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Autoimmune disease

DR LOCKWOOD ON
How ob/gyns can de-stress
Dr. Lockwood was honored with a Lifetime Achievement Award at the Society for Maternal-Fetal Medicine’s 2017 Pregnancy Meeting.

Have a question for the Board? Send it to us at drlockwood@ubm.com

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University of South Florida
Tampa, FL

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Associate Professor of Obstetrics and Gynecology
Harvard Medical School
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Brigham and Women’s Hospital
Boston, MA

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Florida International University College of Medicine
Miami, FL

Joshua A. Copel, MD
Professor, Obstetrics, Gynecology, and Reproductive Sciences, and Pediatrics
Yale School of Medicine
New Haven, CT

Ilana Cass, MD
Vice Chair, Associate Clinical Professor, Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA

Steven J. Ory, MD
Professor of Obstetrics and Gynecology
Florida International University
Miami, FL

Christian Pettler, MD
Associate Professor, Maternal-Fetal Medicine, Department of Obstetrics, Gynecology and Reproductive Sciences
Yale School of Medicine
New Haven, CT

Sharon T. Phelan, MD
Professor, Department of Obstetrics and Gynecology
University of New Mexico
Albuquerque, NM

Joe Leigh Simpson, MD
Executive Associate Dean for Academic Affairs, Professor of Obstetrics and Gynecology, and Human and Molecular Genetics
Florida International University College of Medicine
Miami, FL

Founding Editor

Jonathan T. Queenan, MD
Professor and Chair Emeritus, Department of Obstetrics and Gynecology
Georgetown University School of Medicine
Washington, DC

Reprint Services
877-652-5295 ext. 121
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CONTENT

Sara Michael
VP, Content & Strategy

Miranda Hester
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Group Content Director

Nancy Bittke
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Aviva Belsky
Group Publisher

440-891-2613, renee.schuster@ubm.com

Judith Orvos
Editorial Consultant

Nicole Davis-Slocom
Art Director

Alison O’Connor
Associate Publisher

440-891-2742, maureen.cannon@ubm.com

Susan C. Olmstead
Editorial Director

SALES & MARKETING

Georgiann DeCenzo
Executive Vice President, Managing Director

732-346-3044, aviva.belsky@ubm.com

Maureen Cannon
Permissions/International Licensing
440-891-2742, maureen.cannon@ubm.com

440-891-2704, susan.olmstead@ubm.com

Joanna Shippoli
Account Manager, Recruitment Advertising
440-891-2615, joanna.shippoli@ubm.com

Renee Schuster
List Account Executive
440-891-2613, renee.schuster@ubm.com

Maureen Cannon
Permissions/International Licensing
440-891-2742, maureen.cannon@ubm.com

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In Figure 1 of the After a sexual assault: What to do in the January 2017 issue, the timing of Ulipristal and Plan B One-Step was reversed. Ulipristal should be provided within 120 hours and Plan B One-Step within 72 hours. The editors regret this error.
Introducing
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• Exceptional control and strength.
• No assembly required.
De-stressing Ob/Gyn

Best remedies for stress can start with your choices.

The January 2017 issue of Contemporary OB/GYN provided a window into the minds of some of our colleagues by reporting the results of our second annual Labor Force survey. About 670 of our readers responded. Seventy-five percent were 50 years or older, 68% were in private practice, 56% were male, and 40% had been in practice for more than 30 years. Thus, there is a likely selection bias toward more senior, male ob/gyns on the “exit ramp” of their careers rather than younger, female physicians on the “entry ramp and passing lane” of their careers. Those caveats notwithstanding, the results are revealing and concordant with my conversations with colleagues.

Among the most disturbing findings was that slightly more than half of the respondents would not choose ob/gyn as a career if they could start over. Reasons they cited included a lack of work-life balance (an ironically millennial-sounding complaint), increasing payer and regulatory burdens, the chronic stress and costs of our intractable professional liability insurance crisis, maintenance-of-certification requirements, and a combination of rising overhead and stagnant reimbursements. Anxiety also accrued around uncertainty posed by the Affordable Care Act,

Q. IF YOU COULD START OVER, WOULD YOU CHOOSE TO SPECIALIZE IN OB/GYN AGAIN?


51% of you said no

Now likely exacerbated by uncertainty over GOP repeal and reform efforts. But the primary leitmotif running through individual narratives was that the frantic pace imposed by seeing more and more patients in less and less time, coupled with time wasted on electronic health record (EHR) documentation and the burden of keeping up with accelerating increases in medical knowledge, was sucking the joy out of what should be the most joyful of professions.

Thankfully, these aren’t the good old days

If I had a dollar for every time I have heard an older colleague lament about how much easier medical practice was 30 years ago, I would be a wealthy man. The truth is we had a lot fewer tools and far less to know back then. When I was a third-year medical student in 1980, medical knowledge doubled about every 7 years. By 2020, it will double every 73 days. This fact alone may explain the enormity of the chal-
We face in preventing physician burnout. However, to better frame the problem, simply reflect on changes in our discipline since 1980. Back then in obstetrics we had no aneuploidy screening other than maternal age. Ultrasound was rudimentary, fetal surgery de minimis, and Rh isoimmunization difficult to treat and often fatal. Back then, premature labor was diagnosed based on contractions and cervical dilation, treated acutely with ethanol or ritodrine, and chronically with prolonged bed rest and oral tocolysis. However, our patients were younger, healthier, and thinner, and seldom required induction. In 1980, a national consensus conference was called to address the alarming rise in cesarean deliveries, which had tripled between 1968 and 1978, reaching an inconceivable 15.2% of live births. In 1980, aides were people who helped out and AIDS the disease had yet to be described or HIV discovered. No American obstetrician had ever heard of Zika. A great obstetrician was one who could discern late decelerations from background noise on a fetal heart rate tracing, and was adept at forceps and total breech extractions.

As for gynecology, in 1980 there had been no successful US in vitro fertilization pregnancies, no Da Vinci robots, and no tension-free vaginal tapes. Premarin and Provera therapy for symptomatic menopausal patients was common. Laparoscopy was in its infancy. Ectopic pregnancies were diagnosed by culdocentesis, signs and/or symptoms and managed by laparotomy. Breast cancers were treated with radical mastectomies. A great gynecologist was adept at colposcopy, cone biopsies, vaginal and abdominal hysterectomies, Marshall-Marchetti-Krantz procedures, and reading pathology slides. Then, subspecialists were relatively rare and knew a little more about a little less. And folks were often paid what they charged.

Today, obstetricians must be familiar with the nuances of cell-free fetal DNA testing using massive parallel sequencing, know common microdeletions, and appreciate the advantages of chromosomal microarray. The average ob/gyn’s ultrasound skills are vastly superior to those of 1980 maternal-fetal-medicine specialists, and modern machines have unimaginably improved resolution. Surgery for select fetuses with neural tube defects improves outcomes, and isoimmunization is both rare and easily treated. Premature labor is diagnosed with fetal fibronectin and/or sonographic cervical length determinations, tocolysis is limited to 48 hours, and prematurity potentially prevented with prophylactic progestins. However, our national cesarean delivery rate exceeds 30%, a reflection of an older, obese population with more comorbidities and indications for induction. Also linked to the cesarean epidemic is the decline in operative vaginal and breech deliveries, to the extent that many young ob/gyns will annually perform more cesarean hysterectomies for placenta accreta than forceps deliveries. HIV is a chronic disease and maternal-to-fetal transmission a rarity. Today, keeping up with the obstetrical literature takes herculean stamina, though Contemporary OB/GYN does help!

Today’s gynecologists must be well-versed on all forms of minimally invasive surgery with or without a robot. Ectopics are diagnosed far earlier using sensitive human chorionic gonadotropin assays, and high-resolution transvaginal ultrasound and medical treatment are now used in more than a third of cases. We must keep up with frequent changes in cervical cancer screening protocols. Publication of the Women’s Health Initiative (WHI) study results, linking hormone replacement therapy to increased cardiovascular disease when used in older women and also to breast cancers from the progestin component, has clearly had some public health benefit, but has also greatly complicated treatment of menopausal symptoms and osteoporosis. Breast cancer screening now has legal, not just professional liability ramifications, and breast-conserving surgical therapy is the norm. Across the discipline, subspecialists with deep knowledge of narrow fields have created as much competition with generalists as collaboration. And all of us must also be familiar with expanding lists of new drugs.

In short, everyday ob/gyn practice has evolved dramatically over the
Have you considered NEXPLANON for all appropriate patients?

Laura, 19
College Student

Maria, 27
Young Professional

Jen, 34
Mom

When getting pregnant isn't part of her 3-year plan, talk to her about NEXPLANON.

NEXPLANON must be removed by the end of the third year and may be replaced by a new NEXPLANON at the time of removal, if continued contraceptive protection is desired.

NEXPLANON is indicated for use by women to prevent pregnancy.

SELECTED SAFETY INFORMATION

Who is not appropriate for NEXPLANON

- NEXPLANON should not be used in women who have known or suspected pregnancy; current or past history of thrombosis or thromboembolic disorders; liver tumors, benign or malignant, or active liver disease; undiagnosed abnormal genital bleeding; known or suspected breast cancer, personal history of breast cancer, or other progestin-sensitive cancer, now or in the past; and allergic reaction to any of the components of NEXPLANON.

Complications of insertion and removal

- NEXPLANON should be inserted subdermally and be palpable after insertion. Palpate immediately after insertion to ensure proper placement. Undetected failure to insert the implant may lead to unintended pregnancy. Failure to remove the implant may result in continued effects of etonogestrel, such as compromised fertility, ectopic pregnancy, or persistence or occurrence of a drug-related adverse event.
- Insertion and removal-related complications may include pain, paresthesias, bleeding, hematoma, scarring, or infection. If NEXPLANON is inserted too deeply (intramuscular or in the fascia), neural or vascular injury may occur. Implant removal may be difficult or impossible if the implant is not inserted correctly, inserted too deeply, not palpable, encased in fibrous tissue, or has migrated. If at any time the implant cannot be palpated, it should be localized and removal is recommended.
- There have been postmarketing reports of implants located within the vessels of the arm and the pulmonary artery, which may be related to deep insertions or intravascular insertion. Endovascular or surgical procedures may be needed for removal.

NEXPLANON and pregnancy

- Be alert to the possibility of an ectopic pregnancy in women using NEXPLANON who become pregnant or complain of lower abdominal pain.
- Rule out pregnancy before inserting NEXPLANON.

Educate her about the risk of serious vascular events

- The use of combination hormonal contraceptives increases the risk of vascular events, including arterial events [stroke and myocardial infarction (MI)] or deep venous thrombotic events (venous thromboembolism, deep venous thrombosis (DVT), retinal vein thrombosis, and pulmonary embolism). Women with risk factors known to increase the risk of these events should be carefully assessed. Postmarketing reports in women using the nonradiopaque etonogestrel implant have included pulmonary emboli (some fatal), DVT, MI, and stroke. NEXPLANON should be removed if thrombosis occurs.
- Due to the risk of thromboembolism associated with pregnancy and immediately following delivery, NEXPLANON should not be used prior to 21 days postpartum.
NEXPLANON is a LARC* placed in the arm

*LARC=long-acting reversible contraceptive.

In a clinical trial, mean insertion time† was 27.9 ± 29.3 seconds

† From the removal of the protective cap of the applicator until retraction of the needle from the arm.

SELECTED SAFETY INFORMATION (continued)

• Women with a history of thromboembolic disorders should be made aware of the possibility of a recurrence. Consider removing the NEXPLANON implant in case of long-term immobilization due to surgery or illness.

Counsel her about changes in bleeding patterns

• Women are likely to have changes in their menstrual bleeding pattern with NEXPLANON, including changes in frequency, intensity, or duration. Abnormal bleeding should be evaluated as needed to exclude pathologic conditions or pregnancy. In clinical studies of the non-radiopaque etonogestrel implant, changes in bleeding pattern were the most common reason reported for stopping treatment (11.1%). Counsel women regarding potential changes they may experience.

Be aware of other serious complications, adverse reactions, and drug interactions

• Remove NEXPLANON if jaundice occurs.
• Remove NEXPLANON if blood pressure rises significantly and becomes uncontrolled.
• Prediabetic and diabetic women using NEXPLANON should be carefully monitored.
• Carefully observe women with a history of depressed mood. Consider removing NEXPLANON in patients who become significantly depressed.
• The most common adverse reactions (≥10%) reported in clinical trials were headache (24.9%), vaginitis (14.5%), weight increase (13.7%), acne (13.5%), breast pain (12.8%), abdominal pain (10.9%), and pharyngitis (10.5%).
• Drugs or herbal products that induce enzymes, including CYP3A4, may decrease the effectiveness of NEXPLANON.
• The efficacy of NEXPLANON in women weighing more than 130% of their ideal body weight has not been studied. Serum concentrations of etonogestrel are inversely related to body weight and decrease with time after implant insertion. Therefore, NEXPLANON may be less effective in overweight women.
• Counsel women to contact their health care provider immediately if, at any time, they are unable to palpate the implant.
• NEXPLANON does not protect against HIV or other STDs.

Before prescribing NEXPLANON, please read the adjacent Brief Summary of the Prescribing Information.
The proportion of 90-day intervals with these bleeding patterns are summarized in Table 2.

1. Complications of Insertion and Removal
NEXPLANON should be inserted subdermally so that it is palpable after insertion, and this should be confirmed by palpation. The subdermal insertion site may be tender or sore for a few days after insertion. Failure to confirm subdermal insertion may or may not be apparent unless it is palpated immediately after insertion. Undetected failure to insert the implant may lead to an unintended pregnancy. Complications related to insertion and removal procedures, such as pain, phlebitis, bleeding, hematoma, scarring or infection, may occur.

If NEXPLANON is inserted deeply (intramuscularly in the fascia), neural or vascular injury may occur. To reduce the risk of neural or vascular injury, NEXPLANON should be inserted at the site of the non-radiopaque upper arm about 3-4 inches (6-8 cm) from the biceps and medial epicondy on of the humerus. NEXPLANON should be inserted subdermally just under the skin avoiding the sulcus (groove) between the biceps and triceps muscles and the large blood vessels and nerves that lie there in the subcutaneous bundle deeper in the subcutaneous tissues. Deep insertions of NEXPLANON have been associated with diabetes due to neural injury. Migration of the implant from its subcutaneous or intramuscular site and introduction of neural or vascular injury if development at the insertion site, start suitable treatment. If the infection persists, the implant should be removed. Incomplete insertions or infections may lead to expulsion. Implant removal may be difficult or impossible if the implant is not inserted correctly. Insertion below the skin, encased in fibrous tissue, or has migrated.

There have been reports of migration of the implant within the arm from the insertion site, which may be related to deep insertion. There also have been postmarketing reports of implants located within the vessels of the arm and the pulmonary artery, which may be related to deep insertions or intravascular insertion. In cases where the implant has migrated to the pulmonary artery, endocarditis or pulmonary embolism may be evident. The implant should be removed if the patient develops complications.

Exploratory surgery without knowledge of the exact location of the implant is strongly discouraged. Removal of deep implants is required with caution in order to avoid injury or damage to the large blood vessels and nerves that lie there in the subcutaneous bundle deeper in the subcutaneous tissues. Deep insertions of NEXPLANON have been associated with neural injury (due to neural injury). Migration of the implant from its subcutaneous or intramuscular site and introduction of neural injury if development at the insertion site, start suitable treatment. If the infection persists, the implant should be removed. Incomplete insertions or infections may lead to expulsion. Implant removal may be difficult or impossible if the implant is not inserted correctly. Insertion below the skin, encased in fibrous tissue, or has migrated.

2. Changes in Menstrual Bleeding Patterns
After starting NEXPLANON, women are likely to have a change from their normal menstrual bleeding pattern. These may include changes in bleeding frequency (absent, less, more frequent or continuous), intensity (reduced or increased) or duration. In clinical trials of the non-radiopaque etonogestrel implant (NEXPLANON), bleeding patterns ranged from amenorrhea (1 in 5 women) to frequent and/or prolonged bleeding (1 in 5 women). The bleeding pattern experienced during the first three months of NEXPLANON use is broadly predictive of the future bleeding pattern for many women. Women should be counseled regarding the bleeding pattern changes they may experience so that they know what to expect. Abnormal bleeding should be evaluated as needed to exclude pathologic conditions or pregnancy. In clinical studies of the non-radiopaque etonogestrel implant, reports of changes in bleeding pattern were the most common reason women stopped treatment (11.1%). Irregular bleeding (10.8%) was the most common single most common reason women stopped treatment, while amenorrhea (0.3%) was cited less frequently. In these studies, women had an average of 17.7 days of bleeding or spotting every 90 days (based on 3,315 intervals of 90 days recorded by 780 patients). The percentages of NEXPLANON users having 0, 1-7, 8-21, or >21 days of spotting or bleeding over a 90-day interval while using the non-radiopaque etonogestrel implant are shown in Table 1.

Table 1: Percentages of Patients With 0, 1-7, 8-21, or >21 Days of Spotted or Bleeding Over a 90-Day Interval While Using the Non-Radiopaque Etonogestrel Implant (NEXPLANON)

<table>
<thead>
<tr>
<th>Total Days of Spotted or Bleeding</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Days</td>
<td>15%</td>
</tr>
<tr>
<td>1-7 Days</td>
<td>13%</td>
</tr>
<tr>
<td>8-21 Days</td>
<td>30%</td>
</tr>
<tr>
<td>&gt;21 Days</td>
<td>35%</td>
</tr>
</tbody>
</table>

Bleeding patterns observed with use of the non-radiopaque etonogestrel implant for up to 2 years, and the proportion of 90-day intervals with these bleeding patterns, are summarized in Table 2.

Table 2: Bleeding Patterns Using the Non-Radiopaque Etonogestrel Implant (NEXPLANON) During the First 2 Years of Use

<table>
<thead>
<tr>
<th>Bleeding Patterns</th>
<th>Definitions</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inefrequent</td>
<td>Less than three bleeding and/or spotting episodes in 90 days (excluding amenorrhea)</td>
<td>33.8</td>
</tr>
<tr>
<td>Amenorrhea</td>
<td>No bleeding and/or spotting in 90 days</td>
<td>22.2</td>
</tr>
<tr>
<td>Prolonged</td>
<td>Any bleeding and/or spotting episode lasting more than 14 days in 90 days</td>
<td>17.7</td>
</tr>
<tr>
<td>Frequent</td>
<td>More than 5 bleeding and/or spotting episodes in 90 days</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Based on 3315 recording periods of 90 days duration in 780 women, excluding the first 90 days after implant insertion

% = Percentage of 90-day intervals with this pattern

In case of undiagnosed, persistent, or recurrent abnormal vaginal bleeding, appropriate measures should be conducted to rule out malignancy.

3. Eclectic Pregnancies
As with all progestin-only contraceptive products, be alert to the possibility of an ectopic pregnancy among women using NEXPLANON who become pregnant or complain of lower abdominal pain. Although ectopic pregnancies are uncommon among women using NEXPLANON, a pregnancy that occurs in a woman using NEXPLANON may be more likely to be ectopic than a pregnancy occurring in a woman using no contraception.

4. Use with Breastfeeding
The use of combination hormonal contraceptives (progestogen plus estrogen) increases the risk of vascular events, including arterial events (strokes and myocardial infarctions) or deep venous thrombotic events (venous thromboembolism, deep venous thrombosis, retinal vein thrombosis, and pulmonary embolism). NEXPLANON is a progestin-only contraceptive. It is unknown whether this increased risk is applicable to etonogestrel alone. It is recommended, however, that women with risk factors known to increase the risk of venous and arterial thromboembolism be carefully assessed. There have been postmarketing reports of serious arterial and venous thromboembolic events, including cases of pulmonary emboli (some fatal), deep vein thrombosis, myocardial infarction, and strokes, in women using etonogestrel implants. NEXPLANON should be removed in the event of a thrombosis.

Due to the risk of thromboembolism associated with pregnancy and immediately following delivery, NEXPLANON should not be used prior to 21 days postpartum. Women with a history of thromboembolic disorders should use a non-hormonal contraceptive method of choice. Evidence for pelvic vein thrombosis is minimal if there is unexplained loss of vision, proptosis, diplopia, paresthesia, or retinal vascular lesions. Consider removal of the NEXPLANON implant in case of long-term immobilization due to surgery or illness.

5. Ovarian Cysts
If follicular development occurs, atresia of the follicle is sometimes delayed, and the follicle may continue to grow beyond the size it would attain in a normal cycle. Generally, these enlarged follicles disappear spontaneously. On rare occasion, surgery may be required.

6. Carcinoma of the Breast and Reproductive Organs
Women who currently have or have had breast cancer should not use hormonal contraception because breast cancer may be hormonally sensitive (see Contraindications). Some studies suggest that the use of progestin-only contraceptives might increase the incidence of breast cancer; however, other studies have not confirmed such findings. Some studies suggest that the use of combination hormonal contraceptives is associated with an increased risk in the risk of cervical cancer or intraepithelial neoplasia. However, there is controversy about the extent to which these findings are due to differences in sexual behavior and other factors. Women with a family history of breast cancer or who develop breast nodules should be carefully monitored.

7. Liver Disease
Disturbances of liver function may necessitate the discontinuation of hormonal contraceptive use until markers of liver function return to normal. Remove NEXPLANON if jaundice develops. Hepatic adenomas are associated with combination hormonal contraceptives use. An estimate of the attributable risk is 3.3 cases per 100,000 women taking combination hormonal contraceptives. It is not known whether this increased risk is applicable to etonogestrel alone. It is recommended, however, that women with risk factors known to increase the risk of venous and arterial thromboembolism be carefully assessed. There have been postmarketing reports of serious arterial and venous thromboembolic events, including cases of pulmonary emboli (some fatal), deep vein thrombosis, myocardial infarction, and strokes, in women using etonogestrel implants. NEXPLANON should be removed in the event of a thrombosis.

8. Weight Gain
In clinical studies, mean weight gain in U.S. non-radiopaque etonogestrel implant (NEXPLANON) users was 2.8 pounds after one year and 3.7 pounds after two years. How much of the weight gain was related to the non-radiopaque etonogestrel implant is unknown. In studies, 2.3% of the users reported weight gain as the reason for having the non-radiopaque etonogestrel implant removed.

9. Elevated Blood Pressure
Women with a history of hypertension-related diseases or renal disease should be discouraged from using hormonal contraception. For women with well-controlled hypertension, use of NEXPLANON can be considered. Women with hypertension using NEXPLANON should be closely monitored. If sustained hypertension develops during the use of NEXPLANON, or if a significant increase in blood pressure does not respond adequately to antihypertensive therapy, NEXPLANON should be removed.

10. Gallbladder Disease
Studies suggest a small increased relative risk of developing gallbladder disease among combination hormonal contraceptive users. It is not known whether a similar risk exists with progestin-only methods like NEXPLANON. The progestin in NEXPLANON may be poorly metabolized in women with liver impairment. Use of NEXPLANON in women with active liver disease or liver cancer is contraindicated (see Contraindications).

11. Carbohydrate and Lipid Metabolic Effects
Use of NEXPLANON may induce mild insulin resistance and small changes in glucose concentrations of unknown clinical significance. Carefully monitor prediabetic and diabetic women using NEXPLANON. Women who are being treated for hyperlipidemia should be followed closely if they elect to use NEXPLANON. Some progestins may elevate LDL levels and may render the control of hyperlipidemia more difficult.

12. Depressed Mood
Women with a history of depressed mood should be carefully observed. Consideration should be given to removing NEXPLANON in patients in whom significantly depressed.

13. Return to Ovulation
In clinical trials with the non-radiopaque etonogestrel implant (NEXPLANON), the etonogestrel level is decreased to menstrual levels by one week after removal of the implant. In addition, pregnancies were observed to occur as early as 7 to 14 days after removal. Therefore, a woman should re-start contraception immediately after removal of the implant if continued contraceptive protection is desired.
In clinical trials involving 942 women who were evaluated for safety, change in menstrual bleeding patterns (irregular menses) was the most common adverse reaction causing discontinuation of use of the non-contraceptive etonogestrel implant (IMPLANON®) (11.1% of women).

Adverse reactions that resulted in a rate of discontinuation of ≥1% are shown in Table 3.

Table 3: Adverse Reactions Leading to Discontinuation of Treatment in 1% or More of Subjects in Clinical Trials of the Non-Radiopaque Etonogestrel Implant (IMPLANON)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Studies</th>
<th>N = 942</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding Irregularities*</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td>Emotional Lability†</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Weight Increase</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>1.0%</td>
<td></td>
</tr>
</tbody>
</table>

*Includes “frequent”, “heavy”, “prolonged”, “spotting”, and other patterns of bleeding irregularity.
†Among US subjects (N=330), 6.1% experienced emotional lability that led to discontinuation.
‡Among US subjects (N=330), 2.4% experienced depression that led to discontinuation.

Other adverse reactions that were reported by at least 5% of subjects in the non-radiopaque etonogestrel implant clinical trials are listed in Table 4.

Table 4: Common Adverse Reactions Reported by <5% of Subjects in Clinical Trials With the Non-Radiopaque Etonogestrel Implant (IMPLANON)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Studies</th>
<th>N = 942</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>24.9%</td>
<td></td>
</tr>
<tr>
<td>Vaginitis</td>
<td>14.5%</td>
<td></td>
</tr>
<tr>
<td>Weight increase</td>
<td>13.7%</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>13.5%</td>
<td></td>
</tr>
<tr>
<td>Breast pain</td>
<td>12.8%</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10.9%</td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>10.5%</td>
<td></td>
</tr>
<tr>
<td>Leukorrhea</td>
<td>9.6%</td>
<td></td>
</tr>
<tr>
<td>Influenza-like symptoms</td>
<td>7.6%</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>7.2%</td>
<td></td>
</tr>
<tr>
<td>Dysmenorrhea</td>
<td>7.2%</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>6.8%</td>
<td></td>
</tr>
<tr>
<td>Emotional lability</td>
<td>6.5%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>6.4%</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>Nervousness</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>5.5%</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>5.4%</td>
<td></td>
</tr>
<tr>
<td>Insertion site pain</td>
<td>5.2%</td>
<td></td>
</tr>
</tbody>
</table>

In a clinical trial of NEXPLANON, in which investigators were asked to examine the implant site after insertion, implant site reactions were reported in 8.6% of women. Erythema was the most common implant site complication, reported during and/or shortly after insertion, occurring in 3.3% of subjects. Additionally, hematomas (3.0%), bruising (2.0%), pain (1.0%), and swelling (0.7%) were reported.

**Adverse Reactions**

1. **Drug-Laboratory Test Interactions**

   - Carbamazepine
   - Rifampin

   Some of these drugs or herbal products that induce enzymes, including CYP3A4, include:
   - Griseofulvin
   - Acyclovir
   - Phenytoin
   - Rifampin
   - St. John’s wort
   - Topiramate

   Changes in Plasma Concentrations of Etonogestrel Associated with Coadministered Drugs

   CYP3A4 inhibitors such as itraconazole or ketoconazole may increase plasma concentrations of etonogestrel.

2. **Decrease in Plasma Concentrations of Etonogestrel Associated with Coadministered Drugs**

   Changes in Plasma Concentrations of Coadministered Drugs

   Hormonal contraceptives may affect the metabolism of other drugs. Consequently, plasma concentrations of etonogestrel may either increase or decrease, depending on the coadministered drug.

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

**USE IN SPECIFIC POPULATIONS**

1. **Pediatric Use**

   - NEXPLANON is not indicated for use during pregnancy (see Contraindications).
   - Teratology studies have been performed in rats and rabbits using oral administration up to 390 and 790 times the human etonogestrel dose (based upon body surface, respectively), and revealed no evidence of fetal harm due to etonogestrel exposure. Studies have revealed no increased risk of birth defects in women who have used combination oral contraceptives before pregnancy or during early pregnancy. There is no evidence that NEXPLANON is different from that of combination oral contraceptives. NEXPLANON should be removed if maintaining a pregnancy.

2. **Nursing Mothers**

   - Based on limited clinical data, NEXPLANON may be used during breastfeeding after the fourth postpartum week. Use of NEXPLANON before the fourth postpartum week has not been studied. Small amounts of etonogestrel are excreted in breast milk. During the first months after insertion of NEXPLANON, when maternal blood levels of etonogestrel are highest, about 109 ng of etonogestrel may be ingested by the child per day based on an average daily milk ingestion of 658 mL. Based on daily milk ingestion of 150 mL/kg, the mean daily infant etonogestrel dose one month after insertion of the non-radiopaque etonogestrel implant (IMPLANON) is about 2.2% of the weight-adjusted maternal daily dose, or about 0.2% of the estimated absolute maternal daily dose. The health of breastfed infants whose mothers began using the non-radiopaque etonogestrel implant during the fourth to eighth week postpartum (n=38) was evaluated in a comparative study with infants of mothers using a non-hormonal IUD (n=33).
   - They were breastfed for a mean duration of 14 months and followed up to 36 months of age. No significant effects and no differences between the groups were observed on the physical and psychomotor development of these infants. No differences between groups in the production or quality of breast milk were detected. Healthcare providers should discuss both hormonal and non-hormonal contraceptive options, as steroids may not be the initial choice for these patients.

3. **Geriatric Use**

   - This product has not been studied in women over 65 years of age and is not indicated in this population.

4. **Hepatic Impairment**

   - No studies were conducted to evaluate the effect of hepatic disease on the disposition of NEXPLANON. The use of NEXPLANON in women with active liver disease is contraindicated (see Contraindications).

5. **Renal Impairment**

   - No studies were conducted to evaluate the effect of renal disease on the disposition of NEXPLANON.

6. **Overweight Women**

   - The effectiveness of the etonogestrel implant in women who weighed more than 130% of their ideal body weight has not been defined because such women were not studied in clinical trials. Serum concentrations of etonogestrel are inversely related to body weight and decrease with time after implant insertion. It is therefore possible that NEXPLANON may be less effective in overweight women, especially in the presence of other factors that decrease serum etonogestrel concentrations such as concomitant use of hepatic enzyme inducers.

**OVERDOSAGE**

Overdose may result if more than one implant is inserted. In case of suspected overdose, the implant should be removed.

**NONCLINICAL TOXICITY**

In a 24-month carcinogenicity study in rats with subdermal implants releasing 10 and 20 mcg etonogestrel per day (equal to approximately 1.8-3.6 times the systemic steady state exposure in women using NEXPLANON), no drug-related carcinogenic potential was observed. Etonogestrel was not genotoxic in the in vitro Ames/Salmonella reverse mutation assay, the chromosomal aberration assay in Chinese hamster ovary cells or in the in vivo micronucleus test. Fertility in rats returned after withdrawal from treatment.

**PATIENT COUNSELING INFORMATION**

1. Counsell women about the insertion of the NEXPLANON implant. Provide the woman with a copy of the Patient Labeling and ensure that she understands the information in the Patient Labeling before insertion and/or removal. A USER CARD and consent form are included in the packaging. Have the woman complete a consent form and retain it in your records. The USER CARD should be filled out and given to the woman after insertion of the NEXPLANON implant so that she will have a record of the location of the implant in the upper arm and when it should be removed.

2. Counsell women to contact their healthcare provider immediately if, at any time, they are unable to palpate the implant.

3. Counsell women that NEXPLANON does not protect against HIV or other STDs.

**DRUG INTERACTIONS**

Changes in contraceptive effectiveness associated with coadministered other products or drugs may decrease the plasma concentrations of progestins, and may decrease the effectiveness of NEXPLANON. In women on long-term treatment with hepatic enzyme inducing drugs, it is recommended to remove the implant and to advise a contraceptive method that is unaffected by the interacting drug.

**Manufactured for:** Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. Whitehouse Station, NJ 08889, USA.
past 4 decades. But with this progress the burden of keeping up with new discoveries, medications, devices, and surgical techniques is testing our limits. In addition, the profusion of much-needed, but voluminous, randomized trials, systematic reviews, and meta-analyses is causing constant evolution of evidenced-based practices and further straining our ability to keep pace with evolving practice demands.

have also participated in other CMS experiments such as bundled payments and accountable care organizations. Of course, all these programs are likely to be further jumbled by the new presidential administration, which is likely to head in an entirely different direction with a focus on consumer-driven health plans wherein patients pay more for medical services—pitting patients against their doctors without third-party insurance buffers. Then there are mounting state regulations and increasing legislation affecting medical practice. Finally, our hospitals are mandating clinical pathways, patient safety bundles, team training, structured handoffs, and operating room checklists. Individually, each item in this long list may have some merit, but collectively they add a gargantuan layer of complexity and stress to our professional lives.

But maybe the good old days weren’t so bad after all?
Perhaps the most frustrating aspect of our contemporary practice environment has been the steady flood of regulations over the past 4 decades. The 1980s saw charge-based provider fee-for-service payments evolve to hospital diagnosis-related group payments and practitioner current procedural terminology (CPT) code-based payments. These efforts to limit Medicare and Medicaid spending failed and the mid-1990s witnessed the chaotic introduction of managed care with gatekeepers and discounted fee-for-service payments. And over the past 2 decades both Republican and Democratic administrations have pushed through a cacophony of federal regulations designed to protect patients’ confidentiality, increase access to healthcare, reduce fraud and abuse, and restrain costs. Then there was all the time we spent completing the ICD-10 conversion. Many of us against their doctors without third-party insurance buffers. Then there are mounting state regulations and increasing legislation affecting medical practice. Finally, our hospitals are mandating clinical pathways, patient safety bundles, team training, structured handoffs, and operating room checklists. Individually, each item in this long list may have some merit, but collectively they add a gargantuan layer of complexity and stress to our professional lives.

They don’t train them like they used to!
A second leitmotif of the survey responses is that new residency graduates are less clinically skilled than they once were. There is some evidence to support this assertion. In a survey of practice readiness distributed to all fellowship directors in the 4 ob/gyn subspecialties, directors said that only 46% of first-year fellows were capable of independently performing an abdominal hysterectomy, only 34% a basic hysteroscopy, and a frightening 20% a vaginal hysterectomy. In a similar survey, half of gynecological oncologists reported that incoming fellows could not independently perform a hysterectomy. In a 2007 study, 60% of fourth-year ob/gyn residents reported performing fewer than 20 forceps deliveries during their residency. A number of factors may be responsible for these grim statistics. First, residents are exposed to fewer hysterectomies; in the US between 2002 and 2010, there was a 36.4% decrease in hysterectomies. Implementation of the 80-hour work week regulations and competition with subspecialty fellows may also reduce available surgeries. Finally, the sheer breadth and depth of medical knowledge that must be crammed into 4 years of training may be crowding out core clinical experiences. Today, residents must learn pretty much everything we did in the 1980s plus the vast amount of knowledge cited above that we absorbed over the past 35 years! In other words, residents and young ob/gyns need to know far more than we did in the good old days.

Preventing burn out
All of us, young and old, face the same frenetic pace of patient care and keeping up with new medical knowledge. We all face loss of autonomy from mounting administrative and regulatory burdens, as well as time and financial pressures, the chronic stress of professional liability, and uncertainty about future federal healthcare policies. And at some point we need to ask when these stressors will exceed our ability to adapt, accommodate, and avoid burnout. Burnout occurs when there
is a pervasive sense of emotional exhaustion, depersonalization, and lack of accomplishment. Other manifestations of physician distress include substance abuse, depression, disillusionment, and divorce. Burnout has been linked to an increase in suicidal ideation among medical students. A Medscape Lifestyle Report survey reported that in 2015, 46% of US physicians on the front lines of patient care reported burnout, compared with 40% just 2 years earlier. These numbers are consistent with other studies. In the “happiness at work” metric, ob/gyns scored in the middle of specialties between happy dermatologists and unhappy internists; however, 10% of ob/gyns reported having the highest severity scores for burnout. As with the medical profession in general, female ob/gyns reported a higher prevalence of burnout (55%) than males (42%). Perhaps most concerning, higher rates of burnout were reported in younger physicians, with 53% of ob/gyns ≤ 35 years reporting this symptom. This finding suggests that our survey may not be so biased after all.

**Short-term solutions**

Attempting to implement strategies for reducing physician burnout is difficult. Exercise and good nutrition are tough when you are working 80 hours a week. Taking enough vacation time is also difficult if you are facing declining reimbursements and increased overhead. A rich spiritual life helps, but religion isn’t a pill you can take.

**Long-term solutions**

It is time for our professional organizations to re-examine ob/gyn residency training. Should we track all rising fourth-year residents through either a 2-year subspecialty fellowship or 2 more years of primary care and general ob/gyn surgical training? Similarly, it is past time for a rigorous, empirical, specialty-specific reassessment of the 80-hour resident work week. We should also work through our professional societies and their political action committees to eliminate ineffective, non-evidenced-based and excessive federal and state regulations. Start with EHR Meaningful Use regulations. The government should conduct a definitive study of the public health impact of the widespread introduction of EHRs. If there is no benefit, their use should be curtailed or they should be redesigned to reduce documentation burdens. If there is evidence of benefit, government and commercial payers should reimburse the costs of their use (eg, the 2–3 hours a day busy clinicians waste typing and clicking) or pay the costs of scribes. Finally, in light of the convergence of a Republican Congress, Executive Branch, and Supreme Court, let’s implement true professional liability insurance reform.

**Take-home message**

A confluence of factors has conspired to exert unique stress on ob/gyns. The situation has been exacerbated by an outdated graduate medical education system and partisan political chaos to create a toxic stew that promotes physician burnout and distress. Individuals can take steps to restore their enthusiasm, engagement, and energy for our great profession, but substantial reforms of physician training, a new work-flow model, and reform of our regulatory and payment systems are also needed.

**Dr Lockwood’s Take**

**PREVENT BURNOUT**

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**6 SHORT-TERM SOLUTIONS TO DE-STRESS**

1. Do a gut check—Are you clinically depressed? Is your marriage in trouble? If so, get professional help.
2. Since substance abuse is associated with burnout, ask yourself (and maybe family and friends) if you have a substance abuse problem; if so, get help.
3. Can you work a little less without dire financial consequences? If so, lessen your work load; if not, consider changing jobs. You can’t adjust the wind but you can trim your sails.
4. Does your hospital and practice culture inspire creativity, collaboration, teamwork, patient safety, and the elimination of non-value-added busywork? If not, either lead a change in the culture (ie, be “the change you wish to see in the world”) or move to a practice setting that does all those things.
5. Do you have a hobby? If not, get one, STAT—preferably a year-round one.
6. Finally, be part of your community, whether it’s at church, a civic or community organization, a professional society, etc.
Cervical pessaries and preterm birth prevention

Placing a cervical pessary may not be enough to prevent preterm birth (PTB), according to results of a multicenter randomized controlled trial presented at the 37th annual Pregnancy Meeting for the Society for Maternal-Fetal Medicine, in Las Vegas, Nevada.

The researchers included asymptomatic women with singleton gestations with a transvaginal ultrasound (TVU) cervical length (CL) ≤ 25 mm at 18th to 23rd weeks and no prior PTB. The women were randomly assigned to receive the Bioteque cup pessary or no pessary and the pessaries were inserted by maternal-fetal medicine staff trained in proper placement. Randomization was stratified by CL (≤ 20 mm or >20-25 mm) and study site. Any women with a TV CL ≤ 20 mm were recommended for treatment with vaginal progesterone. Analysis was by intention-to-treat and the researchers required a total sample size of 242.

Of a total of 17,388 screened for TVU CL, 446 (2.6%) were found to have a TVI CL ≤ 25 mm. Three hundred ninety-four (88.3%) met the eligibility criteria and 122 (31.0%) agreed to be randomized. When the study was submitted for the meeting, 111 of the women had delivered: 56 in the pessary and 55 in the no pessary group. Demographic characteristics were similar across both groups and no significant differences were seen between the pessary and no pessary group in the rates of PTB < 37 weeks, PTB < 34 weeks, PTB < 28 weeks, gestational age at delivery, birth weight, and composite neonatal outcome.

The investigators concluded that treatment with a cervical pessary did not appear to prevent PTB in women with a singleton gestation and a TVU CL ≤ 25 mm at 18th to 23rd weeks. The study recruitment was halted before the researchers were able to meet their enrollment goal, but they state that the findings are similar to other recent studies that have also found pessaries to be ineffective.


Is inadvertent HPV vaccination in pregnancy safe?

Inadvertently receiving a dose of the quadrivalent human papillomavirus vaccine (4vHPV) may not be a cause for adverse pregnancy outcomes, according to a retrospective, observational cohort study presented at the 37th annual Pregnancy Meeting for the Society for Maternal-Fetal Medicine in Las Vegas, Nevada.

FINDINGS ARE SIMILAR TO OTHER RECENT STUDIES THAT HAVE ALSO FOUND PESSARIES TO BE INEFFECTIVE.
You see recovery. Your patients may see OINV.

Opioid-Induced Nausea and Vomiting

Opioids can trigger nausea and vomiting in any patient, but the expression and severity is patient-specific.

Is OINV disrupting more recoveries than you realize?


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learn more at KnowOINV.com
The researchers used administrative and healthcare data from the Vaccine Safety Datalink to look at a cohort of insured women aged 11 to 27 with singleton pregnancies that ended in a live birth between January 2007 and September 2013. Women who received the 4vHPV either during pregnancy or in the peri-conception period were classified as exposed. Controls were women with singleton pregnancies and a live birth during the same period who had received the 4vHPV vaccine in the 4 to 18 months prior to the start of pregnancy.

Risks of major structural birth defects, chorioamnionitis, small for gestational age birth, hypertensive disorders of pregnancy, gestational diabetes, and preterm birth (<37 weeks’ gestation) were evaluated. Adjusted relative risk tied to receiving the 4vHPV vaccine pregnancy, the peri-conception period, and the risks for both periods combined were evaluated using a generalized estimating equation method.

The researchers found 720 women who received the 4vHPV vaccine peri-conception and 638 who had received the vaccine during pregnancy with 8166 women with distal 4vHPV exposures. Overall, vaccination with 4vHPV during the peri-conception period and pregnancy was not associated with an increased risk of adverse obstetrical events such as gestational diabetes (peri-conception adjusted risk ratio [aRR] 1.06, 95% confidence interval [CI] [1.02]; during pregnancy aRR .98 [.67 – 1.4]; combined period aRR 1.0 [.77 – 1.3]); birth outcomes like preterm birth (peri-conception aRR .93 [.69 – 1.2]; during pregnancy aRR .97 [.72 – 1.3]; combined period aRR .97 [.79 – 1.2]); and major structural birth defects (peri-conception aRR .49 [.49 – 1.8]; during pregnancy aRR .91 [.46 – 1.8]; combined period aRR .96 [.59 – 1.6]).

The researchers concluded that inadvertent 4vHPV vaccine administration is not linked to adverse outcomes for either mother or infant.


### Brain volume, microcephaly on US associated with Zika

Results of a study by Colombian investigators underscore the correlation between decreased brain volume on fetal magnetic resonance imaging (MRI) and ultrasound-detected microcephaly in Zika-exposed fetuses. The findings were presented at the 37th Annual Pregnancy Meeting of the Society for Maternal-Fetal Medicine, held in Las Vegas.

The goal of the prospective cohort study was to assess fetal brain findings and volumetric composition with MRI in fetuses with confirmed Zika virus from the current outbreak in Barranquilla, Colombia. Among 214 pregnant women with Zika exposure, 13 fetuses were found on ultrasound to have abnormal brain findings such as microcephaly, ventriculomegaly, callosal dysgenesis, calcifications, and cortical anomalies. Seven women who were Zika-positive received fetal MRI at 29±4.4 weeks and were gestational age matched to 7 healthy controls at 29.87±4.61 weeks.

Total brain volume in the Zika-infected fetuses differed significantly from that in controls (9422.42±2169.11 versus 20529.7±7049.95; P<0.001) as did total intracranial volume (16390.42±3690.41 versus 35593.42±12281.71; P<0.01. No significant difference was seen in ventricular volume, brainstem volume, or cerebellar volume. The ratio of cerebrospinal fluid to supratentorial brain parenchyma was higher in Zika-affected fetuses (1.36±0.20 versus 0.99±0.16; P<0.01), suggesting microcephaly.


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READ ABOUT USPSTF reaffirms benefit of folic acid supplementation ON PAGE 44
Gastroschisis
Prenatal diagnosis and management

With incidence of this birth defect on the rise, ob/gyns need to understand how best to spot and deal with it.

by JOSHUA A. COPEL, MD, AND KATHERINE H CAMPBELL, MD, MPH

Case
A 20-year-old gravida 1 presented for a targeted anatomy ultrasound in the setting of an elevated maternal serum alpha fetoprotein (MSAFP) (7.14 multiples of the median [MoM]) obtained from routine prenatal screening. Transabdominal ultrasound revealed a full-thickness abdominal wall defect to the right of the umbilical cord insertion with herniation of abdominal contents. Free-floating loops of bowel were seen in the amniotic fluid without evidence of a covering membrane. The patient underwent serial ultrasounds to assess fetal growth and well-being. At 38 weeks’ gestation, fetal testing revealed a biophysical profile (BPP) that was 4/10 (2 points for fluid and fetal breathing). The patient was subsequently admitted to labor and delivery for repeat fetal testing and ultimately induction. The patient proceeded to have an uncomplicated vaginal delivery. At delivery, the lower half of the neonate’s body was placed in a sterile plastic bag to protect the exposed fetal bowel and promptly handed off to the waiting pediatricians. The neonate underwent a successful reduction of gastroschisis with a silastic silo and subsequent bioclosure of the defect and was discharged from the neonatal intensive care unit at 6 weeks of age.

Definition
The term gastroschisis is derived from the Greek words “gastro,” meaning stomach, and “schism,” meaning cleft. The condition is described as a full-thickness paraumbilical defect in the abdominal wall.1 In the majority of cases, this defect lies to the right of a normally inserted umbilical cord. Abdominal wall defects are usually small (<4 cm), however, their presence invariably leads to herniation of the fetal mid gut (ileum and jejunum) (Figure 1A). The intestinal loops float freely in the amniotic fluid and, by definition, are not covered by peritoneal membrane (Figure 1B). Additional organs

With gastroschisis, the abdominal wall defect is almost always located to the right of the cord insertion.

The recommended mode of delivery is vaginal because there is no evidence that cesarean improves the outcome in uncompromised gastroschisis.

Neither author has a conflict of interest to report in respect to the content of this article.
can herniate including the stomach, liver, spleen, and the genitourinary tract, but that is not common. Fetal assessment with ultrasound after the first trimester reveals free-floating loops of bowel with a "cauliflower-like" appearance in the setting of a normal umbilical cord insertion (Figure 2). Differentiating between gastroschisis and omphalocele is critical. By definition, omphalocele is a ventral wall defect that results in midline herniation of abdominal viscera into the base of the umbilical cord. Prior to the 1950s, gastroschisis was considered a variant of omphalocele. Now, however, the differing pathophysologies, unique risk factors, and different perinatal outcomes of the 2 conditions are appreciated.

**Epidemiology and risk factors**

Worldwide, incidence of gastroschisis has increased over the past 2–3 decades for reasons that are not well understood. Recent data from the Centers for Disease Control and Prevention have shown a 30% increase in incidence in US cases from 3.6 to 4.9 per 10,000 live births when comparing 1995–2005 with 2006–2012. In a multinational study that examined 25 birth defect registries, a significant temporal increase in gastroschisis incidence was also observed, while no similar trend was seen for 36 other malformations examined.

Young maternal age and low maternal body mass index have long been recognized as risk factors for gastroschisis, with rates as much as 7-fold higher in women younger than age 20. Due to the temporal trend of increasing disease incidence combined with these risk factors, epidemiologists have proposed various environmental factors as possible links to the underlying etiology. However, many of the findings have shown only weak associations, including infection, nutrition, medication use, and tobacco exposure. Young maternal age continues to be the single strongest risk factor for fetal gastroschisis.

As opposed to omphalocele, gastroschisis is less commonly associated with chromosomal abnormalities or additional birth defects. In an international population-based study, 14% of gastroschisis cases were associated with other birth defects, central nervous system anomalies being the most common, and 1.2% of gastroschisis cases were associated with chromosomal anomalies. Omphalocele, in contrast, is commonly associated with additional structural anomalies (60%–70%) and chromosomal abnormalities (15%–20%).

**Etiology**

Understanding the development of gastroschisis requires appreciation of normal embryonic development of the midgut, abdominal wall, and umbilical cord. As the embryo develops, the ventral body wall closes by 7 weeks’
METHYLERGONOVINE MALEATE TABLETS

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

INDICATIONS AND USAGES
Methylergonovine Maleate is a semi-synthetic ergot alkaloid used for the prevention and control of postpartum hemorrhage. It is used following delivery of placenta, for routine management of uterine atony, hemorrhage, and subinvolution of the uterus as well as for control of uterine hemorrhage in the second stage of labor following delivery of the anterior shoulder.

CONTRAINDICATIONS
Hypertension, toxemia, pregnancy, and hypersensitivity are contraindications to Methylergonovine Maleate Tablets.

WARNINGS

Methylergonovine Maleate Tablets, USP may produce coronary artery disease or risk factors for coronary artery disease (e.g., smoking, obesity, diabetes, high cholesterol) may be more susceptible to developing myocardial ischemia and infarction associated with methylergonovine-induced vasospasm.

Medication Errors: Inadvertent administration of Methylergonovine Maleate Tablets, USP to newborn infants has been reported. In these cases of

Breast-Feeding: Mothers should not breast-feed during treatment with Methylergonovine Maleate Tablets, USP. Milk secreted during this period should be discarded. Methylergonovine Maleate Tablets, USP may also reduce the yield of breast milk. Mothers should wait at least 12 hours after administration of the last dose of Methylergonovine Maleate Tablets, USP before initiating or resuming breast-feeding.

Coronary Artery Disease: Patients with coronary artery disease or risk factors for coronary artery disease (e.g., smoking, obesity, diabetes, high cholesterol) may be more susceptible to developing myocardial ischemia and infarction associated with methylergonovine-induced vasospasm.

Confidence From Hospital To Home
inadvertent neonatal exposure, symptoms such as respiratory depression, convulsions, cyanosis, and oliguria have been reported. Usual treatment is symptomatic. However, in severe cases, respiratory and cardiovascular support is required. Methylergonovine Maleate Tablets, USP has been administered instead of vitamin K and Hepatitis B vaccine, medications which are routinely administered to the newborn. Due to the potential for accidental neonatal exposure, methylergonovine maleate should be stored separately from medications intended for neonatal administration.

PRECAUTIONS

General: Caution should be exercised in the presence of sepsis, obliterative vascular disease. Also use with caution during the second stage of labor. The necessity for manual removal of a retained placenta should occur only rarely with proper technique and adequate allowance of time for its spontaneous separation.

Drug Interactions

CYP3A4 Inhibitors (e.g., Macrolide Antibiotics and Protease Inhibitors): There have been rare reports of serious adverse events in connection with the coadministration of certain ergot alkaloid drugs (e.g., dicyclomamine and erogotamine) and potent CYP3A4 inhibitors, resulting in vasospasm leading to cerebral ischemia and/or ischemia of the extremities. Although there have been no reports of such interactions with methylergonovine alone, potent CYP3A4 inhibitors should not be coadministered with methylergonovine. Examples of some of the more potent CYP3A4 inhibitors include macrolide antibiotics (e.g., erythromycin, troleandomycin, clarithromycin), HIV protease or reverse transcriptase inhibitors (e.g., ritonavir, indinavir, nelfinavir, delavirdine) or azole antifungals (e.g., ketoconazole, itraconazole, voriconazole). Less potent CYP3A4 inhibitors should be administered with caution. Less potent inhibitors include saquinavir, nefazodone, fluconazole, dihydroergotamine and ergotamine) and potent CYP3A4 inhibitors, resulting in vasospasm leading to cerebral ischemia and/or ischemia of the extremities. However, recovery occurred in all but one case following a period of respiratory depression, hypothermia, hypertonicity with jerking movements, and convulsions. Also, several children 1-3 years of age have accidentally ingested up to 10 tablets (2 mg) with no apparent ill effects. A postpartum patient took 4 tablets at one time in error and reported paresthesias and clamminess as her only symptoms.

CYP3A4 Inducers: Drugs (e.g. nevirapine, rifampin) that are strong inducers of CYP3A4 are likely to decrease the pharmacological action of Methylergonovine Maleate Tablets, USP.

Beta-Blockers: Caution should be exercised when Methylergonovine Maleate Tablets, USP is used concurrently with beta-blockers. Concomitant administration with beta-blockers may enhance the vasoconstrictive action of ergot alkaloids.

Anesthetics: Anesthetics like halothane and methoxyfluran may reduce the oxytocic potency of Methylergonovine Maleate Tablets, USP.

Glyceryl Trinitrate and Other Antianginal Drugs: Methylergonovine maleate produces vasoconstriction and can be expected to reduce the effect of glyceryl trinitrate and other antianginal drugs. No pharmacokinetic interactions involving other cytochrome P450 isozymes are known. Caution should be exercised when methylergonovine maleate is used concurrently with other vasoconstrictors, ergot alkaloids, or progestins.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No long-term studies have been performed in animals to evaluate carcinogenic potential. The effect of the drug on mutagenesis or fertility has not been determined.

Pregnancy: Category C: Animal reproductive studies have not been conducted with methylergonovine maleate. It is also not known whether methylergonovine maleate can cause fetal harm or can affect reproductive capacity. Use of methylergonovine maleate is contraindicated during pregnancy because of its uterotonic effects. (See INDICATIONS AND USAGE).

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

Geriatric Use: Clinical studies of methylergonovine maleate did not include sufficient number of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

The most common adverse reaction is hypertension associated in several cases with seizure and/or headache. Hypotension has also been reported. Abdominal pain (caused by uterine contractions), nausea and vomiting have occurred occasionally. Rarely observed reactions have included: acute myocardial infarction, transient chest pain, vasocoinstriaction, vasospasm, coronary arterial spasm, bradycardia, tachycardia, dyspnea, hematuria, thrombophlebitis, water intoxication, hallucinations, leg cramps, dizziness, tinnitus, nasal congestion, diarrhea, diaphoresis, palpitation, rash, and foul taste. There have been rare isolated reports of anaphylaxis, without a proven causal relationship to the drug product.

Nervous System Disorders: Cerebrovascular accident, paraesthesia.

Cardiac Disorders: Ventricular fibrillation, ventricular tachycardia, angina pectoris, atrioventricular block.

DRUG ABUSE AND DEPENDENCE

Methylergonovine maleate has not been associated with drug abuse or dependence of either a physical or psychological nature.

OVERDOSAGE

Symptoms of acute overdose may include: nausea, vomiting, abdominal pain, numbness, tingling of the extremities, rise in blood pressure, in severe cases followed by hypotension, respiratory depression, hypothermia, convulsions, and coma. Because reports of overdose with methylergonovine maleate are infrequent, the lethal dose in humans has not been established. The oral LD50 (in mg/kg) for the mouse is 187, the rat 93, and the rabbit 4.5. Several cases of accidental methylergonovine maleate injection in newborn infants have been reported, and in such cases 0.2 mg represents an overdose of great magnitude. However, recovery occurred in all but one case following a period of respiratory depression, hypothermia, hypertonicity with jerking movements, and convulsions.

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gestation (35 days post conception). At that time, midgut growth is rapid and the expanding intestines herniate into the umbilical cord soon after abdominal wall closure. The midgut subsequently returns to the abdominal cavity by 11–12 weeks’ gestation\(^9\) (Figure 3a, 3b).

Several hypotheses involve mechanisms that could lead to the development of fetal gastroschisis, all of which include defective formation (malformation) or disruption of the body wall. A well-known hypothesis involves infarction and necrosis of the body wall near the base of the umbilical cord due to disruption of the right omphalomesenteric (vitelline or yolk sac) artery.\(^{10,11}\) The vascular pathogenesis proposal prompted research into the culpability of various vasoactive substances including cocaine, tobacco, and common over-the-counter decongestants. However, no consistent association has been shown between early pregnancy exposure to these substances and subsequent development of gastroschisis.\(^5,6\)

Another hypothesis proposes failure of abdominal body folding impeding the merging of the yolk sac with the body stalk. With embryonic maturation, the intestinal loop attached to the vitelline duct herniates through the defect and into the amniotic cavity instead of undergoing the anticipated transient physiological gut herniation into the umbilical cord.\(^{12}\) A third mechanism proposes that the yolk sac and related vitelline structures fail to be incorporated into the umbilical stalk. This failure leads to persistence of the vitelline duct and yolk sac outside the main body stalk and abdominal wall as the abdominal folds close normally. In this scenario, the developing midgut has 2 areas of egress at the time of physiological gut herniation, leading to abnormal herniation of the expanding midgut into the vitelline duct and amniotic cavity.\(^{10}\)

**Diagnosis and fetal development**

Prior to widespread use of routine early fetal ultrasound assessment, abnormal MSAFP was often the first indication that a birth defect might be present. Elevated MSAFP is seen in virtually all cases of fetal gastroschisis and can be fairly high with median MSAFP MoMs from 7.0–9.4 MoMs, which are higher than seen with fetal omphalocele (median MSAFP 4.2 MoMs).\(^{13}\)

Most cases of gastroschisis are diagnosed by ultrasound. Correct identification of gastroschisis has improved as technological advances have improved the clarity of ultrasound images and interpretation skills have developed. Older population studies show detection rates of approximately 85%, while newer population studies show rates of approximately 97.5%\(^4,14\).

Transabdominal ultrasound assessment reveals loops of fetal bowel in the amniotic cavity which are free-floating and not covered by a membrane. Closer examination of the umbilical cord insertion reveals a normally inserted umbilical cord with a small abdominal wall defect virtually always located to the right of the cord insertion. In contrast, omphalocele presents as a smooth, rounded mass containing abdominal contents. The mass is centrally located at the level of the umbilical cord insertion disrupting the normal cord insertion anatomy and the umbilical vessels can be seen coursing across the surface of the mass. Often, gastroschisis is described as having a cauliflower-like appearance, due to the presence of amniotic fluid between bowel loops creating acoustic interfaces at near and fall bowel walls.
Gastroschisis may be seen on ultrasound after resolution of physiologic gut herniation by 12 weeks’ gestation. The main differential diagnosis at that time includes other abdominal wall defects (omphalocele, ectopia cordis, Pentalogy of Cantrell), amniotic bands and body stalk abnormalities, bladder extrophy, and umbilical cord cysts. Due to the association between fetal anomalies (structural and chromosomal) and omphalocele, early differentiation between omphalocele and gastroschisis is critical to provide correct antepartum counseling to a patient. Although risk of additional birth defects and chromosomal abnormalities is low, associated gastrointestinal abnormalities are more common in gastroschisis.

Amniotic fluid is an irritant to the sensitive intestinal tissue and prolonged exposure of the bowel to amniotic fluid induces inflammation, bowel wall edema, and abnormal motility (hypoperistalsis). In fact, extra-abdominal bowel dilation (defined as diameter greater than 10 mm) is a common finding in gastroschisis, and since the 1980s, dilation of extra-abdominal bowel has been examined as a marker for possible poor postnatal prognosis. A retrospective review of 191 cases of gastroschisis revealed that 45% had extra-abdominal bowel dilation, but no association with adverse neonatal outcome. In addition, a systematic review of 10 observational studies concluded that fetuses with isolated gastroschisis and extra-abdominal bowel dilation are not at increased risk of adverse perinatal outcome compared with fetuses without dilation. Due to the current lack of association between antenatal appearance of extra-abdominal bowel and neonatal outcome, delivery planning should not be based on prenatal assessment of extra-abdominal fetal bowel.

While extra-abdominal bowel dilation is common and does not appear to be significantly associated with postnatal prognosis, it is important to note that there is a significant association between gastroschisis and other gastrointestinal abnormalities. A systematic review and analysis found a 17% risk of gastrointestinal complications including atresia, stenosis volvulus, perforation, or necrosis. In utero bowel obstruction (mechanical or anatomical) may be suspected when progressive intraabdominal dilation of the stomach and intestines is appreciated. Polyhydramnios may serve as a marker for intestinal obstruction and be a risk factor for a more complicated postnatal course. The presence of additional gastrointestinal abnormalities can affect the postnatal course by increasing neonatal morbidity and mortality and prolonging postnatal recovery.

Fetal growth restriction is more common in fetuses with gastroschisis. In part, this is due to the abnormal size of the fetal abdominal circumference (AC). However, even when controlling for the abnormal fetal AC, fetal growth restriction is more common in fetuses with gastroschisis. Additional ultra-
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sound findings can include oligohydramios and abnormal fetal testing.\textsuperscript{15,20}

**Management**

Significant variability exists in antepartum management of pregnancies complicated by fetal gastroschisis. This is due, in part, to the lack of high-quality studies that could guide uniform clinical practice.\textsuperscript{21} Given the prevalence of early ultrasound assessment in the first trimester, early diagnosis of gastroschisis is possible.

Both detailed fetal anatomical survey and fetal echocardiogram in the second trimester are indicated when gastroschisis is identified. A thorough search for additional structural abnormalities will allow for optimal patient counseling and delivery planning. Due to the low association between gastroschisis and chromosomal abnormalities, invasive testing has not been routinely advocated. However, presence of additional anomalies should prompt further consideration for invasive genetic testing. Prenatal chromosomal microarray will identify chromosomal aneuploidy, large changes in the structures of the chromosomes as well as submicroscopic abnormalities that are not detected by karyotype analysis alone. Data on the yield of microarray in isolated gastroschisis remain limited.

Given the association between gastroschisis and fetal growth restriction (25%), spontaneous preterm birth (25%), and stillbirth (5%), serial ultrasound evaluation of fetal growth is warranted.\textsuperscript{15,22} Earlier gestational age at delivery has been associated with worse perinatal outcome,\textsuperscript{16} so optimal delivery planning is critical in cases of threatened preterm labor, including consideration for steroid administration to accelerate fetal maturity.

Assessment of fetal bowel for dilation and wall thickening has been commonly advocated and performed because of the possibility of adverse outcome in the setting of extra-abdominal bowel dilation; however, a systematic review did not find significant association between dilated extra-abdominal bowel and adverse perinatal outcome.\textsuperscript{23} In contrast, intraabdominal bowel dilation has been associated with postnatal diagnosis of bowel atresia and more complicated repair.\textsuperscript{24} It is important to note that existing data conflict on the implications of both extra- and intra-abdominal bowel dilation and the association with perinatal outcome. Additional well-designed studies are needed in this area.

Antenatal testing recommendations are mainly based on expert opinion and retrospective studies, given the association of gastroschisis with stillbirth.\textsuperscript{22,25} A suggested algorithm is to begin antenatal monitoring with non-stress test and amniotic fluid volume assessment or BPP at 32–36 weeks' gestation, with earlier initiation of testing for more complicated cases (eg, in the presence of fetal growth restriction or amniotic fluid volume abnormalities).

There is no single delivery manage-
ment algorithm, and due to the association of gastroschisis with stillbirth, earlier delivery has been advocated.26 A retrospective cohort study that included 860 cases of gastroschisis from a reference population of more than 2 million singleton pregnancies found that risk of stillbirth may be minimized with delivery as early as 37 weeks’ gestation.22 In settings of normal fetal growth and fetal testing, the delivery plan can be made on a case-by-case basis, but due to the increased risk of stillbirth with advancing gestational age, fetuses with gastroschisis should undergo delivery planning by 39 weeks’ gestation. Although newer literature may support elective delivery planning prior to 39 weeks’ gestation, this is not currently standard of care and delivery prior to 39 weeks should be reserved for obstetrical indication.

The recommended mode of delivery is vaginal, with cesarean delivery reserved for obstetrical indication as there is no evidence that cesarean delivery improves the outcome in uncompromised gastroschisis. Use of this obstetrical management algorithm is increasing, as seen in a recent population-based study that showed a rate of attempted vaginal delivery of 59.7% in 2005 and 68.8% in 2013.27

Due to the exposed fetal bowel, the neonate is at risk for insensible losses of fluid and heat (Figure 4). Upon delivery, the neonate should be placed in a sterile plastic bag up to the level of the chest and handed to waiting pediatricians for assessment. The neonate should be placed on its side to avoid kinking the bowel while awaiting pediatric surgery assessment. A nasogastric tube generally is placed to decompress the stomach and intravenous access is obtained.28 One preferred method of closure for uncomplicated gastroschisis is placement of a Silastic spring-loaded silo (Figure 5).29 The defects are reduced in 1–3 days and bio-
closure with umbilical cord may be used (Figure 6). If complications are suspected, exploration in the operating room is required. Approximately 17% of cases are complex due to the presence of additional gastrointestinal pathologies, and will likely require exploratory and corrective surgery prior to placement of the silo.30 Herniated bowel can also be reduced with a staged closure, if needed. The most common postnatal complications are overcoming poor mucosal function and hypoperistalsis of the fetal bowel. The neonatal mortality rate ranges from 2% to 17%, with higher rates for complex cases.15,18

**Summary**

Gastroschisis is a result of a full-thickness paraurbicilcal defect that allows herniation of free-floating fetal bowel into the amniotic cavity. Incidence of this birth defect is increasing worldwide and young maternal age at the time of pregnancy is a significant risk factor for the condition. Fetal gastroschisis is rarely associated with aneuploidy and is commonly isolated. Nearly all cases are associated with elevated MSAFP and the defect is readily diagnosed on ultrasound. Affected fetuses are at increased risk for growth restriction, preterm birth, and stillbirth. Approximately 10% of cases are associated with intestinal atresia requiring more extensive postnatal management and intervention. The atresia may or may not be diagnosed prior to birth. Recommended mode of delivery is vaginal with cesarean delivery reserved for usual obstetrical indications.

**FOR REFERENCES VISIT contemporaryobgyn.net/gastroschisis**
Birth plans
Managing patients’ expectations

Birth plans can be evidence-based collaborations that foster trust.

by SUSAN C. OLMSTEAD

SUSAN OLMSTEAD: As an obstetrician, tell me about how you feel about birth plans.

DR YALDA AFSHAR: I really support a woman’s decision to prepare for pregnancy, for childbirth, and to experience them in a way that she feels empowered. And if that includes writing a physical birth plan, then so be it. I’ll support that decision. The cohort of women who have birth plans is actually increasing in Labor and Delivery (L&D) throughout the country. We have to be cognizant of that. As I’ll discuss a bit later, the term “birth plan” is pretty restrictive. I’m trying to use “birth preference” more because we know that birth really can’t be planned. So these are preferences that can be shared.

MS OLMSTEAD: That’s a very good point. Do you encourage patients to write out their birth preferences or do you wait for them to bring up the topic?

DR AFSHAR: I don’t bring up the topic of a birth plan, per se, but I bring up birth choices. I love to have that discussion prenatally, antenatally, before a woman presents in active labor. That’s really what I think the whole point of a birth preference document should be. It should kind of heighten the therapeutic alliance between the mom and the provider.

In the United States, birth plans aren’t the norm on L and D whereas in other countries and areas, such as the UK and Scotland, they’re part of the national maternity record and a standard of care.

MS OLMSTEAD: I didn’t realize that. In other countries, is there a national form that’s used universally?

DR AFSHAR: Yes. There is a universal, standardized birth-preparedness document.

MS OLMSTEAD: What about patients who write up a birth plan and have unrealistic expectations? How do you help steer them toward more realistic expectations of birth?

DR AFSHAR: That’s actually a big issue in this era of shared decision-making. We know that women who have a higher number of birth plan requests are less satisfied with their birth experience. The fewer things that are fulfilled from their birth document, the more unsatisfied they are. I think what’s important is that if someone lists something that’s unrealistic and not part of the standard of care, we discuss it.

This is an issue with a lot of birth plans that are found on the Internet. Many of them include outdated pro-
procedures like prophylactic enemas and routine episiotomies. The American College of Obstetricians and Gynecologists has had a stance against both of those procedures for a while now. We need to focus birth preferences on things that are a little more tangible, real, and in touch with day-to-day L & D.

I use the topic of birth preparedness to tell my patients that I come to work every single day saying, “How can I make the life of moms in labor better? How can I ensure a safe pregnancy outcome for the mom and the baby?” And I think that spelling that out helps establish a little more trust. A birth document can be a tool to foster that.

**Ms Olmstead:** I’m sure that helps patients feel a lot more confident and comfortable. If you were to develop the ideal plan, one that you would hope a patient might come to you with, what would it include?

**Dr Afshar:** We’ve actually started developing such a tool. The ideal plan, for me, would be a decision-making tool that says, “The evidence shows this about xyz. What is your preference about that?” or “The evidence shows that a vaginal delivery is associated with better outcomes for xyz.” Then a patient would choose.

The focus is on evidence-based practice recommendations in labor, birth, and for the newborn. Ideally, it should be 1 page and very simple.

**Ms Olmstead:** I’m sure you help patients understand that labor is unpredictable and things happen that may cause the plan to shift. Is that right?

**Dr Afshar:** Absolutely. Labor is dynamic. One of the most important discussions to have with the patient is about the fact that neither the provider nor the mom has any control over the course of labor. We can try to optimize some preferences, but really, in the end, labor kind of plays out. So, preparedness is important.

**Ms Olmstead:** It sounds as if you are very in touch with what moms want and eager to work with them. I suppose that’s the takeaway message.

**Dr Afshar:** Yes. We recently looked at birth plans at a larger, provider level. We did a national online survey about plans and childbirth education that was distributed through professional societies and social media. We heard from about 600 respondents, 76% of whom were obstetricians and the rest were midwives. The results were pretty surprising.

Only 26% had favorable views of birth plans. About 67% actually did not recommend birth plans. Thirty percent felt they were predictors of poor obstetrical outcome. Those with more years in practice had more favorable views of birth plans as did those with higher obstetrical volume.

These are not national sentiments but I think they do suggest a trend. Moms are asking for birth plans and it’s important that ob/gyns believe in a therapeutic alliance and shared decision-making with their patients, and that we start bridging the gap on our end.

**Ms Olmstead:** Dr Afshar, thank you so much for talking with us.

**Dr Afshar:** It’s been a privilege.

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**Ms. Olmstead** is the Editorial Director of Contemporary OB/GYN.

**Dr. Afshar** is a Maternal-Fetal Medicine Fellow in the Department of Obstetrics and Gynecology, University of California, Los Angeles.

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**Read more about Dr Afshar’s experience with birth plans at CONTEMPORARYOBGYN.NET/BIRTHPLAN**
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Treating UTIs in the age of antibiotic resistance
Strategies for the practicing OB/GYN

by ROBERT J. STILLER, MD, CHRISTOPHER HICKS, MD, and ZANE SAUL, MD

Ob/gyns have witnessed how development of antibiotic resistance has affected disease management in our specialty. Increased resistance of Neisseria gonorrhoea (N gonorrhoea) to penicillins and quinolones, emergence of methicillin-resistant staphylococcus aureus (MRSA) and resistance of Group B Streptococcus to erythromycin and clindamycin have led us to modify our antibiotic treatment regimens. Whether antibiotics are appropriately or inappropriately prescribed, they can lead to loss of effectiveness by allowing only organisms with resistance to survive and multiply in a process similar to natural selection. Alternatively, organisms can share genetic information through plasmids, which are small segments of DNA that can code for production of resistance factors.

Urinary tract infections (UTIs) complicate 3% to 10% of pregnancies and are among the most common reasons for antibiotic use in obstetrics. Clinical relevant disease may include lower urinary tract conditions such as asymptomatic bacteriuria and acute cystitis or upper tract urinary infections such as pyelonephritis. In pregnancy, these infections are most frequently caused by the Enterobacteriaceae group of organisms, which include the gram negative rods, Escherichia coli (E coli) (82.5%), Klebsiella pneumoniae (K pneumoniae) (7.6%), Proteus mirabilis (4.9%), and Enterobacter species (5.7%). Gram positive organisms such as Streptococcus species (21.4%), Staphylococcus species (6.5%), and Enterococcus species (5.7%) also cause infections, although frequencies of specific organisms vary among case series.

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Antibiotic-resistant UTIs

Otic resistance in *Enterobacteriaceae* has been the production of enzymes, known as beta-lactamases, capable of inactivating some members of the penicillin and cephalosporin class antibiotics, which share a similar beta-lactam chemical ring structure. Most recently within this class of antibiotics, extended-spectrum beta-lactamase (ESBL) enzymes have arisen, which have even greater activity. Besides resistance to penicillins and cephalosporins, ESBL-producing organisms commonly carry other enzymes, which gives them additional resistance to fluoroquinolones, aminoglycosides, and sulfamethoxazole-trimethoprim, and are sometimes known as multidrug-resistant organisms (MDROs). Resistance of gram-negative bacteria in both the community and hospital settings has grown substantially in recent years, with prevalence of ESBL-producing *E coli* increasing from 7.8% to 18.9% in the US from 2010 to 2014. In a review of our own hospital’s 2015 antibiogram, 9% of *E coli* and 13% of *K pneumoniae* were ESBL producers (unpublished data), making infections due to resistant organisms much more frequent. Given ESBL resistance to many of our commonly used antibiotics, these infections are becoming more difficult to treat, leaving the ob/gyn with fewer effective drugs from which to choose, resulting in more drugs that are less familiar to our specialty. In fact, the CDC now lists antibiotic resistance of gram-negative organisms as one of its biggest threats.

Here we describe issues that an ob/gyn might encounter when dealing with multidrug-resistant (MDR) UTIs and reviews antibiotics that are both safe for use in pregnancy and effective against these MDROs.

### Treatment of non-ESBL UTIs

Asymptomatic bacteriuria (ASB) was originally defined as the presence of 105 colony-forming units of the same bacteria obtained in 2 consecutive voided samples. Untreated ASB may result in pyelonephritis in up to 30% to 40% of pregnant patients and screening for ASB is performed at the first prenatal visit. Currently, treatment is recommended after 1 positive culture is obtained. Acute cystitis is defined as a symptomatic lower UTI in the absence of fever, back pain, or systemic symptoms. Gram negative organisms of the *Enterobacteriaceae* family comprise the majority of these infections.

Typical antibiotic regimens for lower tract infections such as ASB and acute cystitis have included nitrofurantoin, oral second- and third-generation cephalosporins, (cefaclor, cefpodoxime), and trimethoprim-sulfamethoxasole. Choice of antibiotic should be based upon either local or individual susceptibility results and treatment continued for 4 to 7 days. All infections should be tested for sensitivity to a given antibiotic. Duration of antibiotic therapy may be modified by patient’s clinical response.

### Antibiotics generally effective against ESBL-producing organisms in pregnancy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade Name</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Tract Infection (asymptomatic bacteriuria or acute cystitis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Macrodantin</td>
<td>50-100 mg orally 4 times daily for 3-7 days</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>Monurol</td>
<td>• 3 g single dose orally</td>
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<tr>
<td></td>
<td></td>
<td>• 3 g every other day for 3 doses orally</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>Invanz</td>
<td>1 g IV for 10-14 days</td>
</tr>
<tr>
<td>Doripenem</td>
<td>Doribax</td>
<td>500 mg q 8 hrs IV for 10-14 days</td>
</tr>
<tr>
<td>Imipenem/Cilastin</td>
<td>Primaxin</td>
<td>500 mg q 8 hrs IV for 10-14 days</td>
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</table>

### Newer antibiotic combinations that may have enhanced activity against MDR organisms

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade Name</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane-Tazobactam</td>
<td>Zerbaxa</td>
<td>1.5 g IV q 8 hrs for 10-14 days</td>
</tr>
<tr>
<td>Ceftazidime-Avibactam</td>
<td>Avicaz</td>
<td>2.5 g IV q 8 hrs for 10-14 days</td>
</tr>
</tbody>
</table>

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**Abbreviations:** ESBL = extended spectrum beta-lactamase; MDR = multidrug-resistant; IV = intravenous

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All drugs listed are FDA Pregnancy Category B. All infections should be tested for sensitivity to a given antibiotic. Duration of antibiotic therapy may be modified by patient’s clinical response.
Implementation of PLAT (Preterm Labor Assessment Toolkit): A System-Wide Initiative to Improve Preterm Labor Outcomes

Preterm birth is a huge healthcare burden. The March of Dimes has set a goal for the U.S. to achieve a preterm birth rate of 8.1% of live births by 2020.* The PLAT algorithm has been designed to improve standardized assessment of preterm labor among women and enable appropriate treatment to improve neonatal outcomes by administering ACS at the time most likely to improve outcomes.

Read the supplement now at: contemporaryobgyn.net/plat-implementation

tis and generally the patient is treated initially with intravenous (IV) therapy followed by oral antibiotics to complete a 10- to 14-day course. Parenteral cephalosporins antibiotics such as ceftriaxone with favorable gram negative organism coverage are often administered.

Use of beta lactam antibiotics

Penicillin and cephalosporins are chemically derived from a beta-lactam ring structure. They work by interfering with bacterial cell wall biosynthesis by binding to the penicillin-binding proteins (PBPs) responsible for the integrity of the bacterial cell wall. A common mechanism of antibiotic resistance involves development of enzymes known as beta-lactamases, which can destroy the beta-lactam ring in penicillins and make the organisms resistant to the antibiotic. Pharmaceutical companies deal with this form of antibiotic resistance by either modifying the beta-lactam ring structure to create a new class of antibiotic—such as cephalexin, cefamandole, monobactams, or carbapenems—or with side chains added to the beta-lactam ring (eg, extended-spectrum penicillins or advanced generation cephalosporins) to make the drug less vulnerable to the microorganism’s beta-lactamase enzymes. Alternatively, the penicillin or cephalosporin can be combined with a beta-lactamase inhibitor such as sulbactam, clavulanic acid, or tazobactam. These beta-lactamase inhibitors inactivate the microorganism’s beta-lactamase enzymes so that the antibiotic partner of the drug can still bind and inhibit the PBPs necessary for cell wall formation and integrity. Examples of these combinations are ampicillin + sulbactam, amoxicillin + clavulanic acid, piperacillin-tazobactam, and ceftolozane-tazobactam. Many different beta-lactamase enzymes have been identified and each carries specific resistance patterns, although individually they generally do not confer complete resistance to the extended-generation cephalosporins, extended-spectrum penicillins, or beta-lactamase inhibitor combination drugs. We refer the reader to these references for more detail.3,4

ESBL-producing organisms are resistant to beta-lactam antibiotics (penicillins, cephalosporins, monobactams), and many penicillin-beta lactamase inhibitor combinations, despite modifications made to their chemical structures. The genetic information for these enzymes is often carried on plasmids, enabling genes to be easily shared among other organisms, thus facilitating their spread. These organisms may also carry resistance factors to nitrofurantoin, aminoglycosides, fluoroquinolones, and sulfonamide-based antibiotics. These broadly active beta-lactamases are responsible for some of the current rise in antibiotic microbial resistance. Similar to the rise of community-acquired MRSA outside of the hospital setting, there has been a substantial rise in ESBL-producing E coli infections in community settings. Given their resistance to many commonly used antibiotics, these infections are becoming more difficult and challenging to treat.

Treatment of ESBL lower UTIs

In cases of ESBL lower UTIs, an oral antibiotic available for use in the US is fosfomycin, which is a phosphonic acid derivative. Discovered in 1969, it has been widely used in Europe and recently has been approved in the US by the FDA for treatment of uncomplicated UTIs. Fosfomycin tromethamine, marketed as Monurol, has bactericidal activity against both gram-negative and gram-positive bacteria, and acts by inhibiting bacterial cell wall synthesis by a mechanism different from beta-lactam antibiotics.5 It is administered as a single 3-g dose mixed in 30 cc of water and had effectiveness similar to a 7-day course of conventional treatment in a study of treatment of asymptomatic bacteriuria during pregnancy.11 Regimens have also included 3 g orally on Days 1, 3, and 5 in patients with symptomatic acute cystitis.12 In a 2010 review, 97% of ESBL-producing E coli and 81% of ESBL-producing K pneumoniae were susceptible to fosfomycin.13 However, a 2016 review showed that while fosfomycin has retained clinical effectiveness against ESBL-producing E coli, increasing resistance patterns are being seen, associated with increased use of fosfomycin in Europe.14

<table>
<thead>
<tr>
<th>TABLE 2 Clinical risk factors for increased antibiotic resistance</th>
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<tr>
<td>• Poor response to standard antibiotic therapy</td>
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<tr>
<td>• Previous antibiotic use</td>
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<td>• Previous hospitalization</td>
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<td>• Presence of indwelling catheters</td>
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<td>• History of international travel</td>
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ESBL pyelonephritis

For women with pyelonephritis from ESBL-producing organisms, IV antibiotics with broad activity and good tissue penetration are recommended, making the carbapenem antibiotic group an ideal choice. Carbapenem antibiotics have a modified beta-lactam ring which is different from penicillins and cephalosporins, and provides significant resistance to beta-lactamase-producing microorganisms, including ESBL-producing Enterobacteriaceae. They have the greatest spectrum of activity within the beta-lactam class of antibiotics with broad gram-negative and gram-positive activity and are also active against N gonorrhoeae, Pseudomonas aeruginosa, gram-positive organisms including Listeria and anaerobes, including Bacteroides fragilis. Carbapenems, like other beta-lactam antibiotics, exhibit bactericidal activity by binding to penicillin-binding proteins in the organism’s cell wall and disrupting peptidoglycan cross-linking, weakening the cell wall and resulting in death of the organism. Carbapenems that have been used for serious UTIs in pregnancy include imipenem, ertapenem, and doripenem, and are listed as FDA Class B medications. Carbapenems are available only in IV formulations. As such, a patient may need prolonged IV access to complete an extended course of therapy.

Imipenem was the first carbapenem antibiotic, approved in 1985. It is inactivated in the proximal renal tubule by the normal human enzyme renal dehydropeptidase I and must be combined with cilastatin, a specific inhibitor of this dehydropeptidase enzyme. Imipenem-cilastatin, marketed as Primaxin, is administered at a dose of 500 mg IV Q6h for complicated UTIs, such as pyelonephritis. Carbapenem dosing must be adjusted in patients with decreased renal function and should be used with caution in individuals with underlying central nervous system (CNS) disease, such as brain lesions or a history of seizures. CNS toxicity has included change in mental state, myoclonus, and seizures. Given its similar beta-lactam ring structure to penicillins, it, like the other beta-lactam-based antibiotics (cephalosporins, monobactams) must be used with caution in patients with a history of significant allergy to penicillin.

Ertapenem, marketed as Invanz, is approved for complicated UTIs and pelvic/intra-abdominal infections. It is active against most Enterobacteriaceae and anaerobes, but less active than the other carbapenems for P aeruginosa, Acinetobacter, and gram-positive bacteria, particularly enterococci and penicillin-resistant pneumococci. It has a long half-life, and can be administered as a single daily dose of 1 g IV/intramuscular, making it convenient for patients who require a prolonged course of therapy. Other approved indications for ertapenem include treatment of postpartum endometritis, septic abortion, and postsurgical infections. In pyelonephritis, it may be given parenterally for 10-14 days. Alternatively, it may be given for 3 days, then switched to oral therapy if clinical response is seen, to complete a 10- to 14-day course of therapy. Veve et al. compared patients with ESBL-producing UTIs, initially hospitalized and then discharged on either ertapenem or fosfomycin for continued outpatient therapy and found cure rates to be comparable.

Dorapenem, marketed as Doribax, is approved for both complicated UTIs and intra-abdominal infections. Dosing is 500 mg every 8 hours to complete a 10- to 14-day course of therapy. It has a spectrum of activity similar to meropenem, although it appears to have more potent in vitro activity against P aeruginosa than ertapenem or meropenem.

Carbapenem resistance

Of great concern is that antibiotic resistance to the carbapenems has also been recently reported. K pneumoniae carbapenemase (KPC) was first identified in 1996 as a beta-lactamase enzyme capable of inactivating the carbapenem class of antibiotics, along with penicillins and cephalosporins. Carbapenems enter gram-negative organisms through outer membrane proteins known as porins and inactivate the enzymes needed for peptidoglycan cross-linking, ulti-
mately causing cell death. Resistance to carbapenems can also develop either by loss of these outer membrane porin channels, or by modifications of the penicillin-binding proteins, so that they do not bind with the carbapenems.\(^{18}\) A recent article by Khari et al highlights the challenges in treating KPC-producing \(K\) \textit{pneumoniae}-associated pyelonephritis in pregnancy, which they managed with a prolonged course of an extended-infusion cefepime and oral fosfomycin.\(^{19}\)

To meet this challenge, a new option in treatment of these MDR gram-negative infections has been the combination of a new beta-lactamase inhibitor, avibactam, combined with a third-generation cephalosporin, ceftazidime. Ceftazidime-avibactam, marketed as Avycaz, demonstrates greater resistance to beta-lactamases produced by MDR pathogens, including some KPC-producing organisms. Avibactam has greater activity than other beta-lactamase inhibitors, such as clavulanic acid, sulbactam, and tazobactam.\(^{20,21}\) Ceftazidime-avibactam is approved for complicated UTIs including pyelonephritis and is given at a dose of 2.5 g IV q 8 hrs for 7 to 14 days. Combinations of avibactam with other beta-lactam antibiotics are in development and may provide additional options in the treatment of MDRO infections. Lastly, investigators are reevaluating the use of colistin, of the polymyxin class of antibiotics, originally used in the 1950s. These antibiotics cause cell death by disrupting the gram-negative cell membrane.\(^{22}\) While they were discontinued due to concerns of nephrotoxicity and due to the development of safer antibiotics, this class of antibiotic is being reintroduced in cases of extensive gram-negative resistance.

An additional concern is that, as patients develop colonization with resistant organisms, this may affect commonly used treatment regimens for conditions such as intra-amniotic infection and postpartum endometritis, in which therapy is often started empirically with combined penicillin, gentamicin, and clindamycin/metronidazole in the absence of genital cultures. The need for organism identification will become more pressing as resistance to our commonly used antibiotics regimens increases, with delay in starting appropriate therapy resulting in increased morbidity.

**Summary**

It is likely that ob/gyns will encounter MDR pathogens previously seen only in the critical care areas that will now occur in both the inpatient and outpatient obstetrical settings. Previous exposure to antibiotics, hospitalization, and the presence of an indwelling catheter increase the risk of resistant organisms. As antibiotic resistance is becoming more widespread, awareness of antibiotic sensitivities and consultation with infectious disease specialists in cases of MDR infections will help practitioners to provide optimum care in these difficult cases. In cases of ESBL-associated UTIs, it is important to obtain a test of cure 10 to 14 days after treatment to confirm eradication of the infection. Carbapenems, fosfomycin, and newer cephalosporin/beta-lactamase inhibitors appear safe for use in pregnancy and provide activity against ESBL-producing \textit{Enterobacteriaceae} that are resistant to our previously used therapies. Strategies such as good handwashing, contact precautions when dealing with patients with resistant organisms, and appropriate antibiotic stewardship (limiting the use of unnecessary antibiotics, limiting broad-spectrum antibiotics when a narrow agent is available, institutional antibiotic cycling) will help us to better deal with these infections in the future.

**Take-home points**

MDRO urinary tract infections are now being seen in the community at higher frequencies with ESBL-producing \textit{E coli} increasing from 7.8% to 18.9% in the US from 2010-2014. Consider antibiotic resistance for infections that do not respond to conventional therapy.

Be knowledgeable of local antibiograms when treating UTIs empirically. Obtain culture and sensitivities studies on all patients at higher risk for antibiotic resistance.

**For references visit**

contemporaryobgyn.net/uti-resistance
Malpractice pitfalls
5 strategies to reduce lawsuit threats

by LIZ SEEGERT

When it comes to getting sued for medical malpractice, it is unfortunately more a case of “when” than “if.”

It’s no secret that physicians are at great risk of being sued by a patient sometime during their career. The good news is, doctors can take steps to reduce the risk of lawsuits, and improve the odds of a favorable outcome if they are sued.

While the frequency of claims and payments actually have declined over the past decade, physicians still have about a one in five chance of making a payment, whether through a trial or settlement.

There are events that occur every day in medical practices that may seem harmless on the surface, but can sow the seeds of a potential lawsuit. From adding an extra note to a patient’s chart after a visit, to rushing through electronic health record (EHR) screens, a minute’s worth of an innocuous action can lead to months of a physician defending his or her actions in court.

To help doctors protect their practices and professional reputations, *Medical Economics* consulted experts to learn the five biggest malpractice hazards facing physicians and how to avoid getting tied up in a malpractice maze.

1. **Document everything**
   
   “Every doctor is taught that if you didn’t put it in the chart, you didn’t do it,” says Steven Fox, MD, an internist and assistant professor of clinical medicine at the Keck School of Medicine at the University of Southern California. If it’s not in the chart, you are deemed not to have done it for the purposes of malpractice litigation, he adds.

   Fox advises documenting all conversations. This includes summarizing patient discussions, having patients verbalize their understanding of why something is important, explaining why any clinical alerts are dismissed and noting conversations with other providers or with family members.

2. **Be transparent with patients**

   The shift to patient-centered care is designed to help patients be part of the decision-making process. But that requires openness and communication by the physician about information in the medical record.

   One approach physicians can take to boost transparency and encourage more patient engagement is to share notes with their patients, says Nitin Damle, MD, an internist with South County Internal Medicine in Wakefield, Rhode Island, and president of the American College of Physicians.

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Doctors may hesitate to do so out of fear that misunderstood comments could lead to lawsuits, but the idea is not unreasonable, he says.

While note-sharing can be tricky if done without appropriate context, it can be helpful when done under the right circumstances, Damle says. Discussing entries with patients promotes more engagement, and helps them become more active participants.

Whether shared in person or through an online portal, physicians should take time to explain what the notes mean, such as why a test or medication was ordered, he says. Additionally, patients should never be permitted to directly modify anything in their chart. If they do need to add information, it should go in as an addendum.

Note sharing helps physicians be more careful about using objective language when describing patient encounters. Damle says common sense should prevail when discussing a patient’s record. Entries should be factual and not derogatory or personal in any way. Keep to the medical specifics of a visit, call or referral, he advises.

Robin Diamond, JD, MSN, chief patient safety officer for physician insurer The Doctors Company, points out that notes need to be objective and unambiguous. “Think about how you’d feel if you saw them projected on a six-foot screen in a courtroom or if they were in the family’s or patient’s possession,” she says.

To increase clarity, she suggests including direct quotes from patients when documenting, especially if the patient seems upset or agitated.

Diamond also recommends that physicians and patients review the notes together. Not only does this practice ensure that entries are appropriate and objective, she adds, it helps patients better understand their situation and any required action on their part. That reduces the potential for claims arising from miscommunication or misunderstandings.

### Show empathy

While there’s a natural inclination to apologize for mistakes, fear of lawsuits prevents many physicians from even expressing empathy if something should go wrong. Instead of sharing information with patients or families, they hesitate to discuss errors, leading to frustration and legal action.

Thirty-six states have so-called “sorry” laws, which generally prohibit using a physician’s apology to patients or families against them in lawsuits. Specifics of these laws vary from state to state, but “showing compassion can sometimes ameliorate a situation over time,” Ellenberg says.

Research from the American Bar Association and elsewhere concludes that apologies do reduce the probability of getting sued. Fox points out that if a case goes to trial, juries tend to be better disposed concerning the amount of liability when doctors are contrite, rather than denying responsibility or shifting blame.

Even with an apology, however, a patient or family may still decide to sue. So before speaking with the patient or family regarding the error, it may be prudent for a physician to seek guidance from their practice’s medical director, hospital’s risk management department or their insurance carrier, advises Carol Keohane, MS, RN, assistant vice president for patient safety at CRICO, a risk management firm that serves the Harvard University medical institutions.

It’s important to assess where communication or other processes may have broken down so as to prevent a recurrence, says Keohane. Common problems include not clearly communicating the significance of test results, not following up on a referral or not providing all necessary documentation to a consulting physician, she says. When evaluating ways to reduce mistakes, take a look at office workflow and staffing as well as ways to educate physicians on process improvements.

### Beware of EHR hazards

Widespread adoption of EHRs adds another layer of potential liability for physicians, according to David Troxel, MD, medical director of The Doctors Company.

Despite the increasing complexity of care, most patients and jurors hold physicians responsible for managing all of a patient’s information. EHRs are supposed to solve information and documentation issues, but don’t always provide correct or complete results, he says.

Providers may be tempted to use shortcuts, such as copying and pasting from templates, auto-filling fields and relying on computer-assisted documentation, he says. But that approach,
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coupled with a lack of updated clinical decision support and “hold harmless” clauses absolving EHR manufacturers of responsibility for errors, leave physicians vulnerable to EHR-related legal problems.

Troxel, who specializes in EHR-related malpractice issues, cites drop-down menu selection errors as a common problem. Even if you know you accidentally selected an item on a menu, you may not be able to correct it. It’s likely that the information already has been transmitted to other parts of the health record and will remain there.

“You basically have a time bomb on your hands,” he says, because it opens the door for another doctor to pull up another part of the record and act based on incorrect information, such as a missed drug allergy or the wrong dose of a medication. Be sure to make copious and visible notes regarding inadvertent errors so other doctors are informed.

In a 2015 CRICO analysis of common communication errors, the absence of the right information, including through EHRs, at a crucial point in the diagnosis or treatment process was a major contributor to patient harm. These types of communication errors are cited as a factor in 38% of all general medicine cases in the survey.

Another common practice, turning off computer-generated warnings, can also trigger liability issues, Troxel notes. Ignoring alerts is especially common when prescribing medications. Missed dosing errors or drug interactions resulting in severe side effects or overdoses can land a physician in court.

Under those circumstances, it’s the physician, not the EHR manufacturer, who is liable for missing alert-generated warnings, especially if documentation is non-existent or incomplete, Troxel says.

Troxel also warns physicians not to develop their own workarounds for common EHR problems, no matter how frustrated they get. The danger is that data may not get included in other areas of the record and if a problem arises, the physician could be held responsible for not using the EHR as it is intended.

Damle says his practice’s system won’t allow a physician to override an alert without a written explanation. He advises that any physician who deviates from clinical guidelines must be certain to document why, or risk being accused of providing suboptimal care.

Maintain good relationships

Physicians must maintain objectivity, even when patient or family dynamics are difficult. It’s important to acknowledge and calmly discuss issues that could affect outcomes, such as non-compliance with the care plan. And of course, document any conversations.

Even if family members are involved, talk to patients directly but recognize that there might be problems with comprehension, cognition or memory, Damle advises. If a patient consents, having a family member or surrogate act as a listener and possible explainer can improve understanding and good will.

Sometimes, it’s the family member who doesn’t agree with the care plan, and that may lead to problems later, because that person may sue or coerce the patient into doing so. But spending a little extra time to explain the diagnosis or disease process can often defuse a tense situation, Damle says.

Part of managing the patient relationship is ensuring transparency and being realistic, Diamond points out. “Be clear with patients about expectations for treatment, follow up, medication,” Diamond says. By helping patients understand their situation thoroughly, they will get better care and be less likely to sue because of a misunderstanding.

Conversely, doctors are more likely to get sued by a patient with whom they have a bad relationship, according to Fox. He adds that there’s no obligation to continue treating patients when there’s a bad relationship.

Good communication and strong relationships are goals physicians and staff members can and should work toward. But even so, “you can do absolutely everything right, make every right decision, do every right test and treatment and still get a bad outcome,” Fox says, “because medicine is not certain.”

FROM THE PAGES OF

Medical Economics

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Autoimmune Disease

AUTHOR: Charles J. Lockwood, Department of Obstetrics and Gynecology, University of South Florida, Morsani College of Medicine, Tampa, FL.

SYNOPSIS In this protocol, Dr Lockwood reviews the pathophysiology, diagnosis, and management of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and scleroderma. One in 2000 pregnancies are complicated by SLE, and RA is the most common autoimmune disease in women of childbearing age. Scleroderma, in contrast, is rare.

KEY MESSAGES ABOUT SLE

- In 98% of patients with SLE, antinuclear antibody is positive. Diagnosis is established when 4 or more criteria for SLE from the American College of Rheumatology are met.
- Four factors determine prognosis for live birth when a pregnancy is complicated by SLE: disease activity at conception and subsequent flares during pregnancy; coexisting lupus nephritis; development of antiphospholipid antibodies (APA); and presence of anti-SSA (Ro) antibodies.
- Many women with SLE and underlying renal disease may be on angiotensin-converting enzyme (ACE) inhibitors to control hypertension and slow progress of the renal disease. ACE inhibitors are teratogenic and should be stopped prior to conception or as soon after it occurs as possible.
- For active SLE in pregnancy, prednisone is the mainstay of therapy. It should also be used for antepartum SLE flare. Azathioprine can be added if a patient's condition is refractory to glucocorticoids. In patients with SLE who have APA, low-molecular-weight aspirin and low-dose aspirin should be used.
- Delivery can be delayed until 40 weeks, provided that twice-weekly fetal testing at 36 weeks is reassuring, if a woman with SLE does not have SSB/SSA antibodies, APA, worsening nephritis or hypertension, fetal growth restriction, oligohydramnios, or superimposed preeclampsia.

KEY MESSAGES ABOUT RA

- Diagnosis of RA requires that 5 different clinical features be present, including inflammatory arthritis involving 3 or more joints and symptom duration of more than 6 weeks.
- In 40% to 80% to patients with RA, the condition improves in pregnancy whereas 90% have postpartum exacerbations.
- Local steroid injections into affected joints should be part of initial treatment of RA in pregnancy. If the condition does not respond, prednisone can be given at a dose of 5 mg every morning and 2.5 mg every evening.
- Acetaminophen is recommended for RA in pregnancy and NSAIDs should be avoided after 20 weeks.


6 tips to help practices adapt to a new EHR

A new system can hurt a practice’s workflow. Here’s how to get back to top form quickly. *by MARY K PRATT*

**MEASURE PROGRESS**
Determine several metrics in advance of the implementation and then measure against them at key intervals, such as 30, 60, 90 and 120 days post-implementation and then again at six months out, says Scott Jacobs, vice president of community outreach services at The HCI Group, a Health IT firm. Physicians should contractually obligate EHR vendors to deliver such results, with stipulations for more training or refunds.

**RELY ON SUPERUSERS**
Tech-savvy organizations identify workers with strong technical acumen to be superusers. Superusers serve as resources for others in their offices, helping colleagues navigate new systems to get the maximum value, says Angela Rose, MHA, RHIA, director of health information management practice excellence at the American Health Information Management Association. When Rose worked at a physician clinic, she attended a full week of training at the EHR vendor’s headquarters.

**PLAN FOR ADDITIONAL TRAINING**
Physicians should schedule additional training to address questions that arise as they and their staff use the system daily, says Rose. Structure your contract so that the EHR vendor must provide training until staff meets certain competencies, instead of stipulating a certain amount of hours. Also, aim for one-on-one or small-group training.

**MONITOR**
Software doesn’t always work perfectly. That’s why physicians should monitor their new EHR and ensure it’s handling functions and data accurately, Rose says. For example, she recommended fact-checking data to ensure data is entered into the EHR accurately and in the right data fields, starting with daily spot checks and moving to less frequent checks if all is well.

**SELL THE UPGRADE**
It’s important to let people know that there’s an adjustment period, says Jacobs. Physicians should tell those in the practice about the upgrade and sell their patients and partners on the change, too. “Tell them, ‘We’re increasing our capabilities. Your data is going to be safer now.’ And if you’ve gotten an EHR integrated (with the local hospital), that’s a huge benefit. I’d let them know that you’ll have all their records—everything [that happened at the] hospital you will know about—and vice versa,” he says.

**TWEAK YOUR NEW SYSTEM**
Similarly, no EHR delivers every function and feature, but physicians shouldn’t accept an unsatisfactory system, either. So plan to address substandard performance in those first few months after the initial implementation, Rose says.
Seema Verma, MPH, a healthcare consultant from Indiana, has been nominated to serve as administrator of the U.S. Centers of Medicare & Medicaid Services (CMS) under President-elect Donald J. Trump.

Here’s what physicians need to know about Verma.

1. Verma is president and chief executive officer of SVC, Inc., a national healthcare consulting company based in Indianapolis, Indiana. According to the SVC website, Verma “has worked extensively on a variety of policy and strategic projects involving Medicaid, insurance, and public health, working with Governor’s offices, State Medicaid agencies, State Health Departments, State Departments of Insurance, as well as the federal government, private companies and foundations.”

2. She is an ally of Vice President-elect Mike Pence, and was responsible for putting together Pence’s Obamacare Medicaid expansion, otherwise known as “Healthy Indiana Plan 2.0.” She has also worked on Medicaid programs in other GOP states, including Kentucky, Iowa, Ohio and Maine.

3. Verma is known as a Medicaid specialist who has worked with Republican governors to introduce conservative ideas to their state Medicaid programs, including health savings accounts and employment requirements, according to Politico.

4. After the Affordable Care Act (ACA) was approved in 2010, Verma was appointed as Indiana’s health reform lead, where she worked to prepare for ACA implementation.

5. Before her consulting work, Verma worked as vice president of planning for the Health & Hospital Corporation of Marion County, Indiana. She was also a director with the Association of State and Territorial Health Officials, a nonprofit public health organization made up of public health.

Ms Seema was interviewed by Indianapolis attorney and radio host Greg Garrison last September on the Affordable Care Act and Indiana state’s Medicaid expansion program under the ACA, the Healthy Indiana Plan (HIP) 2.0, which she worked closely with then Indiana Governor, now Vice President, Mike Pence, to design. Go to http://bit.ly/2ketlG4 to listen.
Should this ectopic pregnancy have been diagnosed earlier?

CONTINUED FROM PAGE 53

to be followed until it was down to 0. Instructions regarding ectopic pregnancy were given to the patient. No complete blood count was ordered.

On October 28, 2011, the plaintiff came back to the WHC for follow-up to evaluate a rising hCG level. She was again seen by Dr A, who had noticed that the ß-hCG level drawn on October 26 was 421.4 and more elevated than 2 days earlier. Additional blood samples were drawn for another ß-hCG level and the result was 447.1, another increase. The woman’s HCT was 32.9 and her Hgb was 11.4. The risk of a possible ectopic pregnancy was discussed with the patient, who expressed that she understood. The treatment plan that day included dilation with suction and curettage and the risks of the procedure—including bleeding, infection, uterine perforation, and damage to the bowel and bladder—were discussed with the patient. The need for possible methotrexate therapy versus a laparoscopic procedure in the future was also discussed.

The plaintiff was admitted that day to the ambulatory surgical unit (ASU) and signed a consent form for a possible salpingectomy. She underwent a diagnostic laparoscopy and dilation and curettage (D&C) and excision of a right ovarian mass. The surgery was performed by Dr A, assisted by defendant PGY-1 ob/gyn Dr B. Intraoperative findings are partially noted in the operative report dictated by Dr B and signed by Dr A, which fails to mention the intraoperative appearance of the fallopian tubes despite the patient being consented for a possible salpingectomy.

CONTINUED ON PAGE 46

Women’s health update

CONTINUED FROM PAGE 43

USPSTF reaffirms benefit of folic acid supplementation

In an update of its 2009 statement on folic acid supplementation in women of childbearing age, the US Preventive Services Task Force (USPSTF) has reaffirmed the value of the vitamin for prevention of neural tube defects (NTDs). Published in JAMA, the new report recommends that all women who are planning or capable of pregnancy take a daily supplement containing 0.4 mg to 0.8 mg of folic acid.

This review of the evidence included 1 randomized clinical trial, 2 cohort studies, 8 case-control studies, and 2 publications from the 2009 analysis and looked at evidence of the effectiveness of folic acid supplementation in at least 41,802 participants. Results were not pooled because of study heterogeneity and differences in food fortification over time. The review did not include evidence on folic acid supplementation in women with a history of pregnancy affected by NTDs or other high-risk factors or on fortification, counseling to increase dietary intake of folic acid or naturally occurring food folate, or screening for NTDs.

As was the case 8 years ago, the USPSTF found that the net benefit of folic acid supplementation is substantial and that the harms to the mother or infant of taking the vitamin at typical doses are no greater than small. No substantial new evidence was identified of either the benefits or harms of folic acid that would have led to a change in the group’s previous recommendation.

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Laparoscopy showed an 8-week-size anteverted uterus, 50 cc of hemoperitoneum, 1- to 2-cm right ovarian mass, normal left ovary and left adnexa, and a grossly normal upper abdomen. Pathology specimens included endometrial curettings and a right ovarian mass.

The surgical pathology report revealed that the endometrial fragments contained decidua tissue only and no chorionic villi, indicating that no intrauterine pregnancy was removed. The right ovarian mass was a pregnancy luteoma, a benign tumor that usually regresses after pregnancy. The patient appeared stable postoperatively and was discharged home with follow-up at the WHC scheduled on November 9, 2011.

On November 2, 2011 the plaintiff was recalled to the WHC to check her hCG levels, which had been steadily rising. She was seen by Dr A, who had noted that the hCG had increased to 884.9, which was suggestive of an ectopic pregnancy rather than an abnormal intrauterine pregnancy. The patient had no pain or appearance of an acute abdomen and so she was told to return to the WHC for possible methotrexate therapy.

On November 4, 2011 the plaintiff returned to the WHC and was seen by non-party Dr C. Her hCG level had risen further to 916.2. The risks, benefits, and adverse effects of methotrexate therapy were explained to the patient and she agreed to try it and was given 85 mg without any adverse effects. Ectopic pregnancy precautions were reviewed and the plaintiff was told to return to the clinic on Day 4 and on Day 7 and then weekly until her hCG levels had dropped to 0. If her hCG levels had decreased less than 15% between Day 4 and Day 7 and there were no other complications, she was to receive a second dose of methotrexate.

On November 8, 2011 the plaintiff returned to the WHC and was seen by Dr B and nonparty Dr D. On that day, her hCG level was noted to have risen to 1385; however, because she was purportedly asymptomatic she was told to return to have her hCG test repeated 3 days later on November 11, 2011. On that day, she returned to the WHC and was seen by Dr E. Her -hCG level was noted to be 1051.0, only a slight decrease from the prior level. The plaintiff complained of bilateral lower abdominal tenderness, and guarding and rebound was noted upon examination. A transvaginal pelvic ultrasound revealed no evidence of a viable intrauterine pregnancy, but there was a large amount of complex fluid in the pelvis. Also noted was a left ovarian cyst and a normal right ovary and a large mass-like area in the cul-de-sac extending to the right adnexa, which was a new finding since the October 24, 2011 study. The report also revealed the suggestion of a ring-like tubal structure. Dr E’s impression was a ruptured ectopic pregnancy despite the decline of the -hCG following methotrexate therapy. The case was discussed with Dr A and the plaintiff was admitted immediately for ambulatory surgery.

The plaintiff underwent an emergent laparoscopic right salpingectomy and a left ovarian cyst aspiration for a right ectopic pregnancy. The surgery was performed by Dr A. Intraoperative findings revealed a right fallopian tube ectopic pregnancy, 2 simple left ovarian cysts, no pelvic adhesions, and a uterus that was small, mobile, and grossly normal.

The pathology report revealed that a segment of the right fallopian tube contained chorionic villi consistent with a fallopian tube pregnancy. The plaintiff was discharged home that day and told to return on November 23, 2011 for a postoperative check. When she came back to the WHC on November 23, 2011 and was seen by Dr A, she was noted to be ambulating, voiding, and passing gas, and that her pain was well controlled with pain medication, which was not needed on that day. She had no fever and her incision was healing well. The result of the ectopic pregnancy in the right tube was noted.

Dr A prescribed a contraceptive vaginal ring and Ms A was to return to the clinic for routine gynecologic care. However, she chose not to follow-up at the defendant hospital.

Allegations

The plaintiff asserted that during the diagnostic laparoscopy, Dr A and Dr B should have detected the ectopic pregnancy in the right fallopian tube. Her attorneys claimed that based upon the plaintiff’s abdominal pain,
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vaginal bleeding, and β-hCG levels, and absent evidence of intrauterine pregnancy on ultrasound, the defendants should have presumed ectopic pregnancy and adequately evaluated the fallopian tube before discharging the patient, thus avoiding rupture.

**Discovery**

At the deposition, the patient claimed that once her tube ruptured she was told by a physician at the defendant hospital that she would never again get pregnant but “could adopt.” She then revealed that she in fact became pregnant a year after the incidents at issue and suffered another ectopic pregnancy. She claimed no knowledge of discussions regarding the possibility of extrauterine pregnancy before the rupture was diagnosed, despite defendants’ testimony and hospital record entries regarding such discussions.

Our obstetric expert opined that the patient’s symptoms of lower back pain and blood in her urine with a positive pregnancy test could have been indicative of an early intrauterine pregnancy, a spontaneous abortion, or an ectopic pregnancy. A β-hCG level of 351 mIU/mL correlates to a 4-week pregnancy from a woman’s LMP and at that early stage it is impossible to see it on ultrasound due to the minuscule size of the fetal sac, they pointed out. The “discriminatory zone” of β-hCG is the level above which an imaging scan should reliably visualize a gestational sac within the uterus in a normal intrauterine pregnancy. It is not until a β-hCG level reaches 1500–1800 mIU/mL that a gestational sac would expect to be visible with transvaginal ultrasonography (TVUS).

The plaintiff’s β-hCG levels remained well below the “discriminatory zone,” making it impossible to see a fetal gestational sac using TVUS. Because it was too early to see a fetal gestational sac, it was impossible to make the diagnosis of an intrauterine pregnancy or spontaneous abortion, so the physicians appropriately decided to monitor the patient’s β-hCG levels, stressing the signs and symptoms of ectopic rupture that could herald a potentially life-threatening complication and advising the patient of the need to return for medical follow-up.

When the patient returned on October 28, Dr A examined all of the adnexal structures, carefully inspecting both fallopian tubes, but the ectopic pregnancy was too small to discriminate in the fallopian tubes at that level of development and β-hCG level. Postoperatively, when plaintiff’s β-hCG levels continued to rise, methotrexate was appropriately administered according to protocol.

When the patient subsequently returned her levels had risen and she properly underwent exploration, at which time the ectopic pregnancy was identified.

**Resolution**

Armed with expert support, the defendants moved for dismissal prior to trial. While the plaintiff contended that her symptoms should have raised the defendants’ index of suspicion for ectopic pregnancy, their expert could not refute the defendants’ contention through expert affidavit that the β-hCG levels on initial presentation were too low to support anything other than a nonviable pregnancy, whether ectopic or intrauterine.

In other words, even if the fallopian tube had been explored no viable pregnancy would have been located and thus plaintiff’s result would have been the same.

**The verdict**

After oral argument before the court, the case was dismissed. The court agreed with the defendants’ experts that given the facts the patient’s result would not have been altered by earlier intervention.

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Should this ectopic pregnancy have been diagnosed earlier?

TVP showed no evidence of a viable intrauterine pregnancy but the patient’s \( \beta \)-hCG levels complicated the picture.

The facts

On October 24, 2011, a 29-year-old patient presented to the defendant hospital’s emergency department complaining of a 4-day history of vaginal bleeding and lower abdominal pain. She was in no acute distress, and had no vomiting, diarrhea, dysuria, or headache. Her complaints were of dizziness and mild shortness of breath. An ultrasound had been performed and blood samples had been drawn when the patient was seen at the co-defendant hospital 2 days earlier.

The woman was told that the imaging showed no intrauterine pregnancy. Her blood sample, however, revealed a beta-human chorionic gonadotropin (\( \beta \)-hCG) level of 313 and rising, which correlated with her last menstrual period (LMP) on September 9, 2011. A basic metabolic panel, coagulation study, and urinalysis were normal, and testing for gonorrhea and chlamydia was negative. Urinalysis did show many bacteria. The patient’s hematocrit (HCT) was 33.2 and her hemoglobin (Hgb) was 11.1.

Physical examination by the emergency medicine attending physician found that the patient’s abdomen was soft with mild left quadrant tenderness but no guarding or rebound. The attending noted mild vaginal bleeding and that the cervical OS was closed. Abdominal and transvaginal pelvic ultrasound were performed and revealed no evidence of an intrauterine pregnancy, no focal uterine masses, a small amount of free fluid in the cul de sac, a small right ovarian cyst, and a normal left ovary. The impression was ectopic pregnancy rather than spontaneous abortion.

Because the patient had no pain or active vaginal bleeding she was discharged home with information about ectopic pregnancies. She was also told to follow up in the women’s health center (WHC) in 48 hours. On October 26, 2011, the plaintiff presented to the WHC as directed and was seen by co-defendant Dr A, who noted that her ultrasound was negative for intrauterine pregnancy. The plaintiff had no pain but was having a small amount of vaginal bleeding. Dr A’s impression was likely complete abortion but he noted that an ectopic pregnancy could not be ruled out.

Blood was drawn for an hCG level and the patient was to be called with the result. The \( \beta \)-hCG blood level was...
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Revolutionizing Hysteroscopic Tissue Removal Using the MyoSure® System

Authors:
Charles E. Miller, MD, FACOG
The Advanced IVF Institute/The Advanced Gynecologic Surgery Institute, Naperville, IL

Karyn M. Solky, MD
Ob/Gyn, Cedars-Sinai Medical Center, Los Angeles, CA

Andreas Thurkow, MD
Ob/Gyn Consultant at Academic Medical Center (University Hospital of the University of Amsterdam), Amsterdam

Introduction
Abnormal uterine bleeding affects approximately 30% of women and has been associated with endometrial polyps, fibroids, particularly submucosal, retained products of conception (RPOC), endometritis, atrophic endometrium, endometrial carcinoma and various entities of endometrial hyperplasia.1–3 Assessment of the endometrium could include endometrial biopsy, ultrasound, saline infused sonography, CT scan and MRI. Ultimately, direct visualization via hysteroscopy is known to provide a minimally invasive approach to visualize the endometrial cavity and enable subsequent removal of structural uterine lesions using electrosurgical loop or hysteroscopic morcellation. Hysteroscopic morcellation offers the advantage of simultaneous visualization and minimally invasive resection and/or sampling of uterine lesions without the use of energy, thereby improving procedure efficiency and outcomes. Three morcellation devices—the TRUCLEAR® Hysteroscopic Morcellator, Symphion™ Tissue Removal System and the MyoSure® Hysteroscopic Tissue Removal System (Myosure Tissue Removal System)—are currently available.4 This supplement will review the technology, data and clinical experiences using the MyoSure Tissue Removal System.

Resection of Polyps and Fibroids
Charles E. Miller, MD, FACOG
Endometrial polyps are a common intrauterine condition and are associated with abnormal uterine bleeding, subfertility, and premalignant and malignant tissue changes.5 Similarly, submucosal leiomyomas or fibroids are also associated with abnormal uterine bleeding, and subfertility and are rarely confused with malignant masses or sarcomas.5 Most recent guidelines therefore recommend polypectomy and myomectomy followed by histopathological examination to exclude the possibility of endometrial cancer.7,8 Electrosurgical resection with monopolar or bipolar current has been traditionally used to remove large polyps and fibroids. However, this has been associated with cervical dilatation to 10 mm and rare risk of hyponatremia related to non-saline distension media utilized with the monopolar resectoscope. Other
risks include: complications associated with excess absorption of some distension media, risk of thermal damage to healthy endometrium leading to synechiae, risk of perforation and visual field limitation from intrauterine chips.\(^9,10\) Hysteroscopic morcellation involves the use of a blade and a suction tube to simultaneously excise and remove tissue as well as clear a bloody field, thereby improving visibility and reducing the risk of perforations. In addition, hysteroscopic morcellation requires less cervical dilation and less anesthesia which improves patient satisfaction and reduces procedure time.\(^11\) A recent meta-analysis of four randomized clinical trials and three retrospective observational studies compared hysteroscopic morcellation with electrosurgical resection for the removal of intracavitary lesions. The authors concluded that patients undergoing intrauterine morcellation with either of the available devices had a smaller fluid deficit as opposed to those treated with electrosurgical resection. In addition, hysteroscopic morcellation of polyps and fibroids with either of the available devices is associated with a shorter procedure duration and lower odds of incomplete lesion removal, respectively. This meta-analysis thus demonstrated the advantages of hysteroscopic morcellation over electrosurgical resection in the removal of structural endometrial lesions 3 cm or less in size.\(^4\) Another systematic review and meta-analysis comparing hysteroscopic morcellation with resectoscopy similarly concluded that hysteroscopic morcellation is associated with a higher success rate and a shorter operative time among patients with endometrial polyps and submucous myomas.\(^12\)

A prospective US multicenter registry determined the feasibility of the MyoSure Tissue Removal System in surgical as well as office-based facilities and among patients treated for abnormal uterine bleeding or infertility. Mean percentage of fibroids removed with the MyoSure system was 95.4%, with the mean fibroid diameter of 2.2 cm and mean polyp diameter of 1.3 cm. While this study provides a representative depiction of hysteroscopic morcellation used in routine practice in the US, it also reports a high level of physician satisfaction with the MyoSure system.\(^13\) In 2015, Rubino and Lukes published a randomized, prospective, comparative trial incorporating nine ob/gyn practices and hospitals in the United States.\(^14\) The authors evaluated 12-month outcomes for patients undergoing MyoSure hysteroscopic morcellation of uterine polyps and myomas. Symptom severity as measured by the UFS-QOL (Uterine Fibroid Symptom—Quality of Life) scale improved significantly (\(P < .01\)) between baseline (mean score of 67.5 ± 15.4) and 12 months post-procedure (mean score of 22.3 ± 22.6). The HRQOL (The Health-Related Quality of Life) scale also improved significantly (\(P < .01\)).\(^14\)

Another prospective cohort study investigated the effectiveness of the MyoSure system for the removal of intrauterine pathology by trainees (61% of cases) and senior clinicians. Results from this report indicated that regardless of clinician experience, polypectomy with the MyoSure system was associated with 92% complete resection including polyps up to 7 cm MyoSure was also effective in removing Type 0, I, and II submucosal fibroids.\(^15\) Additionally, no patients experienced intraoperative complications consistent with previously reported less than <0.1% incidence with hysteroscopic morcellation.\(^16\) This is a 10-fold decrease from the complication rate reported with electrosurgical loop.\(^17\)

More recently, a retrospective case series from two US fertility clinics assessed fertility outcomes among subfertile women after treatment of intrauterine lesions with the MyoSure system. As observed in Table 1, use of the MyoSure system for the removal of intrauterine leiomyomas and polyps supports subsequent conception and live birth rates among subfertile women undergoing fertility treatment.\(^18\)

### TABLE 1: Fertility Outcomes after Hysteroscopic Morcellation of Intrauterine Leiomyomas and Polyps. Modified from Bhalani et al.\(^18\)

<table>
<thead>
<tr>
<th>Fertility Outcomes</th>
<th>Total (n=62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy, no. (% of women)</td>
<td>44 (71)</td>
</tr>
<tr>
<td>Time to pregnancy, months, mean ± SD</td>
<td>8.4 ± 7.0</td>
</tr>
<tr>
<td>Live birth, living child (% of pregnancies)</td>
<td>39 (78)</td>
</tr>
</tbody>
</table>

Taken together, these recent studies highlight the usefulness of the MyoSure system in the removal of polyps and fibroids for both clinicians and patients. As an infertility specialist and surgical innovator, hysteroscopic morcellation has been part of my surgical armamentarium for the management of endometrial polyps, uterine fibroids and retained products of conception for over the past decade. In my experience, as no energy is utilized, the ability to perform hysteroscopic morcellation provides a safe and efficient alternative, which minimizes the risk of tissue necrosis and subsequent intrauterine adhesions. Furthermore, normalizing the uterine cavity with the MyoSure system supports my patients’ ability to achieve successful pregnancies.

### Endometrial Tissue Sampling for Pathology

Karyn M. Solky, MD

Traditionally, blind endometrial biopsy and dilation & curettage (D&C) have been the mainstay of endometrial tissue sampling for pathological evaluation.\(^1\) However, several studies have indicated the limitations of curettage and blind biopsy in obtaining adequate samples and diagnosing focal intrauterine lesions. For instance, one study from 1993 demonstrated that the percentage of endometrial surface area sampled by the Pipelle device was only 4.2%.\(^9\) Similarly in 1975, Stock and Kanbour showed that approximately 60% of curettage specimens sampled less than half of the uterine cavity.\(^20\) A prospective study from 2001 compared the adequacy of D&C vs hysteroscopy with endometrial resection in obtaining a representative endometrial sample in women with postmenopausal bleeding and endometrium...
≥5 mm. This study demonstrated that compared to hysteroscopy, D&C missed 58% of polyps, 50% of hyperplasias, 60% of complex atypical hyperplasias, and 11% of endometrial cancers, thereby indicating that hysteroscopy with visual biopsy is superior to D&C for obtaining a representative endometrial sample.21

Another prospective trial described the low sensitivity and accuracy of blind biopsy with Novak’s curette in the diagnosis of benign focal intracavitary lesions. This study concluded that hysteroscopy enables accurate biopsy and direct visualization of the uterine cavity, which can aid in overcoming the false-negative results of blind biopsy.22 A retrospective cohort study corroborated the opinion, the MyoSure system also allows for a thorough biopsy.23 Resectoscopy with monopolar or bipolar current, however, is associated with the risk of trauma to adjacent endometrial tissue, which can lead to the development of intrauterine adhesions as well as the distortion of tissue morphology from thermal artifact.15 Given that recommendations from the Society for Gynecologic Oncology consider devices yielding crushed, cauterized, or very small samples as “unacceptable” for diagnosis of endometrial carcinoma, there has been a need to improve endometrial sample collection.25 It is widely recognized that endometrial cancer is frequently identified after a biopsy sample of complex atypical hyperplasia (CAH). Indeed, up to 40% of cases of CAH on pre-hysterectomy endometrial curettage will have cancer and on occasion will have significant myometrial invasion.26 Investigators have suggested that greater tissue volume at biopsy provided for pathologic diagnosing could reduce these discrepant results.27

Since the MyoSure Tissue Removal System enables concurrent resection and aspiration of endometrial tissue without electrocautery, it eliminates thermal artifact in tissue samples submitted for histologic evaluation. In my opinion, the MyoSure system also allows for a thorough sampling of the endometrial cavity while constant visualization reduces the risk of perforation compared to blind D&C. A recent analysis used extirpated uteri from postmenopausal women to compare endometrial sampling with the MyoSure system and blind curettage.28 This study demonstrated that use of the MyoSure system for endometrial sampling yielded more tissue for histopathological investigation versus sharp curettage. Further studies are warranted to determine if the extensive sampling capability of the MyoSure system is equivalent to outcomes associated with endometrial resection by loop.

MyoSure Curettage

In my personal practice, I recently encountered a 44-year-old healthy GO who presented with menorrhagia and was unable to tolerate an office endometrial biopsy or saline ultrasound and was taken to the operating room (OR) for hysteroscopy and MyoSure curettage, as well as sharp curette. Use of the MyoSure system enabled easy visualization and removal of multiple polyps. Additional tissue from all quadrants was also removed without difficulty using the MyoSure system. Pathology from the MyoSure sampling demonstrated a minute foci of endometrial adenocarcinoma, with staining concerning for Lynch syndrome. The routine curettage, by comparison, showed no overt abnormal pathology. The patient subsequently tested positive for Lynch syndrome and underwent LAVH, BSO and staging, with grade 1 endometrial adenocarcinoma confirmed in the uterine corpus as well. This case demonstrates for me the benefits of MyoSure Curettage for endometrial sampling compared to blind sharp curette.

In-office Use of the MyoSure System

Charles E. Miller, MD, FACOG

For many gynecologists, diagnostic hysteroscopy in the office setting has become routine for the evaluation of abnormal uterine bleeding. Endometrial sampling or resection of visually identified intrauterine pathology, on the other hand, is primarily deferred to the operating room and completed under general anesthesia. Recent studies have demonstrated that including endometrial sampling and removing endometrial polyps during hysteroscopy can be safely performed in the office with high patient tolerance and satisfaction.29–31 The literature is replete in regards to use of hysteroscopic morcellation for the management of endometrial polyps in an outpatient setting.30–32 A randomized prospective comparative trial comparing office and ambulatory surgical center use of the MyoSure system for removal of polyps and fibroids concluded that the MyoSure system proved to be efficacious in both settings.14 Similarly, a randomized controlled trial comparing two types of paracervical or intracervical block was associated with low pain scores during operative procedures with the MyoSure system.33

A subsequent prospective study on the use of MyoSure hysteroscopic morcellation to manage endometrial polyps in an office-based (outpatient) setting by McIlwaine and McElhinney was published in 2015.32 While this study was performed in a public hospital, evacuation of endometrial polyps was performed under local anesthesia. The mean polyp size was 13 mm and the mean resection time was 39.4 seconds. Complete resection was achieved in 95.2% of the cases. The median visual analogue score (VAS) was 2.7. In general, women were very satisfied; over 97% would recommend the procedure to a friend and over 95% were happy to consider a repeat procedure in the future if required. The complication rate was 4.8% and all were minor in nature.32 The authors determined that in-office polypectomy can also save critical healthcare resources.

In the past, reimbursement rates may have led to some resistance to adoption. However, based on the Centers for Medicare and Medicaid Services (CMS) 2017 Physician Schedule, the physician fee was significantly
increased to $1,382.07 for hysteroscopy and biopsy (CPT Code 58558) performed in the office setting. This is not only encouraging to physicians in their efforts to perform polypectomy in-office, but is more cost-effective for the patient, physician, and overall health system. This also allows the physician to be more efficient and the patient to be in a more comfortable environment.

The MyoSure system is of small enough diameter to allow for use with minimal cervical dilation which can typically be performed using local anesthesia in the form of paracervical block. In addition, the MyoSure system uses no electrical energy and is associated with minimal discomfort to patients during polypectomy under local anesthesia. Furthermore, there are versatile MyoSure devices available that are designed to access hard-to-reach pathology, resect smaller and softer tissue, and remove a range of tissue types and sizes.

**Removal of RPOC**
Andreas Thurkow, MD

RPOC are known to occur after miscarriage, vaginal or cesarean delivery, and medical or surgical pregnancy termination. While bleeding and infections are the RPOC-associated short-term complications, formation of intrauterine adhesions has been described as the long-term complication of RPOC. Indeed, intrauterine adhesions are known to significantly affect future reproductive outcomes due to infertility, miscarriages, and pregnancy complications such as placenta accreta. D&C represents the traditional surgical treatment of RPOC which has been reported to increase the endometrial trauma from the RPOC. Currently, hysteroscopy to identify the areas with the suspected RPOC followed by removal of the RPOC using the loop as curettage with gentle motions without application of current is recommended. A recent meta-analysis reported that hysteroscopic removal of RPOC led to low complication rates, low rates of intrauterine adhesions and high rates of subsequent pregnancies as compared with blind curettage. A retrospective case series evaluated the effectiveness of hysteroscopic morcellation in removing RPOC among women with histologic confirmation of placental remnants after miscarriage, termination of pregnancy or delivery. Data from this analysis reported that hysteroscopic morcellation led to successful removal of placental remnants as the first approach in 94.3% of cases, among which 85.7% of cases were associated with no adverse events. This study supported the expanded utility of hysteroscopic morcellation devices in the removal of RPOC. A 2014 case presentation reported the utility of the MyoSure system in the successful and expeditious removal of RPOC in a 33-year-old patient with a loss at 10 weeks’ gestation. Similarly, the MyoSure system was useful in resecting RPOC in a 24-year-old woman with recurrent miscarriages and intrauterine adhesions following treatment of non-progressive pregnancies. Use of the MyoSure system in this case was not only associated with successful removal of RPOC, but also prevention of adhesion formation and a subsequent ongoing viable pregnancy. Another case report demonstrated the utility of the MyoSure system in the management of a cornual ectopic pregnancy that had failed medical therapy. A prospective cohort study that used the MyoSure system to resect RPOC in 16 cases reported that this device was useful in the removal of smaller volumes of residual tissue (up to 10 mL). Although the experience at present is limited, in our institution the use of the Myosure system for RPOC is actually seen as the best indication for the device—providing excellent removal of the retained tissue without damaging the uterine wall. The technique seems to be especially promising for the prevention of adhesion formation when compared with our experience with traditional D&C. Hysteroscopic removal, specifically with the MyoSure system, seems to improve these results but it remains to be proven.

In light of all these results, removal of RPOC with hysteroscopic morcellation devices appears to be safe and effective.

**Conclusions**

Several clinical studies confirm the effectiveness of the MyoSure Tissue Removal System in the resection of polyps and fibroids in the hospital and office setting. In order to treat a wide range of intrauterine pathology and a full spectrum of intrauterine procedures, the MyoSure Tissue Removal System offers multiple device types: MyoSure LITE, REACH and XL. In previously subfertile women, normalizing the uterine cavity by treating intrauterine pathology with the MyoSure system supports subsequent conception and live birth rates. In addition, MyoSure has shown to obtain adequate and sufficient endometrial samples for histopathological assessment. The utility of the MyoSure system has now been expanded to the removal of retained products of conception.

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**Important Safety Information for the MyoSure® Hysteroscopic Tissue Removal System**

**Indications for Use:** The MyoSure Tissue Removal System is intended for hysteroscopic intrauterine procedures by trained gynecologists to resect and remove tissue including submucous myomas and endometrial polyps.

**Contraindications:** The MyoSure Tissue Removal System should not be used with pregnant patients or patients exhibiting pelvic infection, cervical malignancies, or previously diagnosed endometrial cancer.
You can use the full capabilities of the MyoSure LITE, REACH, and XL devices to:

- Complete a variety of procedures and treat a wide range of intrauterine pathology
- Achieve confidence in resections and tissue collections
- Bring efficiency and consistency to your procedures

See how the complete MyoSure system can improve procedural efficiency.

Learn more at MyoSure.com/ONESYSTEM

IMPORTANT SAFETY INFORMATION

The MyoSure® tissue removal system is intended for hysteroscopic intrauterine procedures by trained gynecologists to resect and remove tissue including submucous myomas, endometrial polyps, and retained products of conception. It is not appropriate for patients who are or may be pregnant, or are exhibiting pelvic infection, cervical malignancies, or previously diagnosed endometrial cancer.


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