and risks for the individual woman.

Please see additional Important Safety Information and Brief Summary of the Full Prescribing Information, including Boxed WARNING, on the following pages.

Select Important Safety Information

Contraindications

- Osphena should not be used in patients with undiagnosed abnormal genital bleeding, known or suspected estrogen-dependent neoplasia, active deep vein thrombosis (DVT), pulmonary embolism (PE) or active arterial thromboembolic disease or a history of these conditions
- Women who are or may become pregnant. Osphena may cause fetal harm when administered to a pregnant woman. Ospemifene was embryo-fetal lethal with labor difficulties and increased pup deaths in rats at doses below clinical exposures, and embryo-fetal lethal in rabbits at 10 times the clinical exposure based on mg/m^2. If this drug is used during pregnancy, or if a woman becomes pregnant while taking this drug, she should be apprised of the potential hazard to a fetus

Warnings and Precautions

Osphena has not been adequately studied in women with breast cancer; therefore it should not be used in women with known or suspected breast cancer or with a history of breast cancer.

Osphena should not be used in women with severe hepatic impairment as it has not been studied.

In clinical trials the more commonly reported adverse reactions in ≥1 percent of patients treated with Osphena 60 mg compared to placebo were: hot flush (7.5% vs. 2.6%), vaginal discharge (3.8% vs. 0.3%), muscle spasms (3.2% vs. 0.9%), hyperhidrosis (1.6% vs. 0.6%), and genital discharge (1.3% vs. 0.1%).

Do not use estrogens or estrogen agonists/antagonists, fluconazole, or rifampin concomitantly with Osphena.

Please see Brief Summary of the Full Prescribing Information, including Boxed WARNING, on the following page.

The first and only NON-ESTROGEN ORAL treatment for moderate to severe dyspareunia, due to menopause

- **REVERSES** key physiological signs of vulvar and vaginal atrophy (VVA), which include increasing superficial cells, decreasing parabasal cells, and decreasing vaginal pH
- Significantly **IMPROVED** the most bothersome symptom (MBS)* of VVA, which was moderate to severe dyspareunia
- Available in a 60-mg **ORAL** tablet taken once daily with food
- Most common adverse reactions include hot flush, vaginal discharge, muscle spasms, hyperhidrosis, and genital discharge

NLY The **FIRST** FDA-approved estrogen agonist/antagonist for moderate to severe dyspareunia, due to menopause.

New Osphena™
(ospemifene) tablets
60 mg

STUDY DESIGN: Two 12-week, randomized, double-blind, placebo-controlled, parallel-group efficacy studies in 1745 generally healthy postmenopausal women. The first clinical study included 3 treatment groups: Osphena 30 mg (n=282), Osphena 60 mg (n=276), and placebo (n=268). The second clinical study included 2 treatment groups: Osphena 60 mg (n=463) and placebo (n=456). Clinical endpoints for both clinical studies included: a mean change from baseline to Week 12 for percentage of superficial cells on a vaginal smear, percentage of parabasal cells on a vaginal smear, vaginal pH, and most bothersome symptom of VVA (dyspareunia) self-reported by the patient.* A 52-week, randomized, double-blind, placebo-controlled, long-term safety study was also conducted with 2 treatment groups: Osphena 60 mg (n=363) and placebo (n=63).

*MBS was defined as the most bothersome moderate to severe symptom at baseline.

osphena.com

OSPHENA™ (ospemifene) 60 mg tablets

BRIEF SUMMARY – See Package Insert for Complete Prescribing Information.

WARNING: ENDOMETRIAL CANCER AND CARDIOVASCULAR DISORDERS

Endometrial Cancer

OSPHENA is an estrogen agonist/antagonist with tissue selective effects. In the endometrium, OSPHENA has estrogen agonistic effects. There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy reduces the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed and random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding [see *Warnings and Precautions (5.2)*].

Cardiovascular Disorders

There is a reported increased risk of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) who received daily oral conjugated estrogens (CE) [0.625 mg]-alone therapy over 7.1 years as part of the Women's Health Initiative (WHI) [see *Warnings and Precautions (5.1)*].

In the clinical trials for OSPHENA (duration of treatment up to 15 months), the incidence rates of thromboembolic and hemorrhagic stroke were 0.72 and 1.45 per thousand women, respectively in OSPHENA 60 mg treatment group and 1.04 and 0 in placebo [see *Warnings and Precautions (5.1)*]. The incidence of DVT was 1.45 per thousand women in OSPHENA 60 mg treatment group and 1.04 per thousand women in placebo [see *Warnings and Precautions (5.1)*]. OSPHENA should be prescribed for the shortest duration consistent with treatment goals and risks for the individual woman.

INDICATIONS AND USAGE: OSPHENA is indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

CONTRAINDICATIONS: OSPHENA is contraindicated in women with any of the following conditions:

- Undiagnosed abnormal genital bleeding
- Known or suspected estrogen-dependent neoplasia
- Active DVT, pulmonary embolism (PE), or a history of these conditions
- Active arterial thromboembolic disease [for example, stroke and myocardial infarction (MI)], or a history of these conditions
- OSPHENA is contraindicated in women who are or may become pregnant. OSPHENA may cause fetal harm when administered to a pregnant woman. Ospemifene was embryo-fetal lethal with labor difficulties and increased pup deaths in rats at doses below clinical exposures, and embryo-fetal lethal in rabbits at 10 times the clinical exposure based on mg/m^2. If this drug is used during pregnancy, or if a woman becomes pregnant while taking this drug, she should be apprised of the potential hazard to a fetus.

WARNINGS AND PRECAUTIONS

Cardiovascular Disorders

Risk factors for cardiovascular disorders, arterial vascular disease (for example, hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) and/or venous thromboembolism (VTE) (for example, personal history or family history of VTE, obesity, and systemic lupus erythematosus), should be managed appropriately.

Stroke

In the WHI estrogen-alone substudy, a statistically significant increased risk of stroke was reported in women 50 to 79 years of age receiving daily CE (0.625 mg)-alone compared to women in the same age group receiving placebo (45 versus 33 per ten thousand women-years). The increase in risk was demonstrated in year 1 and persisted.

In the clinical trials for OSPHENA (duration of treatment up to 15 months), the incidence rates of thromboembolic and hemorrhagic stroke were 0.72 and 1.45 per thousand women, respectively in OSPHENA 60 mg treatment group and 1.04 and 0 per thousand women in placebo.

Should thromboembolic or hemorrhagic stroke occur or be suspected, OSPHENA should be discontinued immediately.

Coronary Heart Disease

In the WHI estrogen-alone substudy, no overall effect on coronary heart disease (CHD) events (defined as non-fatal MI, silent MI, or CHD death) was reported in women receiving estrogen-alone compared to placebo. In the OSPHENA clinical trials, a single MI occurred in a woman receiving 60 mg of ospemifene.

Venous Thromboembolism

In the WHI estrogen-alone substudy, the risk of VTE (DVT and PE), was increased for women receiving daily CE (0.625 mg)-alone compared to placebo (30 versus 22 per ten thousand women-years), although only the increased risk of DVT reached statistical significance (23 versus 15 per ten thousand women-years). The increase in VTE risk was demonstrated during the first 2 years.

In the OSPHENA clinical trials, the incidence of DVT was 1.45 per thousand women in OSPHENA 60 mg treatment group and 1.04 per thousand women in placebo. Should a VTE occur or be suspected, OSPHENA should be discontinued immediately.

If feasible, OSPHENA should be discontinued at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization.

Malignant Neoplasms

Endometrial Cancer

OSPHENA is an estrogen agonist/antagonist with tissue selective effects. In the endometrium, OSPHENA has agonistic effects. In the OSPHENA clinical trials (60 mg treatment group), no cases of endometrial cancer were seen with exposure up to 52 weeks. There was a single case of simple hyperplasia without atypia. Endometrial thickening equal to 5 mm or greater was seen in the OSPHENA treatment groups at a rate of 60.1 per thousand women vs 21.2 per thousand women for placebo. The incidence of any type of proliferative (weakly plus active plus disordered) endometrium was 86.1 per thousand women in OSPHENA vs 13.3 per thousand women for placebo. Uterine polyps occurred at an incidence of 5.9 per thousand women vs 1.8 per thousand women for placebo.

An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in a woman with a uterus. The reported endometrial cancer risk among unopposed estrogen users is about 2 to 12 times greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with the use of estrogens for less than 1 year. The greatest risk appears to be associated with prolonged use, with increased risks of 15- to 24-fold for 5 to 10 years or more. This risk has been shown to persist for at least 8 to 15 years after estrogen therapy is discontinued. Adding a progestin to postmenopausal estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. There are, however, possible risks that may be associated with the use of progestins with estrogens compared to estrogen-alone regimens. These include an increased risk of breast cancer. The use of progestins with OSPHENA therapy was not evaluated in the clinical trials.

Clinical surveillance of all women using OSPHENA is important. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.

Breast Cancer

OSPHENA 60 mg has not been adequately studied in women with breast cancer; therefore it should not be used in women with known or suspected breast cancer or with a history of breast cancer.

Severe Hepatic Impairment

OSPHENA should not be used in women with severe hepatic impairment [see Use in Specific Populations (8.7), and Clinical Pharmacology (12.3)].

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Cardiovascular Disorders [see *Boxed Warnings, Warnings and Precautions (5.1)*]
- Malignant Neoplasms [see *Boxed Warnings, Warnings and Precautions (5.2)*]

Clinical Trial 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.

The safety of OSPHENA has been assessed in nine phase 2/3 trials (N=1892) with doses ranging from 5 to 90 mg per day. The duration of treatment in these studies ranged from 6 weeks to 15 months. Most women (N=1370) had a treatment period of at least 12 weeks, 409 had at least 52 weeks (1 year) of exposure.

The incidence rates of thromboembolic and hemorrhagic stroke were 0.72 per thousand women (1 reported case of thromboembolic stroke) and 1.45 per thousand women (2 reported cases of hemorrhagic stroke), respectively in OSPHENA 60 mg treatment group and 1.04 and 0 per thousand women, respectively in placebo. The incidence of deep vein thrombosis (DVT) was 1.45 per thousand women in OSPHENA 60 mg treatment group (2 reported cases of DVT) and 1.04 (1 case of DVT) in placebo.

In clinical trials the more commonly reported adverse reactions in ≥1 percent of patients treated with Osphena 60 mg compared to placebo were: hot flush (7.5% vs. 2.6%), vaginal discharge (3.8% vs. 0.3%), muscle spasms (3.2% vs. 0.9%), hyperhidrosis (1.6% vs. 0.6%), and genital discharge (1.3% vs. 0.1%).

DRUG INTERACTIONS

OSPHENA is primarily metabolized by CYP3A4 and CYP2C9. CYP2C19 and other pathways contribute to the metabolism of ospemifene.

Estrogens and estrogen agonist/antagonist

OSPHENA should not be used concomitantly with estrogens and estrogen agonists/antagonists. The safety of concomitant use of OSPHENA with estrogens and estrogen agonists/antagonists has not been studied.

Fluconazole

Fluconazole, a moderate CYP3A/strong CYP2C9/moderate CYP2C19 inhibitor, should not be used with OSPHENA. Fluconazole increases the systemic exposure of ospemifene by 2.7-fold. Administration of fluconazole with ospemifene may increase the risk of OSPHENA-related adverse reactions [see *Clinical Pharmacology (12.3)*].

Rifampin

Rifampin, a strong CYP3A4/moderate CYP2C9/moderate CYP2C19 inducer, decreases the systemic exposure of ospemifene by 58%. Therefore, coadministration of OSPHENA with drugs such as rifampin which induce CYP3A4, CYP2C9 and/or CYP2C19 activity would be expected to decrease the systemic exposure of ospemifene, which may decrease the clinical effect [see *Clinical Pharmacology (12.3)*].

Ketoconazole

Ketoconazole, a strong CYP3A4 inhibitor increases the systemic exposure of ospemifene by 1.4-fold. Administration of ketoconazole chronically with ospemifene may increase the risk of OSPHENA-related adverse reactions [see *Clinical Pharmacology (12.3)*].

Warfarin

Repeated administration of ospemifene had no effect on the pharmacokinetics of a single 10 mg dose of warfarin. No study was conducted with multiple doses of warfarin. The effect of ospemifene on clotting time such as the International Normalized Ratio (INR) or prothrombin time (PT) was not studied [see *Clinical Pharmacology (12.3)*].

Highly Protein-Bound Drugs

Ospemifene is more than 99% bound to serum proteins and might affect the protein binding of other drugs. Use of OSPHENA with other drug products that are highly protein bound may lead to increased exposure of either that drug or ospemifene [see *Clinical Pharmacology (12.3)*].

Multiple Enzyme Inhibition

Coadministration of OSPHENA with a drug known to inhibit CYP3A4 and CYP2C9 isoenzymes may increase the risk of OSPHENA-related adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic effects: Pregnancy Category X [see *Contraindications (4)*].

Nursing Mothers

It is not known whether OSPHENA is excreted in human breast milk. In a nonclinical study, ospemifene was excreted in rat milk and detected at concentrations higher than that in maternal plasma.

Pediatric Use

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

Geriatric Use

Of the 1892 OSPHENA-treated women enrolled in the nine phase 2/3 trials of OSPHENA, >19 percent were 65 years of age or older. No clinically meaningful differences in safety or effectiveness were observed between these women and younger women less than 65 years of age.

Renal Impairment

The pharmacokinetics of ospemifene in women with severe renal impairment (CrCL<30 mL/min) was similar to those in women with normal renal function [see *Clinical Pharmacology (12.3)*].

No dose adjustment of OSPHENA is required in women with renal impairment.

Hepatic Impairment

The pharmacokinetics of ospemifene has not been studied in women with severe hepatic impairment (Child-Pugh Class C); therefore, OSPHENA should not be used in women with severe hepatic impairment [see *Warnings and Precautions (5.3)*, and *Clinical Pharmacology (12.3)*].

No clinically important pharmacokinetic differences with OSPHENA were observed between women with mild to moderate hepatic impairment and healthy women [see *Clinical Pharmacology (12.3)*].

No dose adjustment of OSPHENA is required in women with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment.

OVERDOSAGE

There is no specific antidote for OSPHENA.

Based on OSPHENA (ospemifene) 60 mg tablets, Prescribing Information 02/2013.

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7% of requisitions. In the absence of this information, 1 in 5 specimens were described as "metal" or "metallic," reports that would clearly be confusing and potentially damaging in the current climate of escalating regulatory and medicolegal concerns," said Tovia Smith, MD.

Grossly undetectable metal fibers may prevent sectioning. Even fine polypropylene mesh fibers may make tissue evaluation difficult due to splintering or lack of adhesion to slides.

The group suggests that either gross or histopathologic examination is appropriate for mesh explants. They found that documentation of clinical history, mesh product, and material was frequently incomplete and associated with increased submission of tissue for histology and inaccurate gross impression of material type.

They recommend improved documentation to aid pathologic examination and enable future study of the pathophysiology of mesh complications.

Smith TM, Smith SC, DeLancey JO, et al. Pathologic evaluation of explanted vaginal mesh: Interdisciplinary experience from a referral center. *Female Pelvic Med Reconstr Surg*. 2013;19(4):238-241.

'GOHO' course taught by leaders in ultrasound

Residents in obstetrics and gynecology were privileged to receive training last month during a program hosted by The Gottesfeld-Hohler Memorial Foundation, a nonprofit organization dedicated to improving education in ultrasound for ob/gyns.

Contemporary OB/GYN Editorial Board member Joshua A. Copel, MD, John Hobbins, MD, and Larry A. Platt, MD, were among the leaders in the field who taught the course, which was held at the Icahn School of Medicine at Mount Sinai in New York City.

The free course was aimed at reaching second-year residents early in the year, at a time when they have finished off-service rotations, have some general knowledge about ob/gyn, and are preparing to embark on more intensive study exclusive to the specialty. On an August weekend, the first-time 2-day program, which was also supported by the American College of Obstetricians and Gynecologists (ACOG) Council on Resident Education in Obstetrics and Gynecology (CREOG), the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), and the American Institute of Ultrasound in Medicine (AIUM), drew 59 residents.

Founded in the late 1980s, The Gottesfeld-Hohler Memorial Foundation honors the memory of two early pioneers of ob/gyn ultrasound, Kenneth Gottesfeld and Charles Hohler. Founded by Drs. Platt and Hobbins, Jim Binns, and Marty Wilcox, the organization has co-sponsored a research award with ACOG, has run "think tanks," and provides grants for other ultrasound education activities. Faculty for the Foundation receive only expense reimbursements and no honoraria. Dr. Copel, who is the group's treasurer, reports that more than 98% of the money raised goes to support scholarly activities.

The research and educational grants provided by the Foundation in the past benefited only one individual a year. The ultrasound program is the organization's way of leveraging its limited assets to support its goal of improving ultrasound education for ob/gyns. Corporate sponsors for the event were GE, Philips, Samsung, and MedaPhor.

Speaking for the Foundation, Dr. Copel and Dr. Platt extended the organization's gratitude to the staff at Mount Sinai, especially Drs. Joanne Stone, Brian Wagner, Garfield Clunie, and Michael Brodman, and their chief sonographer, Kim Abruzese, and the sponsors. Said Dr. Copel, "We are also tremendously indebeted to our faculty—Joanne Stone, Lynn Simpson, Michael Divon, Peer Dar, Ilan Timor-Tritsch, George Bega, and Lori Crites, RDMS."

PHOTOS COURTESY KIMBERLY ABRUZESE, RDMS

Ample vaccine supply key to combatting unpredictability of flu season

The only predictable aspect of the influenza season is its unpredictability, according to experts.

For example, the 2012–2013 influenza season was moderately severe, started early, and lasted longer than a usual influenza season. On the other hand, the 2011–2012 year was a mild influenza year.

The 2013-2014 influenza season is the first time that quadrivalent influenza vaccines will be available in the United States.

"The best way to be prepared for the upcoming influenza season is to ensure that there is an ample vaccine supply, it is available early and throughout the season, that influenza vaccine be strongly recommended by healthcare providers for all individuals 6 months of age and older, and there is adequate coverage and reimbursement by insurance providers," said Pedro Piedra, MD, professor, department of molecular virology & microbiology at Baylor College of Medicine, Houston, Texas.

The 2013-2014 influenza season is the first time that quadrivalent influenza vaccines will be available in the United States. Previously, only trivalent influenza vaccines were available, which contained 2 influenza A strains and one influenza B strain.

Women, men may experience depression in equal numbers

A new investigation published online by *JAMA Psychiatry* discusses differences in how depression manifests in men and women. Researchers from the University of Michigan and Vanderbilt University found that men meet the criteria for depression in proportions equal to women when evaluated for the condition using a sex-specific symptom checklist.

Women are diagnosed with depression twice as often as men, which the authors theorize is due to diagnostic criteria rather than actual differences in rates of depression.

Rather than appearing sad, the authors write, men experiencing emotional pain are more likely to react with "anger, self-destructive behavior, self-distraction … substance use, gambling, womanizing, and workaholism." They note that many researchers have proposed that irritability could be the key symptom linking men and depression.

Analysis of data from the National Comorbidity Survey Replication was done with a scale that included alternative, "male-type" symptoms of depression found that a higher proportion of men (26.3%) than women (21.9%) (P = .007) met criteria for depression.

When alternative and traditional depression symptoms were included in the analysis, men and women were found to meet the criteria for depression in equal proportions: 30.6% of men and 33.3% of women (P = .57).

Martin LA, Neighbors HW, Griffith DM. The experience of symptoms of depression in men vs women: analysis of the National Comorbidity Survey Replication. *JAMA Psychiatry.* Published online August 28, 2013. doi:10.1001/jamapsychiatry.2013.1985

MRI + mammography reduces risk of familial breast cancer

A recent study in *The Journal of the National Cancer Institute* shows that annual mammography plus magnetic resonance imaging (MRI) screenings can improve survival in women with nongenetic, familial breast cancer. The cost-effectiveness is questionable, however, particularly in younger women.

Fifteen percent to 20% of all breast cancers are familial and associated with development of disease earlier than in women with no family history or gene mutation. Because of that risk, women with a family history of breast cancer typically undergo mammography before age 50.

In the new study, researchers from the Netherlands used data from the largest prospective MRI screening study (MRISC). From 1999 to 2007, 1597 women aged 25 to 70 with an estimated cumulative lifetime cancer risk of 15% to 50% were screened with semi-annual clinical breast examination and annual mammography and MRI. In the 8370 woman-years screened, 47 cases of breast cancer were diagnosed, including 9 cases of ductal carcinoma in situ.

The calculated cost of screening, along with additional MRI costs, was $123,672 per detected cancer. Costs continuously decreased with increased age, likely due to higher incidence rate in older women. Cost per life-year is about 2.5 times higher with MRI, but the reduction in mortality went from 17% to 25% because of earlier detection.

Saadatmand S, Tilanus-Linthorst M, Rutgers E, et al. Cost-effectiveness of screening women with familial risk for breast cancer with magnetic resonance imaging. *J Natl Cancer Inst.* 2013 Aug 12 doi: 10.1093/jnci/djt203.

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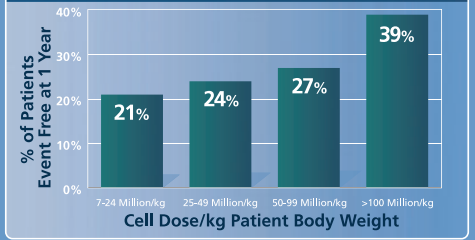

Transplant Success is the % of patients without events defined as death, autologous reconstitution and receipt of a second graft. All such events indicate graft failure.

1. Rubinstein P, Carrier C, Scaradavou A, Kurtzberg J, et al. Outcomes among 562 recipients of placental-blood transplants from unrelated donors. N Engl J Med. 1998;339(22):1565-1577. 2. PR Newswire. The umbilical cord blood stem cells: prime source for transplants and future regenerative medicine. http://www.prnewswire.co.uk/cgi/news/release?id=341146. November 29, 2011. 3. Marrow Donor Program®. Trends in allogeneic transplants. http://www.marrow.org/PHYSICIAN/URD_Search_and_Tx/Number_of_Allogeneic_Tx_Perfor/index.html. Accessed September 14, 2011.

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Excision without consent leads to $2 million settlement

FACTS

On December 17, 2001, a 52-year-old woman saw Dr. A for a gynecology/oncology consult at the direction of her gynecologist. The patient/plaintiff had been diagnosed with lichen sclerosus years earlier. She reported to Dr. A that her condition had been unresponsive to all previous medical treatment, including antifungal, estrogen, testosterone, corticosteroid, and antibacterial medications. Dr. A performed an exam of the external genitalia and observed whitish discoloration in the anterior vulva area consistent with lichen sclerosus. He also noted small fissures in the discolored area and around the perianal area.

He recommended a trial of clobetasol propionate for 4 weeks and then a re-evaluation.

At a January 3, 2002, follow-up appointment, the plaintiff's condition had not responded to the clobetasol and she complained of worsening vulvar itching. Dr. A performed a physical exam and observed scratched fissures on the labia minora and majora, as well as white discoloration on the perianal area. On January 14 he performed a simple vulvectomy. Superficial layers of skin were removed from the labia minora, the anterior part of the labia majora, the clitoral hood, and the posterior areas between the introitus and the perianal area. The full thickness of the skin was not excised and Dr. A's operative report stated that he did not excise the clitoral area.

> "The doctor's operative report stated that he did not excise the clitoral area."

After surgery, the plaintiff was ambulating and afebrile, and Dr. A noted no complaints from her. At discharge, Dr. A instructed the patient to take sitz baths 3 times a day and avoid exaggerated movements and sexual activity.

On February 28, 2002, the patient saw Dr. A for a follow-up appointment. The plaintiff reported no pain or discharge, nor did she have complaints about her gastrointestinal or genitourinary systems. She was healing well except for small superficial wound suppuration in the posterior fourchette. Because of the suppuration, Dr. A advised the plaintiff to rest her pelvis, and specifically to abstain from sexual activity and avoid touching the area or using tampons. He instructed her to return in 4 weeks but she did not and also missed a June 6, 2002, follow-up appointment.

In the meantime, the woman saw another gynecologist on June 8 and again on June 27. She was treated with metronidazole for "a vaginal problem."

On June 13, the plaintiff saw Dr. A for a follow-up appointment. She had no itching or bleeding in the perineal area and had no other complaints. Dr. A noted a whitish dry scar superior to the plaintiff's clitoris, abrasions in the perineal region, and scratch marks along the incision line on the left side of her posterior vulva. He gave her instructions for perineal care and advised her to return in 5 weeks.

The plaintiff returned to Dr. A on September 26, 2002, and complained of vulvar itching. Dr. A observed that the lichen sclerosus had returned and covered the anterior vulva including the clitoral hood, the labia minora, and the posterior fourchette. He prescribed testosterone gel, advised the plaintiff to return in 4 weeks, and noted that if the cream failed, a surgical resection would be considered.

On November 7, 2002, the plaintiff returned to Dr. A and reported that she had not used the testosterone cream that he had prescribed. Dr. A examined the plaintiff and observed the same areas of lichen sclerosus and a rectocele in the front wall of the rectum into the vagina. His

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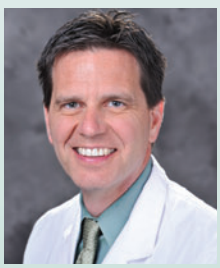

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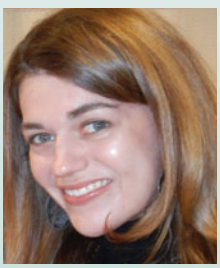
Maternal-Fetal Medicine
Medical University of South Carolina

Founding partner, Physician Maternal-Fetal Specialists
Atlanta, Georgia

Genevieve Fairbrother, MD, MPH

Obstetrics and Gynecology, Board Certified, Tufts University School of Medicine

Chief of Staff, Northside Hospital in Atlanta, GA



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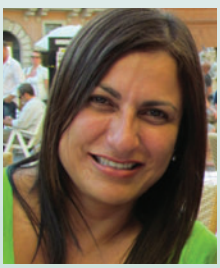

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plan for surgical correction included a second partial/simple vulvectomy and a posterior repair but no work on the rectocele. He later testified that he wanted to take care of the lichen first.

The plaintiff returned to Dr. A on February 14, 2003, complaining of itching. An exam revealed that the lichen sclerosus had returned. On February 24, Dr. A performed a second simple vulvectomy and laser vaporization of the clitoral hood and the affected perianal area. He removed a superficial layer of skin from the clitoral hood but left the rest of the clitoral hood and the clitoris intact. The final pathology report indicates advanced lichen sclerosus.

On May 5, 2003, Dr. A saw the plaintiff again and she complained of itching around the clitoris. An exam revealed lichen sclerosus in the anterior vulvar area, anterior to the clitoral hood, extending to the labia minora on both sides and a small area on the posterior vulva on the left side. A small area with firm nodules at the introitus closest to the perineum did not constitute lichen sclerosus.

Dr. A later testified that he planned for a wide local excision because the lesions observed on May 5 were smaller and localized and did not necessitate taking out a large section of vulvar skin. He also testified that if the clitoris were going to be removed, it would have been mentioned in his notes as a resection of the organ, and not merely a local excision of the skin.

Dr. A's operative report from the radical vulvectomy he performed on May 19, 2003, reads "the decision was made to resect the clitoris together with the gross lesion." He later testified, however, that he did not resect the clitoris and that the statement in the report was a dictation error. Had he removed the clitoris, he said, he would have dictated it in the operative procedure note as a resection of the clitoris, and it would have been written in both his operative note and the pathology report.

When Dr. A saw the plaintiff for the final time on June 27, 2003, she complained of itching at the perineal body. Dr. A observed a lesion of persistent lichen sclerosus in the perineal area. He prescribed clobetasol propionate for 2 weeks and advised the plaintiff to return in 4 weeks. He also noted that a surgical re-excision would be necessary. Subsequent records reveal that the plaintiff's lichen sclerosus returned.

ALLEGATIONS

The plaintiff alleged that Dr. A failed to obtain proper informed consent and failed to use alternate medical therapies—such as retinoids, cryotherapy, photodynamic therapy, and topical macrolide immunosuppressants—instead of surgery.

The plaintiff's lawyers also contended that Dr. A unskillfully and unnecessarily performed multiple vulvar surgeries. They further argued that Dr. A inadvertently and/or negligently removed the clitoris and that the surgeries resulted in a "fused vagina."

DISCOVERY

Dr. A refuted the suggestion that he removed the clitoris, and neither the initial physical examination nor the subsequent treatment records definitively reported that the entire clitoris had been removed. However, physical exam by the plaintiff's expert physician reported the absence of a clitoris, extreme narrowing of the vaginal opening, and thinning and hypopigmentation of the vulva and perineum.

Our expert ob/gyn felt that the case could not be defended because there was no indication for surgical treatment in the absence of vulvar cancer. Lichen sclerosus is known to recur, and excision will not prevent recurrence, our physician noted. Our dermatology expert expressed the same opinion.

Finally, upon review of the pathology slides, it was determined that the clitoris had in fact been removed. At no time did the patient give consent for such an excision.

RESOLUTION

Before this case went to trial it was settled for $2 million.

ANALYSIS

This case is more about poor judgment and surgical inadvertence than about a charting error. Dr. A should have carefully read the operative part of the plaintiff's medical records and corrected the section that suggested that the clitoris had been removed if that was not what he had done or intended. But that was exactly what had occurred.

The resection was not planned, consented to, or indicated, and this was enough reason to reach a settlement in this case rather than allow a jury to price it. Several of the experts we retained led us to believe that it would be better to resolve this case, even though one expert was willing to accept Dr. A's actions as a reasonable—if not entirely prudent—exercise of surgical judgment.

Convincing a jury that surgery was appropriate and that the results did not indicate negligence would have been difficult. COG

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Umbilical cord prolapse
A plan for an ob emergency

Your initial response can make a difference in maternal and infant outcomes.

BY **BRADLEY D. HOLBROOK, MD** AND **SHARON T. PHELAN, MD**

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Neither author has a conflict of interest to disclose with respect to the content of this article.

Umbilical cord prolapse (UCP) is a well-known obstetric emergency in which the umbilical cord passes through the cervix at the same time as or in advance of the fetal presenting part. The cord is then prone to compression between the fetal presenting part and the surrounding soft tissues or bony pelvis, which can lead to fetal hypoxia. Although not a common obstetric emergency, UCP is one in which the initial response can make a difference in the quality of maternal and infant outcomes.

Incidence of UCP is estimated to be between 1.4 and 6.2 per 1000 pregnancies.[1] Although this has not changed in the last century, perinatal outcomes for UCP have improved significantly. Historically, UCP has been associated with poor neonatal outcomes, with perinatal mortality ranging from 32% to 47% in the early to mid 20th century.[2] Current rates of perinatal mortality in cases of UCP are estimated to be 10% or less.[1-4] The most likely explanations for these vastly improved outcomes are the increased availability of cesarean delivery and advances in neonatal resuscitation.

TAKE-HOME MESSAGES

- Incidence of UCP is estimated to be between 1.4 and 6.2 per 1000 pregnancies.
- Approximately half the cases of UCP may be linked to iatrogenic causes.
- The mainstay of management for UCP is urgent cesarean delivery.

Diagnosis

UCP can be occult or overt. Occult prolapse occurs when the cord passes through the cervix alongside the fetal presenting part; it is neither visible nor palpable. In overt prolapse, the cord presents in advance of the fetus and is visible or palpable within the vaginal vault or even past the labia.

Prolapse of the cord often leads to cord compression which, in turn, leads to abnormal findings on fetal heart rate (FHR) tracings in 41% to 67% of cases.[3,5] These changes may present as a severe, sudden deceleration,

often with prolonged bradycardia, or recurrent moderate-to-severe variable decelerations. The diagnosis of overt UCP is made on vaginal examination, which will reveal a palpable umbilical cord (usually a soft, pulsating mass) within or visibly extruding from the vagina. A confirmed diagnosis of occult UCP is rare, because it cannot be definitively diagnosed even when Doppler ultrasound imaging is employed. Attempts to identify occult prolapse with imaging could delay necessary treatment for this emergent condition. Occult UCP likely is the cause of some cases of urgent cesarean delivery for unexplained fetal bradycardia.

Risk factors

Several factors increase the risk of cord prolapse. The main precipitating event is rupture of membranes (ROM), either spontaneous or performed artificially by a healthcare provider. Most risk factors for UCP can be separated into two categories: spontaneous and iatrogenic (Table 1).

Spontaneous causes may be related to fetal factors, uterine distention, or pregnancy complications. Fetal risk factors include malpresentation, fetal anomalies, fetal growth restriction/small for gestational age, funic presentation, and cord abnormalities. Factors related to uterine distention include polyhydramnios, multiple gestation (although this may also be related to increased risk of malpresentation), and grand multiparity. Pregnancy complications that put the fetus at risk of UCP include preterm delivery and preterm premature rupture of membranes.[1-3,5]

A number of iatrogenic causes also exist, some of which are related to routine procedures performed as part of normal labor management. These include artificial ROM (especially if the fetal head or presenting part is not engaged), placement of a fetal scalp electrode or an intrauterine pressure catheter, amnioinfusion, attempted rotation of the fetal head from occiput posterior to occiput anterior, and external cephalic version.[1-3,5]

Approximately half the cases of UCP may be linked to iatrogenic causes, but iatrogenic cord prolapse does not appear to be clinically linked to poor outcomes.[5,6] This is because the procedures in question are generally performed on Labor & Delivery units, where continuous fetal monitoring and any necessary interventions are available. Furthermore, iatrogenic UCP can occur in cases in which risk factors may have led to a spontaneous prolapse without

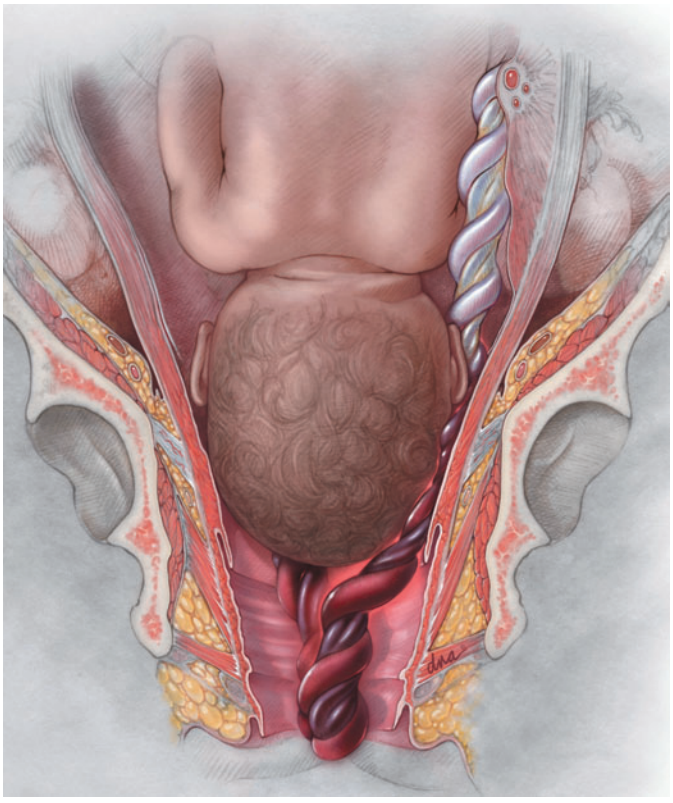


ILLUSTRATION BY ALEX BAKER, DNA ILLUSTRATIONS, INC.

TABLE 1 Risk factors for UCP

Spontaneous
Fetal:
Malpresentation
Fetal anomalies
Prematurity
IUGR/SGA
Funic presentation
Cord abnormalities
Uterine:
Polyhydramnios
Multiple gestation
Pregnancy:
Spontaneous ROM
PPROM
Grand multiparity
Iatrogenic
Amniotomy
Placement of an intrauterine pressure catheter or fetal scalp electrode
Amnioinfusion
Attempted rotation of the fetal head
Placement of a cervical ripening balloon catheter
External cephalic version

Abbreviations: IUGR, intrauterine growth restriction; PPROM, preterm premature rupture of membranes; ROM, rupture of membranes; SGA, small for gestational age; UCP, umbilical cord prolapse

TABLE 2 Step-by-step management for UCP based on anticipated time to cesarean

	In-hospital event (<30 min until delivery)	Out-of-hospital event (>30 min until delivery)
Elevate the presenting part	Manually with 2 fingers or entire hand Consider knee-chest position	Initially elevate manually; consider bladder filling (if equipment available) with 500 mL saline Consider knee-chest position
Get help	Because provider is committed to elevating head, needs help for next steps	Because provider is committed to elevating head, needs help for next steps
Verify FHT present and viable gestational age	Monitoring may already be in place Delivering a previable or demised fetus via cesarean provides no benefit	Fetascope or Doppler Delivering a previable or demised fetus via cesarean provides no benefit
Cesarean	Get staff to prepare for emergent cesarean: notify anesthesia, pediatrics, and/or staff per routine system Consent patient during transport to OR	Call for emergent transport to hospital Notify hospital of impending arrival and need for preparations for surgical delivery on arrival Consent patient during transport
Tocolytics	If cesarean is happening quickly likely not needed	Terbutaline 0.25 mg SQ
Presence of cord out of the vagina	Replace cord into vaginal vault using wet gauze	Replace cord into vaginal vault using wet gauze
Once in delivery suite	Verify FHT, ideally get tracing to see if regional anesthesia is an option	Verify FHT (rule out demise in transit). If present, consider tracing to see if regional anesthesia is an option
When to cease elevation of the presenting part	Just before the uterine incision	If the bladder has been filled, release the clamp once the fascia has been entered

Abbreviations: FHT, fetal heart tones; OR, operating room; SQ, subcutaneous; UCP, umbilical cord prolapse

intervention. Studies seem to support this finding, because different regional obstetric practice styles have no effect on the incidence of UCP.[5]

Prevention

Although a large percentage of UCP cases are attributed to iatrogenic causes, there is no evidence that knowledge of risk factors can reduce the incidence of UCP.[5] At the same time, it is important to be aware of the risks when undertaking the interventions previously described. We recommend avoiding amniotomy unless the fetal head is well-engaged, or if necessary, "needling" the bag for a slower, more controlled release of fluid.[7] If the vertex is not well applied to the cervix, mild fundal pressure during placement of a fetal scalp electrode or intrauterine pressure catheter may help to minimize elevation of the vertex out of pelvis. Providers should exercise caution with any of these procedures and perform them only in cases in which other methods are inadequate.

UCP cannot be prevented, but subsequent fetal complications have been shown to often be preventable, with significant decreases in fetal morbidity and mortality when the condition is promptly and appropriately treated.[5]

Management

Cord prolapse results in fetal hypoxia, and if not rapidly treated, can lead to long-term disability or death.[2,3,8] Prompt delivery has been shown to improve outcomes.[5] This means that cases of UCP should be delivered as quickly as possible, which generally means cesarean delivery. In rare cases, however, UCP can occur when delivery is near. If the provider believes that a vaginal delivery can be performed more rapidly than a cesarean delivery, it is certainly appropriate to proceed with vaginal delivery. Operative delivery should be considered if the FHR tracing shows concerning findings.

The mainstay of management for UCP is urgent cesarean delivery. From the time of diagnosis until cesarean can be performed, the fetal presenting part should be elevated to relieve pressure on the cord and arrangements should be made for urgent cesarean

continued on **PAGE 34**

The only ascending-dose, extended-regimen oral contraceptive

- **A scientific design—**Ethinyl estradiol is gradually increased at specific points across the 91-day cycle[1]
- **Reductions in breakthrough bleeding (BTB) and spotting from cycle to cycle—**BTB was cut in half from cycle 1 to cycle 2, and spotting was cut in half from cycle 1 to cycle 3[1]
- **4 short, light periods a year—**An average of only 3 to 4 days of scheduled bleeding per 91-day cycle[1]
  - —The occurrence of fewer planned menses (4 per year instead of 13 per year) should be weighed against the occurrence of increased unscheduled bleeding and/or spotting
- **Valuable savings—**With the Quartette™ Savings Card, patients can get their first 3-month trial for free* and pay no more than $25† for their next 3 refills‡

*Maximum savings up to $175. †Maximum savings up to $150. ‡Certain restrictions apply.

Quartette™

(levonorgestrel/ethinyl estradiol and ethinyl estradiol) tablets

An ascending composition in oral contraception

Prescribe Quartette™ for the only ascending-dose extended regimen oral contraceptive. Quartette™ is in rhythm with her life.

Reference: 1. Quartette™ [Prescribing Information]. Sellersville, PA: Teva Pharmaceuticals USA, Inc.; 2013.

Quartette™ is indicated for use by females of reproductive age to prevent pregnancy.

IMPORTANT SAFETY INFORMATION

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptives (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs should not be used by women who are over 35 years of age and smoke.

The use of combination oral contraceptives is associated with increased risks of several serious side effects, including blood clots, stroke, and heart attack. Some women should not take Quartette™, including women with a high risk of arterial or venous thrombotic diseases, liver tumors (benign or malignant) or liver disease, undiagnosed abnormal uterine bleeding, breast cancer or other estrogen- or progestin-sensitive cancer (now or in the past), or those who could be pregnant.

Thromboembolic Disorders and Other Vascular Problems: Stop Quartette™ if an arterial or deep venous thrombotic event (VTE) occurs. If feasible, stop Quartette™ at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of VTE. Start Quartette™ no earlier than 4 weeks after delivery, in women who are not breastfeeding. The risk of VTE is highest during the first year of use of a COC. The greatest risk of VTE is present after initially starting a COC or restarting (following a 4-week or greater pill-free interval) the same or a different COC. Use COCs with caution in women with cardiovascular disease risk factors.

Liver Disease: Discontinue Quartette™ if jaundice develops.

High Blood Pressure: Quartette™ is contraindicated in women with uncontrolled hypertension or hypertension with vascular disease. For women with well-controlled hypertension, monitor blood pressure and stop Quartette™ if blood pressure rises significantly. An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women and with extended duration of use.

Carbohydrate and Lipid Metabolic Effects: Carefully monitor prediabetic and diabetic women who are taking Quartette™. Consider alternative contraception for women with uncontrolled dyslipidemias.

Headache: If a woman taking Quartette™ develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue Quartette™ if indicated.

Bleeding Irregularities: If unscheduled bleeding persists or occurs after previously regular cycles on Quartette™, check for causes such as pregnancy or malignancy.

Depression: Carefully observe women with a history of depression and discontinue Quartette™ if depression recurs to a serious degree.

Drug Interactions: Drugs or herbal products that induce certain enzymes, including P450 3A4 (CYP3A4), may decrease the effectiveness of COCs or increase breakthrough bleeding.

Quartette™ does not protect against HIV infection (AIDS) and other sexually transmitted infections.

Most common adverse reactions (≥2%) in clinical trials: headaches (12.2%), heavy/irregular vaginal bleeding (9.7%), nausea/vomiting (8.8%), acne (5.4%), dysmenorrhea (5.4%), increased weight (4.6%), mood changes (2.9%), anxiety/panic attack (2.4%), breast pain (2.2%), and migraine (2.0%).

Use of Quartette™ provides women with more hormonal exposure on a yearly basis than conventional monthly oral contraceptives containing the same strength synthetic estrogens and progestins (an additional 9 and 13 weeks of exposure to progestin and estrogen, respectively, per year). Before prescribing Quartette™, consider the occurrence of fewer scheduled menses (4 per year instead of 13 per year) against the occurrence of increased unscheduled bleeding and/or spotting. In clinical trials, unscheduled bleeding and unscheduled spotting decreased over successive 91-day cycles.

Please see Brief Summary of Prescribing Information on adjacent pages.

In rhythm with her life

Quartette®

(levonorgestrel/ethinyl estradiol) tablets
0.15 mg/0.02 mg, 0.15 mg/0.025 mg, 0.15 mg/0.03 mg

(ethinyl estradiol) tablets
0.01 mg

TEVA Women's Health

QUA-40018
July 2013

Quartette™

(levonorgestrel/ethinyl estradiol) tablets
0.15 mg/0.02 mg, 0.15 mg/0.025 mg, 0.15 mg/0.03 mg

(ethinyl estradiol) tablets
0.01 mg

BRIEF SUMMARY
of Prescribing Information for
Quartette™ (levonorgestrel/ethinyl estradiol and ethinyl estradiol) tablets for oral use

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptives (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs should not be used by women who are over 35 years of age and smoke. *[See Contraindications (4)]*

1 INDICATIONS AND USAGE

Quartette™ is indicated for use by females of reproductive age to prevent pregnancy.

4 CONTRAINDICATIONS

Do not prescribe Quartette to women who are known to have the following conditions:

- A high risk of arterial or venous thrombotic diseases. Examples include women who are known to:
  - Smoke, if over age 35 *[see Boxed Warning and Warnings and Precautions (5.1)]*.
  - Have deep vein thrombosis or pulmonary embolism, now or in the past *[see Warnings and Precautions (5.1)]*.
  - Have cerebrovascular disease *[see Warnings and Precautions (5.1)]*.
  - Have coronary artery disease *[see Warnings and Precautions (5.1)]*.
  - Have thrombogenic valvular or thrombogenic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation) *[see Warnings and Precautions (5.1)]*.
  - Have inherited or acquired hypercoagulopathies *[see Warnings and Precautions (5.1)]*.
  - Have uncontrolled hypertension *[see Warnings and Precautions (5.3)]*.
  - Have diabetes with vascular disease *[see Warnings and Precautions (5.5)]*.
  - Have headaches with focal neurological symptoms or have migraine headaches with or without aura if over age 35 *[see Warnings and Precautions (5.6)]*.
- Liver tumors, benign or malignant, or liver disease *[see Warnings and Precautions (5.2) and Use in Specific Populations (8.6)]*.
- Undiagnosed abnormal uterine bleeding *[see Warnings and Precautions (5.7)]*.
- Pregnancy, because there is no reason to use COCs during pregnancy *[see Warnings and Precautions (5.8) and Use in Specific Populations (8.1)]*.
- Breast cancer or other estrogen- or progestin-sensitive cancer, now or in the past *[see Warnings and Precautions (5.10)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Thromboembolic Disorders and Other Vascular Problems

Stop Quartette if an arterial or deep venous thrombotic event (VTE) occurs. Stop Quartette if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions. Evaluate for retinal vein thrombosis immediately.

If feasible, stop Quartette at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of VTE.

Start Quartette no earlier than 4 weeks after delivery, in women who are not breastfeeding. The risk of postpartum VTE decreases after the third postpartum week, whereas the risk of ovulation increases after the third postpartum week.

The use of COCs increases the risk of VTE. However, pregnancy increases the risk of VTE as much or more than the use of COCs. The risk of VTE in women using COCs is 3 to 9 per 10,000 woman-years. The risk of VTE is highest during the first year of use of a COC. Data from a large, prospective cohort safety study of various COCs suggest that this increased risk, as compared to that in non-COC users, is greatest during the first 6 months of COC use. Data from this safety study indicate that the greatest risk of VTE is present after initially starting a COC or restarting (following a 4-week or greater pill-free interval) the same or a different COC. The risk of thromboembolic disease due to COCs gradually disappears after COC use is discontinued.

Use of Quartette provides women with more hormonal exposure on a yearly basis than conventional monthly oral contraceptives containing the same strength synthetic estrogens and progestins (an additional 9 and 13 weeks of exposure to progestin and estrogen, respectively, per year). In the clinical trial, three cases of deep vein thrombosis were reported.

Use of COCs also increases the risk of arterial thromboses such as strokes and myocardial infarctions, especially in women with other risk factors for these events. COCs have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes), although, in general, the risk is greatest among older (>35 years of age), and hypertensive women who also smoke. COCs also increase the risk for stroke in women with other underlying risk factors.

Use COCs with caution in women with cardiovascular disease risk factors.

5.2 Liver Disease

Impaired Liver Function

Do not use Quartette in women with acute viral hepatitis or severe (decompensated) cirrhosis of the liver *[see Contraindications (4)]*. Acute disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal and COC causation has been excluded. Discontinue Quartette if jaundice develops.

Liver Tumors

Quartette is contraindicated in women with benign and malignant liver tumors *[see Contraindications (4)]*. Hepatic adenomas are associated with COC use. An estimate of the attributable risk is 3.3 cases/100,000 COC users. Rupture of hepatic adenomas may cause death through intra-abdominal hemorrhage. Studies have shown an increased risk of developing hepatocellular carcinoma in long-term (> 8 years) COC users. However, the attributable risk of liver cancers in COC users is less than one case per million users.

5.3 High Blood Pressure

Quartette is contraindicated in women with uncontrolled hypertension or hypertension with vascular disease *[see Contraindications (4)]*. For women with well-controlled hypertension, monitor blood pressure and stop Quartette if blood pressure rises significantly.

An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women and with extended duration of use. The incidence of hypertension increases with increasing concentration of progestin.

5.4 Gallbladder Disease

Studies suggest a small increased relative risk of developing gallbladder disease among COC users. Use of COCs may also worsen existing gallbladder disease. A past history of COC-related cholestasis predicts an increased risk with subsequent COC use. Women with a history of pregnancy-related cholestasis may be at an increased risk for COC-related cholestasis.

5.5 Carbohydrate and Lipid Metabolic Effects

Carefully monitor prediabetic and diabetic women who are taking Quartette. COCs may decrease glucose tolerance in a dose-related fashion.

Consider alternative contraception for women with uncontrolled dyslipidemias. A small proportion of women will have adverse lipid changes while on COCs. Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when using COCs.

5.6 Headache

If a woman taking Quartette develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue Quartette if indicated. Consider discontinuation of Quartette in the case of increased frequency or severity of migraine during COC use (which may be prodromal of a cerebrovascular event) *[see Contraindications (4)]*.

5.7 Bleeding Irregularities

Bleeding and/or spotting that occurs at any time while taking the first 84 tablets (light pink, pink and purple) of each extended-cycle regimen is considered "unscheduled" bleeding/spotting. Bleeding that occurs during the time a woman takes the seven tablets (yellow) containing 10 mcg of ethinyl estradiol is considered "scheduled" bleeding.

Unscheduled and Scheduled Bleeding and Spotting

Unscheduled (breakthrough) bleeding and spotting sometimes occur in patients on COCs, especially during the first 3 months of use. If unscheduled bleeding persists or occurs after previously regular cycles on Quartette, check for causes such as pregnancy or malignancy. If pathology and pregnancy are excluded, bleeding irregularities may resolve over time or with a change to a different COC. Before prescribing Quartette, consider the occurrence of fewer scheduled menses (4 per year instead of 13 per year) against the occurrence of increased unscheduled bleeding and/or spotting. A 12-month open-label study of the efficacy of Quartette in preventing pregnancy assessed scheduled and unscheduled bleeding *[see Clinical Studies (14)]* in 3,597 women who completed 34,087 28-day cycles of exposure. A total of 178 (4.9%) of the women discontinued Quartette, at least in part, due to bleeding or spotting.

Scheduled (withdrawal) bleeding and/or spotting remained fairly stable over time, with an average of 3 to 4 days of bleeding and/or spotting per each 91-day cycle. Unscheduled bleeding and unscheduled spotting decreased over successive 91-day cycles. Table 1 below presents the number of days with unscheduled bleeding, spotting, and unscheduled bleeding and/or spotting in Treatment Cycles 1 to 4.

Table 1: Number of Unscheduled Bleeding, Spotting and Bleeding and/or Spotting Days per 91-day Cycle

Cycle (N)	Days of Unscheduled Bleeding per 84-Day Interval				Median Days Per Subject-Month
	Mean	Q1	Median	Q3	
1 (3330)	7.2	0	4	10	1.0
2 (2820)	3.3	0	0	4	0.0
3 (2433)	2.5	0	0	3	0.0
4 (2213)	2.2	0	0	2	0.0

Cycle (N)	Days of Unscheduled Spotting per 84-Day Interval				Median Days Per Subject-Month
	Mean	Q1	Median	Q3	
1 (3330)	10.7	2	7	15	1.8
2 (2820)	6.7	0	3	9	0.8
3 (2433)	5.2	0	2	6	0.5
4 (2213)	4.4	0	1	5	0.3
Cycle (N)	**Days of Unscheduled Bleeding and/or Spotting per 84-Day Interval**				**Median Days Per Subject-Month**
	Mean	**Q1**	**Median**	**Q3**	
1 (3330)	17.9	5	14	27	3.5
2 (2820)	10.0	1	5	14	1.3
3 (2433)	7.7	0	3	10	0.8
4 (2213)	6.6	0	3	8	0.8

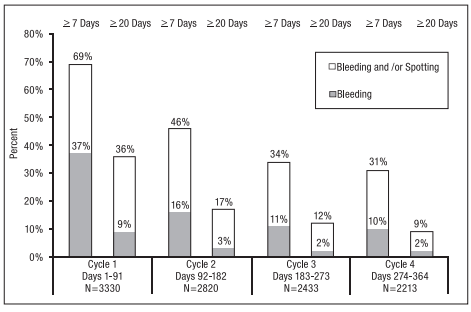
Q1 = Quartile 1: 25% of women had ≤ this number of days of unscheduled bleeding/spotting

Median: 50% of women had ≤ this number of days of unscheduled bleeding/spotting

Q3 = Quartile 3: 75% of women had ≤ this number of days of unscheduled bleeding/spotting

Figure 1 shows the percent of Quartette subjects in the primary clinical trial with ≥ 7 days or ≥ 20 days of unscheduled bleeding and/or spotting, or just unscheduled bleeding, during each 91-day treatment cycle.

Figure 1: Percent of Women Taking Quartette Who Reported Unscheduled Bleeding and/or Spotting



Amenorrhea and Oligomenorrhea

Women who are not pregnant and use Quartette may experience amenorrhea. Based on data from the clinical trial, amenorrhea occurred in approximately 1.9% of women during Cycle 1, 7.7% during Cycle 2, 10.7% during Cycle 3, and 10.1% during Cycle 4 using Quartette. Rule out pregnancy in the event of amenorrhea. Some women may experience amenorrhea or oligomenorrhea after stopping COCs, especially when such a condition was pre-existent.

5.8 COC Use Before or During Early Pregnancy

Extensive epidemiological studies have revealed no increased risk of birth defects in women who have used oral contraceptives prior to pregnancy. Studies also do not suggest a teratogenic effect, particularly in so far as cardiac anomalies and limb-reduction defects are concerned, when taken inadvertently during early pregnancy. Discontinue Quartette if pregnancy is confirmed.

The administration of oral contraceptives to induce withdrawal bleeding should not be used as a test for pregnancy *[see Use in Specific Populations (8.1)]*.

5.9 Depression

Carefully observe women with a history of depression and discontinue Quartette if depression recurs to a serious degree. Six cases of suicidality (suicide attempts and suicidal behavior) were reported in the clinical trial; several of these cases occurred in women with a psychiatric history.

5.10 Carcinoma of the Breast and Cervix

Quartette is contraindicated in women who currently have or have had breast cancer because breast cancer may be hormonally sensitive *[see Contraindications (4)]*.

There is substantial evidence that COCs do not increase the incidence of breast cancer. Although some past studies have suggested that COCs might increase the incidence of breast cancer, more recent studies have not confirmed such findings.

Some studies suggest that COCs are associated with an increase in the risk of cervical cancer or intraepithelial neoplasia. However, there is controversy about the extent to which these findings are due to differences in sexual behavior and other factors.

5.11 Effect on Binding Globulins

The estrogen component of COCs may raise the serum concentrations of thyroxine-binding globulin sex hormone-binding globulin and cortisol-binding globulin. The dose of replacement thyroid hormone or cortisol therapy may need to be increased.

5.12 Monitoring

A woman who is taking COCs should have a yearly visit with her healthcare provider for a blood pressure check and for other indicated health care.

5.13 Hereditary Angioedema

In women with hereditary angioedema, exogenous estrogens may induce or exacerbate symptoms of angioedema.

5.14 Chloasma

Chloasma may occur with COC use, especially in women with a history of chloasma gravidarum. Advise women who tend to develop chloasma to avoid exposure to the sun or ultraviolet radiation while taking Quartette.

6 ADVERSE REACTIONS

The following serious adverse reactions with the use of COCs are discussed elsewhere in the labeling:

- Serious cardiovascular events and stroke *[see Boxed Warning and Warnings and Precautions (5.1)]*
- Vascular events *[see Warnings and Precautions (5.1)]*
- Liver disease *[see Warnings and Precautions (5.2)]*

Adverse reactions commonly reported by COC users are:

- Irregular uterine bleeding
- Nausea
- Breast tenderness
- Headache

6.1 Clinical Trial 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 the rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below are from a 12-month, US, open-label study, which enrolled women aged 18-40, of whom 3,597 took at least one dose of Quartette (2,661 woman-years of exposure) *[see Clinical Studies (14)]*.

Adverse Reactions Leading to Study Discontinuation: 13.3% of the women discontinued from the clinical trial due to an adverse reaction; the most common adverse reactions (≥ 1% of women) leading to discontinuation were heavy/irregular bleeding (5.0%), mood swings/alteration/affect lability (1.4%), headaches/migraines (1.3%), weight increased (1.3%) and acne (1.0%).

Common Adverse Reactions (≥ 2% of women): headaches (12.2%), heavy/irregular vaginal bleeding (9.7%), nausea/vomiting (8.8%), acne (5.4%), dysmenorrhea (5.4%), weight increased (4.6%), mood changes (depression, depressed mood, crying, major depression, affective disorder, depression suicidal, dysthymic disorder) (2.9%), anxiety/panic attack (2.4%), breast tenderness/pain/discomfort (2.2%), migraine (2.0%).

Serious Adverse Reactions (≥ 2 women): Abortion Spontaneous, Suicide Attempt, Cholecystitis/Cholelithiasis, Deep Vein Thrombosis, Ectopic Pregnancy.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of other extended-cycle COCs containing levonorgestrel and ethinyl estradiol. 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.

Gastrointestinal disorders: abdominal distension, vomiting

General disorders and administration site conditions: chest pain, fatigue, malaise, edema peripheral, pain

Immune system disorders: hypersensitivity reaction

Investigations: blood pressure increased

Musculoskeletal and connective tissue disorders: muscle spasms, pain in extremity

Nervous system disorders: dizziness, loss of consciousness

Psychiatric disorders: insomnia

Reproductive and breast disorders: dysmenorrhea

Respiratory, thoracic and mediastinal disorders: pulmonary embolism, pulmonary thrombosis

Skin and subcutaneous tissue disorders: alopecia

Vascular disorders: thrombosis

7 DRUG INTERACTIONS

Consult the labeling of concurrently-used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

No drug-drug interaction studies were conducted with Quartette.

7.1 Effects of Other Drugs on Combined Oral Contraceptives

Substances diminishing the efficacy of COCs: Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the effectiveness of COCs or increase breakthrough bleeding. Some drugs or herbal products that may decrease the effectiveness of hormonal contraceptives include phenytoin, barbiturates, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, rifampicin, topiramate and products containing St. John's wort. Interactions between oral contraceptives and other drugs may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative method of contraception or a back-up method when enzyme inducers are used with COCs, and to continue back-up contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability.

Substances increasing the plasma concentrations of COCs: Co-administration of atorvastatin and certain COCs containing EE increase AUC values for EE by approximately 20%. Ascorbic acid and acetaminophen may increase plasma EE concentrations, possibly by inhibition of conjugation. CYP3A4 inhibitors such as itraconazole or ketoconazole may increase plasma hormone concentrations.

continued from **PAGE 30**

delivery. Specifics of management will vary depending on whether an operative delivery can be accomplished within 30 minutes (typically an in-hospital event) or there will be a delay of more than 30 minutes (an out-of-hospital event). Table 2 lists variations to consider in management, depending on location.

Elevation of the presenting fetal part. The key first step after identifying a UCP is to elevate the presenting fetal part off the prolapsed cord. This is generally performed manually, with the physician placing 2 fingers or an entire hand into the vagina to elevate the fetus off the cord. Care should be taken to avoid palpation of the cord because that may cause vasospasm, potentially leading to a worse outcome.[2] Placing the patient in steep Trendelenburg or in knee-chest position is believed to be helpful by taking advantage of gravity to further relieve pressure on the cord.[9]

In cases in which the interval to delivery is likely to be prolonged (that is, requiring maternal transport to a facility where cesarean delivery can be performed), bladder filling may be a better option. With this technique—commonly called Vago's method, in reference to the physician who first described the technique—a Foley catheter is placed and the bladder is filled with 500 to 750 mL of saline, and then clamped.[10] The patient's enlarging bladder provides upward pressure on the fetus, thus alleviating the compression on the cord. Vago described this as an alternative to manual elevation, which he described as "effective, but . . . unpleasant for the mother and wearying for the doctor." He also noted that in his experience, filling the bladder tends to calm uterine contractions, which would certainly further relieve pressure on the cord. Over the years, studies have shown Vago's method to be effective.[10,11] To employ this strategy requires that a cord prolapse tray be immediately available (Figure 1). Comparison of manual elevation of the presenting part versus bladder filling shows essentially equal outcomes between the 2 groups.[12] It should be noted that the combination of the 2 methods does not lead to any improvement over using either alone.

Funic reduction. Another method that has been used to treat cord prolapse is funic reduction, replacement of the cord back into the uterus by sliding it above the fetal presenting part. This is performed by placing the entire hand in the vagina and gently elevating the fetal head. The cord is then lightly elevated above the fetal head, preferably at its widest point, and replaced back into the uterus; the goal is that the cord should stay in the fetal nuchal region.

Before cesarean delivery became commonplace, funic reduction was a major part of management in cases of UCP. It is now rarely performed, however, because outcomes were worse than cesarean delivery. There has been some discussion of renewed interest in funic reduction, and Dr. Barrett notes that overall, he has had very good outcomes with this strategy.[13] In our experience, the technique is difficult but it can sometimes be successful and is certainly worth an attempt. Nevertheless, we would not recommend delaying preparations for cesarean delivery while attempting to replace the cord.[7]

Tocolysis. Although not a primary treatment for UCP, tocolysis has also been described and it appears to be a useful adjunct.[9] It is likely not necessary in cases in which urgent delivery can be performed, but it can certainly be employed if FHR decelerations persist after the primary procedures have been performed.

Other considerations. Another important consideration is keeping the cord moist. When delivery is imminent, this is less of a concern. But with a prolonged interval to delivery, the cord could dry out, which could lead to vasospasm and thus, potentially worse outcomes. Therefore, if the cord prolapses through the introitus, it should be gently replaced into the vagina. A moist tampon or 4 x 4 gauze can then be inserted gently into the vagina below the cord to help hold it in place.

In rare cases of UCP, contraindications to immediate delivery may exist. In cases of lethal fetal anomalies or absent fetal heart tones, exposing the mother to the risk of urgent cesarean delivery will lead to no benefit to the fetus and thus, should not be performed. Delivery at a previable gestational age falls into this same category, although the definition of previability will vary based on the capabilities of a neonatal intensive care unit (NICU) as well as institutional policies.

It is important to note that there are case reports of UCP at a previable gestational age that were managed expectantly and successfully prolonged pregnancy to viable gestational age.[2,14] Cases of multiple gestations with prolapse of one cord at a periviable gestational age present difficult clinical dilemmas; the risks to each fetus must be discussed in detail but quickly with the patient to make the best management decision.

Outcomes

Despite the potential for extremely poor outcomes, most neonates born after experiencing UCP do very well, especially if delivery is achieved within 30 minutes.[5] The literature shows improved outcomes for cases of UCP that occur when the patient is already in the hospital, even if the fetus is not being monitored.[3]

One study has shown team training exercises to be beneficial in decreasing the mean diagnosis-to-delivery interval in cases of UCP.[15] In addition, although this study was small and the results did not reach statistical significance, there was a trend toward improved Apgar scores and fewer NICU admissions. It appears that such exercises may lead to improved neonatal outcomes. These drills should stress both the steps taken prior to arrival in the operating suite and the role of all members of the team in facilitating an efficient and safe urgent/crash cesarean delivery.

FIGURE 1 Suggested contents of a cord prolapse tray for using the Vago method

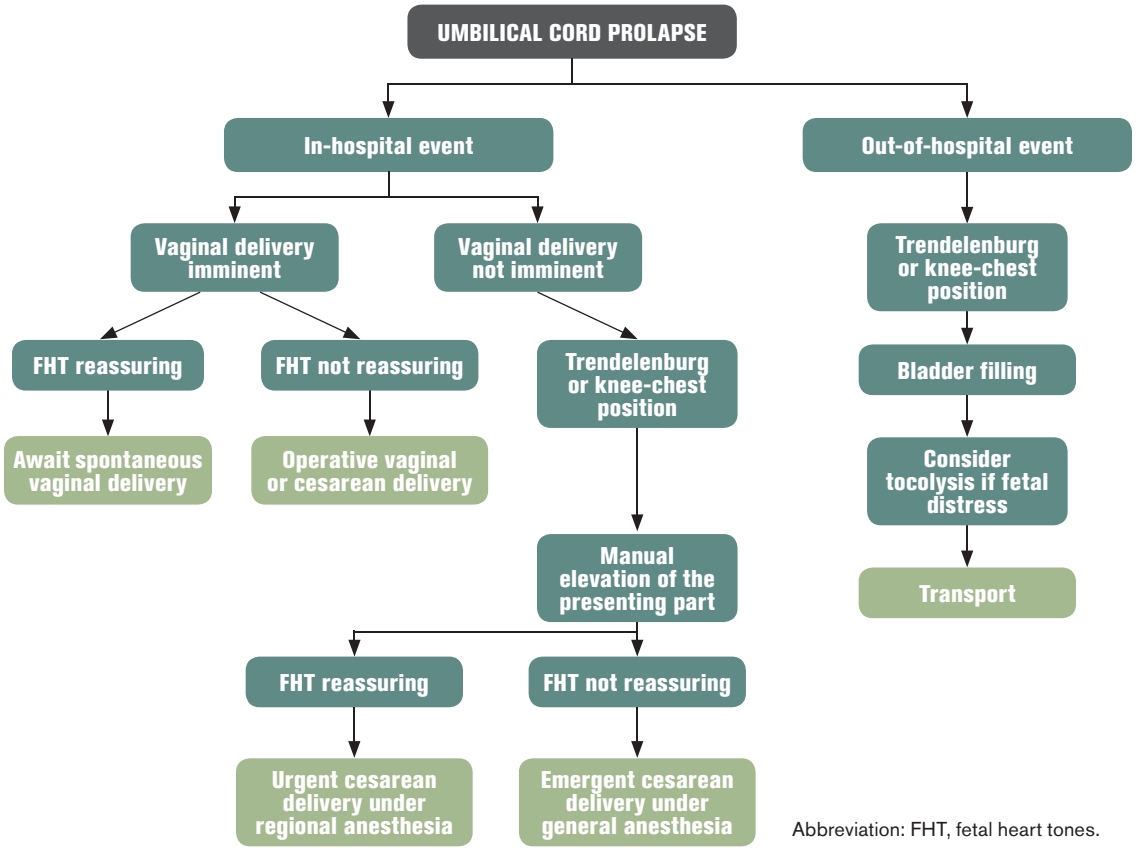
- Foley catheter (ideally with a port that can be used to fill the bladder)
- Two 50-mL syringes (with the appropriate tip for filling the Foley)
- Solution to fill the Foley (normal saline); it can be done using either:
  - A syringe through the port on the Foley (will likely require a bowl for filling syringes) or
  - Tubing similar to hysteroscopy/cystoscopy tubing, allowing for direct infusion
- 2 clamps (Kelly clamps work well) to prevent backflow
- A 4 x 4 gauze—this can be moistened and used to replace the cord into the vagina

Summary

Umbilical cord prolapse is a well-known obstetric emergency that requires prompt delivery to avoid potentially devastating fetal outcomes. Diagnosis is made by the presence of a palpable, pulsating mass within the vagina or visibly extruding from the introitus. It is often accompanied by sudden, severe FHR decelerations. Risk factors for UCP include malpresentation, prematurity, low birth weight, polyhydramnios, and a number of iatrogenic causes related to routine labor interventions. There is no evidence that UCP can be prevented, but rapid diagnosis and delivery have been shown to be advantageous.

Once UCP is diagnosed, the fetal presenting part should be manually elevated off the cord, the patient placed in knee-chest or steep Trendelenburg position, and preparations made for cesarean delivery, unless vaginal delivery is imminent. In cases in which the time to delivery is anticipated to be pro-

FIGURE 2 Management of umbilical cord prolapse



Abbreviation: FHT, fetal heart tones.

longed, backfilling the bladder with approximately 500 mL of saline can safely be substituted for manual elevation of the presenting part. Figure 2 presents an algorithm for management of UCP. Team training exercises have been shown to shorten the interval between diagnosis and delivery and may lead to improved neonatal outcomes.

If managed improperly, UCP can lead to significant fetal morbidity or mortality. Prompt, appropriate management of this condition, however, has been shown to have favorable overall outcomes. COG

REFERENCES

1. Kahana B, Sheiner E, Levy A, et al. Umbilical cord prolapse and perinatal outcomes. *Int J Gynaecol Obstet.* 2004;84:127–132.
2. Lin MG. Umbilical cord prolapse. *Obstet Gynecol Surv.* 2006;61:269–277.
3. Koonings PP, Paul RH, Campbell K. Umbilical cord prolapse. A contemporary look. *J Reprod Med.* 1990;35:690–692.
4. Boyle JJ, Katz VL. Umbilical cord prolapse in current obstetric practice. *J Reprod Med.* 2005;50:303–306.
5. Murphy DJ, MacKenzie IZ. The mortality and morbidity associated with umbilical cord prolapse. *Br J Obstet Gynaecol.* 1995;102:826–830.
6. Usta IM, Mercer BM, Sibai BM. Current obstetrical practice and umbilical cord prolapse. *Am J Perinatol.* 1999;16:479–484.
7. Holbrook BD, Phelan ST. Umbilical cord prolapse. *Obstet Gynecol Clin North Am.* 2013;40:1–14.
8. Critchlow CW, Leet TL, Benedetti TJ, Daling JR. Risk factors and infant outcomes associated with umbilical cord prolapse: a population-based case-control study among births in Washington State. *Am J Obstet Gynecol.* 1994;170:613–618.
9. Katz Z, Lancet M, Borenstein R. Management of labor with umbilical cord prolapse. *Am J Obstet Gynecol.* 1982;142:239–241.
10. Vago T. Prolapse of the umbilical cord: a method of management. *Am J Obstet Gynecol.* 1970;107:967–969.
11. Caspi E, Lotan Y, Schrever PI. Prolapse of the cord: reduction of perinatal mortality by bladder instillation and cesarean section. *Isr J Med Sci.* 1983;19:541–545.
12. Bord I, Gemer O, Anteby EY, Shenhav S. The value of bladder filling in addition to manual elevation of presenting fetal part in cases of cord prolapse. *Arch Gynecol Obstet.* 2011;283:989–991.
13. Barrett JM. Funic reduction for the management of umbilical cord prolapse. *Am J Obstet Gynecol.* 1991;165:654–657.
14. Leong A, Rao J, Opie G, Dobson P. Fetal survival after conservative management of cord prolapse for three weeks. *BJOG.* 2004;111:1476–1477.
15. Siassakos D, Hasafa Z, Sibanda T, et al. Retrospective cohort study of diagnosis-delivery interval with umbilical cord prolapse: the effect of team training. *BJOG.* 2009;116:1089–1096.

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IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants, including selective serotonin reuptake inhibitors (SSRIs), have been shown to increase the risk of suicidal thoughts and behavior in pediatric and young adult patients when used to treat major depressive disorder and other psychiatric disorders. Because BRISDELLE is an SSRI, monitor patients closely for worsening and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber.

CONTRAINDICATIONS:

- Concurrent use with monoamine oxidase inhibitors (MAOIs) or use within 14 days of MAOI use or starting BRISDELLE in a patient who is being treated with linezolid or intravenous methylene blue because of an increased risk of serotonin syndrome.
- Concomitant use with thioridazine or pimozide due to their increased plasma concentrations and because of the potential of QTc prolongation.
- Hypersensitivity to any ingredient in BRISDELLE.
- Pregnancy because BRISDELLE may cause fetal harm.

WARNINGS AND PRECAUTIONS:

- *Serotonin Syndrome*: Serotonin syndrome, which is potentially life-threatening, has been reported with concomitant use of serotonergic drugs, and with drugs that impair metabolism of serotonin (in particular, MAOIs). Monitor patients for the emergence of serotonin syndrome. Discontinue BRISDELLE and any concomitant serotonergic agents and initiate supportive treatment.
- *Tamoxifen*: Efficacy of tamoxifen may be reduced when administered concomitantly with BRISDELLE.
- *Abnormal Bleeding*: SSRIs, including BRISDELLE, may increase the risk of bleeding events. Caution patients about the risk of bleeding associated with the concomitant use of BRISDELLE and non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, or other drugs that affect coagulation.
- *Hyponatremia*: may occur as a result of treatment with SSRIs, including BRISDELLE. Elderly patients may be at greater risk and in many cases it can occur in association with syndrome of inappropriate antidiuretic hormone secretion (SIADH). Consider discontinuation of BRISDELLE in patients with symptomatic hyponatremia and institute appropriate medical intervention.
- *Bone fracture*: Epidemiological studies have reported an association between SSRI treatment and fractures.
- *Activation of Mania/Hypomania*: Screen for bipolar disorder and monitor for mania/hypomania.
- *Seizures*: Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold.
- *Akathisia*: Can occur, most likely in the first few weeks of treatment. Discontinue treatment with BRISDELLE if akathisia occurs.
- *Acute Angle Closure Glaucoma*: May cause acute angle closure in patients with narrow angle glaucoma; tell patients with narrow angle glaucoma to report visual symptoms.
- *Cognitive and Motor Impairment*: May cause impairment; patients should not operate machinery or motor vehicles until certain that BRISDELLE does not affect them adversely.

ADVERSE REACTIONS:

The most common adverse reactions (≥ 2%) reported in clinical trials were: headache, fatigue, and nausea and vomiting. Of these, nausea occurred primarily within the first 4 weeks of treatment and fatigue occurred primarily within the first week of treatment, and decreased in frequency with continued therapy.

To report SUSPECTED ADVERSE REACTIONS, contact Noven Therapeutics, LLC at 1-800-455-8070 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

DRUG INTERACTIONS:

Paroxetine is a strong CYP2D6 inhibitor. Co-administration of BRISDELLE can alter concentrations of other drugs that are metabolized by CYP2D6. Use caution if co-administering BRISDELLE with other drugs that are metabolized by CYP2D6.

These are not all the possible side effects of BRISDELLE. **Please read the Full Prescribing Information and Medication Guide available at www.brisdelle.com**

Please see Brief Summary of full Prescribing Information, including Boxed WARNING, on the following pages.

Reference: 1. Brisdelle™ [Prescribing Information]. Miami, FL: Noven Therapeutics, LLC; 2013.

noven THERAPEUTICS, LLC

BRISDELLE™ (Paroxetine) Capsules Rx only

Brief Summary; Consult package insert for full Prescribing Information

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants, including selective serotonin reuptake inhibitors (SSRIs), have been shown to increase the risk of suicidal thoughts and behavior in pediatric and young adult patients when used to treat major depressive disorder and other psychiatric disorders. Because BRISDELLE is an SSRI, monitor patients closely for worsening and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber *[see Warnings and Precautions (5.1)]*.

INDICATIONS AND USAGE

BRISDELLE is indicated for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.

Limitation of Use:

BRISDELLE is not indicated for the treatment of any psychiatric condition. BRISDELLE contains a lower dose of paroxetine than that used for psychiatric conditions. Patients who require paroxetine for treatment of a psychiatric condition should discontinue BRISDELLE and initiate a paroxetine-containing medication that is indicated for such use.

CONTRAINDICATIONS

Monoamine Oxidase Inhibitors

Concomitant use of an MAOI with BRISDELLE or within 14 days of stopping treatment with BRISDELLE is contraindicated because of an increased risk of serotonin syndrome. The use of BRISDELLE within 14 days of stopping an MAOI is also contraindicated *[see Dosage and Administration (2.2), Warnings and Precautions (5.2) and Drug Interactions (7.3)]*.

Starting BRISDELLE in a patient who is being treated with linezolid or intravenous methylene blue, both of which inhibit monoamine oxidase, is also contraindicated because of an increased risk of serotonin syndrome *[see Dosage and Administration (2.2), Warnings and Precautions (5.2) and Drug Interactions (7.3)]*.

Thioridazine

Concomitant use of BRISDELLE with thioridazine is contraindicated, because thioridazine prolongs the QT interval, and paroxetine can increase thioridazine levels *[see Drug Interactions (7.1)]*.

Pimozide

Concomitant use of BRISDELLE with pimozide is contraindicated because pimozide prolongs the QT interval, and paroxetine increases pimozide levels *[see Drug Interactions (7.1)]*.

Hypersensitivity to any Ingredient in BRISDELLE

BRISDELLE is contraindicated in patients with a history of hypersensitivity to paroxetine or any of the other ingredients in BRISDELLE.

Pregnancy

Menopausal VMS does not occur during pregnancy and BRISDELLE may cause fetal harm *[see Use in Specific Populations (8.1)]*.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors

BRISDELLE is not approved for any psychiatric condition.

Antidepressants, including those that contain an SSRI, increase the risk of suicidal thinking and behavior (suicidality) in pediatric and young adult patients when used to treat major depressive disorder (MDD) and other psychiatric disorders. There is limited information regarding suicidality in women who use BRISDELLE for treatment of VMS. The BRISDELLE trials excluded women with a presence or history of previous psychiatric disorders.

Consider discontinuing BRISDELLE in patients with worsening depression or those who experience emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

All patients being treated with BRISDELLE should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of treatment.

Anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania have been reported in patients being treated with antidepressants for MDD as well as for other psychiatric and nonpsychiatric indications. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Families and caregivers of patients being treated with BRISDELLE should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers.

Serotonin Syndrome

The development of a potentially life-threatening serotonin syndrome has been reported with SSRIs, including paroxetine, alone but particularly with concomitant use of serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort), and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat depression and others such as linezolid and intravenous methylene blue).

Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Monitor patients for the emergence of serotonin syndrome.

The concomitant use of BRISDELLE with MAOIs is contraindicated. Do not start BRISDELLE in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue. All reports with methylene blue that provided information on the route of administration involved intravenous administration in the dose range of 1 mg/kg to 8 mg/kg. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection) or at lower doses. There may be circumstances when it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking BRISDELLE. BRISDELLE should be discontinued before initiating treatment with the MAOI *[see Contraindications (4.1) and Dosage and Administration (2.2)]*.

If concomitant use of BRISDELLE with other serotonergic drugs (e.g., triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) is clinically warranted, consider the increased risk of serotonin syndrome and carefully observe the patient, particularly during treatment initiation *[see Contraindications (4.1) Drug Interactions (7.3)]*.

Discontinue BRISDELLE and any concomitant serotonergic agents immediately if the above events occur and initiate supportive symptomatic treatment.

Potential Impact on Tamoxifen Efficacy

It is uncertain whether the co-administration of paroxetine and tamoxifen has a significant adverse effect on the efficacy of tamoxifen. Some studies have shown that the efficacy of tamoxifen, as measured by the risk of breast cancer relapse/mortality, may be reduced when co-prescribed with paroxetine as a result of paroxetine's irreversible inhibition of CYP2D6 *[see Drug Interactions (7.1)]*. However, other studies have failed to demonstrate such a risk. When tamoxifen is used for the treatment or prevention of breast cancer, weigh the likely benefit of BRISDELLE for treating VMS vs. the risk of possible decreased tamoxifen effectiveness, and consider avoiding the concomitant use of BRISDELLE for VMS treatment.

Abnormal Bleeding

SSRIs, including BRISDELLE, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRIs have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Caution patients about the risk of bleeding associated with the concomitant use of BRISDELLE and NSAIDs, aspirin, or other drugs that affect coagulation *[see Drug Interactions (7.1)]*.

Hyponatremia

Hyponatremia may occur as a result of treatment with SSRIs, including BRISDELLE. Elderly patients may be at greater risk. In many cases, the hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases with serum sodium lower than 110 mmol/L have been reported in patients using SSRIs. Also, patients taking diuretics or who are volume-depleted can be at greater risk. Consider discontinuation of BRISDELLE in patients with symptomatic hyponatremia and institute appropriate medical intervention.

Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death.

Bone Fracture

Epidemiological studies on bone fracture risk following exposure to SSRIs have reported an association between SSRI treatment and fractures. It is unknown to what extent fracture risk is directly attributable to SSRI treatment. If a BRISDELLE-treated patient presents with unexplained bone pain, point tenderness, swelling, or bruising, consider the possibility of a fragility fracture.

Screening Patients for Bipolar Disorder and Monitoring for Mania/Hypomania

BRISDELLE is only indicated for the treatment of moderate to severe VMS and is not approved for use in treating either depression or bipolar depression. However, prior to initiating treatment with BRISDELLE, all patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It is generally believed (though not established in controlled trials) that use of an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder.

Seizures

In premarketing testing of paroxetine, seizures occurred in 0.1% of paroxetine-treated patients. Use BRISDELLE cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold. Evaluate and consider discontinuing use in any patient who develops seizures.

Akathisia

The use of paroxetine or other SSRIs has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment. Discontinue treatment with BRISDELLE if akathisia occurs.

Acute Angle Closure Glaucoma

Mydriasis has been reported in the premarketing studies with paroxetine. Cases of acute angle closure glaucoma associated with paroxetine therapy have been reported in the literature. Because mydriasis can cause acute angle closure in patients with narrow angle glaucoma, when BRISDELLE is prescribed for patients with narrow angle glaucoma, caution them to report visual symptoms.

Potential for Cognitive and Motor Impairment

BRISDELLE has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that the drug treatment does not affect them adversely.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in labeling:

- Suicidality *[see Warnings and Precautions (5.1)]*
- Serotonin syndrome *[see Warnings and Precautions (5.2)]*
- Abnormal bleeding *[see Warnings and Precautions (5.4)]*
- Hyponatremia *[see Warnings and Precautions (5.5)]*
- Bone Fracture *[see Warnings and Precautions (5.6)]*
- Mania/Hypomania *[see Warnings and Precautions (5.7)]*
- Seizure *[see Warnings and Precautions (5.8)]*
- Akathisia *[see Warnings and Precautions (5.9)]*

Clinical Trials Experience

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

The data described below reflect exposure to BRISDELLE in the one 8-week Phase 2 randomized, placebo-controlled trial and the two Phase 3 randomized, placebo-controlled, 12-week and 24-week trials for the treatment of moderate to severe VMS *[see Clinical Studies (14)]*. In these trials, a total of 635 women were exposed to BRISDELLE 7.5 mg administered orally once daily and 641 women received placebo. The majority of BRISDELLE-treated patients were Caucasian (68%) and African American (30%), with a mean age of 55 years (range 40 to 73 years). Women with a history of suicidal ideation or suicidal behavior were excluded from these studies.

Adverse Reactions Leading to Study Discontinuation: A total of 4.7% of women taking BRISDELLE discontinued from the clinical trials due to an adverse reaction, compared to 3.7% of women on placebo; the most frequent adverse reactions leading to discontinuation among paroxetine-treated women were: abdominal pain (0.3%), attention disturbances (0.3%), headache (0.3%), and suicidal ideation (0.3%).

Common Adverse Reactions: Overall, based on investigators' determinations about what events were likely to be drug-related, about 20% of women treated with BRISDELLE reported at least 1 adverse reaction in the three controlled studies. The most common adverse reactions (≥ 2% and more common among BRISDELLE-treated women) reported in these studies were headache, fatigue/malaise/lethargy, and nausea/vomiting. Of these commonly reported adverse reactions, nausea occurred primarily within the first 4 weeks of treatment and fatigue occurred primarily within the first week of treatment, and decreased in frequency with continued therapy.

The adverse reactions that occurred in at least 2% of patients in the BRISDELLE group and at a higher incidence than placebo are shown in Table 1 for the pooled Phase 2 and Phase 3 trials.

Table 1 Frequency of Adverse Reactions in the Phase 2 and Phase 3 Trials (≥ 2% and at a higher incidence than placebo)

	Frequency n (%)	
	BRISDELLE (n = 635)	**Placebo (n = 641)**
Nervous system disorders		
Headache	40 (6.3)	31 (4.8)
General disorders and administration site conditions		
Fatigue, malaise, lethargy	31 (4.9)	18 (2.8)
Gastrointestinal disorders		
Nausea, vomiting	27 (4.3)	15 (2.3)

Certain symptoms were seen more frequently in women at the time of discontinuation of BRISDELLE compared to women discontinuing placebo, and have also been reported upon discontinuation of other formulations of paroxetine, particularly when abrupt. These include increased dreaming/nightmares, muscle cramps/spasms/twitching, headache, nervousness/anxiety, fatigue/tiredness, restless feeling in legs, and trouble sleeping/insomnia. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms with other formulations of paroxetine.

Serious Adverse Reactions: In the pooled Phase 2 and Phase 3 trials, three BRISDELLE-treated patients reported a serious adverse reaction of suicidal ideation and one BRISDELLE-treated patient reported a serious adverse reaction of suicide attempt. There were no serious adverse reactions of suicidal ideation or suicide attempt reported among the placebo-treated patients.

Postmarketing Experience

The following adverse reactions have been identified from clinical studies of paroxetine and during post-approval use of other formulations of paroxetine. Because some of 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.

Blood and Lymphatic System Disorders: Idiopathic thrombocytopenic purpura, Events related to impaired hematopoiesis (including aplastic anemia, pancytopenia, bone marrow aplasia, agranulocytosis).

Cardiac Disorders: Atrial fibrillation, Pulmonary edema, Ventricular fibrillation, Ventricular tachycardia (including torsades de pointes).

Gastrointestinal Disorders: Pancreatitis, Pancreatitis hemorrhagic, Vomiting.

General Disorders and Administration Site Conditions: Death, Drug withdrawal syndrome, Malaise.

Hepatobiliary Disorders: Drug-induced liver injury, Hepatic failure, Jaundice.

Immune System Disorders: Anaphylactoid reaction, Angioedema, Toxic epidermal necrolysis.

Investigations: Elevated liver tests (the most severe cases were deaths due to liver necrosis, and grossly elevated transaminases associated with severe liver dysfunction).

Metabolism and Nutrition Disorders: Diabetes mellitus inadequate control, Type 2 diabetes mellitus.

Nervous System Disorders: Neuroleptic malignant syndrome, Paresthesia, Somnolence, Tremor.

Psychiatric Disorders: Aggression, Agitation, Anxiety, Confusional state, Depression, Disorientation, Homicidal ideation, Insomnia, Restlessness.

Respiratory, Thoracic and Mediastinal Disorders: Pulmonary hypertension.

Skin and Subcutaneous Tissue Disorders: Hyperhidrosis, Stevens-Johnson syndrome.

DRUG INTERACTIONS

No drug-drug interaction studies have been conducted with BRISDELLE.

Potential for BRISDELLE to Affect Other Drugs

Paroxetine is a strong CYP2D6 inhibitor. Clinical drug interaction studies have been performed with substrates of CYP2D6 and show that paroxetine can inhibit the metabolism of drugs metabolized by CYP2D6 *[see Clinical Pharmacology (12.3)]*. Table 2 contains examples of drugs with a metabolism that may be affected by co-administration with BRISDELLE.

Table 2 Effects of Paroxetine on Other Drugs

Concomitant Drug Name	Effect of Paroxetine on Other Drugs	Clinical Recommendations
Thioridazine	Increased plasma concentrations of thioridazine Potential QTc prolongation	Concomitant use of thioridazine and BRISDELLE is contraindicated.
Pimozide	Increased plasma concentrations of pimozide. Potential QTc prolongation	Concomitant use of pimozide and BRISDELLE is contraindicated.
Tamoxifen	Reduced plasma concentrations of active tamoxifen metabolite	Consider avoiding concomitant use of tamoxifen and BRISDELLE.
Tricyclic Antidepressant (TCA) (e.g., Desipramine)	Increased plasma concentrations and elimination half-life	Plasma TCA concentrations may need to be monitored and the dose of TCA may need to be reduced if a TCA is co-administered with BRISDELLE. Monitor tolerability.
Risperidone	Increased plasma concentrations of risperidone	A lower dosage of risperidone may be necessary (see the Full Prescribing Information for risperidone). Monitor tolerability.
Atomoxetine	Increased exposure of atomoxetine	A lower dosage of atomoxetine may be necessary (see Full Prescribing Information for atomoxetine). Monitor tolerability.
Drugs Highly Bound to Plasma Protein (e.g., Warfarin)	Increased free plasma concentrations	The dosage of warfarin may need to be reduced. Monitor tolerability and the International Normalized Ratio.
Digoxin	Decreased plasma concentrations of digoxin	Dosage of digoxin may need to be increased. Monitor digoxin concentrations and clinical effect.
Theophylline	Increased plasma concentrations of theophylline	Dosage of theophylline may need to be decreased. Monitor theophylline concentrations and tolerability.

Use caution if co-administering BRISDELLE with other drugs that are metabolized by CYP2D6, including nortriptyline, amitriptyline, imipramine, desipramine, fluoxetine, phenothiazines, risperidone, and Type 1C antiarrhythmics (e.g., propafenone, flecainide, and encainide).

Potential for Other Drugs to Affect BRISDELLE

The metabolism and pharmacokinetics of paroxetine may be affected by the induction and inhibition of drug metabolizing enzymes such as CYP2D6. Table 3 contains a list of drugs that may affect the pharmacokinetics of BRISDELLE when administered concomitantly *[see Clinical Pharmacology (12.3)]*.

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Table 3 Effects of Other Drugs on Paroxetine

Concomitant Drug Name	Effect of Concomitant Drug on Paroxetine	Clinical Recommendations
Phenobarbital	Decreased paroxetine exposure	No dose adjustment for BRISDELLE. Monitor clinical effect of BRISDELLE.
Phenytoin	Decreased paroxetine exposure	
Fosamprenavir/ Ritonavir	Decreased plasma concentration of paroxetine	
Cimetidine	Increased plasma concentration of paroxetine	

Use caution if co-administering BRISDELLE with other drugs that inhibit CYP2D6 (e.g., quinidine).

Other Potentially Significant Drug Interactions

Monoamine Oxidase Inhibitors (MAOIs)

Serious adverse reactions such as serotonin syndrome have been reported in patients receiving a concomitant SSRI and MAOI, in patients started on an SSRI who recently received an MAOI and in patients started on an MAOI who recently received an SSRI. Therefore, concomitant use of MAOIs with BRISDELLE or use of BRISDELLE and an MAOI within 14 days of each other is contraindicated *[see Dosage and Administration (2.2), Contraindications (4.1) and Warnings and Precautions (5.2)]*.

Serotonergic Drugs

If concomitant use of BRISDELLE with other serotonergic drugs (e.g., triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) is clinically warranted, consider the increased risk of serotonin syndrome and carefully observe the patient, particularly during treatment initiation *[see Warnings and Precautions (5.2)]*.

An interaction between paroxetine and tryptophan may occur when they are co-administered. Adverse experiences, consisting primarily of headache, nausea, sweating, and dizziness, have been reported when tryptophan was administered to patients taking paroxetine. Consequently, concomitant use of BRISDELLE with tryptophan is not recommended.

If concomitant use of BRISDELLE with a serotonergic drug is warranted, carefully observe the patient, particularly during treatment initiation. There have been postmarketing reports of serotonin syndrome with the use of an SSRI and a triptan.

BRISDELLE contains paroxetine, which is also the active ingredient in other drugs. The concomitant use of BRISDELLE with other paroxetine products is not recommended *[see Indications and Usage (1)]*.

Drugs that Interfere with Homeostasis (e.g., NSAIDs, Aspirin, and Warfarin)

Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs are co-administered with NSAIDs, aspirin, and warfarin or other drugs that affect coagulation. There may be a pharmacodynamic interaction between paroxetine and warfarin that causes an increased bleeding diathesis despite unaltered prothrombin time. Carefully monitor patients receiving warfarin therapy when BRISDELLE is initiated or discontinued *[see Warnings and Precautions (5.4)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category X

Risk Summary

BRISDELLE is contraindicated in pregnant women because menopausal VMS does not occur during pregnancy and paroxetine can cause fetal harm. Epidemiological studies have shown that infants exposed to paroxetine in the first trimester of pregnancy may have an increased risk of cardiovascular malformations. Cardiac malformations are a common congenital abnormality. These data would suggest that the risk of a cardiac abnormality following paroxetine exposure in the first trimester may increase the risk from 1% to 2%. Exposure to SSRIs in late pregnancy may lead to an increased risk for neonatal complications requiring prolonged hospitalization, respiratory support, and tube feeding, and/or persistent pulmonary hypertension of the newborn (PPHN). No teratogenicity was seen in reproductive development studies conducted in rats and rabbits. However, an increase in rat pup deaths was seen during the first 4 days of lactation when dosing occurred during the last trimester of gestation and continued throughout lactation, at a dose approximately equal to the maximum recommended human dose (MRHD) for VMS (7.5 mg) on an mg/m^2 basis. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. *[see Use in Specific Populations (8.1)]*

Nursing Mothers

Paroxetine is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from BRISDELLE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established; BRISDELLE is not indicated in the pediatric population.

Geriatric Use

Clinical studies of BRISDELLE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Elderly patients may have elevated paroxetine plasma concentrations compared to younger patients. However, no BRISDELLE dose adjustment is considered necessary in elderly patients [*see Clinical Pharmacology (12.3)]*.

SSRIs have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event *[see Warnings and Precautions (5.5)]*.

Renal Impairment

No BRISDELLE dose adjustment is considered necessary in patients with renal impairment *[see Clinical Pharmacology (12.3)]*.

Hepatic Impairment

No BRISDELLE dose adjustment is considered necessary in patients with liver impairment *[see Clinical Pharmacology (12.3)]*.

OVERDOSAGE

Human Experience with Overdosage

There is limited clinical experience with BRISDELLE overdosage in humans, as there were no overdoses reported in the clinical studies.

Spontaneous cases of deliberate or accidental overdosage during paroxetine treatment have been reported; some of these cases were fatal and some of the fatalities appeared to involve paroxetine alone. Of nonfatal cases with known outcome, most recovered without sequelae. The largest known ingestion involved 2000 mg of paroxetine (267 times the maximum recommended daily dose) in a patient who recovered.

Commonly reported adverse reactions associated with paroxetine overdosage include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. Other notable signs and symptoms observed with overdoses involving paroxetine (alone or with other substances) include mydriasis, convulsions (including status epilepticus), ventricular dysrhythmias (including torsades de pointes), hypertension, aggressive reactions, syncope, hypotension, stupor, bradycardia, dystonia, rhabdomyolysis, symptoms of hepatic dysfunction (including hepatic failure, hepatic necrosis, jaundice, hepatitis, and hepatic steatosis), serotonin syndrome, manic reactions, myoclonus, acute renal failure, and urinary retention.

Management of Overdosage

Treatment should consist of those general measures employed in the management of overdosage with any SSRI. Consult with a certified poison control center for up-to-date guidance and advice on treatment of overdosage.

Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. In managing overdosage, consider the possibility of multiple drug involvement.

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide).

CLINICIAN TO CLINICIAN

For some IVF patients, twins are the best outcome

To properly measure risk, the author argues, researchers must compare 1 twin pregnancy with 2 consecutive singleton pregnancies.

BY **NORBERT GLEICHER, MD**

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What began as a European phenomenon has spread worldwide: defining twins conceived through fertility treatments as adverse outcomes to be avoided. This has led to government interventions in some European countries (and at least one Canadian province) to restrict the number of embryos allowed for transfer during in vitro fertilization (IVF).

Although a majority of twin pregnancies following fertility treatments are generated in ovarian hyperstimulation cycles (with or without intrauterine inseminations [IUI]),[1] these treatments have paradoxically escaped regulatory attempts by medical organizations and/or governments.

By contrast, IVF has increasingly become the focus of professional society recommendations and government interventions. In 2000, our research group pointed out that because IVF controls the number of embryos transferred, it offers an opportunity to control excessive multiple births created by ovulation induction/IUI cycles.[2]

IVF is an easy target exactly because the number of embryos transferred into the uterus so clearly defines the multiple pregnancy risk

TAKE-HOME MESSAGES

- A careful examination of the eSET concept reveals it to be based on statistically incorrect premises.
- Twins after IVF do not demonstrate significantly increased risks over 2 consecutive singleton pregnancies.
- Infertility patients have an absolute right of self-determination in choosing their treatments.

and is so easily controllable. Transferring fewer embryos allows for a very quick—almost immediate—impact on multiple pregnancy rates. This was first demonstrated in a worldwide IVF practice change in the late 1990s, following a groundbreaking paper by Templeton and Morris. They demonstrated that transferring only 2 embryos (rather than multiple embryos, which up to that point had been standard practice) in good-prognosis patients significantly reduced multiple (and especially higher-order multiple) pregnancy rates without negatively affecting pregnancy rates.[3] The so-called 2-embryo transfer (2-ET) was born.

While this switch in transfer policy eliminated most high-order multiples, twin rates remained high. Barely a year after the Templeton and Morris paper, the Finnish group of Vilska et al. promoted the concept of elective single embryo transfer (eSET).[4] Driven by the belief that eSET reduces adverse outcomes to mothers and offspring by minimizing twin deliveries, eSET has since become almost an obsession.[5] A careful examination of the eSET concept, however, reveals it to be based on statistically incorrect premises.

Proposed rationale for eSET

Only one argument fuels the eSET debate: Avoidance of twin pregnancies will reduce excessive adverse outcomes among mothers and their offspring. Proponents of eSET base this opinion on the accepted obstetrical observation that twin pregnancies carry with them higher risks for mothers and newborns than do singleton pregnancies. That is, indeed, the case, but at the same time this representation is also the principal reason why proponents of eSET are incorrect.

The simple fact that a twin pregnancy leads to delivery of 2 children, and a singleton pregnancy to delivery of only 1 child already suggests that twin pregnancies will carry higher risk profiles. It is, however, important to acknowledge that this outcome difference is the consequence of 2 very different outcome products (2 children versus 1).

A comparison of risk profiles between events with greatly differing outcomes makes sense and is statistically appropriate within an obstetrical paradigm that is retroactive and cannot be influenced. But a statistical comparison in a prospective paradigm (ie, infertility paradigm) must be based on identical outcomes (ie, the birth of either 1 or 2 neonates). Thus, to equalize outcomes in a prospective infertility paradigm involving twins, the control group also must claim the birth of 2 offspring as a final outcome. The appropriate comparison, therefore, is not between 1 twin and 1 singleton pregnancy but between 1 twin and 2 consecutive singleton pregnancies.[6]

Our research group noted in a 2009 publication that when risk comparisons are made correctly, higher outcome risks for twin pregnancies almost completely disappear.[6] Aside from patients who for social reasons do not wish to have twins (a minority among infertility patients[7]) and/or patients with medical contraindications for twin pregnancies, no further indications for eSET remain. Indeed, under such circumstances, eSET should, for most patients, be considered contraindicated, because it harms patient outcomes in comparison to 2-ET without offering compensatory benefits.

The literature is unanimous that eSET reduces a woman's pregnancy chances with IVF in comparison to 2-ET.[8] Such a reduction would be palatable if it compensated for real increased risks (infertile women, in fact, are willing to take considerable risks to improve pregnancy chances[7,9]). But in my opinion this breaches most basic ground rules of medical ethics by reducing and delaying pregnancy chances without compensatory benefits.

Proponents of eSET have argued that the combination of 1 fresh eSET followed by a frozen-thawed eSET results in pregnancy chances almost identical to 1 2-ET,[8] but any reduction in pregnancy chances and/or delay in achieving pregnancy absent compensatory benefits must be considered a harmful outcome to infertile women.

This is a crucial point when differentiating between the switch from 2-ET to eSET and the switch from multiple embryo transfer to 2-ET. Templeton and Morris were able to demonstrate that in good-prognosis patients, reducing the number of transferred embryos significantly decreased high-order multiples without negatively affecting IVF pregnancy chances.[3] The practice change driven by the Templeton and Morris paper differs in 2 crucial points from the currently advocated eSET concept: (1) It reduced high-order multiples, which unquestionably represent higher risks than twin pregnancies. Therefore, the potential benefit from reducing multiple births was greater than expected from twin reductions; and (2) It did so without negatively affecting pregnancy chances.

TABLE **Results from Swedish national data comparing maternal and neonatal outcomes of 1 twin to 2 consecutive singleton pregnancies[18]***

INCREASED MATERNAL RISKS	Adjusted OR (95% CI)
Cesarean delivery	4.19 (3.32–5.29)
Premature rupture of membrane	8.43 (4.86–14.63)
Placenta previa	-0.37 (0.17–0.81)
Preeclampsia	2.64 (1.81–3.86)
Gestational diabetes	NS
Maternal mortality	NS
INCREASED NEONATAL RISKS	
Sepsis	2.31 (1.29–4.13)
Respiratory complications	4.92 (3.68–6.58)
Jaundice	5.03 (3.77–6.70)
Perinatal mortality	NS
Apgar < 7 at 5 minutes	NS
Mortality in first year of life	NS
Congenital anomalies	NS

*The study reports on 1982 children born to 991 mothers in IVF twin pregnancies after 2-ET, and on 1842 children born in 2 consecutive IVF singleton pregnancies to 921 mothers. Abbreviation: NS, not significant

In contrast, eSET, as noted above, based on our evaluation of the literature, does not in a clinically very significant way improve outcome risks, yet unquestionably decreases IVF pregnancy chances.[6]

Proof of concept

The validity of eSET depends on whether the central argument made in our 2009 manuscript is correct: Outcomes of 1 twin pregnancy do not represent significantly higher maternal and neonatal risks than outcomes of 2 consecutive singleton pregnancies.[6] We reached this conclusion based on a review of published literature and a systematic review by Helmerhorst et al.[10] These authors, as summarized in a commentary in the same year,[11] reported little if any difference in frequencies of very preterm births, very low birth weights, and small-for-gestational-age births between IVF-conceived and naturally conceived twins.

IVF twins, however, demonstrated lower perinatal mortality and higher rates of neonatal hospital admissions. Their review concluded that IVF twins presented with an approximately 40% lower risk of serious adverse outcomes than did spontaneously conceived twins, whereas IVF singleton pregnancies actually demonstrated higher outcome risks than spontaneously conceived singletons.

Their systemic review suggested that when obstetric outcome data were used to define risks, the data (1) must compare 1 twin pregnancy to 2 singleton pregnancies and (2) must be adjusted for outcome differences between IVF-conceived and spontaneously conceived pregnancies. Doing this, we demonstrated that clinically relevant risks to mothers and neonates no longer differed significantly.[6]

The paper by Helmerhorst and associates was published in 2004.[10] More recently published data are more divergent in their outcome assessments.[12-16] Because some studies did not support the outcome comparisons reported in Helmerhorst's systemic review, perinatal/neonatal colleagues, especially, challenged our assertion that twin pregnancies do not represent excessive risk. Their biggest concern was an alleged highly increased risk of cerebral palsy, although the only recent study we were able to find in the literature suggests no such effects.[17]

We initially welcomed a recent publication that for the first time in statistically correct fashion compared pregnancy outcomes between 1 twin IVF pregnancy and 2 consecutive singleton IVF pregnancies.[18] Our enthusiasm waned after recognizing that the authors misinterpreted their own data by claiming "dramatically" higher maternal and neonatal risks for twin pregnancies, while not showing such outcomes in their results.[19] Very much to the contrary, their results very closely resembled the earlier analysis that has previously been described,[6] demonstrating increased twin risks limited to minor and clinically mostly inconsequential prematurity risks (Table).

Using data from Sweden, Sazonova and colleagues reported on 1982 children born to 991 mothers via twin pregnancies after 2-ET and on 921 mothers who gave birth to 1842 children via 2 consecutive singleton IVF pregnancies. The Table presents a summary of outcome comparisons. Maternal risks differed to minor degrees; twins demonstrated higher risk for preeclampsia (adjusted odds ratio [OR] 2.64; 1.81–3.86), cesarean delivery (adjusted OR 4.19; 3.32–5.29), and premature rupture of membranes (adjusted OR 8.43; 4.86–14.63). Risk of placenta previa was negative (adjusted OR -0.37; 0.17–0.81). Most remarkably, risks of preeclampsia, gestational diabetes, and maternal mortality did not differ.

Differences in neonatal morbidity were even less pronounced. Twins demonstrated increased

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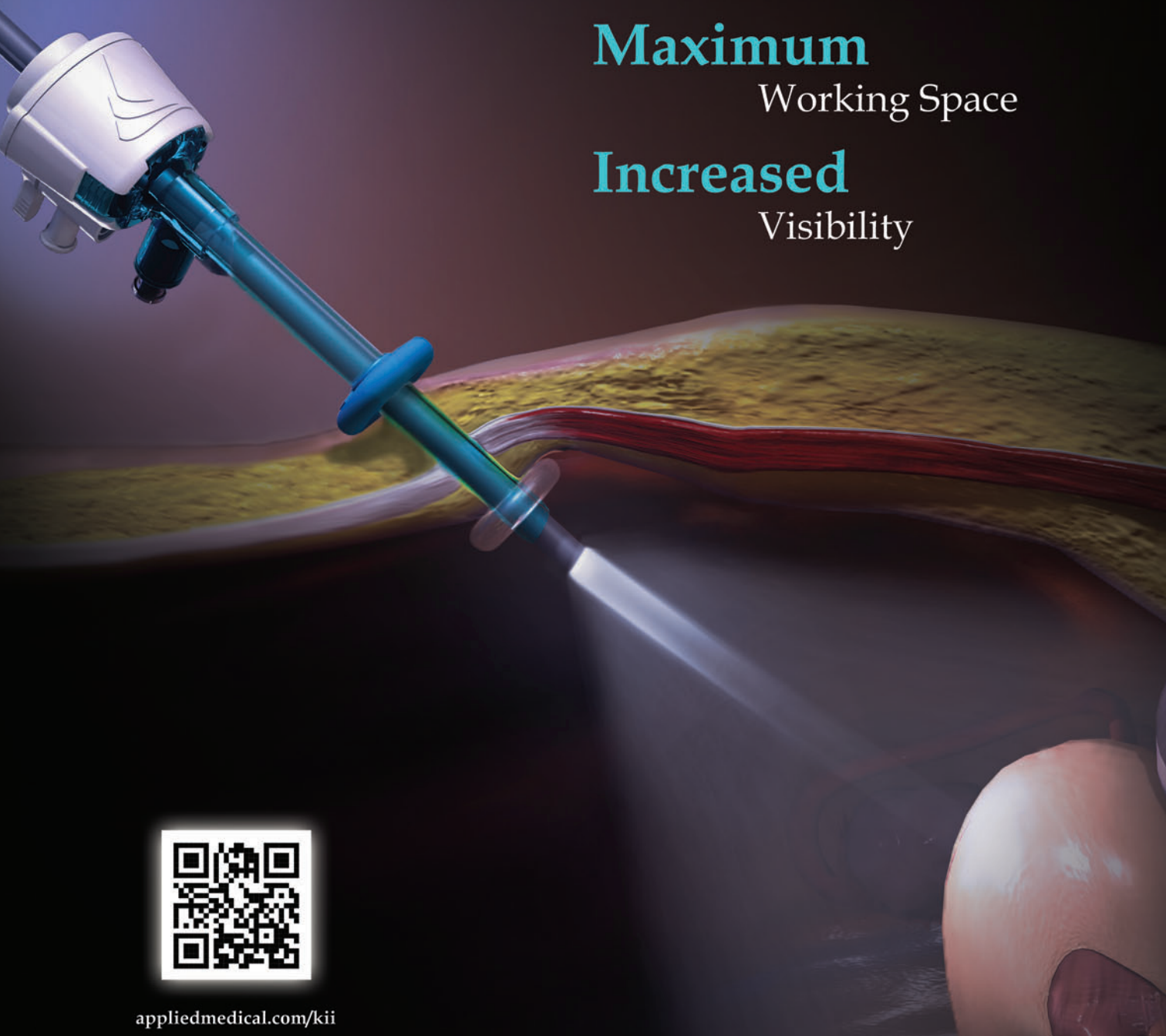

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> Infertile women, even after biased counseling that favors eSET, **favor the opportunity to conceive twins** and are willing to accept even exaggerated risks.

risk only of respiratory complications (adjusted OR 4.92) and jaundice (adjusted OR 5.03), but perinatal mortality, Apgar scores below 7 at 5 minutes, mortality in first year of life, and congenital abnormalities did not differ. In summary, except for minor short-term morbidity, the Swedish study found no evidence of clinically significant and/or long-term increased risks in association with IVF twin pregnancies.

Observed increases in respiratory complications and jaundice, considering no differences in Apgar scores, can be assumed to be relatively minor. These data, indeed, well reflect the findings by Helmerhorst and the associated noted increase in neonatal hospitalizations for twins, although in absence of significant morbidity.[10,11]

If twins after IVF do not demonstrate significantly increased risks over 2 consecutively delivered singleton pregnancies, there really is no meaningful argument left in support of eSET, unless patients simply do not wish to conceive twins and/or have medical contraindications to twin pregnancies.[19]

Social considerations

Evidence demonstrating no practical risk differences between 1 twin and 2 singleton deliveries still exaggerates the risks of twins because data are based on the unrealistic assumption that twin deliveries can be established "at will." That is, of course, not possible. With 2-ET, at most, one-third of pregnancies will be twin pregnancies. Therefore, only one-third of women who choose to take the risks of a twin pregnancy will indeed encounter those risks. The other two-thirds will have experienced the potential of twins but will have failed to receive either the benefits or risks of twin births.

Our disagreement on this subject with many colleagues does not stem from differences in interpretation of published risk data alone. We are also concerned about paternalism, based on how eSET is presented to patients, often denying infertile women the right of self-determination. It puzzles us to see colleagues grant women the right to demand elective cesarean delivery, plastic surgery, and other surgical procedures, yet deny them self-determination in their desire to maximize pregnancy chances.[7,9]

Because infertility is not a medical emergency requiring quick decisions, and because the large majority of infertility patients in the United States are socioeconomically privileged, they are among the best-educated patients in medicine. Yet many colleagues deride these patients' widely reported desire for twin pregnancies as a reflection of poor education or biased counseling.

Neither allegation can be supported by data. Infertile women, even after biased counseling that favors eSET, favor the opportunity to conceive twins and are willing to accept even exaggerated risks.[7,9]

When patients are counseled, of course, the medical risks to mothers and offspring must be fairly described and the social implications of twin deliveries—which can be profound—should be addressed.[20] Yet after such counseling, infertility patients—like patients in all other medical specialty areas—have an absolute right of self-determination in choosing their treatments.

Study after study has demonstrated that quick conception and delivery are the primary goals of most infertile women and that the desire for twins logically increases with advancing patient age and length of infertility.[7]

Reducing and/or delaying pregnancy chances without compensatory benefits might actually be considered unethical. Not even the most accomplished fertility specialist can guarantee patients a second pregnancy chance at least 12 to 18 months after a first delivery, when a second pregnancy may become feasible. By that time, the infertile patient is 12 to 18 months older, her fertility has further declined, and other medical problems may have arisen.

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> **An infertility patient who wants 2 children** should not be prevented from taking the chances of a twin pregnancy.

Arguing, as proponents of eSET do, that 2-ET can be replaced by 2 consecutive eSET pregnancies[8] is misleading. An infertility patient who wants 2 children should not be prevented from taking the chances of a twin pregnancy, which will give her the desired outcome now, and does not require a second successful treatment cycle.

Summary

After appropriate counseling and absent medical contraindications, if a patient desires twins, they should be welcomed. What is surprising to this author is the uncritical acceptance by so many colleagues of the notion that twins are "bad."

How far some colleagues are willing to take this concept is best demonstrated by a recent paper from the same Finnish group that initially introduced eSET to the world.[21] In this paper the authors, who themselves initially proposed eSET only for favorable patients, now propose eSET for women up to age 44.

Can one responsibly suggest to a patient to have an eSET at age 44 because she always can have another child 12 to 18 months later? I don't think so.[5] COG

REFERENCES

1. Jones HW Jr. Iatrogenic multiple births: a 2003 checkup. *Fertil Steril.* 2007;87(3):453-455.

2. Gleicher N, Oleske DM, Tur-Kaspa I, Vidali A, Karande V. Reducing the risk of high-order multiple pregnancy after ovarian stimulation with gonadotropins. *N Engl J Med.* 2000;343(1):2-7.

3. Templeton A, Morris JK. Reducing the risk of multiple births by transfer of two embryos after in vitro fertilization. *N Engl J Med.* 1998;339(9):573-577.

4. Vilska S, Tiitinen A, Hydén-Granskog C, Hovatta O. Elective transfer of one embryo results in an acceptable pregnancy rate and eliminates the risk of multiple births. *Hum Reprod.* 1999;14(9):2392-2395.

5. Gleicher N. The irrational attraction of elective single-embryo transfer (eSET). *Hum Reprod.* 2013;28(2):294-297.

6. Gleicher N, Barad D. Twin pregnancy, contrary to consensus, is a desirable outcome in infertility. *Fertil Steril.* 2009;91(6):2426-2431.

7. Gleicher N, Campbell DP, et al. The desire for multiple births in couples with infertility problems contradicts present practice patterns. *Hum Reprod.* 1995;10(5):1079-1084.

8. Pandian Z, Marjoribanks J, Ozturk O, Serour G, Bhattachaya S. Number of embryos for transfer following in-vitro fertilisation or intracytoplasmic sperm injection. *Cochrane Database Syst Rev.* 2013.

9. Scotland GS, McNamee P, Peddie VL, Bhattacharya S. Safety versus success in elective single embryo transfer: women's preferences for outcomes of in vitro fertilisation. *BJOG.* 2007;114(8):977-983.

10. Helmerhorst FM, Perquin DA, Donker D, Keirse MJ. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ.* 2004;328(7434):261.

11. Keirse MJ, Helmerhorst FM. How many eggs? *BMJ.* 2004;329(7461):302-303.

12. Källén B, Finnström O, Lindam A, Nilsson E, Nygren KG, Olausson PO. Selected neonatal outcomes in dizygotic twins after IVF versus non-IVF pregnancies. *BJOG.* 2010;117(6):676-682.

13. Messerschmidt A, Olischar M, Birnbacher R, Weber M, Pollak A, Leitich H. Perinatal outcome of preterm infants <1500 g after IVF pregnancies compared with natural conception. *Arch Dis Child Fetal Neonatal Ed.* 2010;95(3):F255-229.

14. Vasario E, Borgarello V, Bossotti C, et al. IVF twins have similar obstetric and neonatal outcome as spontaneously conceived twins: a prospective follow-up study. *Reprod Biomed Online.* 2010;21(3):422-428.

15. Yang H, Choi YS, Nam KH, Kwon JY, Park YW, Kim YH. Obstetric and perinatal outcomes of dichorionic twin pregnancies according to methods of conception: spontaneous versus in-vitro fertilization. *Twin Res Hum Genet.* 2011;14(1):98-103.

16. Tomic V, Tomic J. Neonatal outcome of IVF singletons versus naturally conceived in women aged 35 years and over. *Arch Gynecol Obstet.* 2011;284(6):1411-1416.

17. Källén AJ, Finnström OO, Lindam AP, Nilsson EM, Nygren KG, Olausson PM. Cerebral palsy in children born after in vitro fertilization. Is the risk decreasing? *Eur J Paediatr Neurol.* 2010;14(6):526-530.

18. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C. Neonatal and maternal outcomes comparing women undergoing two in vitro fertilization (IVF) singleton pregnancies and women undergoing one IVF twin pregnancy. *Fertil Steril.* 2013;99(3):731-737.

19. Gleicher N, Barad DH. Mistaken advocacy against twin pregnancies following IVF. *J Assist Reprod Genet.* 2013;30(4):575-579.

20. Benute GR, Nozzella DC, Prohaska C, Liao A, de Lucia MC, Zugaib M. Twin pregnancies: evaluation of major depression, stress, and social support. *Twin Res Hum Genet.* 2013;16(2):629-633.

21. Niinimäki M, Suikkari AM, Mäkinen S, Söderström-Antilla V, Martikainen H. Elective single-embryo transfer in women aged 40-44 years. *Hum Reprod.* 2013;28(2):331-335.

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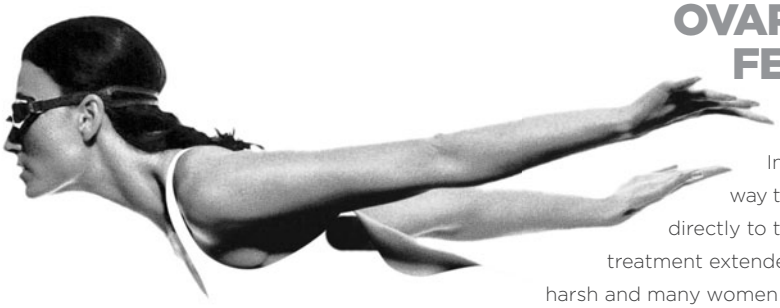


Intraperitoneal (IP) chemotherapy was introduced as a way to treat ovarian cancer by administering chemotherapy directly to the abdomen rather than through a vein. While this treatment extended median survival for women, the side effects were harsh and many women were unable to complete treatment. Our faculty at **Magee-Womens Hospital of UPMC** and **UPMC CancerCenter** played a major role in the adaptation of IP to a modern outpatient regimen, reducing side effects and improving outcomes by adjusting dosing and anticipating and controlling symptoms. Oncologists at Magee and throughout UPMC were also among the first to use hyperthermic IP chemotherapy for the treatment of ovarian cancer. We continue to research new and better ways to treat ovarian cancer, with an emphasis on providing personalized treatment plans. Learn more at **UPMCPhysicianResources.com/OvarianCancer.**

Magee-Womens Hospital of UPMC

UPMC is affiliated with the University of Pittsburgh School of Medicine.

The life course theory

Are public health programs the answer to racial disparities in prematurity and infant mortality?

BY **HAYWOOD L. BROWN, MD, MARK SMITH, MS,** AND **YVONNE BEASLEY, RN, MN**

Reducing infant mortality (deaths in the first year of life) has long been a national priority of the United States. Since 1935, US rates of infant mortality have fallen by more than 400%, mostly due to early detection and treatment of complications (Figure). Despite this success, the current model is challenged to address health problems far outside the scope of the doctor's exam room.

Currently, the World Health Organization (WHO) ranks the United States 41st among 193 other nations in infant mortality, largely due to variations in infant mortality associated with race and ethnicity.

Authors from the National Center for Health Statistics wrote nearly 50 years ago in one of the first public health reports on infant mortality, "although the national infant mortality rate is now at its lowest level, the prospects for a change in the rate of decline in the future do not appear to be as favorable now as they did in 1958 . . . The gap between the rate for white and nonwhite infants has widened during the past decade."

The leading causes of death among newborns during the first year of life are related to prematurity and congenital anomalies. Prematurity as a cause of infant mortality affects non-Hispanic blacks at a rate 3 times higher than non-Hispanic whites. The epidemiology of prematurity and racial disparity of spontaneous preterm birth is quite complex. In 2005, the Institute of Medicine (IOM) estimated the annual price tag for prematurity in the US at $26 billion.[1]

While researchers have long known the impact of social determinants on health behaviors, most public health agencies have focused resources on health education and early prenatal care to reduce infant mortality. In 2007, the IOM recognized the growing importance of social and health determinants, stating:

Preterm birth is a complex cluster of problems with a set of overlapping factors of influence. Its causes may include individual level behavioral and psychosocial factors, neighborhood characteristics, environmental exposures, medical conditions, infertility treatments, biological factors, and genetics. Many of these factors occur in combination, particularly in those who are socioeconomically disadvantaged or who are members of racial and ethnic minority groups.[1]

Because of the recognized complexities in epidemiology of prematurity, in 2010 the Maternal and Child Health Bureau (MCHB) of the US Department of Health and Human Services released a concept paper that applied life course theory (LCT) to its long-term strategic plan to reduce racial and ethnic disparities in infant mortality.[2]

LCT suggests that an individual's environment and culture heavily influence manifestation and management of disease. Social, economic, and environmental inequities persist across generations, collectively limiting individuals' future health and creating variations in incidence and impact of many diseases.

Implicit within LCT are 4 tenets. We will discuss each one as it relates to a particular health behavior and discuss how some interventions use LCT to address the underlying roots of variations in infant mortality.

LCT TENET 1: Timelines. Health behaviors and attitudes persist across generations, often handed down from parent to child.

Intimate partner violence

Intimate partner violence (IPV) not only acts as a barrier

to prenatal care but also results in physical injury, psychological trauma, and sometimes death. Abused women experience more physical health problems and have a higher occurrence of depression; anxiety and stress; tobacco, illicit drug, and alcohol abuse; and suicide attempts, in addition to using more healthcare services. In 2003, the Centers for Disease Control and Prevention (CDC) estimated that IPV accounted for more than 1500 deaths annually, with a price tag of $5.8 billion due to lost productivity and use of healthcare services.[3]

Witnessing violence between one's parents and caretakers is the strongest risk factor for transmitting violent behavior from one generation to the next.[3] Therefore the effects of IPV extend far beyond the period of abuse. Perpetrators of IPV are 30%–60% more likely to abuse children in the home, and boys who witness violence are twice as likely to abuse their partners and children when they grow up.[4]

Parker and others demonstrated the efficacy of programs that teach safety behaviors and build empowerment skills to reduce different types of IPV.[5] More recent IPV interventions have developed integrated models that include other cognitive behavioral interventions to address overlapping health determinants. They have shown significant reductions in IPV as well as rates of prematurity.[6]

LCT TENET 2: Timing. Periods of vulnerability influence lifelong health as well as social and economic trajectories.

Smoking and smoking cessation

The health and economic consequences from smoking are well documented. Smoking during pregnancy is linked to up to 10% of all infant deaths. The direct medical costs of a complicated birth are 66% higher for smokers than for nonsmokers, reflecting the more severe complications and a requirement for more intensive care. Direct medical costs associated with tobacco use and exposure to secondhand smoke during pregnancy are estimated to be $4.6 billion.[7]

Research has shown that parental smoking can contribute to smoking initiation independent of other risk factors such as depression and anxiety.[8] Once the habit of daily smoking begins, most smokers find it very difficult to quit and average 6 attempts before becoming former smokers.[9]

Despite the challenges of quitting smoking, pregnancy is a defining moment in many women's lives when they focus on their own health and the health of their fetus. Women who smoke and become pregnant are twice as likely to attempt to quit smoking as nonpregnant women.[10]

According to the March of Dimes, most pregnant smokers will attempt to quit, but 80% will resume smoking within 6 months after giving birth. Women who quit smoking before the age of 35 have lifespans similar to women who never smoked.[11]

Many efficacious smoking cessation programs exist, yet relatively few are for pregnant women. The March of Dimes developed a motivational counseling program called the 5 As. The 5 As (ask, advise, assess, assist, arrange) program is based on a woman's needs and can be offered by health educators, social workers, and healthcare workers. Published research suggests that this program can increase smoking cessation rates by 30%.

LCT TENET 3: Equity. Diseases and treatments affect individuals (eg, race), families (eg, cultural beliefs), and communities (eg, environment) differently, leading to variations in disease incidence, prevalence, and impact.

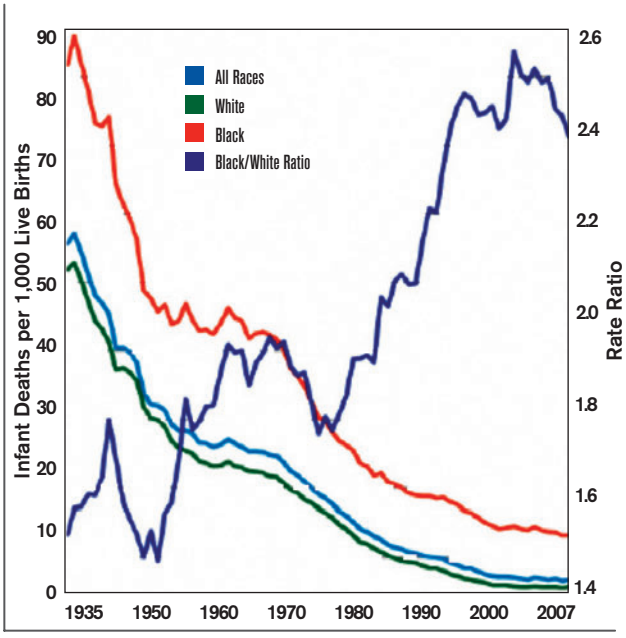
Obesity

By age 65, approximately 1 in 4 US adults are obese and another 34% to 47% are considered overweight (having a body mass index [BMI] of 25 to < 30).[11] The medical consequences of adult obesity are well known. The medical costs of treating obesity are approaching $150 billion each year.[12] Obstetric complications as a result of obesity and its comorbidities increase the risk of adverse outcome for both mother and baby.

The increasing prevalence of obesity in the United States was a factor behind the IOM's reexamination of the recommended weight gain guidelines during pregnancy, which subsequently limited the maximum weight gain for most women. Breastfeeding also plays an important role in helping women achieve healthier interconception weight, and may impact childhood and adult obesity.

Surveys of women who gave birth in 2004–2005 in 26 states showed that race or ethnicity coupled with geographic location had the largest impact on rates of prepregnancy obesity, which ranged from 7.3% in white, non-Hispanic women living in New York City to 34.7%

Infant Mortality Rate by Race, United States, 1935-2007



Source: Singh GK, van Dyck PC. Infant Mortality in the United States, 1935-2007: Over Seven Decades of Progress and Disparities. A 75th Anniversary Publication. Health Resources and Services Administration, Maternal and Child Health Bureau. Rockville, Maryland: U.S. Department of Health and Human Services; 2010. http://www.hrsa.gov/healthit/images/mchb_infantmortality_pub.pdf

in Hispanic women living in Michigan.[13]

New "lifestyle case management" approaches (such as the Strong Healthy Women program) that include individual and group education, support, and referrals can be effective because they take a more holistic approach and can be tailored to specific racial and ethnic groups located in specific communities.

The Indianapolis Healthy Start Program developed a program called Fruits of Our Labor that includes healthy weight education, nutrition support groups, and referrals to cooking programs, fitness centers, and a community garden to assist many urban and African-American women.

LCT TENET 4: Environment. Attributes within a community (eg, lack of transportation) can either directly (eg, air pollution) or indirectly (eg, education) modify the expression of disease or its treatment.

Environmental influences

Where women live is an independent risk factor for prematurity and infant mortality. Socioeconomic confounders including race, ethnicity, and education have typically been employed when describing perinatal outcome. However, more recent research is demonstrating that regardless of race, ethnicity, and education, women residing in certain communities or neighborhoods are at increased risk.[14]

While the reasons are complex and often not well understood, it doesn't appear that all races are affected equally. It may take years of residing in the same community for health impacts to become evident. Many possible factors affect a woman's health, such as drinking-water quality, air quality, lead exposure, sanitation, access to health care, and employment. These important influences vary by neighborhood and are known to impact prematurity.

Recognition of the importance of the environment and community hasn't produced evidence-based practices to reduce infant mortality. Understanding the root causes of fetal and infant mortality requires a coalition of community leaders in health care, government, academia, and industry intent on improving health disparities.

The National Fetal Infant Mortality Review (FIMR) project, created by Dr. Ezra Davidson in his American College of Obstetricians and Gynecologists Presidential Initiative in 1990, is one such collaborative community-health care-focused project. During the past 2 decades, the program has expanded and has been adopted by many Healthy Start grantees under the Health Resources and Services Administration.

The focus of FIMR is to understand causes of infant deaths. FIMR staff and community healthcare providers review detailed records coupled with in-depth interviews of surviving mothers to get a better understanding of specific details and events that contribute to infant deaths. This process identifies community risk factors such as chronic disease; mental health effects from social and economic insecurity; loss of functionality during motherhood due to mental health problems; obstacles to securing safe, healthy, and affordable housing; and consequences of no or inadequate health insurance.

Health behaviors are affected by each LCT tenet. This often results in multiple underlying disparities manifesting as health disparities. Depression, which is common among women, illustrates this multiplicity principle. Depression prevalence varies considerably by race, age, and socioeconomic status.

continued on **PAGE 52**

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continued from **PAGE 50**

Maternal depression during pregnancy and infancy is linked to prematurity, low birth weight, and other adverse birth outcomes.[15] Prenatal depression is also associated with early breastfeeding cessation and newborn crying, fussiness, and inconsolability, which make it difficult for a parent to provide nurturing care.[16] Depressed mothers are also more likely to report IPV and substance abuse.[17]

There is also evidence suggesting that both women and men who suffer from depression have common risk factors during their childhood and adolescence.[18]

Women living in poverty who report severe depression are 8 times more likely to report physical abuse within the previous 2 years than are nondepressed women living in poverty, 2.5 times more likely to report recent binge drinking, and less likely to be living with the father of their child or children (41% vs. 60%).[18]

African-American women already are at a higher risk of adverse birth outcomes and IPV, which is also associated with significantly higher rates of depression and suicide attempts as well as use of tobacco, alcohol, and illicit drugs.[18]

Summary

The implications of chronic risk factors on pregnancy outcome and disease expression are striking. The traditional medical model has often focused on individual health knowledge and access to the healthcare system to mitigate specific risk factors. But LCT directs attention "upstream," to neighborhood conditions, community infrastructure, and social inequalities.

Few good programs applying LCT exist, but we believe there are seeds of hope in those programs that employ LCT. Increasing knowledge, skills, and resources will translate into healthier babies and healthier communities.

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REFERENCES

1. Behrman RE, Butler AS, eds. *Preterm Birth: Causes, Consequences, and Prevention*. Washington, DC: National Academies Press; 2007.

2. Lu MC, Kotelchuck M, Hogan V, Jones L, Jones CP, Halfon N. A 12-point plan. Closing the black-white gap in birth outcomes: a lifecourse health development approach. *Ethn Dis*. 2010;20(1 Suppl 2):S62-76.

3. National Center for Injury Prevention and Control. *Costs of Intimate Partner Violence Against Women in the United States*. Atlanta, GA: Centers for Disease Control and Prevention; 2003.

4. Tjaden P, Thoennes N. *Extent, Nature, and Consequences of Intimate Partner Violence: Findings from the National Violence Against Women Survey*. Washington, DC: National Institute of Justice and the Centers for Disease Control and Prevention; 2000.

5. Parker B, McFarlane J, Soeken K, Silva C, Reel S. Testing an intervention to prevent further abuse to pregnant women. *Res Nurs Health*. 1999;22(1):59–66.

6. Kiely M, El-Mohandes AA, El-Khorazaty MN, Blake SM, Gantz MG. An integrated intervention to reduce intimate partner violence in pregnancy. *Obstet Gynecol*. 2010;115:273–283.

7. Centers for Disease Control and Prevention Office of Surveillance, Epidemiology, and Laboratory Services. Behavioral Risk Factor Surveillance System Prevalence and Trends Data. http://apps.nccd.cdc.gov/brfss/. Accessed June 12, 2012.

8. Hill KG, Hawkins JD, Catalano RF, Abbott RD, Guo J. Family influences on the risk of daily smoking initiation. *J Adolesc Health*. 2005;37(3):202-210.

9. Jones JM. Smoking habits stable; most would like to quit. July 18, 2006. http://www.gallup.com/poll/23791/smoking-habits-stable-most-wouldlike-quit.aspx. Accessed June 12, 2012.

10. Chen X, Stanton B, Shankaran S, Li X. Age of smoking onset as a predictor of smoking cessation during pregnancy. *Am J Health Behav*. 2006;30(3):247-258.

11. Malarcher A, Dube S, Shaw L, Babb S, Kaufmann R. Quitting smoking among adults—United States, 2001–2010. *MMWR*. 2011;60(44):1513-1519.

12. Chu SY, Kim SY, Bish CL. Prepregnancy obesity prevalence in the United States, 2004–2005. *Matern Child Health J*. 2009;13:614–620.

13. Finkelstein EA, Trogdon JG, Cohen JW, Dietz W. Annual medical spending attributable to obesity: payer- and service-specific estimates. *Health Affairs*. 2009;28(5):w822-w831.

14. Collins JW Jr, Wambach J, David RJ, Rankin KM. Women's lifelong exposure to neighborhood poverty and low birth weight: a population-based study. *Matern Child Health J*. 2009;13:326–333.

15. England MJ, Sim LJ, eds. *Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention*. Washington, DC: National Academies Press; 2009.

16. Vericker T, Macomber J, Golden O. *Infants of Depressed Mothers Living in Poverty*. Washington, DC: The Urban Institute; 2010.

17. Green KM, Fothergill KE, Robertson JA, Zebrak KA, Banda DR, Ensminger ME. Early life predictors of adult depression in a community cohort of urban African Americans. *J Urban Health*. 2013; 90(1):101–115.

18. Pickett KE, Collins JW Jr, Masi CM, Wilkinson RG The effects of racial density and income incongruity on pregnancy outcomes. *Soc Sci Med*. 205;60(10):2229–2238.

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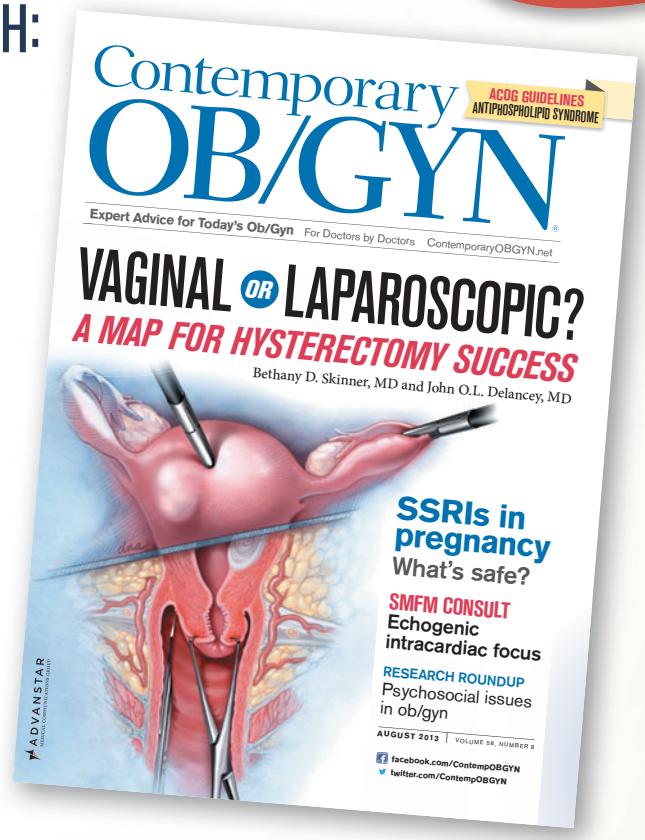

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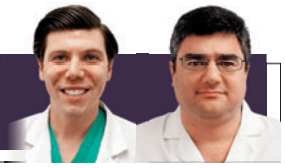


An EHR Primer

Part 2: The price of improved efficiency is the cost of learning a new process for patient care.

In our previous Tech Tools column ("An EHR Primer Part 1: Current laws and incentives," July 2013 *Contemporary OB/GYN*) we introduced the concept of electronic health records (EHRs), the associated technology, and the government-supported programs that encourage their use and adoption. In this installment we will review the perceived versus the actual benefits of EHRs and the costs associated with EHR adoption.

When looking broadly at EHR adoption, the move from paper to digital makes sense. The immediate accessibility of patient demographics, pertinent medical problems, and past medical history is an attractive part of almost every EHR. In fact, embedded safety checks reduce the effort needed to find specific information and help minimize physician errors. However, the price of improved efficiency is the cost of learning a new process for patient care. Until an EHR is completely implemented, it can be cumbersome to retrieve information from patients' records in the same time it took in a traditional "pen & paper" office.

EHRs touch many aspects of health care practice, but the 5 areas in which the technology can have a dramatic impact are these:

1 Improved Communication

For patients with multiple physicians, an open-architecture EHR can facilitate enhanced provider-to-provider communication. Ideally, these relationships would include a given patient's pharmacy, hospital, and any other healthcare entity. Similarly, patient and physician communication can be streamlined through direct and secure "web portals" and other methods of safe electronic communications. Patients can then be empowered to manage their health care needs by accessing their own health records.

2 Reduced paperwork for physician and patient

When data-collection systems communicate better with one another, clipboards will begin to disappear, along will the stacks of paperwork exchanged between patient and provider. As more information is entered into an EHR, those data will support a more productive and streamlined encounter between patient and physician.

3 Streamlined coordination of care

EHR systems will become effective tools to accumulate and share personal health information (PHI), simplifying the sometimes formidable task of coordination of care and reducing medical mistakes. In the future, it would be ideal if all providers could use the same PHI record and, thus access the most current, complete, and accurate data.

4 Enhanced patient safety

EHRs are ideal for alerting providers to allergies, drug interactions, abnormal laboratory test findings, and redundant test orders. As an EHR becomes more comprehensive and "intelligent," it can trigger provider-alerts to health safety issues such as newly identified medication side effects, product recalls, and new strategies for disease management and preventive care. Such a system would allow a provider to "preemptively" notify patients of important health issues based on a continual automated process of cross-referencing of their medical histories with the latest medical findings. That could change health care from an encounter- and patient-complaint-driven system of care to a more proactive approach to complete health management.

5 Patient-controlled direct access to PHI

Patients have a legal right to their health

records. In addition, patient portals to the EHR can further improve the accuracy of the PHI by identifying omissions and inaccuracies. Giving patients secure online access to their PHIs can encourage them to proactively follow up on health-related needs. Establishing protocols for this direct access to PHI will empower patients to manage their health care.

When evaluating how EHRs improve efficiency, the Healthcare Information and Management Systems Society, a nonprofit organization dedicated to promoting discussions about health information technology (HIT), describes 5 broad categories of values attributable to HIT investments (eg, EHRs) for which they use the acronym STEPS (Figure 1).[1]

By the end of 2013 Q1, the Centers for Medicare & Medicaid Services (CMS) had paid doctors and hospitals more than $13.7 billion to facilitate EHR implementation through the HITECH Act of 2009.[2] That has spurred doctors to embrace EHRs because most of the government subsidies require continued use. In fact, an Accenture study showed that 93% of American physicians routinely use EHRs, compared with 95% in Spain, 93% in Germany, and 92% in France. Figure 2 illustrates the results of the survey, which included 3700 physicians in 8 countries.[3]

The Accenture study also revealed a 32% annual increase in routine use of HIT by US physicians, compared with a 15% increase among peers in other countries surveyed. US physicians also had the highest routine use of e-prescribing (65%) and electronic documentation (78%). Most compelling was the finding that 57% of US physicians reported regularly using electronic lab orders—a 21% annual increase versus a 6% global decline.[3]

A case study by the Commonwealth Fund found that one of the most important factors in building support for an EHR was having clinical staff drive the process and involving as many staff members as possible in its design and development.[4] Building support among physicians, the authors note, requires "nurtured physician champions" who are either proponents of adopting a comprehensive EHR from the start or become enthusiastic early in the process, and are viewed as having influence over other physicians. The ultimate goal is to aggregate the physician champions with other EHR "supporters" to build clinical teams for EHR development.

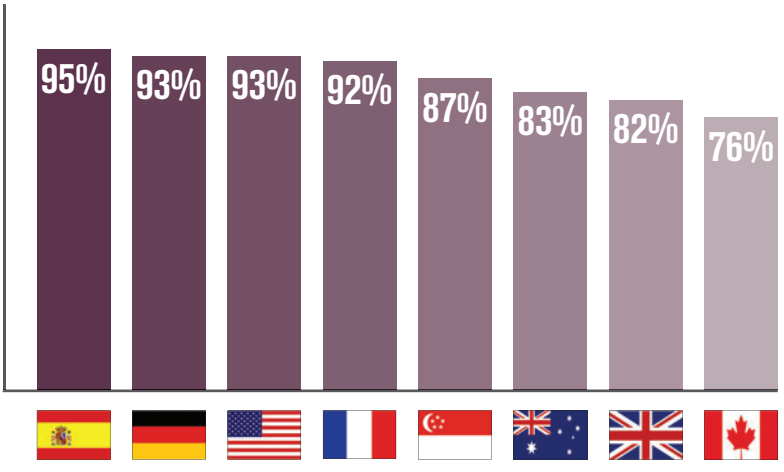
The Table is an overview of how

FIGURE 1 5 categories of values attributable to HIT investments

SATISFACTION	118% Increase in patient satisfaction –Unity Health Care, Inc, 2012	90% Increase in staff retention –Hudson River Healthcare, Inc, 2011
TREATMENT/ CLINICAL	52% Decrease in 30-day readmission rate –Mount Sinai Medical Center, 2012	20% Increase in per-visit physician time spent with each patient –Mount Sinai Medical Center, 2012
ELECTRONIC INFORMATION/ DATA	$500,000 Annual decrease in claim denials –Sentara Health Care, 2012	
PREVENTION/ PATIENT EDUCATION	96% Compliance rate for patient and medication scans –Sentara Health Care, 2012	150% Increase in patients meeting diabetes management metrics –Hawaii Pacific Health, 2012
	191% Increase in immunizations –James Hoslinger, MD	
SAVINGS	$9.7 MILLION From elimination of transcription services –Hawaii Pacific Health, 2012	$3.1 MILLION From reduced length of patient stays –Sentara Health Care, 2012
	ROI TOTALING $17.7 MILLION –Coastal Medical Group, 2012	

Source: HIMSS.org[1]

FIGURE 2 Use of EHRs by doctors in 8 countries



Source: Accenture[3]

TABLE Examples of hospitals' use of clinical teams for EHR development

Gundersen Lutheran	The hospital gradually put together a 50-person clinical team, primarily comprised of nurses with a few physicians, focused on information services. The team focused on ensuring that the EHR was built with patient care as its top priority. They also helped train other staff in use of the new system.
Metro Health	A "core epic" team of about 100 employees was established and met regularly for 18 months; it included nurses, physicians, and staff from throughout the hospital system who focused on workflow.
Carilion	The parent health system used a 3-level implementation team: • executive team with direct oversight of the project that included hospital COOs, CMOs, CNOs, CEO of ambulatory care, and others; • steering committee that developed policies and procedures; and • operating team comprised of frontline staff who incorporated the new system into daily processes in the hospitals and other sites.
Sentara	The parent health system brought in 185 people (many of them floor nurses) from across the integrated system, trained them on the new EHR system, and then sent them back to teach others. These "super users" are embedded throughout the organization and are called on whenever there is a need to tweak or modify the system.
NewYork–Presbyterian	The hospital used clinical specialists to break up the EHR's note template into structured fields so that information can be extracted for meaningful use data reporting. It also has a house staff quality council with an IT subcommittee that meets monthly and discusses issues such as improving hand-off communication using a custom EHR feature, developing an electronic checklist to track safety and regulatory requirements, and working to prevent alert fatigue.
Geisinger	The parent health system selected the "best and brightest" in the organization to implement the EHR. Inpatient implementation involved a physician optimization team, a nursing "super user" team, and an inpatient EHR project IT team for analysis, system development, and issue tracking and management.
Yale–New Haven	The system buys physicians' time away from practice so as not to penalize them for being involved in customizing the EHR; before the rollout of the new EHR, scores of physicians worked on customization every Tuesday morning.

Source: The Commonwealth Fund[4]

some hospitals use their clinical teams.[4] After Gundersen Lutheran Hospital implemented an EHR, for example, medication errors per 1000 hospital days decreased from 17.9 to 15.4, and the percentage of medication-related injuries decreased from 66.5% to 55.2%.[5]

It appears that more physicians are using electronic resources and that CMS is paying more and more physicians. At the same time, however, because of the inability to adhere to strict requirements of EHR meaningful use, some physicians have stopped accepting Medicare & Medicaid Services. In fact, the large upswing in EHR adoption may be due to hospital-associated adoption. According to the CMS nearly 10,000 physicians who had previously accepted Medicare opted out of the program in 2012, up from just over 3500 in 2009 (out of the 685,000 physicians enrolled last year).[6]

A recent Reuters article recounts the story of a patient-advocate who helped transition a family member from a hospital to a rehabilitation facility.[7] During that transfer of care, the patient-advocate noted that the electronic chart that was printed at the hospital had to be retyped into the proprietary system at the rehabilitation facility. During this "repopulation" of the EHR, the patient's hypothyroidism was mistakenly recorded as hyperthyroidism. The patient could have been prescribed the wrong medication, with disastrous results. The record error led the patient's family to question the quality of care the patient was receiving.

Unfortunately, this anecdote is not unique. Although EHRs can catch dangerous medication interactions and physician errors, they are fallible computer programs.

Like paper charts, the information entered EHRs is subject to human error. With an EHR, however, the mistakes may be easier to track. COG

REFERENCES

1. The HIMSS health IT value suite. http://www.himss.org/ValueSuite. Accessed August 19, 2013.

2. Sullivan T. EHR incentives surge to $13.7B. May 8, 2013. http://www.healthcareitnews.com/news/ehr-incentive-payments-surge-137b. Accessed August 19, 2013.

3. EMR and HIE use increases among U.S. doctors, Accenture annual survey finds. May 9, 2013. http://newsroom.accenture.com/news/emr-and-hie-use-increases-among-us-doctors-accenture-annual-survey-finds.htm. Accessed August 19, 2013.

4. Silow-Carroll S, Edwards JN, Rodin D. *Using Electronic Health Records to Improve Quality and Efficiency: The Experiences of Leading Hospitals*. New York: The Commonwealth Fund, July 2012. http://www.commonwealthfund.org/Publications/Issue-Briefs/2012/Jul/Using-EHRs-to-Improve-Quality-and-Efficiency.aspx. Accessed August 19, 2013.

5. Zlabek, JA, Wickus, JW, Mathiason, MA. Early cost and safety benefits of an inpatient electronic health record. *J Am Med Inform Assn*. 2011;18(2):169–172.

6. CMS.gov. Research, statistics, data & systems. http://www.cms.gov/Research-Statistics-Data-and-Systems/Research-Statistics-Data-and-Systems.html. Accessed August 19, 2013.

7. Pinsker B. Your Money: Electronic health records still require manual labor. August 12, 2013. http://www.reuters.com/article/2013/08/12/healthcare-costs-electronicrecords-perso-idUSL1N0GA0SE20130812. Accessed August 19, 2013.

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CALENDAR

2013 SEPTEMBER

18-21: American Gynecological and Obstetrical Society Annual Meeting
Chicago, Illinois
www.agosonline.org/meetings.html

19-21: Reproductive Health 2013 Association of Reproductive Health Professionals (ARHP)
Denver, Colorado
www.arhp.org/RH13

19-21: 3rd Annual Meeting of the Society of OB/GYN Hospitalists
Denver, Colorado
http://societyofobgynhospitalists.com

OCTOBER

2-4: International Society for the Study of Vulvovaginal Disease International Postgraduate Course
Tel Aviv, Israel
www.issvd.org/wordpress

2-6: Pacific Coast Obstetrical and Gynecological Society 80th Annual Meeting
Walla Walla, Washington
www.pcogs.org/meetings.cfm

4-6: Women's and Pediatric Dermatology Seminar
Newport Beach, CA
www.globalacademycme.com/conferences/women-s-and-pediatric-dermatology-seminar-2013/conference-overview.html

9-12: 24th Annual Meeting of the North American Menopause Society
Dallas, Texas
www.menopause.org/annual-meetings/2013-meeting/general-information

12-17: 69th Annual Meeting of the American Society for Reproductive Medicine/International Federation of Fertility Societies (ASRM/IFFS)
Boston, Massachusetts
www.asrm.org/IFFS-ASRM2013

NOVEMBER

6-8: Perinatal Mental Health: Optimizing Maternal Treatment to Improve Infant Outcomes Conference
Chicago, Illinois
http://perinatalmentalhealthmeeting.com/

10-14: 42nd American Association of Gynecologic Laparoscopists Global Congress of Minimally Invasive Gynecology
National Harbor, Maryland
www.aagl.com/annual-meeting

14-15: OB/GYN Clinical Reviews
Rochester, Minnesota
www.mayo.edu/cme/women-s-health-2013r040

2014 FEBRUARY

3-8: Society for Maternal-Fetal Medicine 34th Annual Meeting
New Orleans, Louisiana
www.smfm.org/Annual%20Meeting%20Page.cfm?ht=me

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