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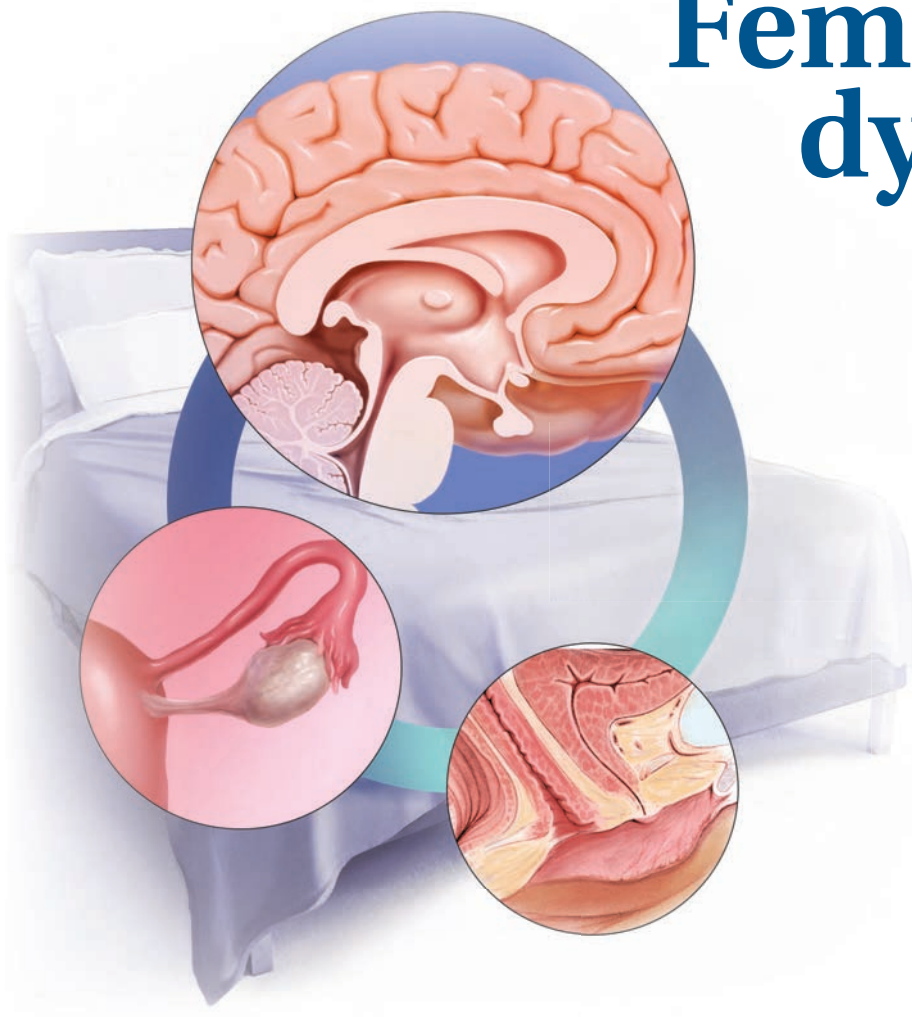
Combination estrogen-progestin contraceptives and cancer risk
Robert L. Barbieri, MD

Surgical catastrophe: Offer a lifeline to the second victim

Oxytocin plus Foley catheter for induction of labor?



Female sexual dysfunction

Understanding pathogenesis defines treatment

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Does HPV testing lead to improved cervical dysplasia diagnosis?

Telehealth and you
ACOG's Lucia DiVenere with Haywood Brown and Peter Nielson

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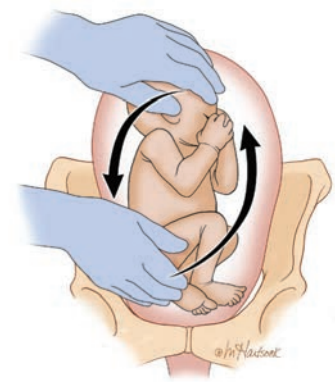

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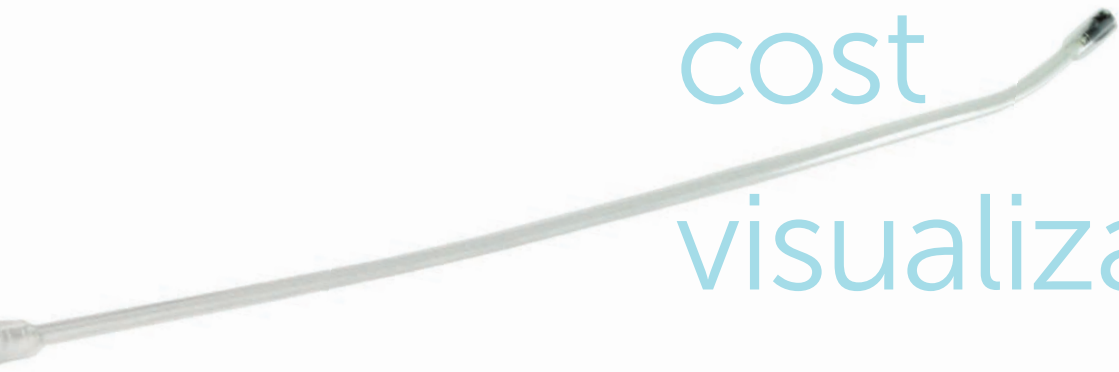

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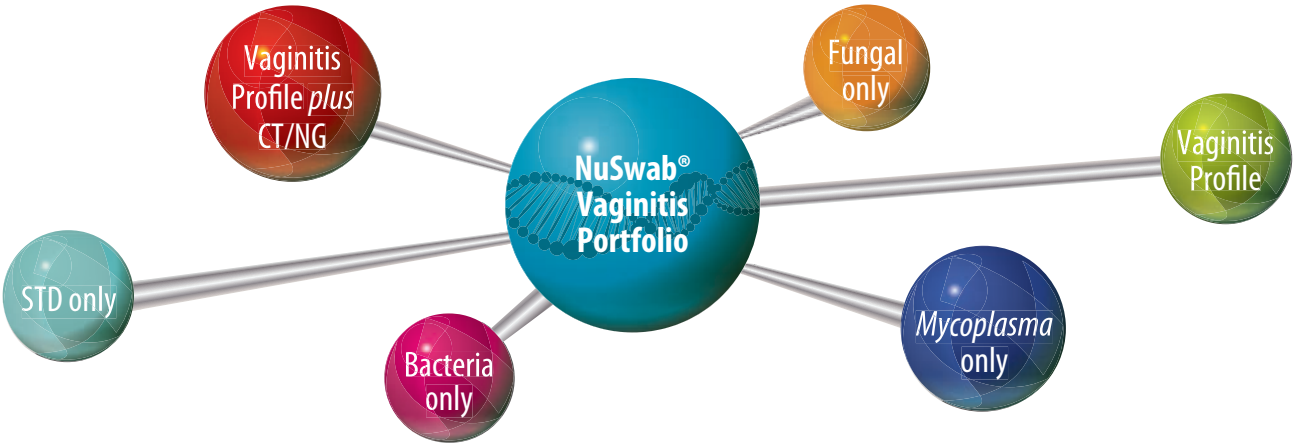

Everything **she** needs

with the services **you** expect.

Vaginitis accounts for approximately 10 million office visits each year.[1] Most women will experience vaginitis symptoms.[2] Recurrence is common.[3] This condition commands a great deal of your daily patient care time. You need a test with diagnostic accuracy to help treat patients properly on the first visit and help reduce recurrence.

Tests **She** Needs - Bacterial

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The NuSwab C *albicans* and C *glabrata* test:

- targets the 2 most common *Candida* species
- helps guide treatment – C *glabrata* is often resistant to fluconazole[5]
- six species test options and add-on testing of 4 additional *Candida* species in refractory or recurrent cases

Tests **She** Needs - Parasitic

The NuSwab *Trichomonas vaginalis* (Tv) test:

- is 100% sensitive and 99% specific for Tv diagnosis[6]
- shown to be more sensitive than culture, microscopy, and Affirm™ VPIII[7]
- can be used as a follow-up test to confirm negative wet mounts[8]

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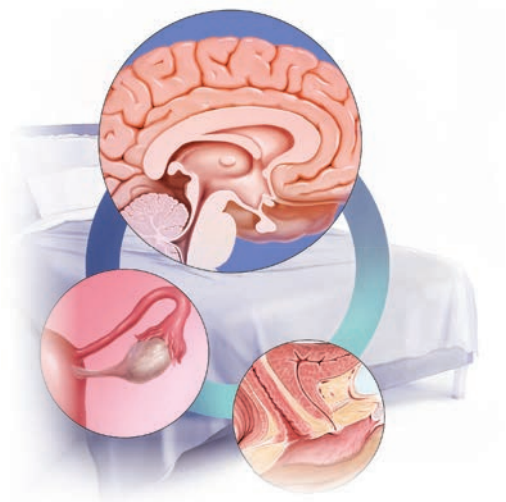

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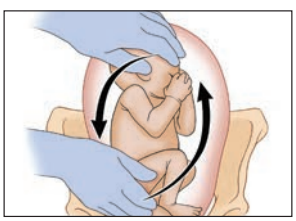

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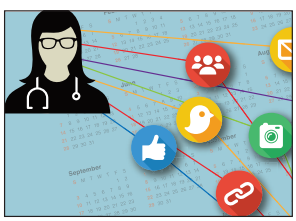

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FAST TRACK is a system to enable you as a reader to move quickly through each issue of **OBG MANAGEMENT**, identifying articles or sections of articles to read in depth.

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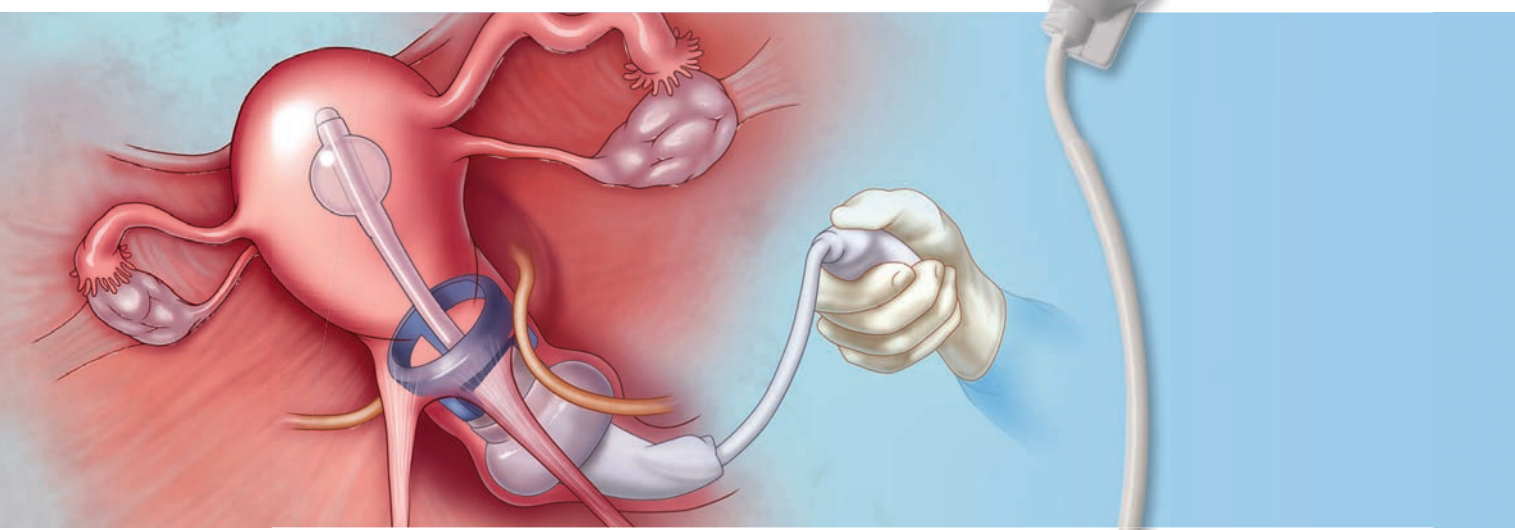

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FROM ENDOMETRIOSIS JOURNEY

Diagnosis and therapy

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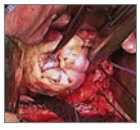

Vaginal salpingo-oophorectomy: Tips and tricks

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Are combination estrogen-progestin oral contraceptives associated with an increased risk of cancer?

Combination estrogen-progestin oral contraceptive (COC) use is associated with a decreased risk of ovarian and endometrial cancer, and the risk reduction persists after discontinuing the COC. In some studies, current use of COCs is associated with a small increased risk of breast cancer. Prolonged COC use is associated with an increased risk of cervical cancer, but confounding factors, including sexual exposures, may account for the association. Following discontinuation of oral contraceptives the increased risk for breast and cervical cancer diminishes.

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

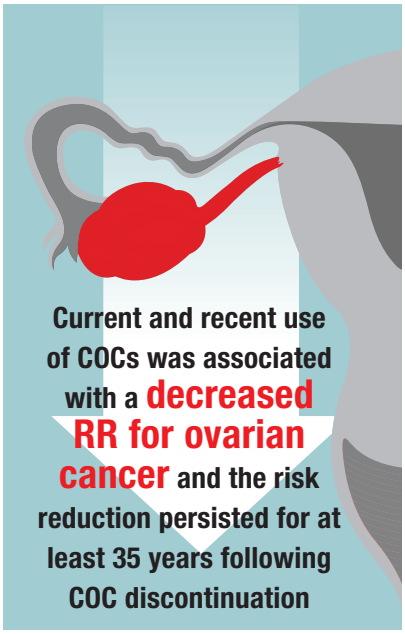
There are no large randomized clinical trials exploring the relationship between COCs and the risk of developing cancer. Many epidemiological studies, however, have investigated the possible association between COC use and the risk of cancer. Such prospective and retrospective studies consistently report that the use of COCs significantly decreases the risk of ovarian and endometrial cancer. The epidemiological data are less consistent concerning the possible association between COC use and the risk of breast cancer. Meta-analyses conclude that current use of COCs may be associated with a small increase in breast cancer risk. In addition, prolonged use of COCs may be associated with an increased risk of cervical cancer.

Ovarian cancer

COC use is associated with reduced risk of ovarian cancer, and the risk reduction persists after discontinuing COC use. In an individual data meta-analysis of 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 women without it, COC use was associated with a relative risk (RR) of 0.73 for ovarian cancer. The magnitude of risk reduction increased with increasing duration of COC use. The RR and 99% confidence interval (CI) for ovarian cancer and mean duration of use was[1]:

- 0.78 (0.73–0.83) for 2.4 years
- 0.64 (0.59–0.69) for 6.8 years
- 0.56 (0.50–0.62) for 11.6 years
- 0.42 (0.36–0.49) for 18.3 years.

In the Royal College of General Practitioners Oral Contraceptive (RCGPOC) study, about 23,000 women who did not use COCs and 23,000 current users of COCs were



CONTINUED ON PAGE 13

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

Typical oral iron dose*

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

*Not intended to represent all possible oral iron regimens.

Typical oral iron absorption

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

INDICATIONS

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

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

Up to 750 mg in a single dose‖¶

+

Up to 750 mg in a single dose‖¶

=

Total cumulative dose **up to 1500 mg** per course

At least 7 days apart

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

injectafer®
ferric carboxymaltose injection

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

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

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

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

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

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

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

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

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

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

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

Daiichi-Sankyo

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

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

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

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

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

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

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

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

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

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

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

CONTRAINDICATIONS: Hypersensitivity to Injectafer or any of its components.

WARNINGS AND PRECAUTIONS

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C.

Risk Summary

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

Animal Data

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

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

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

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

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

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

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

$[FeO_x(OH)_y(H_2O)_z]_n\ [\{(C_6H_{10}O_5)_m\ (C_6H_{12}O7)\}_l]_k$,

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

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

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

Vial closure is not made with natural rubber latex.

CLINICAL PHARMACOLOGY

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

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

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

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

NONCLINICAL TOXICOLOGY

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

PATIENT COUNSELING INFORMATION

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

Daiichi-Sankyo

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

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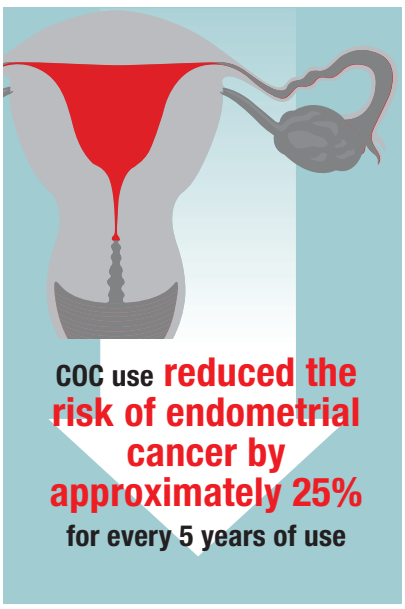
recruited around 1968 and followed for a median of 41 years. In this study, current and recent use of COCs was associated with a decreased RR for ovarian cancer (0.49) and the risk reduction persisted for at least 35 years following COC discontinuation (RR, 0.50; 99% CI, 0.29–0.84).[2]

In the prospective Nurses' Health Study (NHS) I, 121,700 nurses were recruited in 1976 and followed for more than 30 years.[3] For nurses who reported using COCs for more than 5 years, the rate ratio for ovarian cancer at 20 years or less and greater than 20 years since last use was 0.58 (95% CI, 0.61–0.87) and 0.92 (95% CI, 0.61–1.39), respectively. These studies show that the association between COC use and a decreased risk of ovarian cancer persists for many years after discontinuing COCs.

Endometrial cancer

COC use is associated with decreased risk of endometrial cancer, and the risk reduction persists for many years after discontinuing COC use. In an individual data meta-analysis of 36 studies that included 27,276 women with endometrial cancer and 115,743 women without it, COC use reduced the risk of endometrial cancer by approximately 25% for every 5 years of use. With 10 years of COC use the absolute risk of endometrial cancer before age 75 was 2.3 and 1.3 per 1,000 women for never and ever users of COC. Risk reduction varied slightly by histopathology, with risk reduction being greatest for type I endometrial cancer (RR, 0.68), slightly less for type II endometrial cancer (RR, 0.75), and lowest for endometrial sarcoma (RR, 0.83).[4]

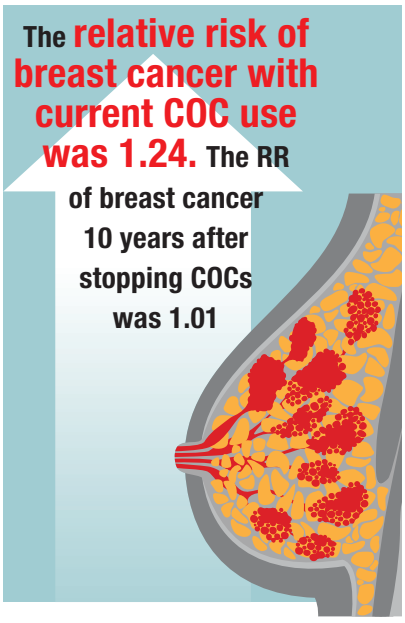


In the RCGPOC study of 46,000 women, the RR of endometrial cancer among current and recent users of COCs was 0.61, and the reduced risk (0.83) persisted for more than 35 years after discontinuing the COC.[2]

It is thought that the progestin in the COC provides most of the beneficial effect. Progestin-only contraceptives, such as depotmedroxyprogesterone acetate, progestin implants, and levonorgestrel-releasing intrauterine devices (LNG-IUDs) are also thought to reduce endometrial cancer risk. For instance, in a study of 93,842 Finnish women who used the LNG-IUD, the standardized incidence ratio for endometrial cancer was 0.50 among LNG-IUD users compared with the general population.[5]

Breast cancer

The relationship between COC use and breast cancer is controversial. However, **most oncologists believe that current use of COCs may be associated with a small increase in the risk of breast cancer diagnosis. The risk is attenuated after discontinuing COC use.** In an individual data meta-analysis of 54 epidemiological studies including 53,297 women with breast cancer and 100,239 without it, the RR of breast cancer with current COC use was 1.24 (95% CI, 1.15–1.33; *P*<.0001). The RR of breast cancer 10 years after stopping COCs was 1.01 (95% CI, 0.96–1.05; NS).[6]



In the prospective NHS study of 116,608 nurses with 1,246,967 years of follow-up, the multivariate relative risk (mRR) of breast cancer with current COC use was 1.33 (95% CI, 1.03–1.73). Past use of COCs was not associated with a significantly increased risk of breast cancer (mRR, 1.12; 95% CI, 0.95–1.33; NS).[7]

In the RCGPOC study (approximately 46,000 women), current use of COCs was associated with an increased risk of breast cancer (incidence rate ratio [IRR], 1.48; 95% CI, 1.10–1.97). Five to 15 years after stopping COCs, there was no significant association between prior COC use and breast cancer (IRR, 1.12; 99% CI, 0.91–1.39; NS).[2]

It is important to note that it is not possible to conclude from these data whether the reported association between current use of COCs

and breast cancer is due to early and accelerated diagnosis of breast cancer, the biological effects of hormones contained in COCs on breast tissue and nascent tumors, or both. In addition, formulations of COCs prescribed in the 1960s and 1970s contained higher doses of estrogen, raising the possibility that the association between COCs and breast cancer is due to COC formulations that are no longer prescribed. However, in animal models and postmenopausal women certain combinations of estrogen plus progestin clearly influence breast cancer biology and cancer risk.[8,9]

Cervical cancer

Prolonged COC use is associated with an increased risk of cervical cancer. The risk is no longer observed 10 years after stopping COC use. In an individual data meta-analysis of 24 epidemiological studies including 16,573 women with cervical cancer and 35,509 women without it, the relative risk of cervical cancer with less than 5 years or 5 or more years of COC use was 1.09 and 1.90, respectively. Analyses of potential confounding exposures, including age at first sexual intercourse, condom use, cigarette smoking, and number of sexual partners, did not significantly weaken the observed association between cervical cancer and COC use of 5 or more years.[10] In a study of women who were positive for HPV DNA, the odds ratio for cervical cancer among women who had used COCs[11]:

- less than 5 years, 0.73 (95% CI, 0.52–1.03)
- 5 to 9 years, 2.82 (95% CI, 1.46–5.42)
- ≥10 years, 4.03 (95% CI, 2.09–8.02).

It is not possible to conclude from these data whether the association between COC use and cervical cancer is due to the biological effects of hormones on the initiation and progression of HPV disease or confounding factors that have yet to be identified. It is known that estrogens and progestins influence the immune defense system of the lower genital tract, and this may be a pathway that influences the acquisition and progression of viral disease.[12] From a clinical perspective, cervical cancer is largely preventable with HPV vaccination and screening. Therefore, the risk between COC use and cervical cancer is likely limited to women who have not been

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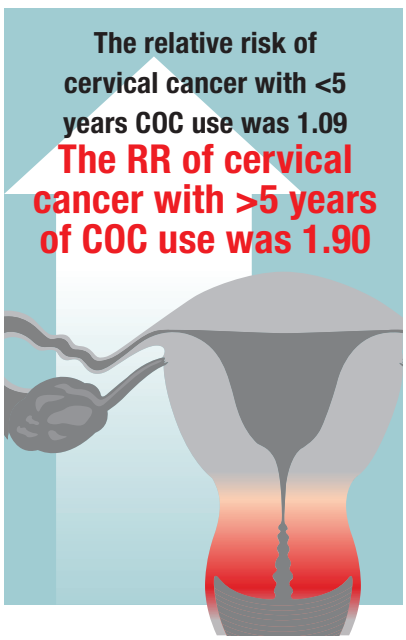

COC use among *BRCA1* and *BRCA2* carriers

Women carrying *BRCA1* and *BRCA2* mutations, which increase the risk of ovarian and breast cancer, are often counseled to consider bilateral salpingectomy between age 35 and 40 years to reduce the risk of developing ovarian cancer. An important clinical question is what is the impact of combination estrogen-progestin oral contraceptives (COC) use on ovarian and breast cancer risk among these women?

Meta-analyses of the association between COC use and ovarian cancer consistently report that COC use reduces the risk of ovarian cancer in women with clinically important *BRCA1* and *BRCA2* mutations.[1,2] For example, a meta-analysis of 6 studies reported that women with *BRCA1* and *BRCA2* mutations who used COCs had a significantly decreased risk of ovarian cancer (odds ratio [OR], 0.58; 95% CI, 0.46–0.73).[1]

The association between COC use and breast cancer risk is not clear. One meta-analysis reported no significant association between COC use and breast cancer risk among *BRCA* mutation carriers (OR, 1.21; 95% CI, 0.93–1.58).[1] Another meta-analysis reported a significant association between COC use before 1975 and breast cancer risk (RR, 1.47; 95% CI, 1.06–2.04) but not with recent low-estrogen formulations of COC (RR, 1.17; 95% CI, 0.74–1.86).[2]

Based on the available data, the Society of Gynecologic Oncologists recommends that women with clinically significant *BRCA1* and *BRCA2* mutations be offered chemoprevention with COCs because the benefit of ovarian cancer risk reduction outweighs the possible impact on breast cancer risk.[3] A contrarian viewpoint espoused by some oncologists is that since women with *BRCA* mutations should have their ovaries removed prior to getting ovarian cancer, the clinical utility of recommending COC chemoprevention of ovarian cancer is largely irrelevant.

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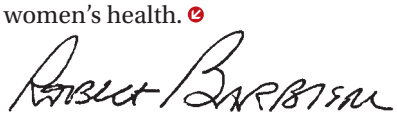
vaccinated and who are not actively participating in cervical cancer screening.

The bottom line

COC use markedly reduces the risk of ovarian and endometrial cancers, and slightly increases the risk of breast cancer. Prolonged COC use may be associated with an increased risk of cervical cancer. Using available epidemiological data, investigators attempted to project the impact of these competing risks on the approximate 12,300,000 females who live in Australia. Based on the pattern of COC use and the cancer incidence in Australia in 2010, the investigators calculated that COC use would cause about 105 breast and 52 cervical cancers and prevent 1,032 endometrial and 308 ovarian cancers.[13] This analysis indicates that the balance of risks and benefits related to COC use and cancer generally favors COC use.

Prevention of unintended pregnancy is a major public health goal. Many women choose COCs as their preferred approach to preventing unintended pregnancy. Evaluated from a whole-life perspective the health benefits of COCs are substantial and represent a great advance in women's health.



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

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"THE PELVIC EXAM REVISITED"
ERIN HIGGINS, MD, AND
CHERYL B. IGLESIA, MD (AUGUST 2017)

Pelvic examination is essential to clinical care

I have contemplated the issue of the routine screening pelvic exam now for several years. But for the last year, I have found various problems in many "asymptomatic women." For example: The 18-year-old who was "not sexually active" but who had *Chlamydia*. Or the 84-year-old who denied itching or other vulvovaginal symptoms who had either vulvar cancer or lichen sclerosis so severe her vagina was almost closed; a 30-minute review of her outside records revealed recurrent urinary tract infections requiring more than 5 courses of antibiotics in 6 months for what was actually contaminants from a urine specimen that passed through the vagina first. I think the move away from actually touching patients has completely gotten out of hand! It is appalling how many women I have seen who visited an emergency department for pelvic or abdominal pain and never had a hands-on examination. If we do not examine the part of the body that many completely ignore we may as well lose our specialty!

Christine Kneer-Aronoff, MD
Cincinnati, Ohio

"EFFECTIVE TREATMENT OF RECURRENT BACTERIAL VAGINOSIS"
ROBERT L. BARBIERI, MD
(EDITORIAL; JULY 2017)

Appreciates treatment options for recurrent BV

I thank Dr. Barbieri for his editorial on effective treatment of recurrent bacterial vaginosis (BV). I practice only outpatient gynecology, and recurrent

AUGUST 2017

BV is the most frustrating condition I have to deal with. Now I have 3 treatment options in my armamentarium for taking care of patients. I clipped the article pages from OBG MANAGEMENT and am keeping them available for easy access when needed.

I have a related question: I see trichomonal vaginitis rarely, maybe 1 to 2 cases in a year. What do you think the reason is?

Vimal Goyle, MD
New York, New York

Beyond BV: Candidiasis and diabetes medications

Thank you for addressing the recurrent BV problem. After many years of throwing antibiotics at this problem I have been underwhelmed. Patients do not want to keep chasing their tails between BV and yeast. I have been suggesting that patients place plain yogurt containing *Lactobacillus* in a tampon applicator and apply it to the vagina weekly at night, after the original "overgrowth" has been treated, to return the "good bacteria" to the vagina. This avoids overuse of antibiotics (an impending epidemic of resistant organisms), boric acid (a dangerous pill to have around toddlers), and the expense that comes with multiple visits and multiple courses of antibiotics. I believe that in Canada a vaginal ovule with vitamin C and probiotics is available (something to ponder).

Another problem is recurrent yeast infections. We are seeing that many new diabetes medications are increasing the clearance of glucose and are causing severe and intractable *Candida* vulvovaginitis. In addition, I would like to know the best topical treatments and skin care for yeast in the folds of the panniculus in the morbidly obese. Unfortunately, these patients often have poor or no insurance and therefore cannot afford the cost of many effective remedies.

John Lewis, MD
Bedford, Massachusetts

Another treatment protocol for BV

For recurrent BV, I treat with standard metronidazole 500 mg orally twice daily for 7 days, then immediately start boric acid suppositories for 3 days in a row followed by 1 weekly for 6 weeks, and that usually takes care of it. However, a few caveats: I instruct patients to keep a supply of boric acid suppositories on hand, and if they start to experience symptoms again, to repeat the 3-day, then weekly-for-6 weeks regimen, so essentially they can manage a recurrence themselves.

For patients who come in thinking they have a recurrent yeast infection or BV, which was initially treated elsewhere, I culture for *Mycoplasma* and *Ureaplasma*. I often find that one of those organisms is responsible for the infection, requiring completely different treatment.

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I also frequently check the vaginal pH, because patients like to see a visual on what I am talking about.

Rebecca Levy-Gantt, DO
Napa, California

Clindamycin appears superior for BV recurrence prevention

In my practice for the past number of years I have been treating BV with clindamycin vaginal cream instead of metronidazole. I have found that the number of women returning with recurrent BV has dropped dramatically. Furthermore, since switching medications, I cannot recall the last time someone required a maintenance dosing regimen. Although anecdotal, the difference between metronidazole and clindamycin treatment seems striking to me.

Daniel N. Sacks, MD
West Palm Beach, Florida

Uses BV regimens in stepwise fashion

To answer Dr. Barbieri's instant poll question, my preference for treating BV is to start off with Regimen 1 (metronidazole treatment followed by twice weekly vaginal metronidazole for 6 months), as described in his editorial. If problem reports resolve but recur at a later date, then I use Regimen 2 (metronidazole treatment plus 21 days of boric acid vaginal capsules followed by twice weekly vaginal metronidazole for 6 months). I am aware of Regimen 3 (single-dose oral metronidazole plus fluconazole followed by once-monthly metronidazole and fluconazole) but rarely use it.

Carole W. Campbell, DNP, CNM
Gadsden, Alabama

›› Dr. Barbieri responds

The readers of OBG Managment *are exceptional clinicians, and I appreciate the sharing of their insights in treating BV with our readers. Dr. Goyle reports that she commonly sees cases of BV but seldom sees cases of trichomoniasis. Two potential explanations for her observation are that her population of women has a low prevalence of trichomoniasis and/or that by using microscopy she is not detecting all the cases of trichomoniasis in her practice. In a recent large US study of women presenting with vaginitis, nucleic acid testing was used to identify the cause of the vaginitis.[1] The most common diagnoses were the following: 36%, bacterial vaginosis only; 24%, no detectable infection; 16%, candidiasis only; 14%, BV and candidiasis; 5%, BV and trichomoniasis; 4%, candidiasis and trichomoniasis; 1.5%, trichomoniasis only; and 0.7%,* Candida glabrata *only.[1] The most sensitive test for trichomoniasis is a nucleic acid test. Microscopy has low sensitivity for the detection of trichomoniasis.*

I agree with Dr. Lewis that for women with BV, lactobacilli and lactic acid treatment have an important role in establishing optimal vaginal flora that is resistant to recurrent infections. Dr. Lewis highlights the link between diabetes, some diabetes medications, and candidiasis. To treat Candida *in the folds of the panniculus, one option is multimodal topical therapy with compounded 2% ketoconazole, 2.5% hydrocortisone, and 1% iodoquinol in a cream base.*

Dr. Levy-Gantt offers a 4th option for treatment of chronic BV—initial metronidazole therapy followed by daily and then weekly use of boric acid vaginal suppositories.

Dr. Sacks reports that in his practice, clindamycin vaginal cream is significantly more effective than metronidazole for the treatment of BV. Most randomized studies comparing these 2 regimens reported no difference in efficacy.[2] Dr. Sacks may have uncovered a previously unreported resistance of organisms to metronidazole.

Dr. Campbell reports that Regimen 1 (metronidazole treatment followed by twice weekly vaginal metronidazole for 6 months) and Regimen 2 (metronidazole treatment plus 21 days of boric acid vaginal capsules followed by twice weekly vaginal metronidazole for 6 months) usually are effective in controlling recurrent BV. Our readers deeply appreciate the help of the clinicians who share their insights and clinical pearls.

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2. Oduyebo OO, Anorlu RI, Ogunsola FL. The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women. Cochrane Database Syst Rev. 2009;(3):CD006055.

"CARING FOR THE TRANSGENDER PATIENT: THE ROLE OF THE GYNECOLOGIST"
CECILE A. UNGER, MD, MPH (JUNE 2017)

Calls for respect for transgender patients

We must keep in mind that transgender males are still sexually anatomically female, with all of the medical needs of any other female. Transgender is merely a social construct. We must treat them with kindness and respect.

Laurence Burns, DO
Grand Rapids, Michigan

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Does HPV testing lead to improved diagnosis of cervical dysplasia for patients with ASC-US cytology?

Yes, according to an analysis from the New Mexico HPV Pap Registry that looked at long-term outcomes of atypical squamous cells of undetermined significance (ASC-US) cytology with and without human papillomavirus (HPV) testing. The investigators found **increased early detection rates of cervical intraepithelial neoplasia** (CIN) but an **increased risk of additional cervical biopsies and excisional procedures**.

Cuzick J, Myers O, Lee JH, et al; New Mexico HPV Pap Registry Steering Committee. Outcomes in women with cytology showing atypical squamous cells of undetermined significance with vs without human papillomavirus testing [published online ahead of print June 22, 2017]. JAMA Oncol. doi:10.1001/jamaoncol.2017.1040.

EXPERT COMMENTARY

›› **Sarah Dilley, MD, MPH,** is a Gynecologic Oncology Fellow, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Alabama at Birmingham.

›› **Warner K. Huh, MD,** is Professor and Division Director, Division of Gynecologic Oncology, Margaret Cameron Spain Endowed Chair in Obstetrics and Gynecology, Department of Obstetrics and Gynecology, University of Alabama at Birmingham.

The American Society for Colposcopy and Cervical Pathology (ASCCP) has recommended HPV triage for ASC-US cytology for more than 15 years. Since the ALTS trial demonstrated improved detection of CIN2+ in women with ASC-US cytology, HPV testing has become the preferred triage strategy for women with ASC-US cytology, except for women under age 25.[1] However, we do not know the long-term outcomes for these women. The study by Cuzick and colleagues uniquely addresses this question.

The authors report no financial relationships relevant to this article.

Details of the study

The retrospective review of data from the New Mexico HPV Pap Registry examined the influence of HPV testing on outcomes in 20,677 women with ASC-US cytology between 2008 and 2012. Of those women, 80.5% had an HPV test, and the authors estimated that 80.6% of those HPV tests were for triage after ASC-US cytology as opposed to co-testing (that is, cytology and HPV testing together). Of note, the majority of these Pap tests were performed prior to the 2012 ASCCP guidelines that recommend HPV co-testing for all women aged 30 to 64 years regardless of cytology. Of the HPV tests performed, 43.1% were positive. The investigators then examined rates of CIN in the interval between ASC-US cytology and biopsy-confirmed CIN, and rates of loop electrosurgical excision procedures (LEEP) and results at 5 years.

FAST TRACK

To assess long-term outcomes of women with ASC-US cytology and HPV triage, researchers examined the interval between ASC-US cytology and biopsy-confirmed CIN, LEEP rates, and results at 5 years

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FAST TRACK

HPV testing in women with ASC-US cytology leads to earlier detection of high-grade disease, but HPV positivity results in more interventions, largely due to overdiagnosis of CIN1

The investigators found a non–statistically significant increase in overall detection of CIN3 (relative risk [RR], 1.16; 95% confidence interval [CI], 0.92–1.45) in women who had been triaged with HPV testing, and a significant increase in overall detection of CIN2 (RR, 1.27; 95% CI, 1.06–1.53) and CIN1 (RR, 1.76; 95% CI, 1.56–2.00). CIN1, CIN2, and CIN3 were detected significantly earlier in patients with HPV testing. As expected, the majority of CIN2 and CIN3 was diagnosed in women who were HPV positive.

The proportion of women undergoing either endocervical curettage or cervical biopsy was higher in those with HPV testing (32.1% vs 20.6%, $P<.001$), as were LEEP rates (4.9% vs 4.0%, $P = .03$). LEEP rates were highest in the year after a positive HPV test and were mostly attributable to CIN1 results. However, the overall ratio of LEEP to CIN3+ diagnosis was similar in women who were tested for HPV compared with those who were not. A larger proportion of patients with HPV testing had follow-up compared with those without HPV testing (84.1% vs 78.9%, $P<.001$).

The authors concluded that HPV testing in women with ASC-US cytology leads to detecting high-grade disease earlier, but that HPV positivity results in more interventions, largely due to an overdiagnosis of CIN1. They also confirmed that the majority of high-grade lesions are found in women with positive HPV tests.

Study strengths and weaknesses

This is the first comprehensive long-term look at women with ASC-US cytology and the impact of HPV testing. The New Mexico HPV Pap Registry is the only US state-based registry with comprehensive follow-up data. This study's results build on previous data that showed sensitivity is increased with the addition of HPV testing to cervical cytology,[1] and they support current ASCCP guidelines that emphasize HPV triage or co-testing for women age 25 or older.

Potential bias. While this study has the benefit of a large cohort, it is limited by biases inherent in retrospective study design. One important potential bias is the differential utilization of HPV testing or procedures by providers. The authors acknowledge preliminary analyses that show that some clinics (rural, federally qualified health centers, public health clinics) serving underserved populations may underutilize or inappropriately utilize HPV testing.

Further, the 2008–2012 study period may make the results less generalizable to current practices since the ASCCP guidelines were adjusted to include more HPV testing in women aged 25 and older in 2012.

Finally, this study examines CIN but does not specifically look at the impact of HPV testing on the ultimate outcome of interest, cervical cancer rates.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

The data from the study by Cuzick and colleagues support the importance of continued screening for cervical cancer and its precursors with HPV testing. However, the results also show that we need to improve our strategies for stratifying patients who actually need colposcopy. The authors assert an "enormous predictive value of HPV testing," but this comes at the expense of many unnecessary procedures. Clinicians should continue to use cytology with HPV triage in women aged 25 years and older, but the ASCCP should reconsider guidelines to improve screening specificity. The addition of other screening modalities, such as extended genotyping, methylation testing, and p16/Ki-67 staining, are considerations for ASC-US triage.

›› SARAH DILLEY, MD, MPH, AND WARNER K. HUH, MD

Reference

1. ASCUS-LSIL Triage Study (ALTS) Group. Results of a randomized trial on the management of cytology interpretations of atypical squamous cells of undetermined significance. Am J Obstet Gynecol. 2003;188(6):1383–1392.

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Surgical catastrophe: Offering a lifeline to the second victim

Jose Antonio Carugno, MD, and Fausto Andrade, MD

When an adverse medical event occurs, clinicians need emotional first aid, peer support, and positive coping strategies

IN THIS ARTICLE

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page 24

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CASE A surgeon's story of patient loss

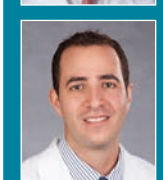
It was a Wednesday morning and Ms. M was my first case of the day. I knew her well, having delivered her 2 children. Now she had a 7-cm complex cyst on her right ovary, she was in pain, and she was possibly experiencing ovarian torsion. My resident took care of the paperwork, I met the patient in preop, answered her few questions, and reassured her husband that I would call him as soon as surgery was over. She was rolled to the operating room.

When I entered the OR, Ms. M was under general anesthesia, draped, and placed on the operating table in the usual position. I made a 5-mm incision at the umbilicus and inserted the trocar under direct visualization. There was blood and the camera became blurry. I removed the camera to clean it, and the anesthesiologist alerted me that there was sudden hypotension. I reinserted the camera and saw blood in the abdomen. I feared the worst—major vessel injury. I requested a scalpel and made a midline skin sub–umbilical incision, entered the peritoneal cavity, and observed blood everywhere. The massive transfusion protocol was activated and vascular surgery was called in. I could not find the source of the bleeding. Using a laparotomy towel I applied pressure on the aorta. The vascular surgeon arrived and pushed my resident away. He identified the source of the bleeding: The right common iliac artery was injured.

The patient coded, the anesthesiologist initiated CPR, bleeding continued, blood was being transfused, and after 20 long minutes of CPR the lifeless body of my patient could not hold any more. She was pronounced dead on the table.

At that moment, there were multiple victims: Ms. M lying on the surgical table; her family members, who did not know what was happening; and the surgical team members, who were looking at each other in denial and feeling that we had failed this patient, hoping that we would wake up from this nightmare.

Dr. Carugno is Assistant Professor of Obstetrics and Gynecology, Gynecologic Minimally Invasive Surgery and Robotics Unit Director, University of Miami Miller School of Medicine, Miami, Florida.



Dr. Andrade is Assistant Professor of Obstetrics and Gynecology, Gynecologic Minimally Invasive Surgery and Robotics Unit Associate Director, University of Miami Miller School of Medicine.

The authors report no financial relationships relevant to this article.

Defining patient harm

Many patients experience harm each year because of an adverse medical event or preventable medical error.[1] A 2013 report

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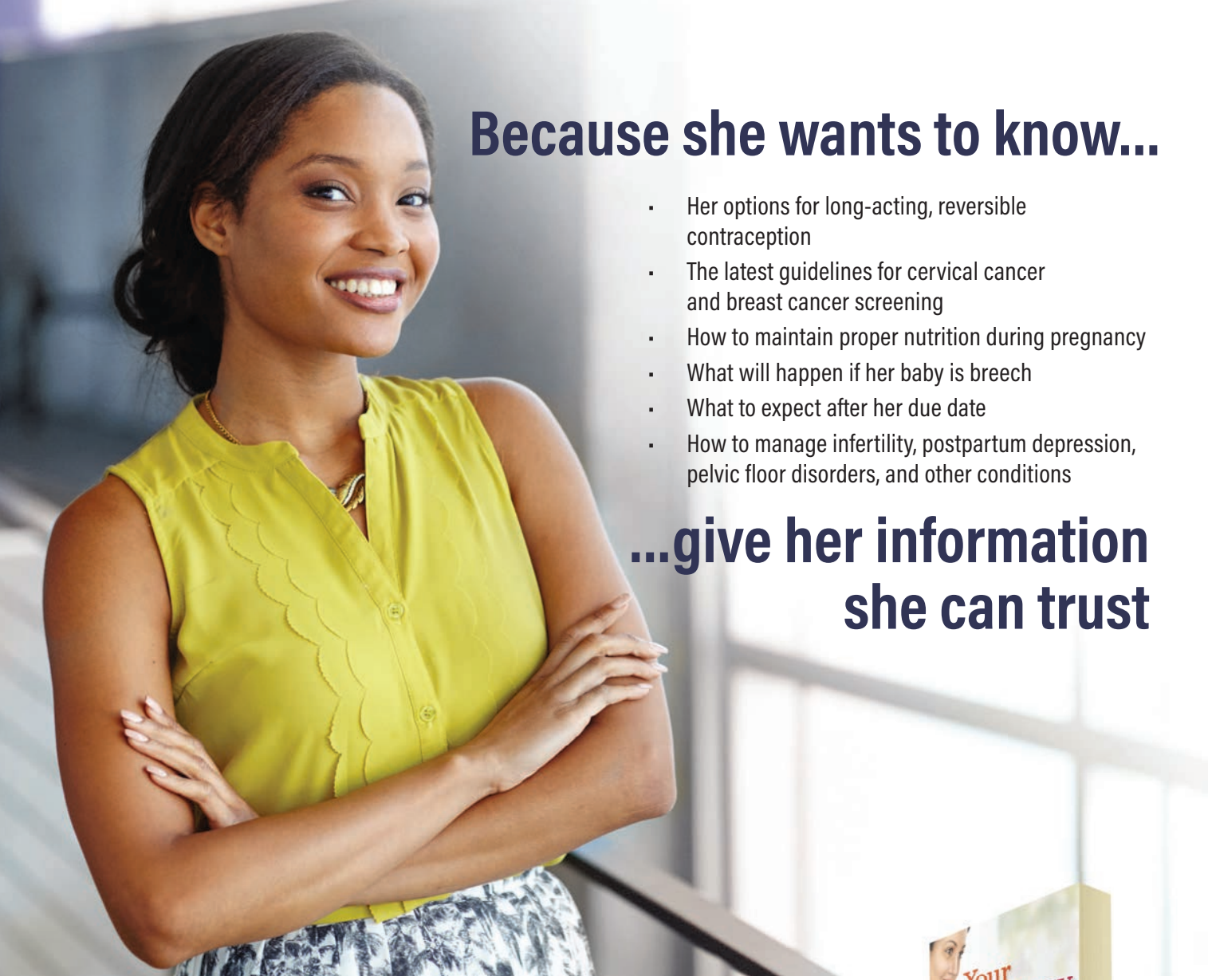

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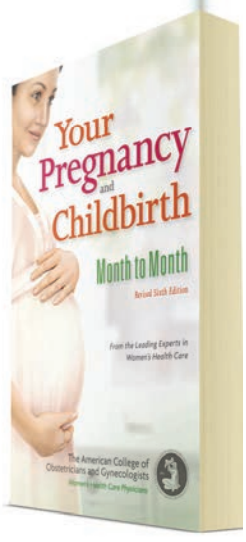

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CONTINUED FROM PAGE 22

TABLE 1 Signs and symptoms that second victims describe experiencing after an adverse medical event[5]

Physical signs and symptoms	Psychological signs and symptoms
• Extreme fatigue	• Anger
• Increased blood pressure	• Decreased job satisfaction
• Muscle tension	• Difficulty concentrating
• Rapid breathing	• Extreme sadness
• Rapid heart rate	• Fear of reputation damage
• Sleep disturbances	• Flashbacks
	• Frustration
	• Grief/remorse
	• Loss of confidence
	• Return to work anxiety

revealed that 210,000 to 440,000 deaths occur each year in the United States related to preventable patient harm.[2] Although this fact is deeply disturbing, it is well known that modern health care is a high-risk industry.

Medical errors vary in terms of the degree of potential or actual damage. A "near miss" is any event that could have resulted in adverse consequences but did not (for example, an incorrect drug or dose ordered but not administered). On the other hand, an "adverse event" describes an error that resulted in some degree of patient harm or suffering.[3]

FAST TRACK

A "near miss" is any event that could have resulted in adverse consequences but did not. An "adverse event" describes an error that resulted in some degree of patient harm or suffering.

Deep impact on the clinician

For each patient who dies because of a medical error or a surgical complication, whether preventable or not, many clinicians are involved in the unfolding of the case. These events have a profound impact on well-intentioned, competent, and caring physicians, and they elicit intense emotional responses.[4] When a patient experiences an unexpected adverse surgical outcome, the surgeons involved in their care may become "second victims." They may feel that they have failed the patient and they second-guess their surgical skills and knowledge base; some express concern about their reputation and perhaps career choice.

Psychological responses. It is important to understand this process to ensure a healthy recovery. Psychological responses to an adverse medical event include guilt; distress, anxiety, and fear; frustration and anger; feelings of insufficiency; and long-standing suffering. Clinicians who experienced an adverse medical event have reported additional psychological as well as physical symptoms in the aftermath of the event (**TABLE 1**).[5]

Risk factors. Certain factors are associated with a greater emotional impact of an adverse medical event, including[6]:

- severity of the harm or leaving permanent sequelae
- death of a healthy patient or a child (for example, from a motor vehicle accident)
- self-blame for the error
- unexpected patient death (for example, a catastrophic complication after a relatively benign procedure)
- physicians-in-training responsible for the patient
- first death under a clinician's watch.

While most research in the field of medical error focuses on systems or process improvement, it is important not to neglect the individual and personal aspects of the clinicians involved in the event. The health care system must include care for our injured colleagues, the so-called second victims.

Steps in recovery for the second victim

Based on a semistructured interview of 31 physicians involved in adverse events, Scott and colleagues described the following 6 stages of healing[5]:

Chaos and accident response. Immediately after the event, the physician feels a sense of confusion, panic, and denial. *How can this be happening to me?* The physician is frequently distracted, immersed in self-reflection.

Intrusive reflections. This is a period of self-questioning. Thoughts of the event and different possible scenarios dominate the physician's mind. *What if I had done this or that?*

Restoring personal integrity. During

this phase, the physician seeks support from individuals with whom trusted relationships exist, such as colleagues, peers, close friends, and family members. Advice from a colleague who has your same level of expertise is precious. The second victim often fears that friends and family will not be understanding.

Enduring the inquisition. Root cause analysis and in-depth case review is an important part of the quality improvement process after an adverse event. A debriefing or departmental morbidity and mortality conference can trigger emotions and increase the sense of shame, guilt, and self-doubt. The second victim starts to wonder about repercussions that may affect job security, licensure, and future litigation.

Obtaining emotional first aid. At this stage, the second victim begins to heal, but it is important to obtain external help from a colleague, mentor, counselor, department chair, or loved ones. Many physicians express concerns about not knowing who is a "safe person" to trust in this situation. Often, second victims perceive that their loved ones just do not understand their professional life or should be protected from this situation.

Moving on. There is an urge to move forward with life and simply put the event behind. This is difficult, however. A second victim may follow one of these paths:

- drop out—stop practicing clinical medicine
- survive—maintain the same career but with significant residual emotional burden from the event
- thrive—make something good out of the unfortunate clinical experience.

Institution and peer support programs aid recovery process

Recognizing that peer support can play an important role in the recovery process has led to the development of specific peer support programs. Large academic institutions have created structured support programs to assist physicians involved in cases resulting in adverse outcomes. For example, the Center for Professionalism and Peer Support at Boston's Brigham and Women's Hospital was founded in 2008 to provide one-on-one peer support.[7] A similar program, RISE (Resilience In Stressful Events), was created at Johns Hopkins University in Baltimore.[8] In Ohio, the Cleveland Clinic instituted "Code Lavender," a rapid-response holistic support team for clinicians who are experiencing acute emotional stress.[9]

TABLE 2 Hallmarks of the peer support team model[10]

- Confidential
- Credulity of peers
- Emotional "first aid" (not therapy)
- Facilitated access to the next level of support (eg, employee assistance program)
- Immediate availability
- Voluntary access

All these programs offer immediate help to any clinician in psychological distress. They provide confidentiality, and the individual is reassured that he or she can safely use the service without further consequences (**TABLE 2**).[10]

The normal human response to an adverse medical event can lead to significant psychological consequences, long-term emotional incapacity, impaired performance of clinical care, and feelings of guilt, fear, isolation, or even suicide. At some point during his or her career, almost every physician will be involved in a serious adverse medical event and is at risk of experiencing strong emotional reactions. Health care facilities should have a support system in place to help clinicians cope with these stressful circumstances.

Use these 5 strategies to facilitate recovery

1. **Be determined.** No matter how bad you feel about the event, you need to get up and moving.
2. **Avoid isolation.** Get outside and interact with people. Avoid long periods in isolation. Bring your team together and talk about the event.
3. **Sleep well.** Most symptoms of

FAST TRACK

At some point in his or her career, almost every physician will be involved in a serious adverse medical event and is at risk of experiencing strong emotional reactions

CONTINUED ON PAGE 48

External cephalic version: How to increase the chances for success

Henry Michael Lerner, MD

Increasing the use of ECV in breech-presenting fetuses at term has the potential to turn the tide on cesarean delivery rates in this population. Certain techniques can help facilitate successful version and the likelihood of vaginal delivery, with low risk to mother and baby.

IN THIS ARTICLE

Timing the ECV procedure
page 28

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page 31

About 3% to 4% of all fetuses at term are in breech presentation. Since 2000, when Hannah and colleagues reported finding that vaginal delivery of breech-presenting babies was riskier than cesarean delivery,[1] most breech-presenting neonates in the United States have been delivered abdominally[2]—despite subsequent questioning of some of that study's conclusions.

Each year in the United States, approximately 4 million babies are born, and fetal malpresentation accounts for 110,000 to 150,000 cesarean deliveries. In fact, about 15% of all cesarean deliveries in the United States are for breech presentation or transverse lie; in England the percentage is 10%.[3] Fortunately, the repopularized technique of external cephalic version (ECV), in which the clinician externally rotates a breech- or transverse-lying fetus to a vertex position (**FIGURE**, page 30), along with the facilitating tools of tocolysis and neuraxial analgesia/anesthesia, is helping to reduce the number of breech presentations in fetuses at term and thus the number of cesarean deliveries and their sequelae—placenta accreta, prolonged recovery, and cesarean deliveries in subsequent pregnancies.

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

The author reports no financial relationships relevant to this article.

Reluctance to perform ECV is unfounded

In the United States, the practice of offering ECV to women who present with their fetus in breech presentation at term varies tremendously. It is routine at some institutions but not even offered at others.

Many ObGyns are reluctant to perform ECV. Cited reasons include the potential for injury to the fetus and mother (and related liability concerns), the ease of elective cesarean delivery, the variable success rate of ECV (35% to 86%),[4] and the pain that women often have with the procedure. According to the literature, however, these concerns either are unfounded or can be mitigated with use of current techniques. Multiple studies have found that the risk of ECV to the fetus and mother is minimal, and that tocolysis and neuraxial anesthesia can facilitate the success of ECV and relieve the pain associated with the procedure.

CONTINUED ON PAGE 28

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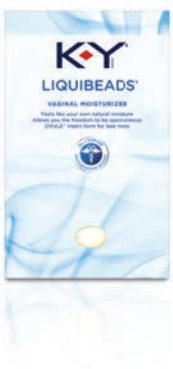

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CONTINUED FROM PAGE 26

Indications for ECV

The indications for ECV include breech, oblique, or transverse lie presentation after 36 weeks' gestation and the mother's desire to avoid cesarean delivery. A clinician skilled in ECV and a facility where emergency cesarean delivery is possible are essential.

There are several instances in which ECV should not be attempted.

Contraindications include:

- concerns about fetal status, including nonreactive nonstress test, biophysical profile score <6/8, severe intrauterine growth restriction, decreased end-diastolic umbilical blood flow
- placenta previa
- multifetal gestation before delivery of first twin
- severe oligohydramnios
- severe preeclampsia
- significant fetal anomaly
- known malformation of uterus
- breech with hyperextended head or arms above shoulders, as seen on ultrasonography.

More controversial contraindications include prior uterine incision, maternal obesity (body mass index >40 kg/m^2), ruptured membranes, and fetal macrosomia.

FAST TRACK

Current practice is to wait until 36 to 37 weeks of gestation to perform ECV, since most fetuses spontaneously move into vertex presentation by 36 weeks

Optimal timing for the ECV procedure

Current practice is to wait until 36 to 37 weeks to perform ECV, as most fetuses spontaneously move into vertex presentation by 36 weeks' gestation. This time frame has several advantages: Many unnecessary attempts at ECV are avoided; only 8% of fetuses in breech presentation after 36 weeks spontaneously change to vertex[5]; many fetuses revert to breech if ECV is performed too early; and prematurity generally is not an issue in the rare case that immediate delivery is required during or just after attempted ECV.

ECV during labor. Performing ECV during labor appears to pose no increased risk to mother or fetus if membranes are intact and there are no other contraindications to the procedure. Some clinicians perform ECV *only* during labor. The advantages are that the fetus has had every chance to move into vertex presentation on its own, the equipment used to continuously monitor the fetus during ECV is in place, and cesarean delivery and anesthesia are immediately available in the event ECV is unsuccessful.

The major disadvantage of waiting until labor is that the increased size of the fetus makes ECV more difficult. In addition, the membranes may have already ruptured, and the breech may have descended deeply into the pelvis.

Success rates in breech-to-vertex conversions

In 2016, the American College of Obstetricians and Gynecologists (ACOG) reported an average ECV success rate of 58% (range, 16% to 100%).[6] ACOG noted that, with transverse lie, the success rate was significantly higher. Other studies have found a wide range of rates: 58% in 1,308 patients in a Cochrane review by Hofmeyr and colleagues[7]; 47% in a study by Beuckens and colleagues[8]; and 63.1% for primiparas and 82.7% for multiparas in a study by Tong Leung and colleagues.[9] These rates were affected by whether ECV was performed with or without tocolysis, with or without intravenous analgesia, and with or without neuraxial analgesia/anesthesia (**TABLE**, page 29).

Likelihood of vaginal delivery after successful ECV

The rate of vaginal delivery after successful ECV is roughly half that of fetuses that were never in breech presentation.[10] In successful ECV cases, dystocia and nonreassuring fetal heart rate patterns are the major indications for cesarean delivery. Some experts have speculated that the factors leading to near-term breech presentation—such as an unengaged presenting part or a mother's smaller pelvis—also may be risk factors for dystocia in labor. Despite this, the rate of vaginal delivery of successfully verted babies has been reported to be as high as 80%.[10]

As might be expected, post-ECV vaginal

CONTINUED ON PAGE 29

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Led by: Rosanne M. Kho, MD

8:30 AM **Hands-On Laparoscopic Suturing - The "Vertical Zone"** (Simulation Lab)
Led by: Charles H. Koh, MD

1:30 PM **Hands-On Hysteroscopy Workshop**
Led by: Andrew I. Brill, MD

1:30 PM **Hands-On Ultrasound Workshop**
Led by: James M. Shwayder, MD, JD

1:30 PM **Technical Aspects of Vaginal Hysterectomy & Cystourethroscopy for the Gynecologist**
Led by: Mickey M. Karram, MD

THURSDAY, DECEMBER 14, 2017

6:30 AM **Registration/Breakfast/Exhibits**

7:10 AM **Breakfast Symposium**

7:55 AM **Course Overview**
Mickey M. Karram, MD

Pelvic Anatomy

8:00 AM **Pelvic and Abdominal Anatomy from the Laparoscopic Surgeon's View**
Tommaso Falcone, MD

8:40 AM **Anatomic Considerations: Facilitating Vaginal Procedures Safely and Effectively**
Mickey M. Karram, MD

Incontinence and Prolapse Surgery

9:10 AM **Case Discussions: How Best to Evaluate a Variety of Female Pelvic Floor Disorders**
John B. Gebhart, MD, MS
Mickey M. Karram, MD

9:55 AM **Question and Answer Session**

10:25 AM **Break/Exhibits**

11:10 AM **Surgery for Stress Incontinence: Does One Sling Fit All?**
Mark D. Walters, MD

11:40 AM **Surgery for Pelvic Organ Prolapse: Getting Back to Basics - Native Tissue Suture Repairs**
John B. Gebhart, MD, MS

12:00 PM **Mesh Augmented Prolapse Repair; Vaginal Mesh vs. Sacrocolpopexy**
Mark D. Walters, MD

12:40 PM **Question and Answer Session**

1:10 PM **Luncheon Symposium**

2:10 PM **Dessert Break/ Exhibits**

Thursday's Keynote Lecture

2:40 PM **Avoiding and Managing Postpartum Perineal Disorders**
Bahaeddine M.Sibai, MD

Fibroid Management & Principles of Electrosurgery

3:25 PM **Myomectomy: Open to Robotic Approaches**
Tommaso Falcone, MD

3:55 PM **The Hysteroscopic Treatment of Submucosal Fibroids and Polyps**
Linda D. Bradley, MD

4:25 PM **Break/Exhibits**

4:40 PM **Safe Use of Electrosurgical Devices for Gynecologic Surgery**
Andrew I. Brill, MD

5:10 PM **Question and Answer Session**

FRIDAY, DECEMBER 15, 2017

7:00 AM **Breakfast/Exhibits**

7:10 AM **Breakfast Symposium**

Hysterectomy - Technique

8:15 AM **The Difficult Vaginal Hysterectomy**
Rosanne M. Kho, MD

8:50 AM **Single Port Approaches to Hysterectomy**
Amanda Nickles Fader, MD

9:25 AM **Total Laparoscopic Hysterectomy**
Andrew I. Brill, MD

10:00 AM **Break /Exhibits**

10:45 AM **Robotic Hysterectomy**
Javier F. Magrina, MD

11:15 AM **Tissue Extraction Techniques (Morcellation)**
Tommaso Falcone, MD

11:45 AM **Techniques to Preserve Level 1 Support at the Time of Vaginal Laparoscopic and Robotic Hysterectomy**
Mark D. Walters, MD

12:15 PM **Which Hysterectomy Approach is Best?** Case Presentation and Audience Participation

12:45 PM **Question and Answer Session**

1:00 PM **Luncheon Symposium**

2:00 PM **Dessert Break/Exhibits**

Friday's Keynote Lecture

2:30 PM **Management of Obstetric Hemorrhage**
Bahaeddine M. Sibai, MD

Oncology For The Generalist

3:15 PM **Surgical Management of Pre-Cancer Vulvovaginal Lesions**
Amanda Nickles Fader, MD

4:00 PM **Laparoscopic and Robotic Management of the Adnexal Mass**
Javier F. Magrina, MD

4:45 PM **Spectrum of Vulvovaginal Disorders**
Michael S. Baggish, MD

5:30 PM **Question and Answer Session**

SATURDAY, DECEMBER 16, 2017

6:30 AM **Breakfast**

7:30 AM **Management of Endometriosis**
Tommaso Falcone, MD

8:30 AM **Avoiding and Managing Urogynecologic Complications**
John B. Gebhart, MD, MS
Mickey M. Karram, MD

9:30 AM **Avoiding and Managing Laparoscopic Complications**
Tommaso Falcone, MD

10:30 AM **Break**

10:45 AM **Medical Legal Cases**
Michael S. Baggish, MD
Tommaso Falcone, MD

11:30 AM **Surgical Tips for Successful Pelvic Surgery: Video Session**
Surgical Management of Cornual Ectopic & Dermoid Cysts
Tommaso Falcone, MD
Techniques to Suspend the Apex at the Time of Vaginal Surgery
Mickey M. Karram, MD

1:00 PM **PAGS Scientific Program Adjournment**

P.E.P. PRACTICE ENHANCEMENT PROGRAM AGENDA

(Optional. Separate fee required)

Open to Non-Attendees so bring your staff!

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Director
Neil H. Baum, MD
Associate Clinical Professor of Urology
Tulane Medical School and Louisiana State University
New Orleans, Louisiana

Dr. Neil Baum is the author of *The Complete Business Guide to a Successful Medical Practice* and *3-Stages of a Physician's Career*

SATURDAY, DECEMBER 16, 2017

2:00 PM **Course Overview**

2:10 PM
Looking at the 4 Pillars of a Successful Practice in the Current Healthcare Environment
- Keeping patients already in your practice
- Attracting new patients to your practice (social media techniques to add 3-5 new patients a day to your practice)
- Communicating with your professional colleagues
- Enhancing staff morale

3:00 PM
Moving from Volume to Value-The New Metric of Healthcare
- Fee for Service and volume of work performed will no longer be the method of reimbursement in the near future
- Define quality (outcomes\costs)
- Provide the 7 steps to measure cost-of-care

3:30 PM **Break**

3:45 PM
Online Reputation Management
- The importance of a physician's reputation
- How it can be ruined with the click of a mouse
- How to obtain positive reviews
- Management of negative reviews

4:15 PM
Patient Satisfaction
- Discuss why patient satisfaction is important
- What are the needs and wants of today's primary care patient
- How we measure patient satisfaction
- Practical suggestions for enhancing patient satisfaction

4:45 PM
Numbers you Need to Know
- Obstetricians and gynecologists need to know and monitor just a few numbers
- Without understanding these concepts, you will not understand the value of the services that you provide
- Will review 5 numbers that need to be monitored (charges\receipts, RVUs, ARs\days in AR, charge lag, denials)

5:00 PM **Q and A**

5:15 PM
The Future of Medical Practice and Conclusion
- What is the current situation
- What happens if ACA is repealed
- What can primary care providers do pro-actively to enhance their practices in the near future

5:30 PM **Adjourn**

PAGS Scientific Faculty

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Cleveland, Ohio

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Cleveland Clinic
Cleveland, Ohio

Pre-Conference Workshops

(Optional. Separate fee required)

Please note: PAGS workshops have limited space available and do sell out. First come. First served!

Wednesday, December 13, 2017 The Cosmopolitan of Las Vegas

HANDS-ON TISSUE EXTRACTION TECHNIQUES WORKSHOP NEW!
4 CME Credits Available
8:30 AM - 12:30 PM
Director: Rosanne M. Kho, MD
Faculty: Andrew I. Brill, MD; Tommaso Falcone, MD; Keith B. Isaacson, MD

HANDS-ON LAPAROSCOPIC SUTURING - THE "VERTICAL ZONE" (SIMULATION LAB)
4 CME Credits Available
8:30 AM - 12:30 PM
Led by: Charles H. Koh, MD

HANDS-ON HYSTEROSCOPY WORKSHOP
4 CME Credits Available
1:30-PM - 5:30 PM
Led by: Andrew I. Brill, MD
Faculty: Linda D. Bradley, MD; Tommaso Falcone, MD; Keith B. Isaacson, MD

HANDS-ON ULTRASOUND WORKSHOP
4 CME Credits Available
1:30 PM - 5:30 PM
Led by: James M. Shwayder, MD, JD
Faculty: William W. Brown, III, MD; Todd Deutch, MD; Tommaso Falcone, MD

HANDS-ON TECHNICAL ASPECTS OF VAGINAL HYSTERECTOMY & CYSTOURETHROSCOPY FOR THE GYNECOLOGIST
4 CME Credits Available
1:30 PM - 5:30 PM
Led by: Mickey Karram, MD
Faculty: Rosanne M. Kho, MD and Douglas Miyazaki, MD

Who Should Attend?

The PAGS conference is designed for obstetricians/gynecologists, second, third and fourth-year residents in Ob/Gyn, as well as sub-specialty fellows and advanced practice clinicians. Residents and advanced practice health clinicians are welcome at reduced rates.

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About Our Venue
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The 2017 Pelvic Anatomy and Gynecologic Surgery Symposium will take place at the ultra-modern Cosmopolitan of Las Vegas, where we have arranged for a discount room rate of just $179* a night for PAGS participants. To make your reservation call- 855.435.0005 (domestic toll free) or 855.455.1055 (international toll free) and reference the code SGAME7.

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- Hysterectomy Techniques
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  - Morcellation • Preserving Level 1 Support
  - Which Approach is Best?
- Avoiding and Managing Complications
- Fibroid Management & Principles of Electrosurgery
- Surgical Tips for Successful Pelvic Surgery

SPECIAL KEYNOTES: Bahaeddine M. Sibai, MD

- **Avoiding and Managing Postpartum Perineal Disorders**
- **Management of Obstetric Hemorrhage**

Plus! "PEP" Practice Management Workshop*
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Cancellation Policy: Full refund less a $50 administrative fee as follows: Cancellations can be made using our online registration system until November 14, 2017. After November 14, 2017 no refunds will be granted. After the refund date, you have two options: you can send someone in your place, or we can mark a credit in the amount you paid minus $50 administration fee (plus additional $35 administration fee per workshop) to be applied to your registration for next year's conference. Refunds will not be issued to no-shows.

To register and for complete information please see our website: PAGS-cme.org.

CONTINUED FROM PAGE 28

deliveries are more common in multiparous than in primiparous women.

Risks of ECV: Generally low and manageable

Although multiple problems may occur with ECV, generally they are rare and reversible. For instance, Grootscholten and colleagues found a stillbirth and placental abruption rate of only 0.25% in a large group of patients who underwent ECV.[11] Similarly, the rate of emergency cesarean delivery was 0.35%. In addition, Hofmeyr and Kulier, in their Cochrane Data Review of 2015, found no significant differences in the Apgar scores and pH's of babies in the ECV group compared with babies in breech presentation whose mothers did not undergo ECV.[7] Results of other studies have confirmed the safety of ECV.[12,13]

One significant risk of ECV attempts is fetal-to-maternal blood transfer. Boucher and colleagues found that 2.4% of 1,244 women who underwent ECV had a positive Kleihauer-Betke test result, and, in one-third of the positive cases, more than 1 mL of fetal blood was found in maternal circulation.[14] This risk can be minimized by administering Rh_o (D) immune globulin to all Rh-negative mothers after the procedure.

Even these small risks, however, should not be considered in isolation. The infrequent complications of ECV must be compared with what can occur with breech-presenting fetuses during labor or cesarean delivery: complications of breech vaginal delivery, cord prolapse, difficulties with cesarean delivery, and maternal operative complications related to present and future cesarean deliveries.

Alternative approaches to converting breech presentation of unproven efficacy

Over the years, attempts have been made to address breech presentations with measures short of ECV. There is little evidence that these measures work, or work consistently.

- **Observation.** After 36 weeks' gestation, only 8% of fetuses in breech presentation spontaneously move into vertex presentation.[5]
- **Maternal positioning.** There is no good evidence that such maneuvers are effective in changing fetal presentation.[15]
- **Moxibustion and acupuncture.** Moxibustion is inhalation of smoke from burning herbal compounds. In formal studies using controls, these techniques did not consistently increase the rate of movement from breech to vertex presentation.[16–18] Likewise, studies with the use of acupuncture have not shown consistent success in changing fetal presentation.[19]

TABLE Factors that affect the ECV success rate

Increase ECV success rate	Decrease ECV success rate
Transverse or oblique lie	Ruptured membranes
Multiparity	Macrosomic fetus
Amniotic fluid index >18	Relative oligohydramnios
Breech unengaged	Maternal obesity
Smaller fetus	Primigravida status
Patient with normal body mass index	Anterior placenta
Clinician experienced in ECV	Mother's inability to relax anterior abdominal wall muscles
Placenta on posterior wall of uterus	Clinician's inability to locate fetal head by palpation
Complete (vs footling) breech	Contracting or tense myometrium
Tocolysis	
Neuraxial analgesia/anesthesia	

Abbreviation: ECV, external cephalic version.

Methods to facilitate ECV success

Two techniques that can facilitate ECV success are tocolysis, which relaxes the uterus, and neuraxial analgesia/anesthesia, which relaxes anterior abdominal wall muscles and reduces or relieves ECV-associated pain.

Tocolysis

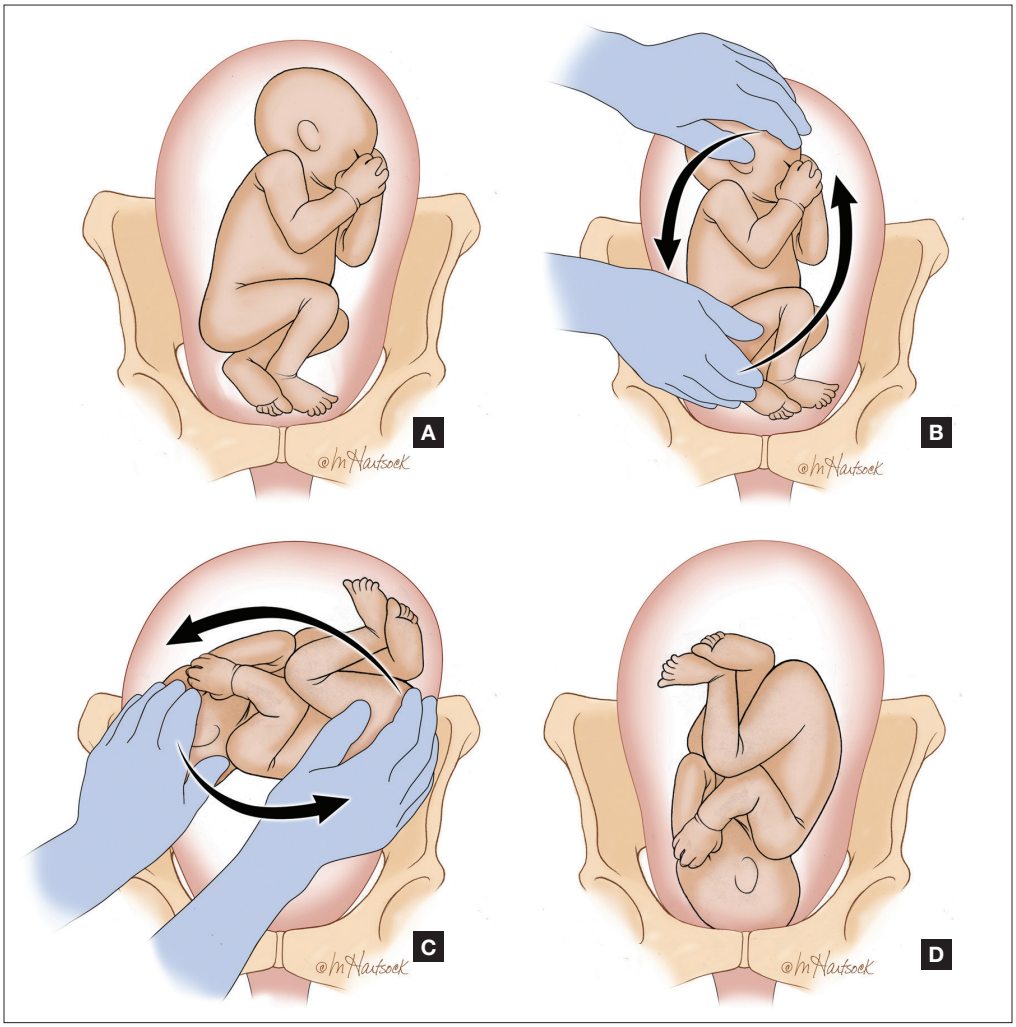
In tocolysis, a medication is administered to reduce myometrial activity and to relax the uterine muscle so that it stretches more easily around the fetus during repositioning. Tocolytic medications originally were studied for

FAST TRACK

Tocolysis, which relaxes the uterus, and neuraxial analgesia/anesthesia, which relaxes anterior abdominal wall muscles and reduces ECV-associated pain, can facilitate ECV success

CONTINUED FROM PAGE 25

FIGURE External cephalic version technique



In external cephalic version, the clinician externally rotates a breech- or transverse-lying fetus to a vertex position. The illustration shows a backflip rotation maneuver. The American College of Obstetricians and Gynecologists recommends a forward rotational maneuver to be attempted first.

Source: Koutrouvelis GO; American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics. Practice Bulletin No. 161: External cephalic version. Obstet Gynecol. 2016;127(2):e54–e61.

FAST TRACK

Several studies have found that nifedipine is less effective than terbutaline in facilitating ECV

their use in decreasing myometrial tone during preterm labor.

Tocolysis clearly is effective in increasing ECV success rates. Reviewing the results of 4 randomized trials, Cluver showed a 1.38 risk ratio for successful ECV when terbutaline was used versus when there was no tocolysis. The risk ratio for cesarean delivery was 0.82.[20] Fernandez, in a study of 103 women divided into terbutaline versus placebo groups, had a 52% success rate for ECV with the terbutaline group versus only a 27% success rate with the placebo group.[21]

Tocolytic medications include terbutaline, nifedipine, and nitroglycerin.

Tocolysis most often involves the use of β_2-adrenergic receptor agonists, particularly terbutaline (despite the boxed safety warning in its prescribing information). A 0.25-mg dose of terbutaline is given subcutaneously 15 to 30 minutes before ECV. Clinicians have successfully used β_2-adrenergic receptor agonists in the treatment of patients in preterm labor, and there are more data on this

ILLUSTRATION: MARCIA HARTSOCK FOR OBG MANAGEMENT

class of medications than on other agents used to facilitate ECV.

Although nifedipine is as effective as terbutaline in the temporary treatment of preterm uterine contractions, several studies have found this calcium channel blocker less effective than terbutaline in facilitating ECV.[22,23]

The uterus-relaxing effect of nitroglycerin was once thought to make this medication appropriate for facilitating ECV, but multiple studies have found success rates unimproved. In some cases, the drug performed more poorly than placebo.[24] Moreover, nitroglycerin is associated with a fairly high rate of adverse effects, such as headaches and blood pressure changes.

Neuraxial analgesia/anesthesia

Over the past 2 decades, there has been a resurgence in the use of neuraxial analgesia/anesthesia in ECV. This technique is more effective than others in improving ECV success rates, it reduces maternal discomfort, and it is very safe. Specifically, it relaxes the maternal abdominal wall muscles and thereby facilitates ECV. Another benefit is that the anesthesia is in place and available for use should emergency cesarean delivery be needed during or after attempted ECV. Neuraxial anesthesia, which includes spinal, epidural, and combined spinal-epidural techniques, is almost always used with tocolysis.

The major complications of neuraxial analgesia/anesthesia are maternal hypotension and fetal bradycardia. Each is dose related and usually transient.

In the past, there was concern that using regional anesthesia to control pain would reduce a patient's natural warning symptoms and result in a clinician applying excessive force, thus increasing the chances of fetal and maternal injury and even fetal death. However, multiple studies have found that ECV complication rates are not increased with use of neuraxial methods.

Higher doses of neuraxial anesthesia produce higher ECV success rates. This dose-dependent relationship is almost surely attributable to the fact that, although lower dose neuraxial *analgesia* can relieve the pain associated with ECV, an *anesthetic* dose is needed to relax the abdominal wall muscles and facilitate fetus repositioning.

The literature is clear: ECV success rates are significantly increased with the use of neuraxial techniques, with anesthesia having higher success rates than analgesia. Reviewing the results of 6 controlled trials in which a total of 508 patients underwent ECV with tocolysis, Goetzinger and colleagues found that the chance of ECV success was almost 60% higher in the 253 patients who received regional anesthesia than in the 255 patients who received intravenous or no analgesia.[25] Moreover, only 48.4% of the regional anesthesia patients as compared with 59.3% of patients who did not have regional anesthesia underwent cesarean delivery, roughly a 20% decrease. Pain scores were consistently lower in the regional anesthesia group. Multiple other studies have reported similar results.

Although the use of neuraxial anesthesia increases the ECV success rate, and decreases the cesarean delivery rate for breech presentation by 5% to 15%,[25] some groups of obstetrics professionals, noting that the decreased cesarean delivery rate does not meet the formal criterion for statistical significance, have expressed reservations about recommending regional anesthesia for ECV. Thus, despite the positive results obtained with neuraxial anesthesia, neither the literature nor authoritative professional organizations definitively recommend the use of neuraxial anesthesia in facilitating ECV.

This lack of official recommendation, however, overlooks an important point: While the cesarean delivery percentage decrease that occurs with the use of neuraxial anesthesia may not be *statistically* significant, the promise of a pain-free procedure will encourage more women to undergo ECV. If the procedure population increases, then the average ECV success rate of roughly 60%[6] applies to a larger base of patients, reducing the total number of cesarean deliveries for breech presentation. As only a small percentage of the 110,000 to 150,000 women with breech presentation at 36 weeks currently elects to

FAST TRACK

Higher doses of neuraxial anesthesia produce higher ECV success rates, possibly because the higher anesthetic dose relaxes the abdominal wall muscles and facilitates fetus repositioning

undergo ECV, any increase in the number of women who proceed with attempts at fetal repositioning **once procedural pain is no longer an issue** will accordingly reduce the number of cesarean deliveries for the indication of malpresentation.

Overarching goal: Reduce cesarean delivery rate and associated risks

In the United States, increasing the use of ECV in cases of breech-presenting fetuses would reduce the cesarean delivery rate by about 10%, thereby reducing recovery time for cesarean deliveries, minimizing the risks associated with these deliveries (current and future), and providing the health care system with a major cost savings.

Tocolysis and the use of neuraxial anesthesia each increases the ECV success rate and each is remarkably safe within the context of a well-defined protocol. Reducing the pain associated with ECV by administering neuraxial anesthesia will increase the number of women electing to undergo the procedure and ultimately will reduce the number of cesarean deliveries performed for the indication of breech presentation.

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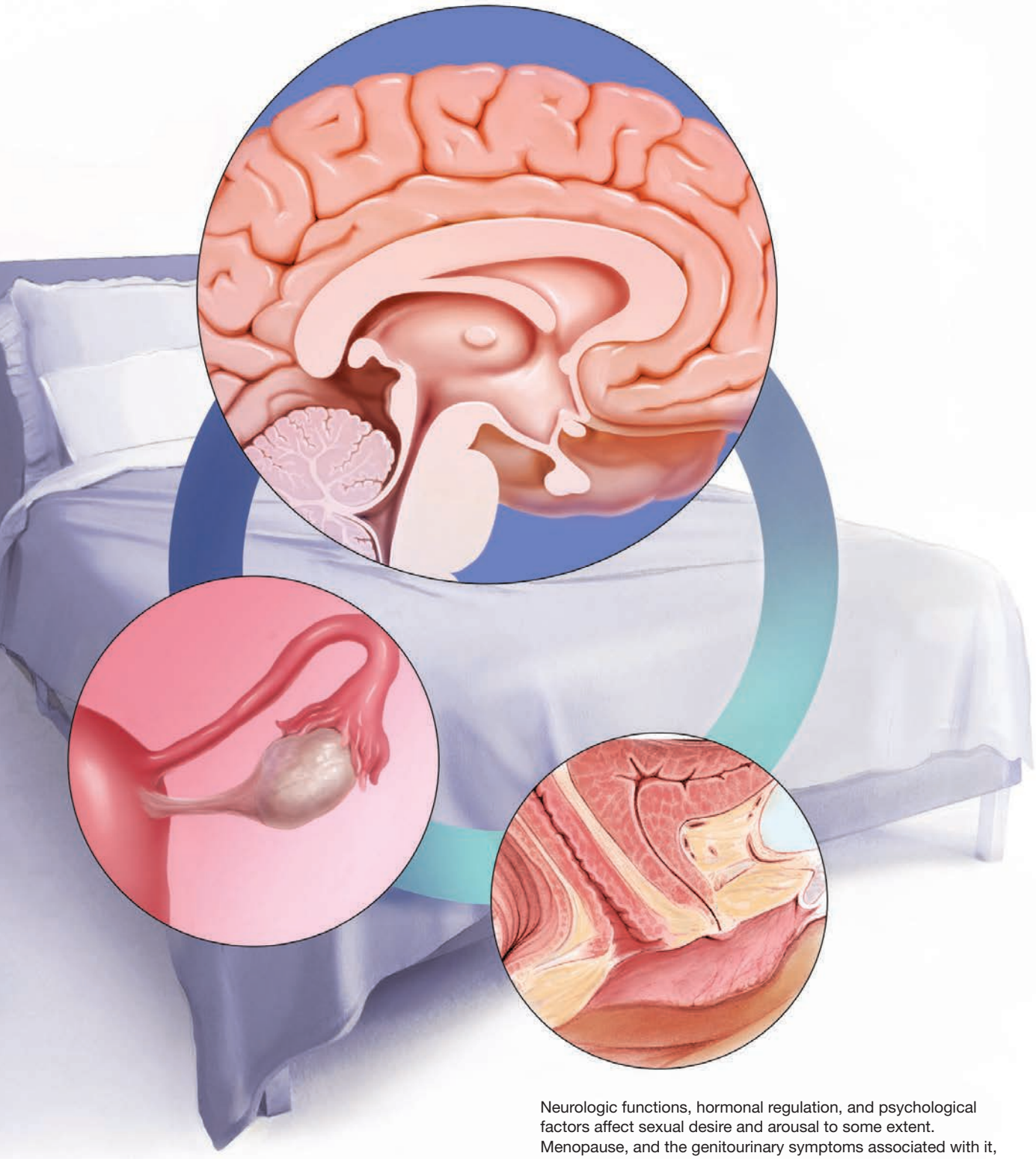

Neurologic functions, hormonal regulation, and psychological factors affect sexual desire and arousal to some extent. Menopause, and the genitourinary symptoms associated with it, also affect sexual function. Understanding the pathogenesis of sexual dysfunction is key to management decisions.

ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

FEMALE SEXUAL DYSFUNCTION

New and emerging treatment options hold promise for improving outcomes in this undertreated disorder

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The author reports no financial relationships relevant to this article.

Sexual function is a complex, multifaceted process mediated by neurologic functions, hormonal regulation, and psychological factors. What could possibly go wrong?

As it turns out, quite a lot. Female sexual dysfunction is a common, vastly undertreated sexual health problem that can have wide-reaching effects on a woman's life. These effects may include impaired body image, self-confidence, and self-worth. Sexual dysfunction also can contribute to relationship dissatisfaction and leave one feeling less connected with her partner.[1,2] Studies have shown women with sexual dysfunction have higher health care expenditures[3] and that depression and fatigue are common comorbidities, as is frequently seen in other chronic conditions such as diabetes and back pain.[4]

Understanding the pathogenesis of female sexual dysfunction helps to guide our approach to its management. Indeed, increased understanding of its pathology has helped to usher in new and emerging treatment options, as well as a personalized, biopsychosocial approach to its management.

In this Update, I discuss the interplay of physiologic and psychological factors that affect female sexual function as well as the latest options for its management. I have also assembled a panel of experts to discuss 2 cases representative of sexual dysfunction that you may encounter in your clinical practice and how prescribing decisions are made for their management.

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Multiple transmitters in the brain can increase or decrease sexual desire and function

Neurotransmitters involved in sexual excitation include brain dopamine, melanocortin, oxytocin, vasopressin, and norepinephrine, whereas brain opioids, serotonin, prolactin, and endocannabinoids function as sexual inhibitors. Inhibitory

transmitters are activated normally during sexual refractoriness but also from primary aversion or secondary avoidance disorders.[1] Drugs or conditions that reduce brain dopamine levels, increase the action of brain serotonin, or enhance brain opioid pathways have been shown to inhibit sexual desire, while those that increase hypothalamic and mesolimbic dopamine or decrease serotonin release have been shown to stimulate sexual desire.[1]

Estradiol and progesterone can impact sexual function and desire

In addition to the neurotransmitters, hormones are important modulators of female sexual function. Decreasing levels of circulating estrogen after menopause lead to physiologic, biologic, and clinical changes in the urogenital tissues, such as decreased elastin, thinning of the epithelium, reduced vaginal blood flow, diminished lubrication, and decreased flexibility and elasticity. These changes result in the symptoms of genitourinary syndrome of menopause (GSM), which affects as many as half of all menopausal women.[5,6] In clinical trials, dyspareunia and vaginal dryness are the most bothersome GSM symptoms reported.[7]

The role of hormonal regulation in sexual dysfunction among premenopausal women is not yet fully understood, but we do know that estradiol has been shown to improve sexual desire, progesterone tends to dampen sexual desire, and that testosterone at physiological levels has been shown in most studies to have a neutral effect on sexual desire in a well-estrogenized patient.[8]

Experience and behavior modulate or reinforce sexual dysfunction

The most common psychological factors that trigger or amplify female sexual dysfunction are depression, anxiety, distraction, negative body image, sexual abuse, and emotional neglect.[9] Contextual or sociocultural factors, such as relationship discord, life-stage stressors (the empty nest syndrome or anxiety and sleep deprivation from a new baby), as well as cultural or religious values that suppress sexuality, also should be considered.[9] Experience-based neuroplasticity (changes in brain pathways that become solidified by negative or positive experiences) may elucidate how a multimodal approach, utilizing medical and psychological treatment, can be beneficial for patients, particularly those with hypoactive sexual desire disorder (HSDD).[1]

FAST TRACK

Although not fully understood how, estradiol can improve sexual desire, progesterone tends to dampen sexual desire, and testosterone has a neutral effect in premenopausal women

New and emerging approaches to managing female sexual dysfunction

Three agents, one of which has been available for prescription for some time, one that is newly available, and one in the pipeline, are or may soon be in the gynecologist's armamentarium.

Flibanserin

Medications that target excitatory pathways or blunt inhibitory pathways are in development, and one, flibanserin (Addyi), has been US Food and Drug Administration (FDA)–approved for the treatment of acquired, generalized HSDD in premenopausal women.[1,10] Flibanserin is a nonhormonal, centrally acting, postsynaptic serotonin 1A receptor agonist and a serotonin 2A receptor antagonist that is taken daily at bedtime (100 mg); several weeks are usually needed before any effects are noted.[1] It is not approved for postmenopausal women and has a boxed warning about the risks of hypotension and syncope; its use is

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contraindicated in women who drink alcohol, in those who have hepatic impairment, and with the use of moderate or strong CYP3A4 inhibitors.[11]

Also keep in mind that flibanserin is only available through a Risk Evaluation and Mitigation Strategy program, so clinicians who wish to prescribe it must enroll in and complete training to become certified providers.[9]

Prasterone

Prasterone (Intrarosa), a once-daily intravaginal dehydroepiandrosterone (DHEA) product, is a prohormone that increases local estrogen and testosterone and has the advantage of improved sexual function, desire, arousal, lubrication, orgasm, satisfaction, as well as pain at sexual activity.[12] It was approved by the FDA in November 2016 to treat moderate to severe dyspareunia and has been available for prescribing since July 2017. Its cost is comparable to topical estrogen products, with a $25 copay program.

Because prasterone is not an estrogen, it does not have the boxed warning that all estrogen products are mandated by the FDA to have. This may make it more acceptable to patients, who often decline to use an estrogen product after seeing the boxed warning on the package. The Centers for Medicare and Medicaid Services (CMS) does not have prasterone on its list of potentially hazardous drugs for the elderly. However, keep in mind that because its label is for dyspareunia and not specifically for GSM, CMS considers it a drug of choice—in other words, like sildenafil (Viagra), a lifestyle choice and not for treatment of a medical condition. As such, at the present time, Medicare does not cover it.

Bremelanotide

Late-stage trials of bremelanotide, a melanocortin receptor agonist, are underway. Its mechanism of action is somewhat like that of flibanserin in that both drugs increase dopamine and norepinephrine levels. The advantage of bremelanotide is that it is used as needed. It is dosed subcutaneously (1.75 mg) and it can be used as often as a woman would like to use it. The FDA is expected to consider it for approval in about a year. Unpublished data from poster sessions at recent meetings show that, in a phase 3 study of 1,247 premenopausal women with HSDD (who had already been screened for depression and were found to have a physiologic condition), improvements in desire, arousal, lubrication, and orgasm were shown with bremelanotide. About 18% of women stopped using the drug because of adverse effects (nausea, vomiting, flushing, or headache) versus 2% for placebo. Like flibanserin, it is expected to be approved

FAST TRACK

Newly available since July 2017, prasterone is a once-daily intravaginal agent that treats moderate to severe dyspareunia and has costs similar to topical estrogens

What would you prescribe for these patients?

CASE Genitourinary syndrome of menopause (GSM) in a 55-year-old woman

A 55-year-old widow is beginning a new relationship. She has not had partnered sexual activity for several years, but she recently has begun a relationship. She describes pain with attempted penetration with her new partner. Her last menstrual period was 3 years ago and she has experienced very minor menopausal symptoms, which are not bothersome. On examination, the vulva and vagina are pale, with thin epithelium and absent rugae. The tissue lacks elasticity. A virginal speculum is needed to visualize the cervix.

How would you go about deciding which of the many options for management of GSM you will recommend for this patient? What do you weigh as you consider DHEA versus estrogen and topical versus oral therapy?

JoAnn V. Pinkerton, MD: Vulvovaginal atrophy (VVA), part of GSM, is associated with postmenopausal estrogen deficiency and includes the signs and symptoms seen

on this patient's physical exam: vaginal narrowing, pallor, loss of elasticity, as well as pain with intercourse.[6] Estrogen therapy is the most effective treatment for vaginal atrophy.[13] Since she does not have significant menopausal symptoms, low-dose vaginal estrogen preparations are effective and generally safe treatments for VVA; these include creams, tablets containing estradiol or conjugated equine estrogen (CEE), and a low-dose vaginal estradiol ring—all available at doses that result in minimal systemic absorption.

Choice is usually made based on patient desire and likely adherence. If the patient prefers nonestrogen therapies that improve VVA and have been approved for relief of dyspareunia in postmenopausal women, I would discuss with the patient the oral selective estrogen receptor modulator ospemifene,[14] and the new intravaginal DHEA suppositories, prasterone.[15] Ospemifene is taken daily as an oral tablet, has a small risk of blood clots, and is my choice for women who do not need systemic hormone therapy and prefer to avoid vaginal therapy.

Andrew M. Kaunitz, MD: GSM is prevalent in menopausal women and, if not treated, causes progressive vaginal dryness and sexual discomfort. When the main indication for hormonal management in a menopausal woman is GSM (as opposed to treatment of vasomotor symptoms or prevention of osteoporosis), the treatment of choice is low-dose local vaginal estrogen, ospemifene, or prasterone (DHEA). Prasterone is a vaginally administered nonestrogen steroid that was approved by the FDA to treat dyspareunia associated with GSM. DHEA is an endogenous inactive steroid that is converted locally into androgens and estrogens; one vaginal insert is placed nightly.[16,17]

This 55-year-old widow has not been sexually active for some time. The facts that attempted penetration was painful and only an ultrathin (virginal) speculum could be used for examination indicate that contraction of the pelvic floor muscles is likely present. Simply starting medical management may not lead to comfortable/successful penetrative sex for this woman. In addition to medical management, she would likely benefit from referral for physical therapy. Using dilators and other strategies, along with the positive impact that medical management will have on the vaginal mucosa, a woman's physical therapist can work with this patient to help the pelvic floor muscles relax and facilitate comfortable penetrative sex.

James A. Simon, MD: With only minor vasomotor symptoms, I would assess the other potential benefits of a systemic therapy. These might include cardiovascular risk reduction (systemic estrogens or estrogens/progesterone in some), breast cancer risk

EXPERT PANEL

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Dr. Pinkerton reports that she receives grant or research support from Grants/Research at TherapeuticsMD (fees go to the University of Virginia). She is a member of the OBG Management Board of Editors.

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reduction (some data suggesting ospemifene can accomplish this), osteoporosis prevention (systemic estrogens and estrogen/androgens), etc. If there is an option for a treatment to address more than one symptom, in this case GSM, assessing the risks/benefits of each of these therapies should be estimated for this specific patient.

If there are no systemic benefits to be had, then any of the local treatments should be helpful. As there are no head-to-head comparisons available, local estrogen cream, tablets, rings, local DHEA, or systemic ospemifene each should be considered possible treatments. I also feel this patient may benefit from supplementary self-dilation and/or physical therapy.

CASE Dyspareunia and vasomotor symptoms in a 42-year-old breast cancer survivor

A 42-year-old woman with a *BRCA1* mutation has undergone prophylactic mastectomies as well as hysterectomy with bilateral salpingo-oophorectomy. She reports mild to moderate hot flashes and bothersome vaginal dryness and dyspareunia. Examination confirms GSM.

Would you advise systemic hormone therapy for this patient? What would your recommendation be for management of her GSM symptoms?

Dr. Simon: While one's gut reaction would be to avoid systemic estrogen therapy in a patient with a *BRCA1* mutation, the scientific information confirming this fear is lacking.[18] Such patients may benefit significantly from systemic estrogen therapy (reduced risk of cardiovascular disease and cognitive decline, etc.), and with both breasts and both ovaries removed, estrogen's breast cancer risks, if any in this population, are largely avoided. The patient also may benefit from additional local therapy with either estrogens or DHEA.

Dr. Kaunitz: Due to her high lifetime risk of breast and ovarian cancer, this woman has proceeded with risk-reducing breast and gynecologic surgery. As more *BRCA* mutation carriers are being identified and undergo risk-reducing bilateral mastectomy (usually with reconstruction) and salpingo-oophorectomy, clinicians and mutation carriers more frequently face decisions regarding use of systemic hormone therapy.

Mutation carriers who have undergone bilateral risk-reducing mastectomy experience a very low baseline future risk for breast cancer; accordingly, concerns regarding this disease should not prevent use of systemic hormone therapy. Furthermore, without hormone replacement, induced menopause in women this age is associated with an elevated risk of osteoporosis, persistent vasomotor symptoms, cardiovascular disease, stroke, mood changes, dementia, Parkinson disease, and overall mortality. Recognizing the safety of estrogen therapy in this setting, this 42-year-old *BRCA1* mutation carrier can initiate estrogen therapy. Standard dose estrogen therapy refers to oral estradiol 1.0 mg, conjugated equine estrogen 0.625 mg, or transdermal estradiol 0.05 mg. In younger women like this 42-year-old with surgically induced menopause, higher than standard replacement doses of estrogen are often appropriate.[17]

Due to concerns the hormone therapy might further increase future risk of breast cancer, some mutation carriers may delay or avoid risk-reducing bilateral salpingo-oophorectomy, a potentially lifesaving surgery which reduces not only future risk of ovarian cancer but also future risk for breast cancer.

Among mutation carriers with intact breasts, several studies address risk of breast cancer with use of systemic hormone therapy. Although limited in numbers of participants and years of follow-up, in aggregate, these studies provide reassurance that short-term use of systemic hormone therapy does not increase breast cancer risk in women with *BRCA1* or *BRCA2* mutations and intact breasts.[19]

Dr. Pinkerton: For this woman with early surgical menopause and hysterectomy, estrogen therapy could improve her vasomotor symptoms and decrease her risk of bone loss and GSM.[17] In the Women's Health Initiative trial, there were 7 fewer breast cancers per 10,000 women-years in the estrogen-only

FAST TRACK

Estrogen therapy may be considered in a breast cancer mutation carrier who has undergone prophylactic mastectomies and bilateral salpingo-oophorectomy

arm.[20] Observational studies suggest that hormone therapy, when given to the average age of menopause, decreases the risks of heart disease, Parkinson disease, and dementia.[21] Limited observational evidence suggests that hormone therapy use does not further increase risk of breast cancer in women following oophorectomy for *BRCA1* or *BRCA2* gene mutation.[22]

The absolute risks observed with hormone therapy tended to be small, especially in younger, healthy women. Systemic hormone therapy could treat her hot flashes and her GSM symptoms and potentially decrease health risks associated with premature estrogen deficiency. Nonestrogen therapies for hot flashes include low-dose antidepressants, gabapentin, and mind-body options, such as cognitive behavioral therapy and hypnosis, but these would not decrease her health risks or treat her GSM.

If she only requests treatment of her GSM symptoms, she would be a candidate for low-dose vaginal estrogen therapy, given as a cream, tablet, or ring depending on her choice. I would not choose ospemifene as my first choice as she is having hot flashes, and there are no data yet on the drug's health benefits in early menopause. If she prefers nonestrogen vaginal therapy, the new intravaginal DHEA might be a good choice as both estrogen and testosterone are increased locally in the vagina while hormone levels remain in the postmenopausal range. There is no boxed warning on the patient insert, although safety in women with breast cancer or in those with elevated risk of breast cancer has not been tested.

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Create an effective social media campaign to market your practice: Here's how

Target the type of patient you want to treat

David S. Kim, MD, PhD, MBA

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Developing an effective social media marketing campaign can expand your practice to bring you more of the type of patient you want to treat. Although ObGyns are often not trained in marketing, we can bring our practices to the attention of women who need our services with a few simple processes.

The American Marketing Association defines marketing as "the activity, set of institutions, and processes for creating, communicating, delivering, and exchanging offerings that have value for customers, clients, partners, and society at large."[1] Social media is described as various forms of online and mobile electronic communication with user-generated content.[2] Social media marketing is the application of traditional marketing strategies to a social media platform. Delivering an effective social media marketing campaign requires focused targeting of a particular community to match the needs of those patients with the value of services and products your practice provides.

By communicating and connecting with the spoken and unspoken needs and desires of potential patients, you will generate greater enthusiasm for your medical services. Social media marketing benefits include: accessibility, low cost, the ability to build brand recognition and social capital, and the availability of analytics that provide large amounts of data to measure the effectiveness of the campaign.[3]

Though social media is pervasive, the medical community has not rapidly embraced it for marketing.[4,5] Creating a social media strategy, rather than randomly or impulsively posting on social media, allows for more effective marketing. The discussion here focuses on Facebook, which has 2 billion monthly users,[6] but these strategies and tactics can be applied to any social media platform, including YouTube, Instagram, and Twitter.[7]

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Use Facebook to create a business page

Your medical practice needs to have a Facebook account and a Facebook page, separate from your personal account. A business-related Facebook page is similar to a personal Facebook profile except that pages are

designed for organizations, brands, businesses, and public figures to share photos, stories, and events with the public.

If you do not have a Facebook account, you can create a new account and profile at http://www.facebook.com. After creating a profile, click on the "create a Facebook page" link. Follow the instructions and select the page category you would like to create; most physicians would select the "Company," "Organization," or "Institution" category. Next, follow the instructions to complete the registration.[8] Once your Facebook page is created, build an audience asking others to "like" your page. Start posting content and use hashtags in your posts to make them discoverable to others (ie, #fibroids #noscar #singlesitesurgery).[9]

One benefit to having a practice-based Facebook page is the automated visible analytics that come with the page, which are not available for personal profiles. When you write a post or upload a photo or video, Facebook provides the demographics of those engaged with your posts plus analytics on that post, including the number of people who viewed the post, clicked on a photo, and viewed the video for more than 3 seconds.

Develop a social media marketing strategy

There are several key factors to consider when planning a strategy. First, know the mission of your organization and the specific service, value, or benefit you would like to provide to the targeted community.[8]

Segment, target, and position (STP)

It is tempting to try to reach out to all women because your ObGyn practice entails prenatal care, family planning, and gynecologic surgery, but by narrowing your target audience, your campaign will be better focused. A very specific target audience can reduce the costs for "boosting" (paid promotion of your posts on Facebook to a chosen audience based on demographics, interests, and behaviors) your posts and improve your return on investment (ROI).

Create different marketing campaigns, but focus on one at a time. Decide on the ideal patient you want to serve in your practice. The more detailed and focused you are about the demographics and type of medical needs to be served, the better you can target this patient.[10]

Segment. Divide the communities you are considering into different segments. For instance, even though you may do obstetrics *and* gynecologic surgery, consider breaking up the campaign to focus on 1 specific group, such as those interested in fibroid management.

Target. Identify the kinds of communities where you might find this patient. For example, if you want to focus on laparoscopic hysterectomies or myomectomies, start looking on Facebook for groups, pages, or website discussion boards or blogs that discuss abnormal uterine bleeding or fibroids and follow those pages.

Also, think about what other characteristics are associated with these ideal patients. For example, you might narrow it down to perimenopausal women with fibroids. A potential targeted group could be 40- to 50-year-old women who participate in yoga or running who have concerns about fibroids interfering in their active lifestyle. Perhaps this type of patient would want a minimally invasive surgical approach. A holistic health activist might be interested in nonsurgical management of fibroids.

Position. Once you have identified the specific community to target, position your practice within the community with the value proposition you are offering. For example, as an ObGyn who is focused on surgery, your position might be that your practice will provide the best experience for those medical services, with specific counseling to patients about resuming their active lifestyle.

Get your potential patient to "raise her hand." In the campaign, you are not trying to convince everyone up front to schedule an appointment from one post. First, try to get people who may be interested in your service(s) to "raise their hands." Once your target market has expressed interest, either by their likes of your post, likes of your page, or other

FAST TRACK

Open a business Facebook page, compile an email list from those who like your postings, and send out useful information and updates on your practice

FAST TRACK

Develop an office policy for social media, supervise postings, ensure patient privacy, and obey copyright laws

engagement, reach out to them with links for more information, such as free fibroid surgery education materials located on your website. On your website, create an opt-in page asking them to register their email address; once you have a compiled email list, send out monthly newsletters on your practice.[11]

Understand that marketing is a process

Think of marketing as an overall process in which you are guiding potential patients to come to your office. Your campaign has several steps; recognize that just one post will not make a huge difference. Use Facebook analytics to measure cost per engagement to calculate your return on investment and the campaign's effectiveness, and revise as necessary.

Rather than just considering social media as a soap box to advertise your practice, break up the marketing process into 3 units: the before unit, the during unit, and the after unit.[11] The word "unit" denotes the service, benefit, or product you are providing.

The before unit refers to the initial marketing that identifies potential patients—initially getting them to raise their hands and ultimately building an audience. (Once a potential patient provides her email address, you can send her a monthly newsletter or updates about your practice to continue the engagement.) Statistics show that an ObGyn needs to have 7 contacts, on average, with a patient over 18 months to "penetrate" her consciousness in a given market.[12] Of course if there is an urgent or emergent need to see a physician, that timeline would be much shorter.

The during unit occurs when the patient comes to your practice and service is being provided. Since you know what she is coming for, you can create informational packets focused on her particular needs, perhaps about different management options for fibroids.

The after unit includes following up with the patient in some automated way. For those being treated for fibroids, it may be a reminder email that discusses the value of follow-up ultrasonography or the various kinds of surgical interventions for fibroids.

In order to continue your campaign, it is helpful to have a designated social media manager who will continue the social media posts and engagement.

When creating the posts, consider developing prescheduled assets (posts that are already produced with photos or links to articles), which can be done through Facebook or Hootsuite (http://www.hootsuite.com).

Manage the risks of social media interaction

There are risks associated with social media. Some things to consider are:

- **Policy.** Develop a policy for your practice; if you work for an institution, align your policy with the institution's.
- **Postings.** Supervise content being posted. Never allow social media to be placed by someone without supervision. Either you should do this or assign a manager to be accountable to check on social media interactions so that any inappropriate comments can be addressed immediately.
- **Privacy.** Never mention patients' private health information or use the platform to

publicly engage with a patient or future patient about their care. Do not post any references to patients or their photos without written consent.

- **Images.** Use photographs and other images properly: obtain releases and obey copyright laws.

Bottom line

Social media is a powerful platform. Combined with good marketing strategies, social media campaigns can have a significant impact on expanding your practice to offer the kind of medical services you want to provide.

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Premature birth after preeclampsia: $23.1M verdict

WHEN A WOMAN SAW HER OBGYN on August 16 at 24 weeks' gestation, test results showed proteinuria and high blood pressure (BP). The following day, she was hospitalized for a 24-hour urine test and BP evaluation supervised by an on-call ObGyn and her ObGyn. Test results confirmed preeclampsia. She was released from the hospital. A few days later, she was found to have continued high BP and increased proteinuria, and restricted fetal growth was detected. On August 29 at 26 weeks' gestation, the baby girl was born with severe cystic periventricular leukomalacia by emergency cesarean delivery. She cannot perform basic tasks and will need 24-hour care for the rest of her life.

PARENT'S CLAIM: The hospital staff and 2 ObGyns failed to timely diagnose and treat preeclampsia. The treating ObGyn neither prescribed medication to treat preeclampsia nor administered antenatal corticosteroids to enhance fetal lung and brain development, both of which should have been started on August 17. Hospital health care providers failed to transfer her to a Level III facility equipped to handle a premature birth of less than 33 weeks' gestation.

DEFENDANTS' DEFENSE: The hospital and ObGyn denied negligence.

VERDICT: Prior to trial, the mother settled with the on-call ObGyn for an undisclosed amount. A $23.15 million Florida verdict was returned, apportioning 70% liability to the treating ObGyn and 30% to the hospital.

Suture found in bladder after hysterectomy

A 40-YEAR-OLD WOMAN underwent a hysterectomy due to dysmenorrhea. Despite the presence of blood in the catheter bag after the procedure, the surgeon did not consult a urologist or perform a cystoscopy. Later, when the patient reported urinary retention, urinary leakage, and dyspareunia, a urologist performed a cystoscopy and discovered a suture in the bladder wall and a vesicovaginal fistula.

PATIENT'S CLAIM: During the procedure, the gynecologic surgeon inadvertently placed a suture in the bladder wall. The presence of blood in the Foley catheter required an immediate urology consult and cystoscopy, during which the presence of the errant suture would have been discovered. Repair surgery then would have prevented subsequent injuries.

PHYSICIAN'S DEFENSE: The surgeon used reasonable judgment, as there were explanations for the blood in the catheter due to a difficult catheter placement and lysis of bladder adhesions.

VERDICT: A Michigan defense verdict was returned.

Shoulder dystocia, paralysis: $950,000 settlement

DURING DELIVERY, shoulder dystocia was encountered. The ObGyn used maneuvers to release the shoulder and completed the delivery. The child has a brachial plexus injury. Despite nerve graft surgery, her right arm, shoulder, and hand are paralyzed.

PARENTS' CLAIM: The ObGyn failed to properly manage the delivery. Shoulder dystocia had been encountered during the delivery of a sibling, but the ObGyn failed to communicate the need for cesarean delivery in future pregnancies.

DEFENDANTS' DEFENSE: There was no negligence. The case settled during trial.

VERDICT: A $950,000 California settlement was reached with the hospital and ObGyn.

Bowel injury during tubal ligation

A 40-YEAR-OLD WOMAN underwent laparoscopic tubal ligation using cauterization at an outpatient surgery center. Two hours after the procedure, her BP began to drop. She was promptly transferred to a hospital and underwent emergency surgery that revealed a bowel injury. Part of the patient's small intestine was resected.

PATIENT'S CLAIM: The gynecologic surgeon committed a medical error when she injured the bowel during trocar insertion.

DEFENDANTS' DEFENSE: The bowel injury was a known complication of the surgery.

VERDICT: A Louisiana defense verdict was returned.

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

PHOTO: SHUTTERSTOCK

Colon injured twice: $1M settlement

A 59-YEAR-OLD WOMAN underwent laparoscopic total hysterectomy and salpingectomy. Her history included an umbilical hernia repair.

Two days after surgery, the patient experienced abdominal pain, chills, abdominal distention, and a foul-smelling discharge from her umbilical suture site. She went to the emergency department where a computed tomography scan revealed 2 injuries in the bowel. Emergency laparotomy included transverse colon resection and right colon colostomy with Hartmann's pouch. She wore an ostomy bag for 8 months. She developed an infection because of the colostomy and also required operations to resolve a bowel obstruction and repair incisional hernias.

PATIENT'S CLAIM: The gynecologic surgeon was negligent when performing the surgery. When he inserted the Veress needle and trocar through the patient's umbilicus, the transverse colon was injured twice with a 3-cm anterior tear and a 1-cm posterior laceration. The injuries were not discovered during the procedure. He should have been more careful knowing that she had undergone prior umbilical hernia surgery.

PHYSICIANS' DEFENSE: The case was settled before the trial began.

VERDICT: A $1 million Virginia settlement was reached.

Chronic pain after sling procedure: $2M verdict

A 63-YEAR-OLD WOMAN reported urinary incontinence to her gynecologist, who performed a transobturator midurethral sling procedure. After surgery, the patient experienced pelvic pain, urinary urgency, intermittent incontinence, and dyspareunia. She returned to the gynecologist twice. He performed a cystoscopy after the second visit but found nothing wrong.

The patient sought a second opinion. A gynecologic surgeon found a large mass in the patient's bladder consisting of a crystallized piece of tape that had been used to secure the sling supporting the bladder. The mass was removed and the patient reported that, although surgery alleviated many symptoms, she was not pain-free.

PATIENT'S CLAIM: The gynecologist negligently inserted the end of the sling through one wall of her bladder and failed to detect the malpositioning during surgery or later. He failed to diagnose and treat bladder stones that resulted from the sling's malpositioning. He failed to perform a cystoscopy when she first reported symptoms and improperly performed cystoscopy at the second visit.

DEFENDANTS' DEFENSE: There was no negligence on the part of the gynecologist. The patient did not report ongoing symptoms until 1 year after sling insertion.

VERDICT: A $2 million Pennsylvania verdict was returned.

Child has brachial plexus injury

A MOTHER WAS ADMITTED to the hospital shortly after her membranes broke. Meconium was detected but the fetal heart-rate (FHR) monitor results were normal. About 15 minutes after admission, she was seen by an attending ObGyn, who started oxytocin to induce labor. FHR monitoring results were acceptable throughout the day, and by midafternoon, the mother was ready to deliver. A fetal baseline heart rate of less than 110 bpm was detected as staff prepared for the delivery. Less than an hour later, the baby's head crowned and the ObGyn quickly identified shoulder dystocia. Nurses repositioned the mother, the baby rotated, and was delivered. Apgar scores were normal despite a shoulder injury.

PARENTS' CLAIM: The ObGyn caused the injury by using excessive force during delivery. After attempting gentle traction, the ObGyn should have changed strategies.

DEFENDANTS' DEFENSE: The ObGyn asserted that she used gentle traction that prevented twisting or stretching the baby's nerves. The birth was normal and she followed all protocols, resulting in the birth of a cognitively intact baby, as evidenced by the child's Apgar scores. The baby was large and labor and delivery went very quickly, both factors that could have led to the baby's injuries. The ObGyn's actions did not cause the injuries.

VERDICT: A Pennsylvania defense verdict was returned.

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Surgical catastrophe

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posttraumatic stress disorder occur at night. If you have trouble falling asleep or you wake up in the middle of the night with nightmares related to the event, attempt to regulate your body's sleep schedule. Seek professional help if needed.

4. **Avoid negative coping habits.** Sometimes people turn to alcohol, cigarettes, food, or drugs to cope. Although these strategies may help in the short term, they will do more harm than good over time.
5. **Enroll in activities that provide positive distraction.** While the mind focuses on the traumatic event (this is normal), you need to get busy with such positive distractions as sports, going to the movies, and engaging in outdoor activities. Do things that you enjoy.

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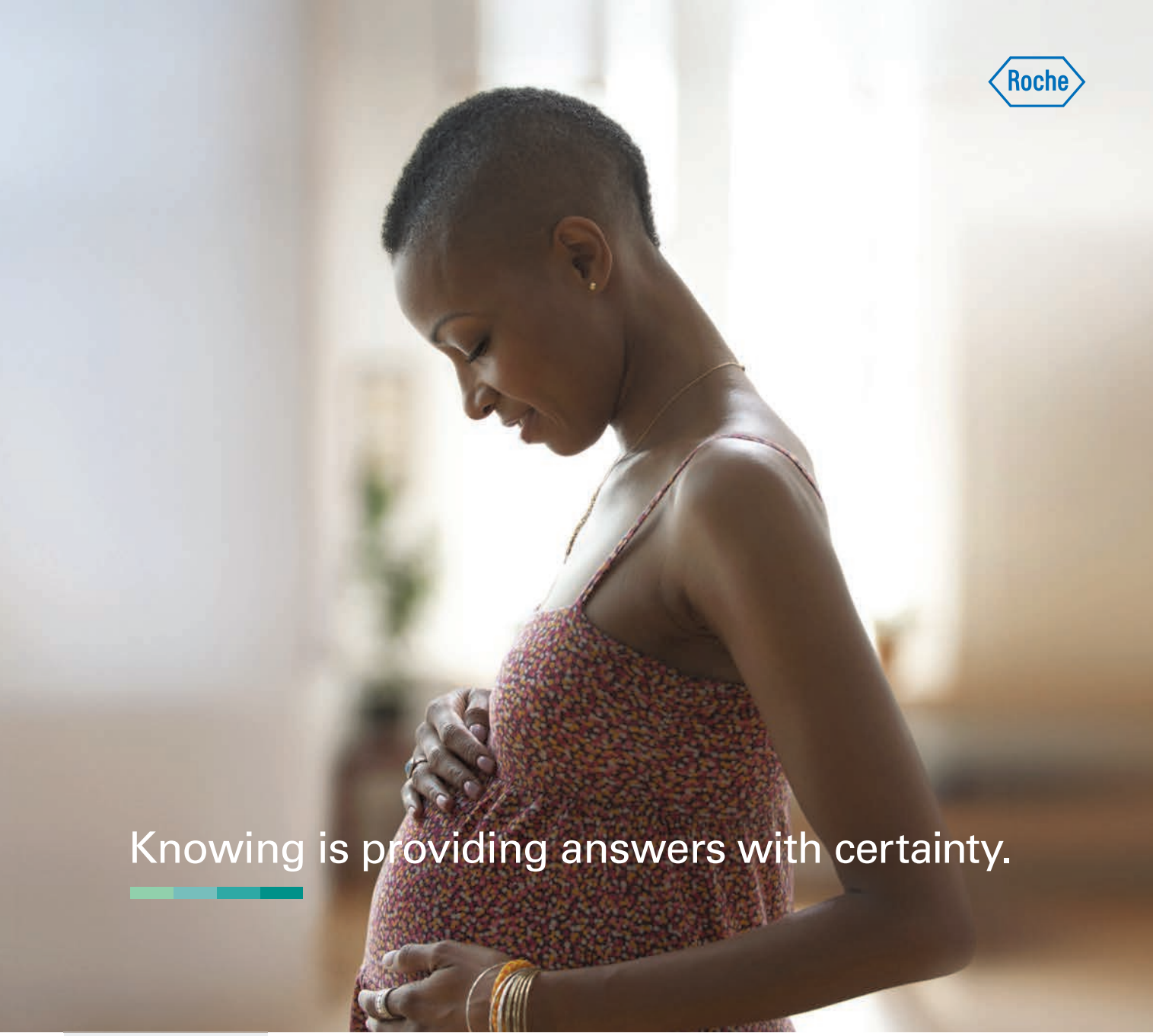

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*The combined false positive rate is for trisomies 21, 18 and 13.

[1]Stokowski R. et al. (2015). Prenatal Diagnosis: Clinical performance of non-invasive prenatal testing (NIPT) using targeted cell-free DNA analysis in maternal plasma with microarrays or next generation sequencing (NGS) is consistent across multiple controlled clinical studies.

The Harmony Prenatal Test was developed by Ariosa Diagnostics, a CLIA-certified laboratory. As with other lab-developed tests, it has not been cleared or approved by the FDA and is not available for sale as an IVD in the US. Noninvasive prenatal testing (NIPT) based on cell-free DNA analysis is not diagnostic; results should be confirmed by diagnostic testing.

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maternal and neonatal outcomes also were examined, including tachysystole, chorioamnionitis, meconium, postpartum hemorrhage, birth weight, maternal intensive care unit (ICU) admission, and neonatal ICU admission.

Women receiving concurrent Foley and oxytocin delivered sooner. Among nulliparous women, the overall rate of delivery within 24 hours of Foley catheter placement was 64% in the Foley with concurrent oxytocin group compared with 43% in those who received a Foley catheter alone followed by oxytocin ($P = .003$). The overall time to delivery was 5 hours less in nulliparous women who received combination cervical ripening compared with those who had a Foley catheter alone.

Similarly, multiparous women had an overall rate of delivery within 24 hours of 87% in the concurrent Foley and oxytocin group compared with 72% in women who received Foley catheter followed by oxytocin ($P = .022$).

Meanwhile, there were no statistically significant differences in mode of delivery between groups for either multiparous or nulliparous patients, and there were no differences in adverse maternal or neonatal outcomes between groups.

Study strengths and weaknesses

This well-designed, randomized control trial clearly demonstrated that the combination of Foley catheter and oxytocin for cervical ripening increases the rate of delivery within 24 hours compared with use of Foley catheter alone. This finding is consistent with those of 2 other large randomized trials in the past 2 years that similarly demonstrated reduced time to delivery when oxytocin infusion was used in combination with Foley catheter compared with Foley alone.[1,2]

Despite these findings, important questions remain regarding concurrent use of cervical ripening agents. The study by Schoen and colleagues does not address the other option for dual cervical ripening, namely, concurrent use of Foley catheter and misoprostol. Several large randomized trials using Foley catheter with vaginal or oral misoprostol demonstrated reduced time to delivery compared with using either method alone.[1,3,4] Only 1 randomized study has compared these 2 dual cervical ripening regimens head-to-head; that study demonstrated that the misoprostol and Foley combination significantly reduced time to delivery compared with combining Foley catheter and oxytocin together.[1]

Additionally, it is important to note that the study by Schoen and colleagues was not large enough to adequately evaluate potential safety risks with dual combination cervical ripening. More safety data are needed before combination cervical ripening methods can be recommended universally.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Combination cervical ripening, in which both a mechanical and a pharmacologic cervical ripening agent are used simultaneously, may be employed for induction of labor in both nulliparous and multiparous women with an unfavorable cervix. However, more safety data and comparative effectiveness studies of Foley catheter with misoprostol versus Foley catheter with oxytocin are needed before 1 combination regimen can be recommended over the other.

›› CHRISTINA A. PENFIELD, MD, MPH, AND DEBORAH A. WING, MD, MBA

FAST TRACK

Among nulliparous women, 64% of those who had a Foley catheter with concurrent oxytocin delivered within 24 hours of Foley placement, compared with 43% of those who had a Foley alone followed by oxytocin

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Should oxytocin and a Foley catheter be used concurrently for cervical ripening in induction of labor?

Yes. Administering oxytocin infusion with an intracervical Foley catheter in place significantly increased the proportion of women who delivered within 24 hours, as shown in a trial involving more than 320 nulliparous and multiparous women. Additional safety and comparative effectiveness data, however, are needed before this regimen can be recommended universally over other combination approaches.

FAST TRACK

Recent randomized trials suggest that using 2 cervical ripening agents together may be superior to 1 agent, challenging the long-standing belief that using 2 agents simultaneously has no benefit compared with 1 agent

Schoen CN, Grant G, Berghella V, Hoffman MK, Sciscione A. Intracervical Foley catheter with and without oxytocin for labor induction: a randomized controlled trial. Obstet Gynecol. 2017;129(6):1046–1053.

EXPERT COMMENTARY

›› **Christina A. Penfield, MD, MPH,** is Clinical Instructor and Maternal-Fetal Medicine Fellow, Department of Obstetrics and Gynecology, University of California, Irvine, School of Medicine.

›› **Deborah A. Wing, MD, MBA,** is Professor, Department of Obstetrics and Gynecology, University of California, Irvine, School of Medicine.

The concurrent use of mechanical and pharmacologic cervical ripening is an area of active interest. Combination methods typically involve placing a Foley catheter and simultaneously administering either prostaglandins or oxytocin. Despite the long-standing belief that using 2 cervical ripening agents simultaneously has no benefit compared with using only 1 cervical ripening agent, several recent large randomized trials are challenging this paradigm by suggesting that using 2 cervical ripening agents together may in fact be superior.

The authors report no financial relationships relevant to this article.

Details of the study

Schoen and colleagues conducted a randomized controlled trial that included 184 nulliparous and 139 multiparous women with an unfavorable cervix undergoing induction of labor after 24 weeks of gestation. All participants had a Foley catheter placed intracervically and then were randomly assigned to receive either concurrent oxytocin infusion within 60 minutes or no oxytocin until after Foley catheter expulsion or removal. Nulliparous and multiparous women were randomly assigned separately. Women with premature rupture of membranes and with 1 prior cesarean delivery were included in the trial, but women were excluded if they were in active labor, had suspected abruption, or had a nonreassuring fetal tracing.

The study was powered to detect a 20% increase in total delivery rate within 24 hours of Foley placement, which was the primary study outcome. Secondary induction outcomes of note included time to Foley expulsion, time to second stage, delivery within 12 hours, total time to delivery, duration of oxytocin use, and mode of delivery. Several

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PRODUCT UPDATE

COLPOSCOPY BRUSHES SHOW BETTER TISSUE YIELD

A new study from the University of California–Riverside and Aurora Diagnostics in Palm Beach, Florida, evaluated 10,000 colposcopy workups and found that the disposable **Histologics Soft-ECC** and **SoftBiopsy** curettes were superior in tissue yield and offered a lower risk of cross contamination than metal curettes.

The **Soft-ECC Endocervical Curette Tissue Collection System** is used to biopsy the endocervical canal during colposcopy or evaluation for abnormal uterine bleeding. It gently frictionally abrades and collects transepithelial tissue samples into the Kylon fabric. The **Soft-ECC-S** has a smaller pad for the short, shallow, or stenotic cervix.

During exocervical biopsy with the **SoftBiopsy Gynecological Biopsy Device,** the Kylon fabric hooks rake across the tissue plane dislodging and shearing tissue strips and fragments from just below the basement membrane to collect in the fabric.

Both products have tips that are snapped off at the scored handle and placed in a fixative vial for transport to the laboratory.

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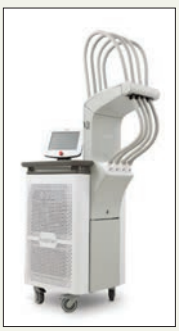

The **Cynosure** division of **Hologic** has just received US Food and Drug Administration (FDA) expanded clearance for **SculpSure** for noninvasive body contouring (lipolysis) of back, inner, and outer thighs. **SculpSure** is clinically proven to permanently eliminate fat cells and is already FDA-cleared to treat the abdomen and love handles (flanks).

According to **Hologic, SculpSure** uses a selective wavelength laser that precisely targets fat cells under the skin without affecting the skin's surface. The laser raises the temperature of body fat to disrupt and destroy these cells, which are naturally eliminated over time and do not return or regenerate. Hologic says that patients are able to achieve desired results, without downtime or surgery, through customized treatment plans, each lasting only 25 minutes. Results can be seen as quickly as 6 weeks; optimal results typically are seen at 12 weeks, they say.

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

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drchrono offers software platforms for medical offices, including electronic health records (EHR), practice management, medical billing, revenue cycle management (RCM), and health care application programming interface (API) tools for iPad, iPhone, and web. Products are available for small and large practice groups, urgent care centers, and specialties, including ObGyns. A patient can complete forms and schedule visits through the Patient Portal as well as receive educational materials through HIPAA-compliant messaging and face-to-face telemedicine.

drchrono says its cloud-based platform allows ObGyns to chart in seconds using customizable medical forms, medical speech-to-text, and photo/drawing tools. ObGyn-specific ICD10, Current Procedural Terminology, and E&M codes can autopopulate into forms. Prenatal flow sheets and other clinical forms can be sent to L&D, other providers, or billing departments using **drchrono**'s direct messaging integration with the local hospital EHR or e-Fax. Prenatal and blood testing, ultrasounds, paper charts, and photographs can be ordered, tracked, and shared with patients and providers.

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A nonmagnetic full dilator set is available for women who are trying to get pregnant and for women with pacemakers or defibrillators.

This product is not FDA approved, is not sold as a medical device, and is not intended to diagnose, treat, cure, or prevent any disease. Effectiveness varies, according to the manufacturer.

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