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OBG MANAGEMENT

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Managing genitourinary endometriosis

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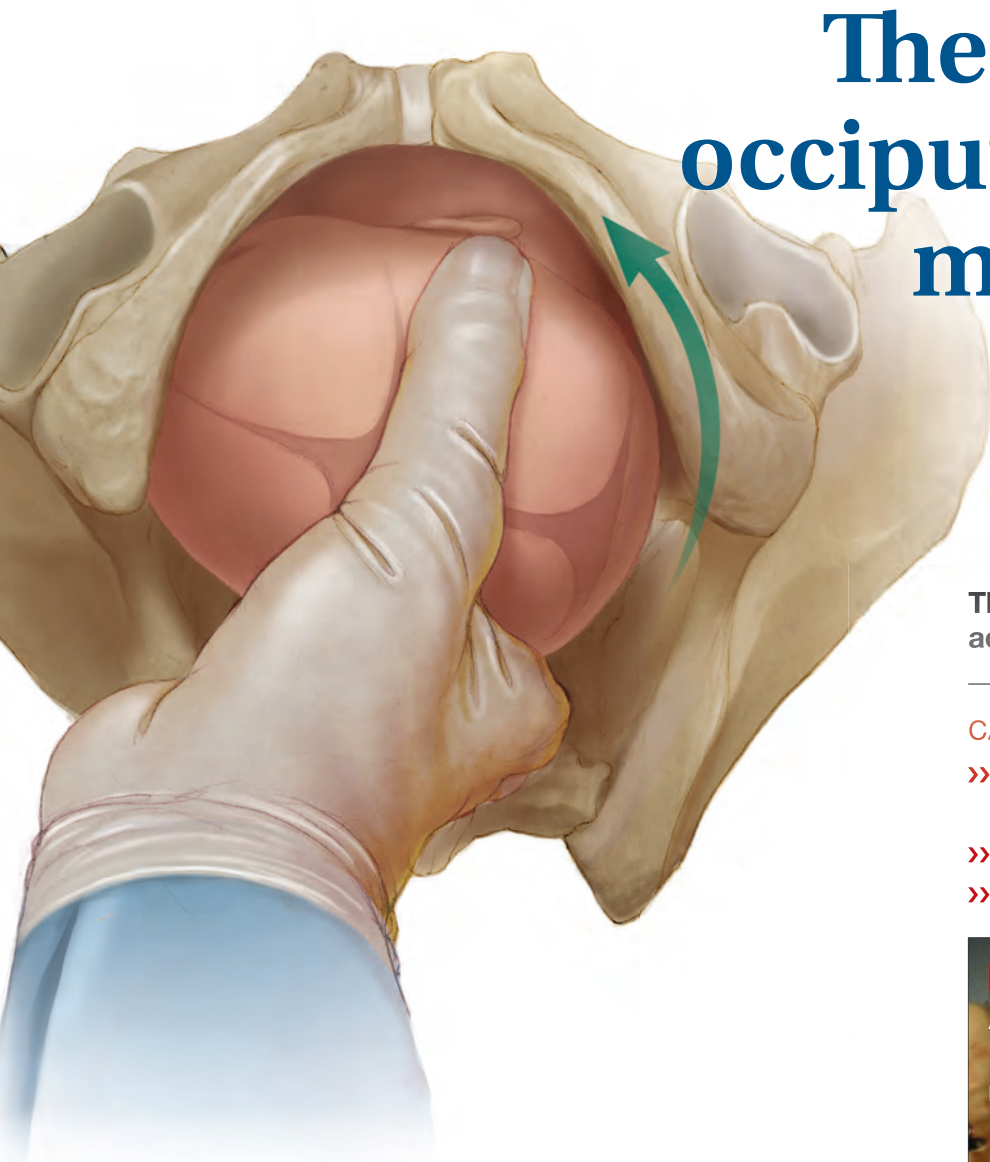


The persistent occiput posterior malposition

Steps for decision making from Robert L. Barbieri, MD

The dilemmas of adolescent consent

CANCER UPDATES

- IP chemotherapy for ovarian cancer
- PARP inhibitors
- MIS for cervical cancer

TAKE A NEXT STEP IN MODERATE TO SEVERE ENDOMETRIOSIS PAIN[1]

Orilissa
elagolix tablets 150 mg 200 mg

Clinical study design: Two robust, similar, multicenter, double-blind, prospective, placebo-controlled phase 3 trials of 6-month treatment at 2 doses as compared with placebo in premenopausal women (18 to 49 years of age) with surgically diagnosed endometriosis and moderate or severe endometriosis-associated pain (N=1686).[1,2]

- Co-primary efficacy endpoints (independently evaluated): proportion of responders for dysmenorrhea at month 3 and proportion of responders for NMPP at month 3[1]

*Statistical significance for dyspareunia was not achieved with the 150 mg QD dose of ORILISSA.

INDICATION

ORILISSA® (elagolix) is indicated for the management of moderate to severe pain associated with endometriosis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- ORILISSA is contraindicated in women who are pregnant (exposure to ORILISSA early in pregnancy may increase the risk of early pregnancy loss), in women with known osteoporosis or severe hepatic impairment (due to risk of bone loss), or with concomitant use of strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine and gemfibrozil).

WARNINGS AND PRECAUTIONS

Bone Loss

- ORILISSA causes a dose-dependent decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORILISSA-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider assessment of BMD in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, and do not use in women with known osteoporosis.
- Limit the duration of use to reduce the extent of bone loss.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- Women who take ORILISSA may experience a reduction in the amount, intensity, or duration of menstrual bleeding, which may reduce the ability to recognize the occurrence of pregnancy in a timely manner. Perform pregnancy testing if pregnancy is suspected, and discontinue ORILISSA if pregnancy is confirmed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

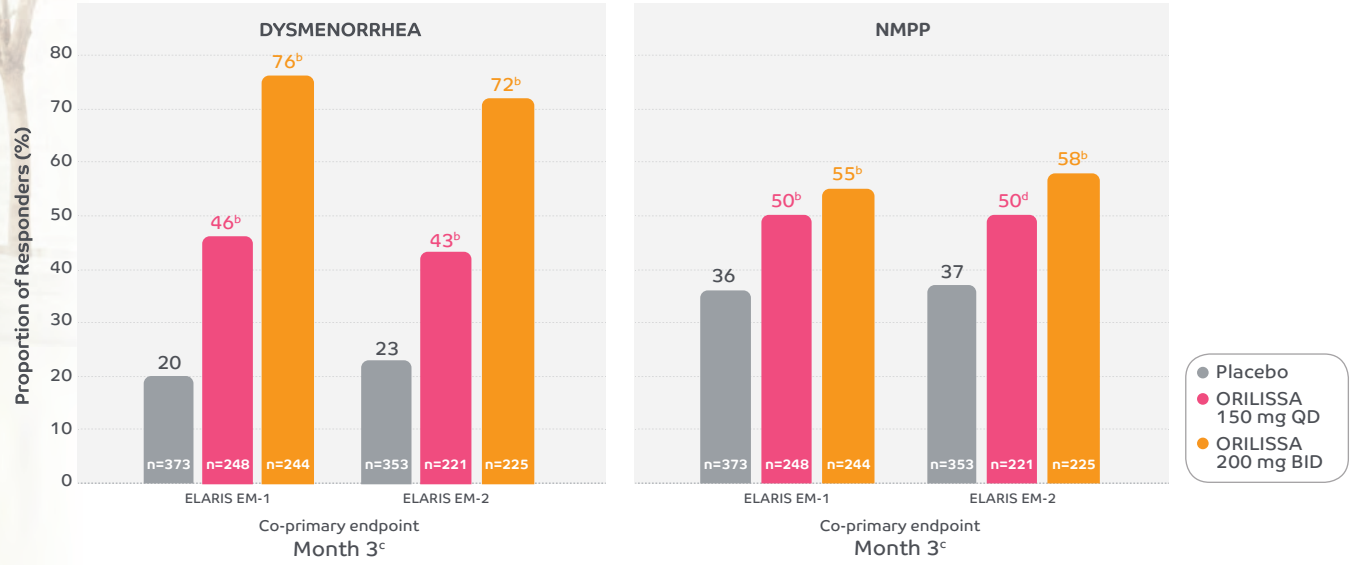
- Suicidal ideation and behavior, including one completed suicide, occurred in subjects treated with ORILISSA in the endometriosis clinical trials.
- ORILISSA users had a higher incidence of depression and mood changes compared to placebo and ORILISSA users with a history of suicidality or depression had an increased incidence of depression. Promptly evaluate patients with depressive symptoms to determine whether the risks of continued therapy outweigh the benefits. Patients with new or worsening depression, anxiety, or other mood changes should be referred to a mental health professional, as appropriate.
- Advise patients to seek immediate medical attention for suicidal ideation and behavior. Reevaluate the benefits and risks of continuing ORILISSA if such events occur.

abbvie

PROVEN PAIN RELIEF IN 2 ORAL DOSING OPTIONS

EM-1 and EM-2: Response Rates vs Placebo[1,2,a-f]

Women were defined as responders only if they experienced clinically meaningful[a] pain reduction and stable or decreased rescue analgesic use for endometriosis-associated pain, as recorded in a daily electronic diary.



EM=ELARIS ENDOMETRIOSIS.

[a]Clinically meaningful reduction in pain was defined as a calculated threshold of improvement in pain score in each study. The threshold was determined based on an analysis of the change in pain score that corresponded to "much improved" or "very much improved" on the Patient Global Impression of Change questionnaire.

[b]$P \leq 0.001$ vs placebo.

[c]The co-primary efficacy endpoints were the proportion of responders for dysmenorrhea and pelvic pain not related to menses (NMPP) at month 3 compared with placebo.

[d]$P \leq 0.01$ vs placebo.

[e]Study EM-1—Dysmenorrhea responder threshold: at least 0.81-point decrease from baseline in dysmenorrhea score; NMPP responder threshold: at least 0.36-point decrease from baseline in NMPP score.

[f]Study EM-2—Dysmenorrhea responder threshold: at least 0.85-point decrease from baseline in dysmenorrhea score; NMPP responder threshold: at least 0.43-point decrease from baseline in NMPP score.

- The **most common adverse reactions** (>5%) in clinical trials included hot flushes and night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions, and mood changes[1]

Hepatic Transaminase Elevations

- In clinical trials, dose-dependent elevations of serum alanine aminotransferase (ALT) at least 3 times the upper limit of the reference range occurred with ORILISSA.
- Use the lowest effective dose and instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.
- Promptly evaluate patients with elevations in liver tests to determine whether the benefits of continued therapy outweigh the risks.

Reduced Efficacy with Estrogen-Containing Contraceptives

- Based on the mechanism of action of ORILISSA, estrogen-containing contraceptives are expected to reduce the efficacy of ORILISSA. The effect of progestin-only contraceptives on the efficacy of ORILISSA is unknown.
- Advise women to use non-hormonal contraceptives during treatment and for one week after discontinuing ORILISSA.

ADVERSE REACTIONS

- The most common adverse reactions (>5%) in clinical trials included hot flushes and night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions, and mood changes.

These are not all the possible side effects of ORILISSA.

Safety and effectiveness of ORILISSA in patients less than 18 years of age have not been established.

References: 1. Orilissa [package insert]. North Chicago, IL: AbbVie Inc; 2018. **2.** Taylor HS, Giudice LC, Lessey BA, et al. Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. *N Engl J Med.* 2017;377(1):28-40.

Consider ORILISSA for your patients with moderate to severe endometriosis pain.
Take a next step at ORILISSA.com/hcp

Please see Brief Summary of full Prescribing Information on the following page of this advertisement.

Orilissa®
elagolix tablets 150 mg 200 mg

ORILISSA™ (elagolix) tablets, for oral use

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

ORILISSA is indicated for the management of moderate to severe pain associated with endometriosis.

DOSAGE AND ADMINISTRATION

Important Dosing Information

- Exclude pregnancy before starting ORILISSA or start ORILISSA within 7 days from the onset of menses.
- Take ORILISSA at approximately the same time each day, with or without food.
- Use the lowest effective dose, taking into account the severity of symptoms and treatment objectives *[see Warnings and Precautions]*.
- Limit the duration of use because of bone loss (Table 1) *[see Warnings and Precautions]*.

Table 1. Recommended Dosage and Duration of Use

Dosing Regimen	Maximum Treatment Duration	Coexisting Condition
Initiate treatment with ORILISSA 150 mg once daily	24 months	None
Consider initiating treatment with ORILISSA 200 mg twice daily	6 months	Dyspareunia
Initiate treatment with ORILISSA 150 mg once daily. Use of 200 mg twice daily is not recommended.	6 months	Moderate hepatic impairment (Child-Pugh Class B)

Hepatic Impairment

No dosage adjustment of ORILISSA is required in women with mild hepatic impairment (Child-Pugh A).

Compared to women with normal liver function, those with moderate hepatic impairment had approximately 3-fold higher elagolix exposures and those with severe hepatic impairment had approximately 7-fold higher elagolix exposures. Because of these increased exposures and risk for bone loss:

- ORILISSA 150 mg once daily is recommended for women with moderate hepatic impairment (Child-Pugh B) with the duration of treatment limited to 6 months. Use of ORILISSA 200 mg twice daily is not recommended for women with moderate hepatic impairment *[see Use in Specific Populations]*.
- ORILISSA is contraindicated in women with severe hepatic impairment (Child-Pugh C) *[see Contraindications and Use in Specific Populations]*.

Missed Dose

Instruct the patient to take a missed dose of ORILISSA on the same day as soon as she remembers and then resume the regular dosing schedule.

- 150 mg once daily: take no more than 1 tablet each day.
- 200 mg twice daily: take no more than 2 tablets each day.

CONTRAINDICATIONS

ORILISSA is contraindicated in women:

- Who are pregnant *[see Use in Specific Populations]*. Exposure to ORILISSA early in pregnancy may increase the risk of early pregnancy loss.
- With known osteoporosis because of the risk of further bone loss *[see Warnings and Precautions]*
- With severe hepatic impairment because of the risk of bone loss *[see Use in Specific Populations]*
- With concomitant use of strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine and gemfibrozil) *[see Drug Interactions]*

WARNINGS AND PRECAUTIONS

Bone Loss

ORILISSA causes a dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment *[see Adverse Reactions]*. The impact of these BMD decreases on long-term bone health and future fracture risk are unknown. Consider assessment of BMD in patients with a history of a low-trauma fracture or other risk factors for osteoporosis or bone loss, and do not use in women with known osteoporosis. Limit the duration of use to reduce the extent of bone loss.

Although the effect of supplementation with calcium and vitamin D was not studied, such supplementation may be beneficial for all patients.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

Women who take ORILISSA may experience a reduction in the amount, intensity or duration of menstrual bleeding, which may reduce the ability to recognize the occurrence of a pregnancy in a timely manner *[see Adverse Reactions]*. Perform pregnancy testing if pregnancy is suspected, and discontinue ORILISSA if pregnancy is confirmed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

Suicidal ideation and behavior, including one completed suicide, occurred in subjects treated with ORILISSA in the endometriosis clinical trials. ORILISSA subjects had a higher incidence of depression and mood changes compared to placebo, and ORILISSA subjects with a history of suicidality or depression had a higher incidence of depression compared to subjects without such a history *[see Adverse Reactions]*. Promptly evaluate patients with depressive symptoms to determine whether the risks of continued therapy outweigh the benefits *[see Adverse Reactions]*. Patients with new or worsening depression, anxiety or other mood changes should be referred to a mental health professional, as appropriate. Advise patients to seek immediate medical attention for suicidal ideation and behavior. Reevaluate the benefits and risks of continuing ORILISSA if such events occur.

Hepatic Transaminase Elevations

In clinical trials, dose-dependent elevations of serum alanine aminotransferase (ALT) at least 3-times the upper limit of the reference range occurred with ORILISSA. Use the lowest effective dose of ORILISSA and instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice. Promptly evaluate patients with elevations in liver tests to determine whether the benefits of continued therapy outweigh the risks *[see Adverse Reactions]*.

Reduced Efficacy with Estrogen-Containing Contraceptives

Based on the mechanism of action of ORILISSA, estrogen containing contraceptives are expected to reduce the efficacy of ORILISSA. The effect of progestin-only contraceptives on the efficacy of ORILISSA is unknown. Advise women to use non-hormonal contraceptives during treatment with ORILISSA and for one week after discontinuing ORILISSA *[see Use in Specific Populations, Drug Interactions]*.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in labeling:

- Bone loss *[see Warnings and Precautions]*
- Change in menstrual bleeding pattern and reduced ability to recognize pregnancy *[see Warnings and Precautions]*
- Suicidal ideation, suicidal behavior, and exacerbation of mood disorders *[see Warnings and Precautions]*
- Hepatic transaminase elevations *[see Warnings and Precautions]*

Clinical Trials Experience

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

The safety of ORILISSA was evaluated in two six-month, randomized, double-blind, placebo-controlled clinical trials [EM-1 (NCT01620528) and EM-2 (NCT01931670)] in which a total of 952 adult women with moderate to severe pain associated with endometriosis were treated with ORILISSA (475 with 150 mg once daily and 477 with 200 mg twice daily) and 734 were treated with placebo. The population age range was 18-49 years old. Women who completed six months of treatment and met eligibility criteria continued treatment in two uncontrolled, blinded six-month extension trials [EM-3 (NCT01760954) and EM-4 (NCT02143713)], for a total treatment duration of up to 12 months.

Serious Adverse Events

Overall, the most common serious adverse events reported for subjects treated with ORILISSA in the two placebo-controlled clinical trials (Studies EM-1 and EM-2) included appendicitis (0.3%), abdominal pain (0.2%), and back pain (0.2%). In these trials, 0.2% of subjects treated with ORILISSA 150 mg once daily and 0.2% of subjects treated with ORILISSA 200 mg twice daily discontinued therapy due to serious adverse reactions compared to 0.5% of those given placebo.

Adverse Reactions Leading to Study Discontinuation

In the two placebo-controlled clinical trials (Studies EM-1 and EM-2), 5.5% of subjects treated with ORILISSA 150 mg once daily and 9.6% of subjects treated with ORILISSA 200 mg twice daily discontinued therapy due to adverse reactions compared to 6.0% of those given placebo. Discontinuations were most commonly due to hot flushes or night sweats (1.1% with 150 mg once daily and 2.5% with 200 mg twice daily) and nausea (0.8% with 150 mg once daily and 1.5% with 200 mg twice daily) and were dose-related. The majority of discontinuations due to hot flushes or night sweats (10 of 17, 59%) and nausea (7 of 11, 64%) occurred within the first 2 months of therapy.

In the two extension trials (Studies EM-3 and EM-4), discontinuations were most commonly due to decreased BMD and were dose-related. In these trials, 0.3% of subjects treated with ORILISSA 150 mg once daily and 3.6% of subjects treated with ORILISSA 200 mg twice daily discontinued therapy due to decreased BMD.

Common Adverse Reactions:

Adverse reactions reported in ≥ 5% of women in the two placebo-controlled trials in either ORILISSA dose group and at a greater frequency than placebo are noted in the following table.

Table 2. Percentage of Subjects in Studies EM-1 and EM-2 with Treatment-Emergent Adverse Reactions Occurring in at Least 5% of Subjects (either ORILISSA Dose Group) and at a Greater Incidence than with Placebo

	ORILISSA 150 mg Once Daily N=475	ORILISSA 200 mg Twice Daily N=477	Placebo N=734
	%	%	%
Hot Flush or Night Sweats	24	46	9
Headache	17	20	12
Nausea	11	16	13
Insomnia	6	9	3
Mood altered, mood swings	6	5	3
Amenorrhea	4	7	<1
Depressed mood, depression, depressive symptoms and/or tearfulness	3	6	2
Anxiety	3	5	3
Arthralgia	3	5	3

Less Common Adverse Reactions:

In Study EM-1 and Study EM-2, adverse reactions reported in ≥ 3% and < 5% in either ORILISSA dose group and greater than placebo included: decreased libido, diarrhea, abdominal pain, weight gain, dizziness, constipation and irritability.

The most commonly reported adverse reactions in the extension trials (EM-3 and EM-4) were similar to those in the placebo-controlled trials.

Bone Loss

The effect of ORILISSA on BMD was assessed by dual-energy X-ray absorptiometry (DXA).

In Studies EM-1 and EM-2, there was a dose-dependent decrease in BMD in ORILISSA-treated subjects compared to an increase in placebo-treated subjects.

In Study EM-1, compared to placebo, the mean change from baseline in lumbar spine BMD at 6 months was -0.9% (95% CI: -1.3, -0.4) with ORILISSA 150 mg once daily and -3.1% (95% CI: -3.6, -2.6) with ORILISSA 200 mg twice daily (Table 3). The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the placebo-controlled treatment period was 2% with ORILISSA 150 mg once daily, 7% with ORILISSA 200 mg twice daily and < 1% with placebo. In the blinded extension Study EM-3, continued bone loss was observed with 12 months of continuous treatment with ORILISSA. The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the extension treatment period was 8% with continuous ORILISSA 150 mg once daily and 21% with continuous ORILISSA 200 mg twice daily.

In Study EM-2, compared to placebo, the mean change from baseline in lumbar spine BMD at 6 months was -1.3% (95% CI: -1.8, -0.8) with ORILISSA 150 mg once daily and -3.0% (95% CI: -3.5, -2.6) with ORILISSA 200 mg twice daily (Table 3). The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the placebo-controlled treatment period was < 1% with ORILISSA 150 mg once daily, 6% with ORILISSA 200 mg twice daily and 0% with placebo. In the blinded extension Study EM-4, continued bone loss was observed with 12 months of continuous treatment with ORILISSA. The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the extension treatment period was 2% with continuous ORILISSA 150 mg once daily and 21% with continuous ORILISSA 200 mg twice daily.

Table 3. Percent Change from Baseline in Lumbar Spine BMD at Month 6

	ORILISSA 150 mg Once Daily	ORILISSA 200 mg Twice Daily	Placebo
EM-1			
N	183	180	277
Percent Change from Baseline, %	-0.3	-2.6	0.5
Treatment Difference, % (95% CI)	-0.9 (-1.3, -0.4)	-3.1 (-3.6, -2.6)	
EM-2			
N	174	183	271
Percent Change from Baseline, %	-0.7	-2.5	0.6
Treatment Difference, % (95% CI)	-1.3 (-1.8, -0.8)	-3.0 (-3.5, -2.6)	

To assess for recovery, the change in lumbar spine BMD over time was analyzed for subjects who received continuous treatment with ORILISSA 150 mg once daily or ORILISSA 200 mg twice daily for up to 12 months and who were then followed after cessation of therapy for an additional 6 months. Partial recovery of BMD was seen in these subjects (Figure 1).

In Study EM-3, if a subject had BMD loss of more than 1.5% at the lumbar spine or more than 2.5% at the total hip at the end of treatment, follow-up DXA was required after 6 months off-treatment. In Study EM-4, all subjects were required to have a follow-up DXA 6 months off treatment regardless of change in BMD and if a subject had BMD loss of more than 1.5% at the lumbar spine or more than 2.5% at the total hip after 6 months off treatment, follow-up DXA was required after 12 months off-treatment. Figure 2 shows the change in lumbar spine BMD for the subjects in Study EM-2/EM-4 who completed 12 months of treatment with ORILISSA and who had a follow-up DXA 12-months off treatment.

Figure 1. Percent Change from Baseline in Lumbar Spine BMD in Subjects Who Received 12 Months of ORILISSA and Had Follow-up BMD 6 Months off Therapy in Studies EM-2/EM-4

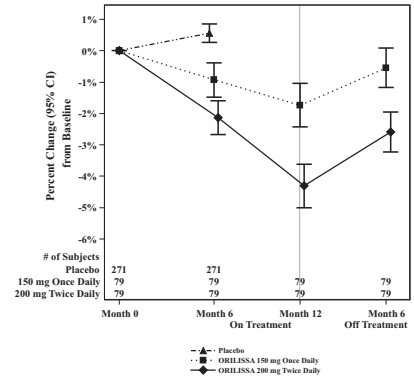
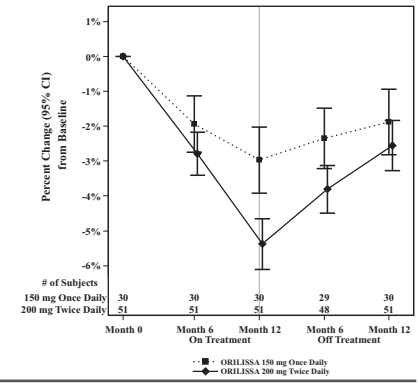


Figure 2. Percent Change from Baseline in Lumbar Spine BMD in Subjects Who Received 12 Months of ORILISSA and Had Follow-up BMD 12 Months off Therapy in Studies EM-2/EM-4



Suicidal Ideation, Suicidal Behavior and Exacerbation of Mood Disorders

In the placebo-controlled trials (Studies EM-1 and EM-2), ORILISSA was associated with adverse mood changes (see Table 2 and Table 4), particularly in those with a history of depression.

Table 4. Suicidal Ideation and Suicidal Behavior in Studies EM-1 and EM-2

Adverse Reactions	ORILISSA 150 mg Once Daily (N=475) n (%)	ORILISSA 200 mg Twice Daily (N=477) n (%)	Placebo (N=734) n (%)
Completed suicide	1 (0.2)	0	0
Suicidal ideation	1 (0.2)	1 (0.2)	0

A 44-year-old woman received 31 days of ORILISSA 150 mg once daily then completed suicide 2 days after ORILISSA discontinuation. She had no relevant past medical history; life stressors were noted.

Among the 2090 subjects exposed to ORILISSA in the endometriosis Phase 2 and Phase 3 studies, there were four reports of suicidal ideation. In addition to the two subjects in Table 4, there were two additional reports of suicidal ideation: one subject in EM-3 (150 mg once daily) and one in a Phase 2 study (75 mg once daily, an unapproved dose). Three of these subjects had a history of depression. Two subjects discontinued ORILISSA and two completed the clinical trial treatment periods.

Hepatic Transaminase Elevations

In the placebo-controlled clinical trials (Studies EM-1 and EM-2), dose-dependent asymptomatic elevations of serum ALT to at least 3-times the upper limit of the reference range occurred during treatment with ORILISSA (150 mg once daily – 1/450, 0.2%; 200 mg twice daily – 5/443, 1.1%; placebo – 1/696, 0.1%). Similar increases were seen in the extension trials (Studies EM-3 and EM-4).

Changes in Lipid Parameters

Dose-dependent increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and serum triglycerides were noted during ORILISSA treatment in EM-1 and EM-2. In EM-1 and EM-2, 12% and 1% of subjects with mildly elevated LDL-C (130-159 mg/dL) at baseline had an increase in LDL-C concentrations to 190 mg/dL or higher during treatment with ORILISSA and placebo, respectively. In EM-1 and EM-2, 4% and 1% of subjects with mildly elevated serum triglycerides (150-300 mg/dL) at baseline had an increase in serum triglycerides to at least 500 mg/dL during treatment with ORILISSA and placebo, respectively. The highest measured serum triglyceride concentration during treatment with ORILISSA was 982 mg/dL.

Table 5. Mean Change and Maximum Increase from Baseline in Serum Lipids in Studies EM-1 and EM-2

	ORILISSA 150 mg Once Daily N=475	ORILISSA 200 mg Twice Daily N=477	Placebo N=734
LDL-C (mg/dL)			
Mean change at Month 6	5	13	-3
Maximum increase during Treatment Period	137	107	122
HDL-C (mg/dL)			
Mean change at Month 6	2	4	1
Maximum increase during Treatment Period	43	52	45
Triglycerides (mg/dL)			
Mean change at Month 6	<1	11	-3
Maximum increase during Treatment Period	624	484	440

Lipid increases occurred within 1 to 2 months after the start of ORILISSA and remained stable thereafter over 12 months.

Hypersensitivity Reactions

In Studies EM-1 and EM-2, non-serious hypersensitivity reactions including rash occurred in 5.8% of ORILISSA treated-subjects and 6.1% of placebo-treated subjects. These events led to study drug discontinuation in 0.4% of ORILISSA-treated subjects and 0.5% of placebo-treated subjects.

Endometrial Effects

Endometrial biopsies were performed in subjects in Study EM-1 and its extension at Month 6 and Month 12. These biopsies showed a dose-dependent decrease in proliferative and secretory biopsy patterns and an increase in quiescent/minimally stimulated biopsy patterns. There were no abnormal biopsy findings on treatment, such as endometrial hyperplasia or cancer.

Based on transvaginal ultrasound, during the course of a 3-menstrual cycle study in healthy women, ORILISSA 150 mg once daily and 200 mg twice daily resulted in a dose-dependent decrease from baseline in mean endometrial thickness.

Effects on menstrual bleeding patterns

The effects of ORILISSA on menstrual bleeding were evaluated for up to 12 months using an electronic daily diary where subjects classified their flow of menstrual bleeding (if present in the last 24 hours) as spotting, light, medium, or heavy. ORILISSA led to a dose-dependent reduction in mean number of bleeding and spotting days and bleeding intensity in those subjects who reported menstrual bleeding.

Table 6. Mean Bleeding/Spotting Days and Mean Intensity Scores at Month 3

	ORILISSA 150mg Once Daily		ORILISSA 200mg Twice Daily		Placebo	
	Baseline	Month 3	Baseline	Month 3	Baseline	Month 3
Mean bleeding/ spotting days in prior 28 days	5.3	2.8	5.7	0.8	5.4	4.6
Mean Intensity score[a]	2.6	2.2	2.5	2.0	2.6	2.4

[a]Intensity for subjects who reported at least 1 day of bleeding or spotting during 28 day interval. Scale ranges from 1 to 4, 1 = spotting, 2 = light, 3 = medium, 4 = heavy

ORILISSA also demonstrated a dose-dependent increase in the percentage of women with amenorrhea (defined as no bleeding or spotting in a 56-day interval) over the treatment period. The incidence of amenorrhea during the first six months of treatment ranged from 6-17% for ORILISSA 150 mg once daily, 13-52% for ORILISSA 200 mg twice daily and less than 1% for placebo. During the second 6 months of treatment, the incidence of amenorrhea ranged from 11-15% for ORILISSA 150 mg once daily and 46-57% for ORILISSA 200 mg twice daily.

After 6 months of therapy with ORILISSA 150 mg once daily, resumption of menses after stopping treatment was reported by 59%, 87% and 95% of women within 1, 2, and 6 months, respectively. After 6 months of therapy with ORILISSA 200 mg twice daily, resumption of menses after stopping treatment was reported by 60%, 88%, and 97% of women within 1, 2, and 6 months, respectively.

After 12 months of therapy with ORILISSA 150 mg once daily resumption of menses after stopping treatment was reported by 77%, 95% and 98% of women within 1, 2, and 6 months respectively. After 12 months of therapy with ORILISSA 200 mg twice daily resumption of menses after stopping treatment was reported by 55%, 91% and 96% of women within 1, 2, and 6 months respectively.

DRUG INTERACTIONS

Potential for ORILISSA to Affect Other Drugs

Elagolix is a weak to moderate inducer of cytochrome P450 (CYP) 3A. Co-administration with ORILISSA may decrease plasma concentrations of drugs that are substrates of CYP3A.

Elagolix is an inhibitor of efflux transporter P-glycoprotein (P-gp). Co-administration with ORILISSA may increase plasma concentrations of drugs that are substrates of P-gp (e.g., digoxin).

Potential for Other Drugs to Affect ORILISSA

Elagolix is a substrate of CYP3A, P-gp, and OATP1B1.

Concomitant use of ORILISSA 200 mg twice daily and strong CYP3A inhibitors for more than 1 month is not recommended. Limit concomitant use of ORILISSA 150 mg once daily and strong CYP3A inhibitors to 6 months.

Co-administration of ORILISSA with drugs that induce CYP3A may decrease elagolix plasma concentrations.

The effect of concomitant use of P-gp inhibitors or inducers on the pharmacokinetics of ORILISSA is unknown. Co-administration of ORILISSA with drugs that inhibit OATP1B1 may increase elagolix plasma concentrations. Concomitant use of ORILISSA and strong OATP1B1 inhibitors (e.g., cyclosporine and gemfibrozil) is contraindicated.

Drug Interactions - Examples and Clinical Management

Table 7 summarizes the effect of co-administration of ORILISSA on concentrations of concomitant drugs and the effect of concomitant drugs on ORILISSA.

Table 7. Established Drug Interactions Based on Drug Interaction Trials

Concomitant Drug Class: Drug Name	Effect on Plasma Exposure of Elagolix or Concomitant Drug	Clinical Recommendations
Antiarrhythmics digoxin	↑ digoxin	Clinical monitoring is recommended for digoxin when co-administered with ORILISSA.
Antimycobacteria rifampin	↑ elagolix	Concomitant use of ORILISSA 200 mg twice daily and rifampin is not recommended. Limit concomitant use of ORILISSA 150 mg once daily and rifampin to 6 months.
Benzodiazepines oral midazolam	↓ midazolam	Consider increasing the dose of midazolam and individualize therapy based on the patient's response.
Statins rosuvastatin	↓ rosuvastatin	Consider increasing the dose of rosuvastatin.
The direction of the arrow indicates the direction of the change in the area under the curve (AUC) (↑= increase, ↓ = decrease).		

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Exposure to ORILISSA early in pregnancy may increase the risk of early pregnancy loss. Use of ORILISSA is contraindicated in pregnant women. Discontinue ORILISSA if pregnancy occurs during treatment.

The limited human data with the use of ORILISSA in pregnant women are insufficient to determine whether there is a risk for major birth defects or miscarriage. Although two cases of congenital malformations were reported in clinical trials with ORILISSA, no pattern was identified and miscarriages were reported at a similar incidence across treatment groups *(see Data)*.

When pregnant rats and rabbits were orally dosed with elagolix during the period of organogenesis, postimplantation loss was observed in pregnant rats at doses 20 times the maximum recommended human dose (MRHD). Spontaneous abortion and total litter loss was observed in rabbits at doses 7 and 12 times the MRHD. There were no structural abnormalities in the fetuses at exposures up to 40 and 12 times the MRHD for the rat and rabbit, respectively *(see Data)*.

The background risk for major birth defects and miscarriage in the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

There were 49 pregnancies reported in clinical trials of more than 3,500 women (of whom more than 2,000 had endometriosis) treated with ORILISSA for up to 12 months. These pregnancies occurred while the women were receiving ORILISSA or within 30 days after stopping ORILISSA. Among these 49 pregnancies, two major congenital malformations were reported. In one case of infant cleft palate, the mother was treated with ORILISSA 150 mg daily and the estimated fetal exposure to ORILISSA occurred during the first 30 days of pregnancy. In one case of infant tracheoesophageal fistula, the mother was treated with ORILISSA 150 mg daily and the estimated fetal exposure to ORILISSA occurred during the first 15 days of pregnancy.

Among these 49 pregnancies, there were five cases of spontaneous abortion (miscarriage) compared to five cases among the 20 pregnancies that occurred in more than 1100 women treated with placebo. Although the duration of fetal exposure was limited in ORILISSA clinical trials, there were no apparent decreases in birth weights associated with ORILISSA in comparison to placebo.

Animal Data

Embryofetal development studies were conducted in the rat and rabbit. Elagolix was administered by oral gavage to pregnant rats (25 animals/dose) at doses of 0, 300, 600 and 1200 mg/kg/day and to rabbits (20 animals/dose) at doses of 0, 100, 150, and 200 mg/kg/day, during the period of organogenesis (gestation day 6-17 in the rat and gestation day 7-20 in the rabbit).

In rats, maternal toxicity was present at all doses and included six deaths and decreases in body weight gain and food consumption. Increased postimplantation losses were present in the mid dose group, which was 20 times the MRHD based on AUC. In rabbits, three spontaneous abortions and a single total litter loss were observed at the highest, maternally toxic dose, which was 12 times the MRHD based on AUC. A single total litter loss occurred at a lower non-maternally toxic dose of 150 mg/kg/day, which was 7 times the MRHD.

No fetal malformations were present at any dose level tested in either species even in the presence of maternal toxicity. At the highest doses tested, the exposure margins were 40 and 12 times the MRHD for the rat and rabbit, respectively. However, because elagolix binds poorly to the rat gonadotropin-releasing hormone (GnRH) receptor (~1000 fold less than to the human GnRH receptor), the rat study is unlikely to identify pharmacologically mediated effects of elagolix on embryofetal development. The rat study is still expected to provide information on potential non-target-related effects of elagolix.

In a pre- and postnatal development study in rats, elagolix was given in the diet to achieve doses of 0, 100 and 300 mg/kg/day (25 per dose group) from gestation day 6 to lactation day 20. There was no evidence of maternal toxicity. At the highest dose, two dams had total litter loss, and one failed to deliver. Pup survival was decreased from birth to postnatal day 4. Pups had lower birth weights and lower body weight gains were observed throughout the pre-weaning period at 300 mg/kg/day. Smaller body size and effect on startle response were associated with lower pup weights at 300 mg/kg/day. Post-weaning growth, development and behavioral endpoints were unaffected.

Maternal plasma concentrations in rats on lactation day 21 at 100 and 300 mg/kg/day (47 and 125 ng/mL) were 0.06-fold and 0.16-fold the maximal elagolix concentration (C_{max}) in humans at the MRHD. Because the exposures achieved in rats were much lower than the human MRHD, this study is not predictive of potentially higher lactational exposure in humans.

Lactation

Risk Summary

There is no information on the presence of elagolix or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. There are no adequate animal data on the excretion of ORILISSA in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ORILISSA and any potential adverse effects on the breastfed child from ORILISSA.

Data

There are no adequate animal data on excretion of ORILISSA in milk.

Females and Males of Reproductive Potential

Based on the mechanism of action, there is a risk of early pregnancy loss if ORILISSA is administered to a pregnant woman *[see Use in Specific Populations]*.

Pregnancy Testing

Exclude pregnancy before initiating treatment with ORILISSA. Perform pregnancy testing if pregnancy is suspected during treatment with ORILISSA *[see Warnings and Precautions]*.

Contraception

Advise women to use effective non-hormonal contraception during treatment with ORILISSA and for one week after discontinuing ORILISSA *[see Warnings and Precautions and Drug Interactions]*.

Pediatric Use

Safety and effectiveness of ORILISSA in patients less than 18 years of age have not been established.

Renal Impairment

No dose adjustment of ORILISSA is required in women with any degree of renal impairment or end-stage renal disease (including women on dialysis).

Hepatic Impairment

No dosage adjustment of ORILISSA is required for women with mild hepatic impairment (Child-Pugh A). Only the 150 mg once daily regimen is recommended for women with moderate hepatic impairment (Child-Pugh B) and the duration of treatment should be limited to 6 months.

ORILISSA is contraindicated in women with severe hepatic impairment (Child-Pugh C) *[see Contraindications]*.

OVERDOSAGE

In case of overdose, monitor the patient for any signs or symptoms of adverse reactions and initiate appropriate symptomatic treatment, as needed.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Two-year carcinogenicity studies conducted in mice (50, 150, or 500 mg/kg/day) and rats (150, 300, or 800 mg/kg/day) that administered elagolix by the dietary route revealed no increase in tumors in mice at up to 19-fold the MRHD based on AUC. In the rat, there was an increase in thyroid (male and female) and liver (males only) tumors at the high dose (12 to 13-fold the MRHD). The rat tumors were likely species-specific and of negligible relevance to humans.

Elagolix was not genotoxic or mutagenic in a battery of tests, including the *in vitro* bacterial reverse mutation assay, the *in vitro* mammalian cell forward mutation assay at the thymidine kinase (TK+/-) locus in L5178Y mouse lymphoma cells, and the *in vivo* mouse micronucleus assay.

In a fertility study conducted in the rat, there was no effect of elagolix on fertility at any dose (50, 150, or 300 mg/kg/day). Based on AUC, the exposure multiple for the MRHD in women compared to the highest dose of 300 mg/kg/day in female rats is approximately 5-fold. However, because elagolix has low affinity for the GnRH receptor in the rat *[see Use in Specific Populations]*, and because effects on fertility are most likely to be mediated via the GnRH receptor, these data have low relevance to humans.

PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide).

- Advise patients on contraceptive options, not to get pregnant while using ORILISSA, to be mindful that menstrual changes could reflect pregnancy and to discontinue ORILISSA if pregnancy occurs *[see Contraindications and Warnings and Precautions]*.
- Inform patients that estrogen containing contraceptives are expected to reduce the efficacy of ORILISSA.
- Inform patients about the risk of bone loss. Advise adequate intake of calcium and vitamin D *[see Warnings and Precautions]*.
- Advise patients to seek immediate medical attention for suicidal ideation and behavior. Instruct patients with new onset or worsening depression, anxiety, or other mood changes to promptly seek medical attention *[see Warnings and Precautions]*.
- Counsel patients on signs and symptoms of liver injury *[see Warnings and Precautions]*.
- Instruct patients who miss a dose of ORILISSA to take the missed dose on the same day as soon as she remembers and then resume the regular dosing schedule:
  - 150 mg once daily: no more than 1 tablet each day should be taken.
  - 200 mg twice daily: no more than 2 tablets each day should be taken.
- Instruct patients to dispose of unused medication via a take-back option if available or to otherwise follow FDA instructions for disposing of medication in the household trash, www.fda.gov/drugdisposal, and not to flush down the toilet.

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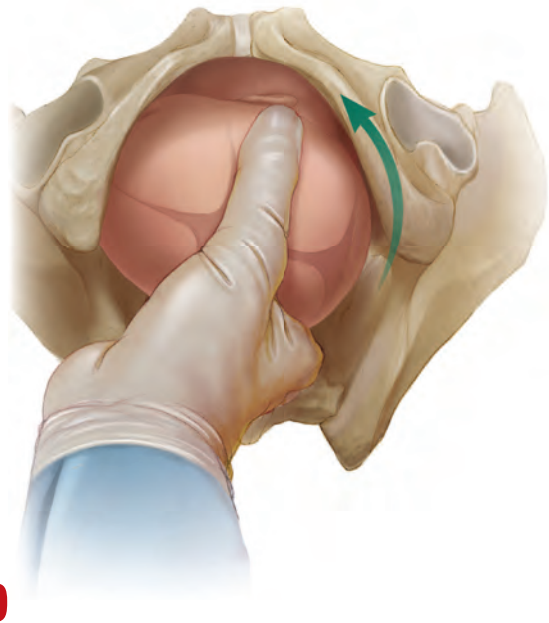
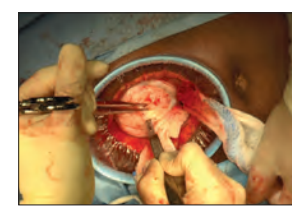


See what's ON THE WEB! page 9

Apps for contraception **29**



Minilaparotomy **52**

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COVER IMAGE: KIMBERLY MARTENS

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Indication

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

Important Safety Information

INTRAROSA is contraindicated in women with undiagnosed abnormal genital bleeding.

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

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

Please see the following page for a Brief Summary of full Prescribing Information.

References: 1. Intrarosa [package insert]. Waltham, MA: AMAG Pharmaceuticals, Inc.; 2018. **2.** Archer DF, Labrie F, Bouchard C, et al. *Menopause*. 2015;22(9):950-963. **3.** Labrie F, Archer DF, Koltun W, et al. *Menopause*. 2016;23(3):243-256.

amag PHARMACEUTICALS

Intrarosa®
Prasterone VAGINAL INSERTS 6.5 mg

INTRAROSA® (prasterone) vaginal inserts

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

INDICATION

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS Current or Past History of Breast Cancer

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

ADVERSE REACTIONS Clinical Trials Experience

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

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

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

amag PHARMACEUTICALS

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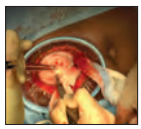
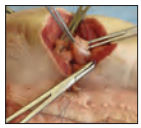


Minilaparotomy: Minimally invasive approach to abdominal myomectomy
SIERRA J. SEAMAN, MD;
PATRICIA J. MATTINGLY, MD;
AND ARNOLD P. ADVINCULA, MD

See QR code on page 52



Instructional video for 4th-degree obstetric laceration repair using modified beef tongue model
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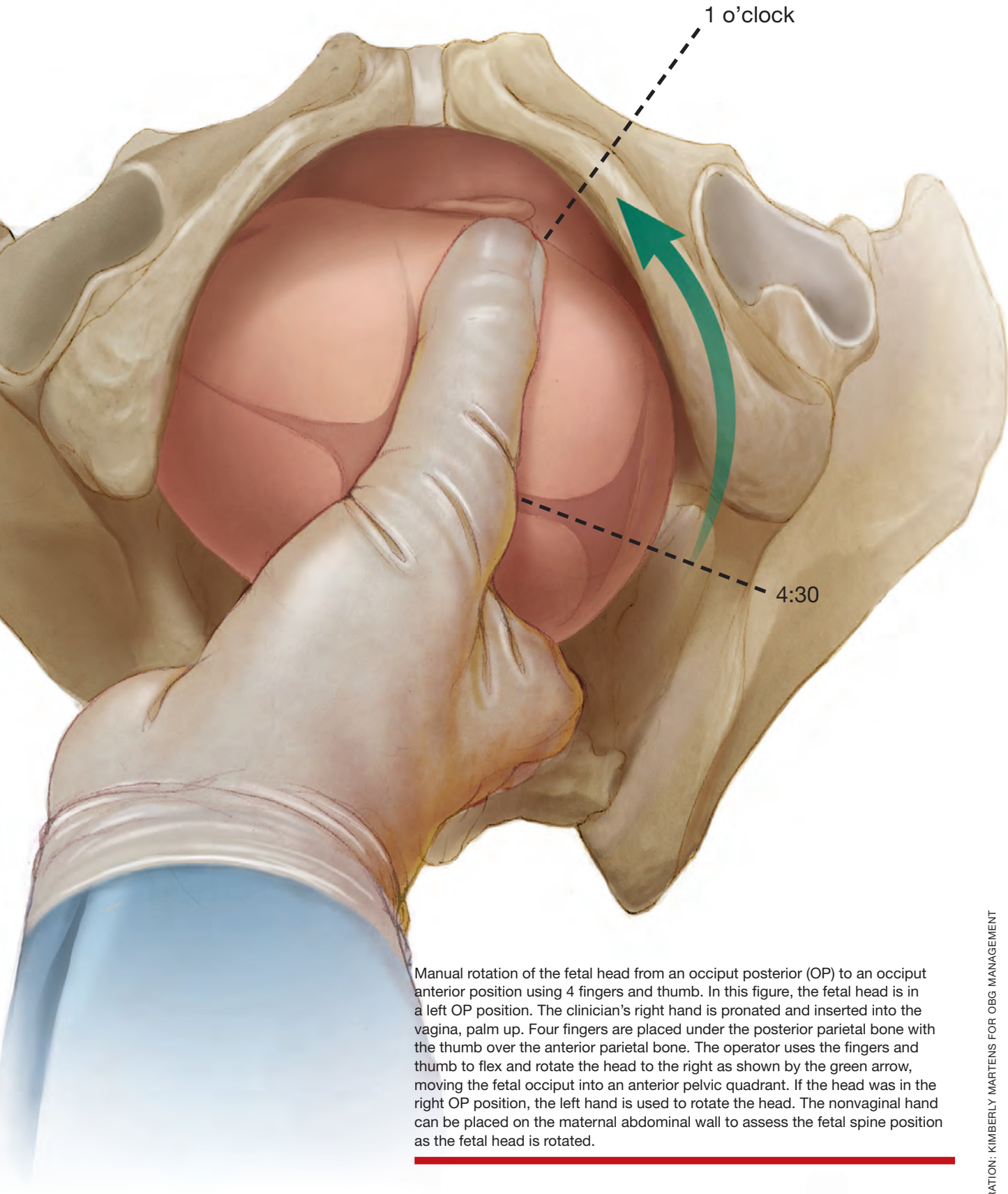

Manual rotation of the fetal head from an occiput posterior (OP) to an occiput anterior position using 4 fingers and thumb. In this figure, the fetal head is in a left OP position. The clinician's right hand is pronated and inserted into the vagina, palm up. Four fingers are placed under the posterior parietal bone with the thumb over the anterior parietal bone. The operator uses the fingers and thumb to flex and rotate the head to the right as shown by the green arrow, moving the fetal occiput into an anterior pelvic quadrant. If the head was in the right OP position, the left hand is used to rotate the head. The nonvaginal hand can be placed on the maternal abdominal wall to assess the fetal spine position as the fetal head is rotated.

ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

What is your approach to the persistent occiput posterior malposition?

One of the peskiest problems in labor obstetrics is the persistent OP position

Robert L. Barbieri, MD
Editor in Chief, OBG Management
Chair, Obstetrics and Gynecology
Brigham and Women's Hospital, Boston, Massachusetts
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Harvard Medical School, Boston

CASE 7- to 8-lb baby suspected to be in occiput posterior (OP) position

A certified nurse midwife (CNM) asks you to consult on a 37-year-old woman (G1P0) at 41 weeks' gestation who was admitted to labor and delivery for a late-term induction. The patient had a normal first stage of labor with placement of a combined spinal-epidural anesthetic at a cervical dilation of 4 cm. She has been fully dilated for 3.5 hours and pushing for 2.5 hours with a Category 1 fetal heart rate tracing. The CNM reports that the estimated fetal weight is 7 to 8 lb and the station is +3/5. She suspects that the fetus is in the left OP position. She asks for your advice on how to best deliver the fetus. The patient strongly prefers not to have a cesarean delivery (CD).

What is your recommended approach?

The cardinal movements of labor include cephalic engagement, descent, flexion, internal rotation, extension and rotation of the head at delivery, internal rotation of the shoulders, and expulsion of the body. In the first stage of labor many fetuses are in the OP position. Flexion and internal rotation of the fetal head in a mother with a gynecoid pelvis results in most fetuses assuming an occiput anterior (OA) position with the presenting diameter of the head (occipitobregmatic) being optimal for spontaneous vaginal delivery. Late in the second stage of labor only about 5% of fetuses are in the OP position with the presenting diameter of the head being large (occipitofrontal) with an extended head attitude, thereby reducing the probability of a rapid spontaneous vaginal delivery.

Risk factors for OP position late in the second stage of labor include[1,2]:

- nulliparity
- body mass index > 29 kg/m^2
- gestation age ≥ 41 weeks
- birth weight > 4 kg
- regional anesthesia.

Maternal outcomes associated with persistent OP position include protracted first and second stage of labor, arrest of second stage of labor, and increased rates of operative vaginal delivery, anal sphincter injury, CD, postpartum hemorrhage, chorioamnionitis, and endomyometritis.[1,3,4] The neonatal complications of persistent OP position include increased rates of shoulder dystocia, low Apgar score, umbilical artery acidemia, meconium, and admission to a neonatal intensive care unit.[1,5]

Diagnosis

Many obstetricians report that they can reliably detect a fetus in the OP position based upon abdominal palpation of the fetal spine and digital vaginal examination of the fetal sutures, fontanels, and ears. Such self-confidence may not be wholly warranted, however. Most contemporary data indicate that digital vaginal examination has an error rate of approximately 20% for identifying the position of the cephalic fetus, especially in the presence of fetal caput succedaneum and asynclitism.[6-10]

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) recommends that cephalic position be determined by transabdominal imaging.[11] By placing the ultrasound probe on the maternal abdomen, a view of the fetal body at the level of the chest helps determine

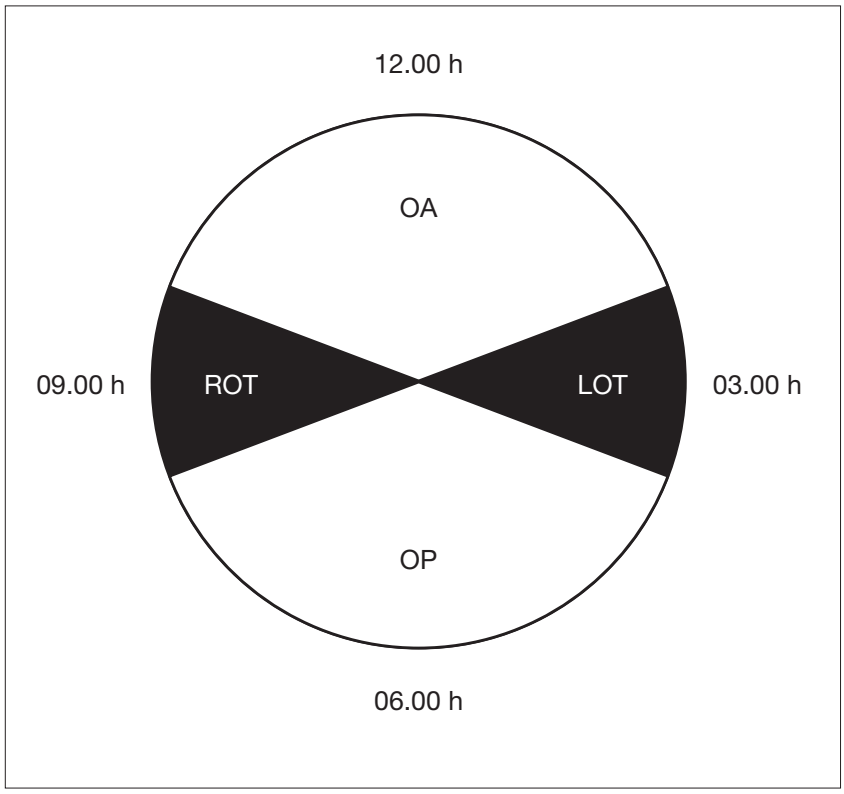

FIGURE International Society of Ultrasound in Obstetrics and Gynecology–recommended classification of fetal position based on positions of the hour on a clock face. Occiput positions from 03.30 h to 08.30 h are indicative of an occiput posterior (OP) position. Positions from 09.30 h to 02.30 h are indicative of an occiput anterior (OA) position. The remaining small 1-hour slivers on the left and right side of the clock face represent occiput transverse (LOT; ROT) positions.

Source: Ghi T, Eggebo T, Lees C, et al. ISUOG practice guidelines: intrapartum ultrasound. *Ultrasound Obstet Gynecol*. 2018;52:128-139. Used with permission.

the position of the fetal spine. When the probe is placed in a suprapubic position, the observation of the fetal orbits facing the probe indicates an OP position.

When the presenting part is at a very low station, a transperineal ultrasound may be helpful to determine the position of the occiput. The ISUOG recommends that position be defined using a clock face, with positions from 330 h to 830 h being indicative of OP and positions from 930 h to 230 h being indicative of OA.[11] The small remaining slivers on the clock face indicate an occiput transverse position (**FIGURE**).[11]

Approaches to managing the OP position

First stage of labor

Identification of a cephalic-presenting fetus in the OP position in the first stage of labor might warrant increased attention to fetal position in the second stage of labor, but does not usually alter management of the first stage.

Second stage of labor

If an OP position is identified in the second stage of labor, many obstetricians will consider manual rotation of the fetal occiput to an anterior pelvic quadrant to facilitate labor progress. Because a fetus in the OP position may spontaneously rotate to the OA position at any point during the second stage, a judicious interval of waiting is reasonable before attempting a manual rotation in the second stage. For example, allowing the second stage to progress for 60 to 90 min in a nulliparous woman or 30 to 60 min in a multiparous woman will permit some fetuses to rotate to the OA position without intervention.

If the OP position persists beyond these time points, a manual rotation could be considered. There are no high-quality clinical trials to support this maneuver,[12] but observational reports suggest that this low-risk maneuver may help reduce the rate of CD and anal sphincter trauma.[13-15]

Manual rotation from OP to OA. Prior to performing the rotation, the maternal bladder should be emptied and an adequate anesthetic provided. One technique is to use the 4 fingers of the hand as a "spatula" to turn the head. If the fetus is in a left OP position, the operator's right hand is pronated and inserted into the vagina, palm up. Four fingers are placed under the posterior parietal bone with the thumb over the anterior parietal bone (**ILLUSTRATION**, page 10).[4] The operator uses the fingers and thumb to flex and rotate the head to the right, moving the fetal occiput into an anterior pelvic quadrant.[4] If the head is in the right OP position, the left hand is used to rotate the head. The nonvaginal hand can be placed on the maternal abdominal wall to assess the fetal spine position as the fetal head is rotated. The fetal head may need to be held in the anterior pelvic quadrant during a few maternal pushes to prevent the head from rotating back into the OP position.

CONTINUED ON PAGE 14

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CONTINUED FROM PAGE 12

Approaching delivery late in the second stage

If the second stage has progressed for 3 or 4 hours, as in the case described above, and the fetus remains in the OP position, delivery may be indicated to avoid the maternal and fetal complications of an even more prolonged second stage. At some point in a prolonged second stage, expectant management carries more maternal and fetal risks than intervention.

Late in the second stage, options for delivery of the fetus in the OP include: CD, rotational forceps delivery, direct forceps delivery from the OP position, and vacuum delivery.

Cesarean delivery. CD of the fetus in the OP position may be indicated when the fetus is estimated to be macrosomic, the station is high (biparietal diameter palpable on abdominal examination), or when the parturient has an android pelvis (narrow fore-pelvis and anterior convergence of the pelvic bone structures in a wedge shape). During CD, if difficulty is encountered in delivering the fetal head, a hand from below, extension of the uterine incision, or reverse breech extraction may be necessary to complete the delivery. If the clinical situation is conducive to operative vaginal delivery, forceps or vacuum can be used.

Rotational forceps delivery. During residency I was told to always use rotational forceps to deliver a fetus in the persistently OP position if the parturient had a gynecoid pelvis (wide oval shape of pelvic bones, wide subpubic arch). Dr. Frederick Irving wrote[16]:

> "Although textbooks almost universally advocate the extraction of the occiput directly posterior without rotation we do not advise it.... Such an extraction maneuver is inartistic and show[s] a lack of regard for the mechanical factors involved in the mechanism of labor. The method used at the Boston Lying-In Hospital presupposes an accurate diagnosis of the primary position. If the fetal back is on the right the head should be rotated to the right; if on the left, toward the left. The head is always rotated in the direction in which the back lies. The forceps are applied as if the occiput was directly anterior. Carrying the forceps handles in a wide sweep the occiput is now rotated to the anterior quadrant of the pelvis or 135 degrees. It will be found that the head turns easily in the way it should go but that it is difficult or impossible to rotate it in the improper direction. The instrument is then reapplied as in the second part of the Scanzoni maneuver."

Rotation of the fetus from the OP to the OA position may reduce the risk of sphincter injury with vaginal birth. With the waning of rotational forceps skills, many obstetricians prefer a nonrotational approach with direct forceps or vacuum delivery from the OP position.

Direct forceps delivery from the OP position. A fetus in the OP position for 3 to 4 hours of the second stage of labor will often have a significant degree of head molding. The Simpson forceps, with its shallow and longer cephalic curve, accommodates significant fetal head molding and is a good forceps choice in this situation.

Vacuum delivery. In the United States, approximately 5% of vaginal deliveries are performed with a vacuum device, and 1% with forceps.[17] Consequently, many obstetricians frequently perform operative vaginal delivery with a vacuum device and infrequently or never perform operative vaginal delivery with forceps. Vacuum vaginal delivery may be the instrument of choice for many obstetricians performing an operative delivery of a fetus in the OP position. However, the vacuum has a higher rate of failure, especially if the OP fetus is at a higher station.[18]

In some centers, direct forceps delivery from the OP position is preferred over an attempt at vacuum delivery, because in contemporary obstetric practice most centers do not permit the sequential use of vacuum followed by forceps (due to the higher rate of fetal trauma of combination operative delivery). Since vacuum delivery of the fetus in the OP position has a greater rate of failure than forceps, it may be best to initiate operative vaginal delivery of the fetus in the OP position with forceps. If vacuum is used to attempt a vaginal delivery and fails due to too many pop-offs, a CD would be the next step.

Take action when needed to optimize outcomes

The persistent OP position is associated with a longer second stage of labor. It is common during a change of shift for an obstetrician to sign out to the on-coming clinician a case of a prolonged second stage with the fetus in the OP position. In this situation, the on-coming clinician cannot wait hour after hour after hour hoping for a spontaneous delivery. If the on-coming clinician has a clear plan of how to deal with the persistent OP position—including ultrasound confirmation of position and physical examination to determine station, fetal size and adequacy of the pelvis, and timely selection of a delivery technique—the adverse maternal and neonatal outcomes sometimes

CONTINUED ON PAGE 48

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Paragard is intended for intrauterine contraception for up to 10 years.

Important Safety Information

- Paragard must not be used by women who have acute pelvic inflammatory disease (PID); have had a postpregnancy or postabortion uterine infection in the past 3 months; have cancer of the uterus or cervix; have an infection of the cervix; have an allergy to any component; or have Wilson's disease.
- If a woman misses her period, she must be promptly evaluated for pregnancy.
- Possible serious complications that have been associated with intrauterine contraceptives are PID, embedment, perforation of the uterus, and expulsion.
- Paragard must not be used by women who are pregnant as this can be life threatening and may result in loss of pregnancy or infertility.
- The most common side effects of Paragard are bleeding and spotting; for most women, these typically subside after 2 to 3 months.
- **Paragard does not protect against HIV or other sexually transmitted infections (STI).**

Please see the following page for a brief summary of full Prescribing Information.

Over 6 million Paragard units distributed[3]

Paragard® T380A
intrauterine copper contraceptive
simple, honest pregnancy prevention™

CooperSurgical

References: 1. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion. Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use; 2017. **2.** Kaneshiro B, Aeby T. Long-term safety, efficacy, and patient acceptability of the intrauterine Copper T-380A contraceptive device. *Int J Womens Health*. 2010;2:211-220. **3.** Data on file, March 2018. CooperSurgical, Inc.

*According to the Centers for Disease Control and Prevention (CDC), Paragard is one of the least restrictive birth control options across all patient types compared to other IUDs.

BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR
ParaGard® T 380A Intrauterine Copper Contraceptive

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

ParaGard® is indicated for intrauterine contraception for up to 10 years. The pregnancy rate in clinical studies has been less than 1 pregnancy per 100 women each year.

CONTRAINDICATIONS

ParaGard® should not be placed when one or more of the following conditions exist:

1. Pregnancy or suspicion of pregnancy
2. Abnormalities of the uterus resulting in distortion of the uterine cavity
3. Acute pelvic inflammatory disease, or current behavior suggesting a high risk for pelvic inflammatory disease
4. Postpartum endometritis or postabortal endometritis in the past 3 months
5. Known or suspected uterine or cervical malignancy
6. Genital bleeding of unknown etiology
7. Mucopurulent cervicitis
8. Wilson's disease
9. Allergy to any component of ParaGard®
10. A previously placed IUD that has not been removed

WARNINGS

1. Intrauterine Pregnancy

If intrauterine pregnancy occurs with ParaGard® in place and the string is visible, ParaGard® should be removed because of the risk of spontaneous abortion, premature delivery, sepsis, septic shock, and, rarely, death. Removal may be followed by pregnancy loss.

If the string is not visible, and the woman decides to continue her pregnancy, check if the ParaGard® is in her uterus (for example, by ultrasound). If ParaGard® is in her uterus, warn her that there is an increased risk of spontaneous abortion and sepsis, septic shock, and rarely, death. In addition, the risk of premature labor and delivery is increased.

Human data about risk of birth defects from copper exposure are limited. However, studies have not detected a pattern of abnormalities, and published reports do not suggest a risk that is higher than the baseline risk for birth defects.

2. Ectopic Pregnancy

Women who become pregnant while using ParaGard® should be evaluated for ectopic pregnancy. A pregnancy that occurs with ParaGard® in place is more likely to be ectopic than a pregnancy in the general population. However, because ParaGard® prevents most pregnancies, women who use ParaGard® have a lower risk of an ectopic pregnancy than sexually active women who do not use any contraception.

3. Pelvic Infection

Although pelvic inflammatory disease (PID) in women using IUDs is uncommon, IUDs may be associated with an increased relative risk of PID compared to other forms of contraception and to no contraception. The highest incidence of PID occurs within 20 days following insertion. Therefore, the visit following the first post-insertion menstrual period is an opportunity to assess the patient for infection, as well as to check that the IUD is in place. Since pelvic infection is most frequently associated with sexually transmitted organisms, IUDs are not recommended for women at high risk for sexual infection. Prophylactic antibiotics at the time of insertion do not appear to lower the incidence of PID.

PID can have serious consequences, such as tubal damage (leading to ectopic pregnancy or infertility), hysterectomy, sepsis, and, rarely, death. It is therefore important to promptly assess and treat any woman who develops signs or symptoms of PID.

Guidelines for treatment of PID are available from the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia at www.cdc.gov or 1-800-311-3435. Antibiotics are the mainstay of therapy. Most healthcare professionals also remove the IUD.

The significance of actinomyces-like organisms on Papanicolaou smear in an asymptomatic IUD user is unknown, and so this finding alone does not always require IUD removal and treatment. However, because pelvic actinomycosis is a serious infection, a woman who has *symptoms* of pelvic infection possibly due to actinomyces should be treated and have her IUD removed.

4. Immunocompromise

Women with AIDS should not have IUDs inserted unless they are clinically stable on antiretroviral therapy. Limited data suggest that asymptomatic women infected with human immunodeficiency virus may use intrauterine devices. Little is known about the use of IUDs in women who have illnesses causing serious immunocompromise. Therefore these women should be carefully monitored for infection if they choose to use an IUD. The risk of pregnancy should be weighed against the theoretical risk of infection.

5. Embedment

Partial penetration or embedment of ParaGard® in the myometrium can make removal difficult. In some cases, surgical removal may be necessary.

6. Perforation

Partial or total perforation of the uterine wall or cervix may occur rarely during placement, although it may not be detected until later. Spontaneous migration has also been reported. If perforation does occur, remove ParaGard® promptly, since the copper can lead to intraperitoneal adhesions. Intestinal penetration, intestinal obstruction, and/or damage to adjacent organs may result if an IUD is left in the peritoneal cavity. Pre-operative imaging followed by laparoscopy or laparotomy is often required to remove an IUD from the peritoneal cavity.

7. Expulsion

Expulsion can occur, usually during the menses and usually in the first few months after insertion. There is an increased risk of expulsion in the nulliparous patient. If unnoticed, an unintended pregnancy could occur.

8. Wilson's Disease

Theoretically, ParaGard® can exacerbate Wilson's disease, a rare genetic disease affecting copper excretion.

PRECAUTIONS

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

1. Information for patients

Before inserting ParaGard® discuss the Patient Package Insert with the patient, and give her time to read the information. Discuss any questions she may have concerning ParaGard® as well as other methods of contraception. Instruct her to promptly report symptoms of infection, pregnancy, or missing strings.

2. Insertion precautions, continuing care, and removal.

3. Vaginal bleeding

In the 2 largest clinical trials with ParaGard®, menstrual changes were the most common medical reason for discontinuation of ParaGard®. Discontinuation rates for pain and bleeding combined are highest in the first year of use and diminish thereafter. The percentage of women who discontinued ParaGard® because of bleeding problems or pain during these studies ranged from 11.9% in the first year to 2.2 % in year 9. Women complaining of heavy vaginal bleeding should be evaluated and treated, and may need to discontinue ParaGard®.

4. Vasovagal reactions, including fainting

Some women have vasovagal reactions immediately after insertion. Hence, patients should remain supine until feeling well and should be cautious when getting up.

5. Expulsion following placement after a birth or abortion

ParaGard® has been placed immediately after delivery, although risk of expulsion may be higher than when ParaGard® is placed at times unrelated to delivery. However, unless done immediately postpartum, insertion should be delayed to the second postpartum month because insertion during the first postpartum month (except for immediately after delivery) has been associated with increased risk of perforation.

ParaGard® can be placed immediately after abortion, although immediate placement has a slightly higher risk of expulsion than placement at other times. Placement after second trimester abortion is associated with a higher risk of expulsion than placement after the first trimester abortion.

6. Magnetic resonance imaging (MRI)

Limited data suggest that MRI at the level of 1.5 Tesla is acceptable in women using ParaGard®. One study examined the effect of MRI on the CU-7® Intrauterine Copper Contraceptive and Lippes Loop™ intrauterine devices. Neither device moved under the influence of the magnetic field or heated during the spin-echo sequences usually employed for pelvic imaging. An in vitro study did not detect movement or temperature change when ParaGard® was subjected to MRI.

7. Medical diathermy

Theoretically, medical (non-surgical) diathermy (short-wave and microwave heat therapy) in a patient with a metal-containing IUD may cause heat injury to the surrounding tissue. However, a small study of eight women did not detect a significant elevation of intrauterine temperature when diathermy was performed in the presence of a copper IUD.

8. Pregnancy

ParaGard® is contraindicated during pregnancy.

9. Nursing mothers

Nursing mothers may use ParaGard®. No difference has been detected in concentration of copper in human milk before and after insertion of copper IUDs. The literature is conflicting, but limited data suggest that there may be an increased risk of perforation and expulsion if a woman is lactating.

10. Pediatric use

ParaGard® is not indicated before menarche. Safety and efficacy have been established in women over 16 years old.

ADVERSE REACTIONS

The most serious adverse events associated with intrauterine contraception are discussed in **WARNINGS** and **PRECAUTIONS**. These include:

Intrauterine pregnancy	Pelvic infection
Septic abortion	Perforation
Ectopic pregnancy	Embedment

The following adverse events have also been observed. These are listed alphabetically and not by order of frequency or severity.

Anemia	Menstrual flow, prolonged
Backache	Menstrual spotting
Dysmenorrhea	Pain and cramping
Dyspareunia	Urticarial allergic skin reaction
Expulsion, complete or partial	Vaginitis
Leukorrhea	

CooperSurgical

CooperSurgical, Inc
95 Corporate Drive
Trumbull, CT 06611

This brief summary is based on the ParaGard full prescribing information dated September 2014.

PAR-41287 01/18

Is oral or IV iron therapy more beneficial for postpartum anemia?

IV iron is the better choice for a select group of women. In a systematic review that evaluated more than 1,000 women who received oral iron versus 1,000 women who received intravenous (IV) iron for postpartum anemia (defined as hemoglobin level less than 12 g/dL), IV iron preparations were more effective in raising hemoglobin levels (almost 1 g/dL higher) at 6 weeks postpartum and were better tolerated than oral iron.

EXPERT COMMENTARY
Julianna Schantz-Dunn, MD, MPH, is Instructor, Division of Global Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

Sultan P, Bampoe S, Shah R, et al. Oral versus intravenous iron therapy for postpartum anemia: a systematic review and meta-analysis. Am J Obstet Gynecol. Published online December 19, 2018. DOI:10.1016/j.ajog.2018.12.016.

Iron deficiency anemia in pregnancy is associated with increased risk for adverse birth outcomes, including preterm delivery, cesarean delivery, and need for blood transfusion.[1,2] Although the outcomes with postpartum iron deficiency anemia are more difficult to study, this condition is associated with increased risk of maternal fatigue and depression, and it is often overlooked as a significant issue during the postpartum period.

In a recent systematic review, Sultan and colleagues sought to provide an updated assessment of IV versus oral iron treatment for postpartum anemia. The 6-week postpartum hemoglobin concentration was the primary outcome.

The author reports no financial relationships relevant to this article.

Details of the study

The authors screened 2,744 articles for randomized controlled trials (RCTs) comparing oral and IV iron in the treatment of postpartum anemia. Fifteen RCTs were included in the review, with 1,001 women receiving oral iron therapy and 1,181 women receiving IV iron. The baseline postpartum hemoglobin concentration in the 15 studies ranged from less than 8 g/dL to 10.5 g/dL.

In all but 1 study, the women in the IV treatment arm experienced a significant increase in postpartum hemoglobin concentration, with the mean difference being 1.0 g/dL at postpartum week 1 (95% confidence interval [CI], 0.5–1.5; $P<.0001$) and 0.9 g/dL at postpartum week 6 (95% CI, 0.4–1.3; $P = .0003$).

Only 4 studies were included in the meta-analysis; specifically, 6-week postpartum hemoglobin levels were measured in 251 women who received IV iron and in 134 who received oral iron. Significant differences were seen in the IV iron group compared with the oral iron group for 3 of the secondary outcomes evaluated: flushing (odds ratio

FAST TRACK

Postpartum iron deficiency anemia is associated with increased risk of maternal fatigue and depression and is often overlooked as a significant issue during the postpartum period

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Given the efficacy and reduced adverse effects associated with IV iron therapy demonstrated in the systematic review by Sultan and colleagues, I recommend treatment with IV iron for women with moderate to severe postpartum anemia (defined in pregnancy as a hemoglobin level less than 10 g/dL and ferritin less than 40 µg/L) who have not received blood products or for women who are unable to tolerate or absorb oral iron (such as those with a history of bariatric surgery, gastritis, or inflammatory bowel disease). In our institution, we frequently give IV iron sucrose 300 mg prior to discharge due to ease of administration. For women with mild iron deficiency anemia (hemoglobin greater than 10 g/dL), I prescribe every-other-day oral iron in the form of ferrous sulfate 325 mg, which effectively raises the hemoglobin level and limits the gastrointestinal side effects associated with more frequent dosing.

JULIANNA SCHANTZ-DUNN, MD, MPH

[OR], 6.95), decreased constipation (OR, 0.08), and decreased dyspepsia (OR, 0.07).

None of the other secondary outcomes associated with IV iron (muscle cramps, headache, urticaria, rash, or anaphylaxis) occurred at statistically significant rates. Notably, adherence was not assessed in the majority of the studies. Although constipation was increased in the oral iron therapy group, it was reported at only 12%.

Study strengths and weaknesses

Results of this study support previous findings that IV iron is better tolerated, with fewer gastrointestinal adverse effects, than oral iron, and they re-emphasize that IV iron therapy is both safe (the authors identified only 2 cases of anaphylaxis) and effective in improving hematologic indices.

The systematic review included studies, however, that excluded women treated for antepartum anemia, a group that may benefit from aggressive correction of iron deficiency. Another study weakness is that all the oral iron regimens used were dosed either daily or multiple times per day, which may lead to difficulty with adherence and can decrease overall iron absorption compared with an every-other-day regimen.[3]

Future studies are needed to determine 1) which women with what level of anemia will benefit the most from postpartum IV iron and 2) the hemoglobin level at which IV iron is a cost-effective therapy. ●

FAST TRACK

These study results support previous findings: IV iron is better tolerated, with fewer GI side effects, than oral iron and is both safe and effective in improving hematologic indices

References

1. Drukker L, Hants Y, Farkash R, et al. Iron deficiency anemia at admission for labor and delivery is associated with an increased risk for Cesarean section and adverse maternal and neonatal outcomes. *Transfusion.* 2015;55:2799-2806.
2. Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr.* 2016;103:495-504.
3. Stoffel NU, Cercamondi CI, Brittenham G, et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. *Lancet Haematol.* 2017;4:e524-e533.

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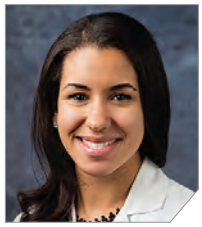

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Dr. Wright reports that he is a consultant to Clovis Oncology and Tesaro, Inc. Dr. Gamble reports no financial relationships relevant to this article.

Gynecologic malignancies continue to be among the most deadly cancers for women. In this article: HIPEC, PARP, and minimally invasive hysterectomy.

Of the major developments in 2018 that changed practice in gynecologic oncology, we highlight 3 here.

First, a trial on the use of hyperthermic intraperitoneal chemotherapy (HIPEC) for patients with ovarian cancer after neoadjuvant chemotherapy demonstrated an overall survival benefit of 12 months for patients treated with HIPEC. Second, a trial on poly-adenosine diphosphate–ribose polymerase (PARP) inhibitors as maintenance therapy after adjuvant chemotherapy showed that women with a *BRCA* mutation had a progression-free survival benefit of nearly 3 years. Third, the Laparoscopic Approach to Cervical Cancer trial revealed a significant decrease in survival in women with early-stage cervical cancer who underwent minimally invasive radical hysterectomy compared with those who had the traditional open approach. In addition, a retrospective study that analyzed information from large cancer databases showed that national survival rates decreased for patients with cervical cancer as the use of laparoscopic radical hysterectomy rose.

In this Update, we summarize the major findings of these trials, provide background on treatment strategies, and discuss how our practice as cancer specialists has changed in light of these studies' findings.

IN THIS ARTICLE

HIPEC improves overall survival in advanced ovarian cancer—by a lot

Van Driel WJ, Koole SN, Sikorska K, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med. 2018;378:230-240.

In the United States, women with advanced-stage ovarian cancer typically are treated with primary cytoreductive (debulking) surgery followed by platinum- and taxane-based chemotherapy. The goal of cytoreductive surgery is the resection of all grossly visible tumor. While associated with favorable oncologic outcomes, cytoreductive surgery also is accompanied by significant morbidity, and surgery is not always feasible.

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Neoadjuvant chemotherapy (NACT) has emerged as an alternative treatment strategy to primary cytoreductive surgery. Women treated with NACT typically undergo 3 to 4 cycles of platinum- and taxane-based chemotherapy, receive interval cytoreduction, and then are treated with an additional 3 to 4 cycles of chemotherapy postoperatively. Several large, randomized controlled trials have demonstrated that survival is similar for women with advanced-stage ovarian cancer treated with either primary cytoreduction or NACT.[1,2] Importantly, perioperative morbidity is substantially lower with NACT and the rate of complete tumor resection is improved. Use of NACT for ovarian cancer has increased substantially in recent years.[3]

Rationale for intraperitoneal chemotherapy

Intraperitoneal (IP) chemotherapy has long been utilized in the treatment of ovarian cancer.[4] Given that the abdomen is the most common site of metastatic spread for ovarian cancer, there is a strong rationale for direct infusion of chemotherapy into the abdominal cavity. Several early trials showed that adjuvant IP chemotherapy improves survival compared with intravenous chemotherapy alone.[5,6] Yet complete adoption of IP chemotherapy has been limited by evidence of moderately increased toxicities, such as pain, infections, and bowel obstructions, as well as IP catheter complications.[5,7]

FAST TRACK

HIPEC treatment was associated with a 3.5-month improvement in recurrence-free survival compared with surgery alone and a 12-month improvement in overall survival

Heated IP chemotherapy for recurrent ovarian cancer

More recently, interest has focused on HIPEC. In this approach, chemotherapy is heated to 42°C and administered into the abdominal cavity immediately after cytoreductive surgery; a temperature of 40°C to 41°C is maintained for total perfusion over a 90-minute period. The increased temperature induces apoptosis and protein degeneration, leading to greater penetration by the chemotherapy along peritoneal surfaces.[8]

For ovarian cancer, HIPEC has been explored in a number of small studies, predominately for women with recurrent disease.[9] These studies demonstrated that HIPEC increased toxicities with gastrointestinal and renal complications but improved overall and disease-free survival.

HIPEC for primary treatment

Van Driel and colleagues explored the safety and efficacy of HIPEC for the primary treatment of ovarian cancer.[10] In their multicenter trial, the authors sought to determine if there was a survival benefit with HIPEC in patients with stage III ovarian, fallopian tube, or peritoneal cancer treated with NACT. Eligible participants initially were treated with 3 cycles of chemotherapy with carboplatin and paclitaxel. Two-hundred forty-five patients who had a response or stable disease were then randomly assigned to undergo either interval cytoreductive surgery alone or surgery with HIPEC using cisplatin. Both groups received 3 additional cycles of carboplatin and paclitaxel after surgery.

Results. Treatment with HIPEC was associated with a 3.5-month improvement in recurrence-free survival compared with surgery alone (14.2 vs 10.7 months) and a 12-month improvement in overall survival (45.7 vs 33.9 months). After a median follow-up of 4.7 years, 62% of patients in the surgery group and 50% of the patients in the HIPEC group had died.

Adverse events. Rates of grade 3 and 4 adverse events were similar for both treatment arms (25% in the surgery group vs 27% in the HIPEC plus surgery group), and there was no significant difference in hospital length of stay (8 vs 10 days, which included a mandatory 1-night stay in the intensive care unit for HIPEC-treated patients).

WHAT THIS EVIDENCE MEANS FOR PRACTICE

For carefully selected women with advanced ovarian cancer treated with neoadjuvant chemotherapy, HIPEC at the time of interval cytoreductive surgery may improve survival by a year.

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PARP inhibitors extend survival in ovarian cancer, especially for women with a *BRCA* mutation

Moore K, Colombo N, Scambia G, et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. 2018;379:2495-2505.

FAST TRACK

After 41 months of follow-up, the olaparib group had a disease-free survival rate of 60% versus 27% in the placebo group

Ovarian cancer is the deadliest malignancy affecting women in the United States. While patients are likely to respond to their initial chemotherapy and surgery, there is a significant risk for cancer recurrence, from which the high mortality rates arise.

Maintenance therapy has considerable potential for preventing recurrences. Based on the results of a large Gynecologic Oncology Group study,[11] in 2017 the US Food and Drug Administration (FDA) approved bevacizumab for use in combination with and following standard carboplatin and paclitaxel chemotherapy for women with advanced ovarian cancer. In the trial, maintenance therapy with 10 months of bevacizumab improved progression-free survival by 4 months; however, it did not improve overall survival, and adverse events included bowel perforations and hypertension.[11] Alternative targets for maintenance therapy to prevent or minimize the risk of recurrence in women with ovarian cancer have been actively investigated.

PARP inhibitors work by damaging cancer cell DNA

PARP is a key enzyme that repairs DNA damage within cells. Drugs that inhibit PARP trap this enzyme at the site of single-strand breaks, disrupting single-strand repair and inducing double-strand breaks. Since the homologous recombination pathway used to repair double-strand DNA breaks does not function in *BRCA*-mutated tissues, PARP inhibitors ultimately induce targeted DNA damage and apoptosis in both germline and somatic *BRCA* mutation carriers.[12]

In the United States, 3 PARP inhibitors (olaparib, niraparib, and rucaparib) are FDA approved as maintenance therapy for use in women with recurrent ovarian cancer that had responded completely or partially to platinum-based chemotherapy, regardless of *BRCA* status. PARP inhibitors also have been approved for treatment of advanced ovarian cancer in *BRCA* mutation carriers who have received 3 or more lines of platinum-based chemotherapy. Because of their efficacy in the treatment of recurrent ovarian cancer, there is great interest in using PARP inhibitors earlier in the disease course.

Olaparib is effective in women with *BRCA* mutations

In an international, randomized, double-blind, phase 3 trial, Moore and colleagues sought to determine the efficacy of the PARP inhibitor olaparib administered as maintenance therapy in women with germline or somatic *BRCA* mutations.[13] Women were eligible if they had *BRCA1* or *BRCA2* mutations with newly diagnosed advanced (stage III or IV) ovarian, fallopian tube, or peritoneal cancer and a complete or partial response to platinum-based chemotherapy after cytoreduction.

Women were randomly assigned in a 2:1 ratio, with 260 participants receiving twice daily olaparib and 131 receiving placebo.

Results. After 41 months of follow-up, the disease-free survival rate was 60% in the olaparib group, compared with 27% in the placebo arm. Progression-free survival was 36 months longer in the olaparib maintenance group than in the placebo group.

Adverse events. While 21% of women

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treated with olaparib experienced serious adverse events (compared with 12% in the placebo group), most were related to anemia. Acute myeloid leukemia occurred in 3 (1%) of the 260 patients receiving olaparib.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

For women with deleterious *BRCA1* and/or *BRCA2* mutations, administering PARP inhibitors as a maintenance therapy following primary treatment with the standard platinum-based chemotherapy improves progression-free survival by at least 3 years.

Is MIS radical hysterectomy (vs open) for cervical cancer safe?

Ramirez PT, Frumovitz M, Pareja R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. N Engl J Med. 2018;379:1895-1904.

Melamed A, Margul DJ, Chen L, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. N Engl J Med. 2018;379:1905-1914.

For various procedures, minimally invasive surgery (MIS) is associated with decreased blood loss, shorter postoperative stay, and decreased postoperative complications and readmission rates. In oncology, MIS has demonstrated equivalent outcomes compared with open procedures for colorectal and endometrial cancers.[14,15]

Increasing use of MIS in cervical cancer

For patients with cervical cancer, minimally invasive radical hysterectomy has more favorable perioperative outcomes, less morbidity, and decreased costs than open radical hysterectomy.[16-20] However, many of the studies used to justify these benefits were small, lacked adequate follow-up, and were not adequately powered to detect a true survival difference. Some trials compared contemporary MIS enrollees to historical open surgery controls, who may have had more advanced-stage disease and may have been treated with different adjuvant chemoradiation.

Despite these major limitations, minimally invasive radical hysterectomy became an acceptable—and often preferable—alternative to open radical hysterectomy for early-stage cervical cancer. This acceptance was written into National Comprehensive Cancer Network guidelines,[21] and minimally invasive radical hysterectomy rapidly gained popularity, increasing from 1.8% in 2006 to 31% in 2010.[22]

Randomized trial revealed surprising findings

Ramirez and colleagues recently published the results of the Laparoscopic Approach to Cervical Cancer (LACC) trial, a randomized controlled trial that compared open with minimally invasive radical hysterectomy in women with stage IA1–IB1 cervical cancer.[23] The study was designed as a noninferiority trial in which researchers set a threshold of -7.2% for how much worse the survival of MIS patients could be compared with open surgery before MIS could be declared an inferior treatment. A total of 631 patients were enrolled at 33 centers worldwide. After an interim analysis demonstrated a safety signal in the MIS radical hysterectomy cohort, the study was closed before completion of enrollment.

Overall, 91% of patients randomly assigned to treatment had stage IB1 tumors.

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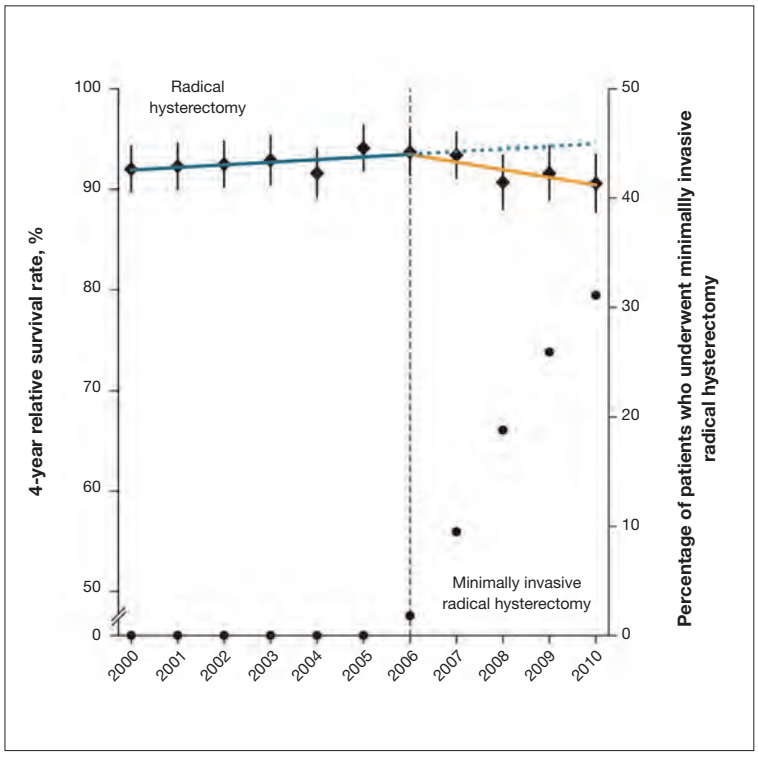
FIGURE Interrupted time-series evaluation of radical hysterectomy[22]



Shown are the 4-year relative survival rates among women who underwent radical hysterectomy for cervical cancer by any surgical approach (diamonds) with 95% confidence interval (CI) (error bars) and the percentages of radical hysterectomies that were undertaken with the use of a minimally invasive approach (circles). The adoption of minimally invasive radical hysterectomy in 2006 was associated with a significant change of temporal trend (as indicated by the dotted blue line) (P = .01) and a declining 4-year relative survival rate after 2006 (yellow line) (annual percentage change, 0.8%; 95% CI, 0.3–1.4). Used with permission.

At the time of analysis, nearly 60% of enrollees had survival data at 4.5 years to provide adequate power for full analysis.

Results. Disease-free survival (the time from randomization to recurrence or death from cervical cancer) was 86.0% in the MIS group and 96.5% in the open hysterectomy group. At 4.5 years, 27 MIS patients had recurrent disease, compared with 7 patients who underwent abdominal radical hysterectomy. There were 14 cancer-related deaths in the MIS group, compared with 2 in the open group.

Three-year disease-free survival was 91.2% in the MIS group versus 97.1% in the abdominal radical hysterectomy group (hazard ratio, 3.74; 95% confidence interval, 1.63–8.58) The overall 3-year survival was 93.8% in the MIS group, compared with 99.0% in the open group.[23]

Retrospective cohort study had similar results

Concurrent with publication of the LACC trial results, Melamed and colleagues published an observational study on the safety of MIS radical hysterectomy for early-stage cervical cancer.[22] They used data from the National Cancer Database to examine 2,461 women with stage IA2–IB1 cervical cancer who underwent radical hysterectomy from 2010 to 2013. Approximately half of the women (49.8%) underwent minimally invasive radical hysterectomy.

Results. After a median follow-up of 45 months, the 4-year mortality rate was 9.1% among women who underwent MIS radical hysterectomy, compared with 5.3% for those who had an abdominal radical hysterectomy.

Using the complimentary Surveillance, Epidemiology, and End Results (SEER) registry dataset, the authors examined population-level trends in use of MIS radical hysterectomy and survival. From 2000 to 2006, when MIS radical hysterectomy was rarely utilized, 4-year survival for cervical cancer was relatively stable. After adoption of MIS radical hysterectomy in 2006, 4-year relative survival declined by 0.8% annually for cervical cancer (**FIGURE**).[22]

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Both a randomized controlled trial and a large observational study demonstrated decreased survival for women with early-stage cervical cancer who underwent minimally invasive radical hysterectomy. Use of minimally invasive radical hysterectomy should be used with caution in women with early-stage cervical cancer.

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References

1. Vergote I, Trope CG, Amant F, et al; European Organization for Research and Treatment of Cancer–Gynaecological Cancer Group; NCIC Clinical Trials Group. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med.* 2010;363:943-953.
2. Kehoe S, Hook J, Nankivell M, et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet.* 2015;386:249-257.
3. Melamed A, Hinchcliff EM, Clemmer JT, et al. Trends in the use of neoadjuvant chemotherapy for advanced ovarian cancer in the United States. *Gynecol Oncol.* 2016;143:236-240.
4. Markman M. Intraperitoneal antineoplastic drug delivery: rationale and results. *Lancet Oncol.* 2003;4:277-283.
5. Markman M, Bundy BN, Alberts DS, et al. Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. *J Clin Oncol.* 2001;19:1001-1007.
6. Armstrong DK, Bundy B, Wenzel L, et al; Gynecologic Oncology Group. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med.* 2006;354:34-43.
7. Alberts DS, Liu PY, Hannigan EV, et al. Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. *N Engl J Med.* 1996;335:1950-1955.
8. van de Vaart PJ, van der Vange N, Zoetmulder FA, et al. Intraperitoneal cisplatin with regional hyperthermia in advanced ovarian cancer: pharmacokinetics and cisplatin-DNA adduct formation in patients and ovarian cancer cell lines. *Eur J Cancer.* 1998;34:148-154.
9. Bakrin N, Cotte E, Golfier F, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for persistent and recurrent advanced ovarian carcinoma: a multicenter, prospective study of 246 patients. *Ann Surg Oncol.* 2012;19:4052-4058.
10. van Driel WJ, Koole SN, Sikorska K, et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. *N Engl J Med.* 2018;378:230-240.
11. Burger RA, Brady MF, Bookman MA, et al; Gynecologic Oncology Group. Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med.* 2011;365:2473-2483.
12. Farmer H, McCabe N, Lord CJ, et al. Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature.* 2005;434:917-921.
13. Moore K, Colombo N, Scambia G, et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med.* 2018;379:2495-2505.
14. Walker JL, Piedmonte MR, Spirtos NM, et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *J Clin Oncol.* 2012;30:695-700.
15. Clinical Outcomes of Surgical Therapy Study Group, Nelson H, Sargent DJ, et al. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med.* 2004;350:2050-2059.
16. Lee EJ, Kang H, Kim DH. A comparative study of laparoscopic radical hysterectomy with radical abdominal hysterectomy for early-stage cervical cancer: a long-term follow-up study. *Eur J Obstet Gynecol Reprod Biol.* 2011;156:83-86.
17. Malzoni M, Tinelli R, Cosentino F, et al. Total laparoscopic radical hysterectomy versus abdominal radical hysterectomy with lymphadenectomy in patients with early cervical cancer: our experience. *Ann Surg Oncol.* 2009;16:1316-1323.
18. Nam JH, Park JY, Kim DY, et al. Laparoscopic versus open radical hysterectomy in early-stage cervical cancer: long-term survival outcomes in a matched cohort study. *Ann Oncol.* 2012;23:903-911.
19. Obermair A, Gebski V, Frumovitz M, et al. A phase III randomized clinical trial comparing laparoscopic or robotic radical hysterectomy with abdominal radical hysterectomy in patients with early stage cervical cancer. *J Minim Invasive Gynecol.* 2008;15:584-588.
20. Mendivil AA, Rettenmaier MA, Abaid LN, et al. Survival rate comparisons amongst cervical cancer patients treated with an open, robotic-assisted or laparoscopic radical hysterectomy: a five year experience. *Surg Oncol.* 2016;25:66-71.
21. National Comprehensive Care Network. NCCN clinical practice guidelines in oncology: cervical cancer, version 1.2018. http://oncolife.com.ua/doc/nccn/Cervical_Cancer.pdf. Accessed February 11, 2019.
22. Melamed A, Margul DJ, Chen L, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N Engl J Med.* 2018;379:1905-1914.
23. Ramirez PT, Frumovitz M, Pareja R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med.* 2018;379:1895-1904.

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Two free contraception apps for providers of family planning

These tech tools offer the opportunity to improve your family planning services

Katherine T. Chen, MD, MPH

Evidence-based research and guidelines regarding contraception are continually changing. Health care providers often have difficulty memorizing and staying up-to-date on all the important developments around family planning. Those who provide contraceptive counseling may not all use guidelines to inform their choices, and some may have misperceptions about patient eligibility for certain methods.[1,2] Mobile health applications (apps) that present this information in an easily accessible fashion have the potential to improve family planning services.

In a search for contraception apps, Dr. Rachel Perry and colleagues identified two contraception apps that were evaluated highly: 1) the Centers for Disease Control and Prevention (CDC) US Medical Eligibility Criteria for Contraceptive Use (MEC) app and 2) the iContraception app.[3]

Two free contraception apps for clinician use. Both the CDC Contraception and iContraception apps are based on CDC MEC information and provide guidance on contraceptive initiation and maintenance.[4] Notably, the American College of Obstetricians and Gynecologists (ACOG) endorses the use of the CDC MEC.[5]

These two apps can aid physicians in prescribing appropriate and safe contraceptive methods and can help them tailor the extensive CDC MEC guidelines for an individual patient. Additionally, the iContraception app allows a user to input multiple clinical and demographic characteristics to determine an individual patient's eligibility for a specific contraceptive method (that is, it incorporates a clinical decision tree).

The recommended contraception apps are listed in the **TABLE** (page 30) and are detailed with a shortened version of the APPLICATIONS scoring system, APPLI (app comprehensiveness, price, platform, literature used, and important special features).[6] I hope that the apps described here will assist you in managing patients who need contraception counseling. ●

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References

1. Russo JA, Chen BA, Creinin MD. Primary care physician familiarity with US medical eligibility for contraceptive use. *Fam Med.* 2015;47:15-21.
2. Dehlendorf C, Levy K, Ruskin R, et al. Health care providers' knowledge about contraceptive evidence: a barrier to quality family planning care? *Contraception.* 2010;81:292-298.
3. Perry R, Lunde B, Chen KT. An evaluation of contraception mobile applications for providers of family planning services. *Contraception.* 2016;93:539-544.
4. Curtis KM, Tepper NK, Jatlaoui TC, et al. US Medical Eligibility Criteria for Contraceptive Use, 2016. *MMWR Recomm Rep.* 2016;65(3):1-103.
5. American College of Obstetricians and Gynecologists. Committee opinion no. 505: understanding and using the US Medical Eligibility Criteria for Contraceptive Use. *Obstet Gynecol.* 2011;118:754-760.
6. Chyjek K, Farag S, Chen KT. Rating pregnancy wheel applications using the APPLICATIONS scoring system. *Obstet Gynecol.* 2015;125:1478-1483.

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Details on recommended apps

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TABLE Recommended contraception apps

App	App comprehensiveness	Price	Platform	Literature used	Important special features
 **CDC US Medical Eligibility Criteria for Contraceptive Use** iTunes: https://itunes.apple.com/us/app/contraception/id595752188?mt=8 Google Play: https://play.google.com/store/apps/details?id=gov.cdc.ondieh.nccdphp.contraception2&hl=en_US	• Clinical decision making (clinical decision support systems, clinical treatment guidelines) • Reference (drug reference guides, medical literature)	Free	iTunes and Google Play store	• US Medical Eligibility Criteria for Contraceptive Use (*MMWR Recomm Rep.* 2016;65[3]:1-103) • US Selected Practice Recommendations for Contraceptive Use (*MMWR Recomm Rep.* 2016;65[4]:1-66)	• Includes more than 60 characteristics and medical conditions that may affect people seeking family planning services • Includes selected practice recommendations for contraceptive use
 **iContraception** iTunes: https://itunes.apple.com/us/app/icontraception/id668520861?mt=8 Google Play: https://play.google.com/store/apps/details?id=com.itiox.icontraception	• Clinical decision making (clinical decision support systems) • Reference (medical literature)	Free	iTunes and Google Play store	• WHO Medical Eligibility Criteria for Contraceptive Use, 2015 (https://www.who.int/reproductivehealth/publications/family_planning/MEC-5/en/) • Other primary sources	Clinical decision tree

Abbreviations: US MEC, US Medical Eligibility Criteria for Contraceptive Use; US SPR, US Selected Practice Recommendations for Contraceptive Use.

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Dr. Katherine T. Chen's App Reviews at mdedge.com/obgyn

- Medical calculator apps allow point of care, rapid decision-making
- CDC apps specific for ObGyns
- Two good apps for management of cervical cancer screening results
- ACOG app and applets: Tools to augment your practice
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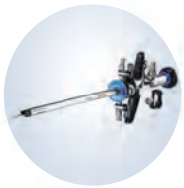
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Genitourinary endometriosis: Diagnosis and management

Early recognition of this rare but potentially devastating disorder is essential to facilitate effective management and optimal outcomes for patients

Megan Kennedy Burns, MD, MA; Michelle A. Wood, DO; Camran Nezhat, MD; and Farr Nezhat, MD

Endometriosis is a benign disease characterized by endometrial glands and stroma outside of the uterine cavity. It is commonly associated with pelvic pain and infertility. Ectopic endometrial tissue is predominantly located in the pelvis, but it can appear anywhere in the body, where it is referred to as extragenital endometriosis. The bowel and urinary tract are the most common sites of extragenital endometriosis.[1]

Laparoscopic management of extragenital endometriosis has been described since the 1980s.[2] However, laparoscopic management of genitourinary endometriosis is still not widespread.[3,4] Physicians are often unfamiliar with the signs and symptoms of genitourinary endometriosis and fail to consider it when a patient presents with bladder pain or hematuria, which may or may not be cyclic. Furthermore, many gynecologists do not have the experience to correctly identify the various forms of endometriosis that may appear on the pelvic organ, including the serosa and peritoneum, as variable colored spots, blebs, lesions, or adhesions. Many surgeons are also not adequately trained in the advanced laparoscopic techniques required to treat genitourinary endometriosis.[4]

In this article, we describe the clinical presentation and diagnosis of genitourinary endometriosis and discuss laparoscopic management strategies with and without robotic assistance.

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The authors report no financial relationships relevant to this article.

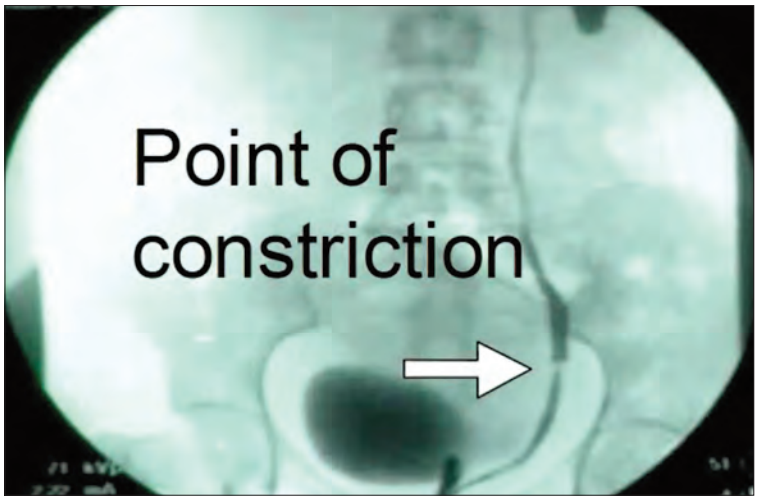
Clinical presentation and diagnosis of genitourinary endometriosis

While ureteral and bladder endometriosis are both diseases of the urinary tract, they are not always found together in the same patient. The bladder is the most commonly affected organ, followed by the ureter and kidney.[3,5,6] Endometriosis of the bladder usually presents with significant lower urinary tract symptoms. In contrast, ureteral endometriosis is usually silent with no apparent urinary symptoms.

Ureteral endometriosis. Cyclic hematuria is present in less than 15% of patients with ureteral endometriosis. Some patients experience cyclic, nonspecific colicky flank

IN THIS ARTICLE

FIGURE 1 Ureteral involvement



Ureteral constriction due to endometriosis, causing proximal hydroureter. If untreated, this may lead to silent kidney loss.

FAST TRACK

Lack of symptoms makes early diagnosis of ureteral endometriosis difficult; histologic evaluation of a biopsy sample is diagnostic

pain.[7-9] Otherwise, most patients present with the usual symptoms of endometriosis, such as pelvic pain and dysmenorrhea. In a systematic review, Cavaco-Gomes and colleagues described 700 patients with ureteral endometriosis; 81% reported dysmenorrhea, 70% had pelvic pain, and 66% had dyspareunia.[10] Rarely, ureteral endometriosis can result in silent kidney loss if the ureter becomes severely obstructed without treatment.[11,12]

The lack of symptoms makes the early diagnosis of ureteral endometriosis difficult. As with all types of endometriosis, histologic evaluation of a biopsy sample is diagnostic. Multiple imaging modalities have been used to preoperatively diagnose ureteral involvement, including computed tomography,[13] magnetic resonance imaging (MRI),[14] intravenous pyelogram (IVP), and pelvic ultrasonography. However, each of these imaging modalities is limited in both sensitivity and the ability to characterize depth of tissue invasion.

In a study of 245 women undergoing pelvic ultrasonography, Pateman and colleagues reported that an experienced sonographer was able to visualize the bilateral ureters in 93% of cases.[15] Renal ultrasonography is indicated in any woman suspected of having genitourinary tract involvement with the degree of hydroureter and level of obstruction noted during the exam.[16]

In our group, we perform renography to assess kidney function when hydroureter is noted preoperatively. Studies suggest that if greater than 10% of normal glomerular filtration rate remains, the kidney is considered salvageable, and near-normal function often returns following resection of disease. If preoperative kidney function is noted to be less than 10%, consultation with a nephrologist for possible nephrectomy is warranted.

We find that IVP is often helpful for preoperatively identifying the level and degree of ureteral involvement, and it also can be used postoperatively to evaluate for ureteral continuity (**FIGURE 1**). Sillou and colleagues showed MRI to be adequately sensitive for the detection of intrinsic ureteral endometriosis, but they reported that MRI often overestimates the frequency of disease.[17] Authors of a 2016 Cochrane review of imaging modalities for endometriosis, including 4,807 women in 49 studies, reported that no imaging test was superior to surgery for diagnosing endometriosis.[18] However, the review notably excluded genitourinary tract endometriosis, as surgery is not an acceptable reference standard, given that many surgeons cannot reliably identify such lesions.[18]

Bladder endometriosis. Unlike patients with ureteral endometriosis, those with bladder endometriosis are typically symptomatic and experience dysuria, hematuria, urinary frequency, and suprapubic tenderness.[7,19] Urinary tract infection, interstitial cystitis, and cancer must be considered in the differential diagnosis. Urinalysis and urine culture should be performed, and other diagnostic procedures such as ultrasonography, MRI, and cystoscopy should be considered to evaluate for endometriosis of the bladder.

Ultrasound and MRI of the bladder both demonstrate a high specificity for detecting bladder endometriosis, but they lack sensitivity for lesions less than 3 cm.[20] Deep infiltrating endometriosis of the bladder can be identified at the time of cystoscopy, which can assist in determining the need for ureteroneocystostomy if lesions are within 2 cm

of the urethral opening.[20] Cystoscopy also allows for biopsy to be performed if underlying malignancy is of concern.[19]

In our group, when bladder endometriosis is suspected, we routinely perform preoperative bladder ultrasonography to identify the lesion and plan to perform intraoperative cystoscopy at the time of laparoscopic resection.[19,21]

Treatment

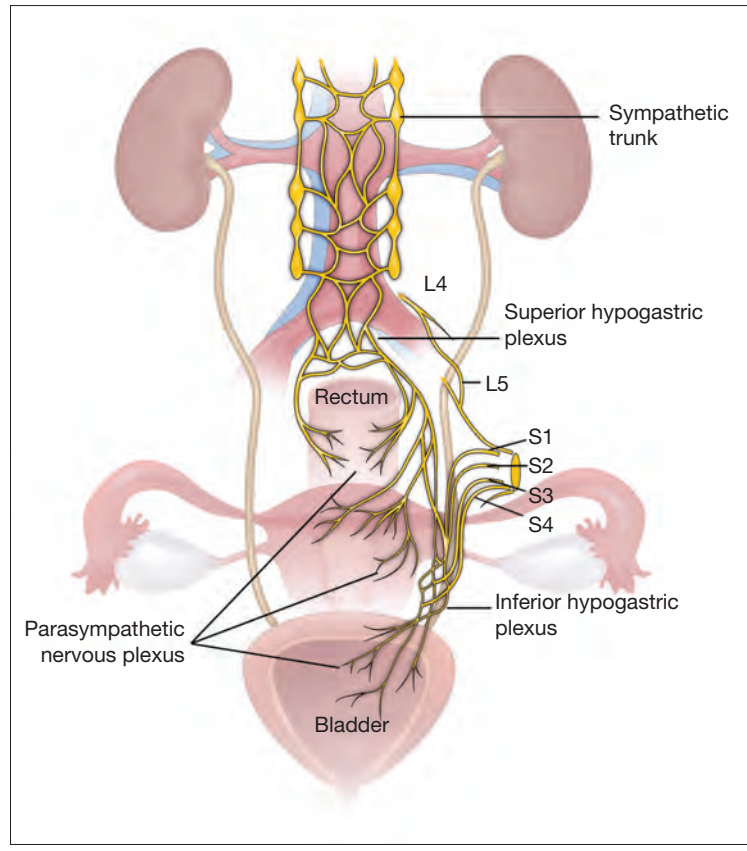
Medical management

Empiric medical therapies for endometriosis are centered around the idea that ectopic endometrial tissue responds to treatment in a similar manner as normal eutopic endometrium. The goals of treatment are to reduce or eliminate cyclic menstruation, thereby decreasing peritoneal seeding and suppressing the growth and activity of established ectopic implants. Medical therapy commonly involves the use of gonadotropin-releasing hormone agonists or antagonists, danazol, combined oral contraceptives, progestins, and aromatase inhibitors.

Medical therapy is commonly employed for patients with mild or early-stage disease and in those who are poor surgical candidates or decline surgery. Medical management alone clearly is contraindicated in the setting of ureteral obstruction and—in our opinion—may not be a good option for those with endometriosis of the ureter, given the potential for recurrence and potential serious sequelae of reduced renal function.[22] Therefore, surgery has become the standard approach to therapy for mild to moderate cases of ureteral endometriosis.[3]

Medical therapy for patients with endometriosis of the bladder is generally considered a temporary solution as hormonal suppression, with its associated adverse effects, must be maintained throughout menopause. However, if endometriosis lesions lie within close proximity to the trigone, medical management is preferred, as surgical excision in the area of the trigone may predispose patients to neurogenic bladder and retrograde bladder reflux.[23,24]

FIGURE 2 Innervation of the pelvic organs



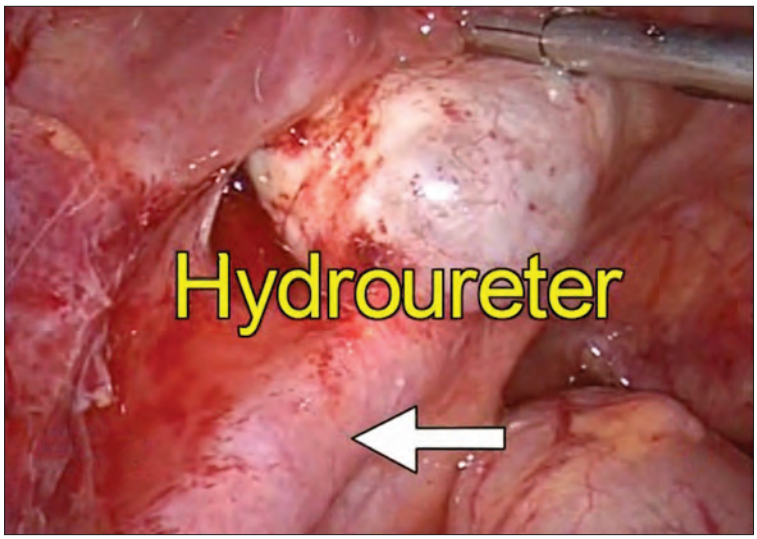
Surgical management

The objectives of surgical treatment for genitourinary tract endometriosis are to excise all visible disease, to prevent or delay recurrence of the disease to the extent possible, and to avoid any further morbidity—in particular, to preserve renal function in cases of ureteral endometriosis—and to avoid iatrogenic injury to surrounding pelvic nervous structures[25-27] (**FIGURE 2**). The surgical approach depends on the technical expertise of the surgeon and the availability of necessary instrumentation. In our experience, laparoscopy with or without robotic assistance is the preferred surgical approach.[3,4,6,11,28-32]

Others have reported on the benefits of laparoscopy over laparotomy for the surgical management of genitourinary endometriosis. In a review of 61 patients who underwent either robot-assisted laparoscopic (n = 25) or open (n = 41) ureteroneocystostomy (n = 41), Isac and colleagues reported the procedure

ILLUSTRATION: JOE GORMAN FOR OBG MANAGEMENT

FIGURE 3 Hydroureter caused by extrinsic compression of the ureter from endometriosis



FAST TRACK

Compared with other approaches, laparoscopic resection of bladder endometriomas is associated with better results in terms of symptom relief, disease progression, and recurrence risk, in our experience

was longer in the laparoscopic group (279 min vs 200 min, *P*<.001), but the laparoscopic group had a shorter hospital stay (3 days vs 5 days, *P*<.001), used fewer narcotics postoperatively (*P*<.001), and had lower intraoperative blood loss (100 mL vs 150 mL, *P*<.001).[32] No differences in long-term outcomes were observed in either cohort.

In a systematic review of 700 patients undergoing laparoscopic surgery for ureteral endometriosis, Cavaco-Gomes and colleagues reported that conversion to laparotomy occurred in only 3% to 7% of cases.[10] In instances of ureteral endometriosis, laparoscopy provides greater visualization of the intraperitoneal contents over laparotomy, enabling better evaluation and treatment of lesions.[3,29,33,34] Robot-assisted laparoscopy provides the additional advantages of 3D visualization, potential for an accelerated learning curve over traditional laparoscopy, improvement in dissection technique, and ease of suturing technique.[6,35,36]

Extrinsic disease. In our group, we perform ureterolysis for extrinsic disease.[25] The peritoneal incision is made in an area unaffected by endometriosis. Using the suction irrigator, a potential space is developed under the serosa of the ureter by injecting normal saline or lactated Ringer's solution. By creating a fluid barrier between the serosa and underlying tissues, the depth of surgical incision and lateral thermal spread are minimized. Grasping forceps are used to peel the peritoneum away.[25,37,38]

Intrinsic disease. Unlike extrinsic disease, intrinsic disease can infiltrate the muscularis, lamina propria, and ureteral lumen, resulting in proximal dilation of the ureter with strictures.[8] In this situation, ureteral compromise is likely and resection of the ureter is indicated[3,28] (**FIGURE 3**). Intrinsic disease can be suggested by preoperative imaging or when there is evidence of deep infiltrating disease on physical exam, such as rectovaginal nodularity.[30,39] When intrinsic ureteral disease is known, consultation with a urologist to plan a joint procedure is advisable. The procedure chosen to re-establish a functional ureter following resection depends on the location and extent of the involved ureter. Resection in close proximity to the bladder may be repaired by ureteroneocystostomy with or without psoas hitch,[30,39,40] whereas resection of more proximal ureter may be repaired using Boari flap, ileal interposition, or autotransplantation. Lesions in the upper third or middle ureter may be repaired using ureterouretral anastomosis.[6,7,30,41-43]

Bladder endometriosis. Surgical treatment for bladder endometriosis depends on the depth of invasion and the location of the lesion (**FIGURE 4**). Lesions of the superficial aspect of the bladder identified at the time of laparoscopy can be treated with either excision or fulguration.[28,35,44] In our group, we perform excision over fulguration to remove the entire lesion and obtain a pathologic diagnosis. Deeper lesions involving the detrusor muscle are likely to be an endometrioma of the bladder. In these cases, laparoscopic excision is recommended.[7] Rarely, lesions close to the interureteric ridge may require ureteroneocystostomy.[19,45]

In our experience, laparoscopic resection of bladder endometriomas is associated with better results in terms of symptom relief, progression of disease, and recurrence risk compared with other approaches. When performing laparoscopic excision of blad-

der lesions, we concomitantly evaluate the bladder lesion via cystoscopy to ensure adequate margins are obtained. Double-J stent placement is advised when lesions are within 2 cm of the urethral meatus to ensure ureteral patency during the postoperative period.[45] A postoperative cystogram routinely is performed 7 to 14 days after surgery to ensure adequate repair prior to removing the urinary catheter.[9,25,46,47]

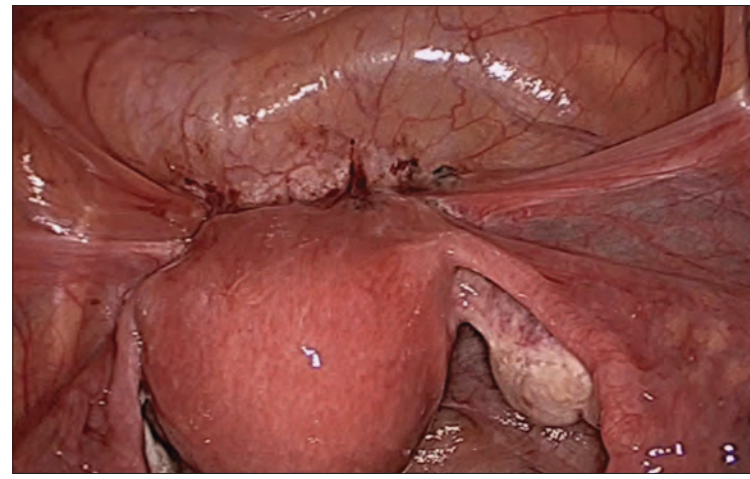
Postsurgical follow-up

Follow-up after treatment of genitourinary tract endometriosis should include monitoring the patient for symptoms of recurrence. Regular history and physical examination, renal function testing, and, in some instances, pelvic ultrasonography, all have a role in surveillance for recurrent ureteric disease. IVP or MRI may be warranted if a recurrence is suspected. A high index of suspicion should be maintained on the part of the clinician to avoid the devastating consequences of silent kidney loss. Patients should be counseled about the risk of disease recurrence, especially in those not undergoing postoperative hormonal suppression.

In conclusion

While endometriosis of the genitourinary tract is rare, patients can experience significant morbidity. Medical management of the disease is often limited by substantial adverse effects that limit treatment duration and is best used postoperatively after excision. An adequate physical exam and preoperative diagnostic imaging can be employed to characterize the extent of disease. When extensive disease involving the ureter is suspected, preoperative consultation with a urologist is encouraged to plan a multidisciplinary approach to surgical resection.

FIGURE 4 Severe endometriosis of the bladder serosa causing adhesions to the anterior uterus



The surgical approach in this case depends on the technical expertise of the surgeon and the availability of necessary instrumentation. Image captured through video-assisted endoscopic surgery, which was first introduced by Camran Nezhat, MD.[48-50]

The ideal approach to surgery is laparoscopic resection with or without robotic assistance. Treatment of ureteral disease most commonly involves ureterolysis for cases of extrinsic disease but may require total resection of the ureter with concurrent ureteral reconstruction when disease is intrinsic to the ureter. Surgery for bladder endometriosis depends on the depth of invasion and location of the lesion. Superficial bladder lesions can be treated with fulguration or excision, while deeper lesions involving the detrusor muscle require excision. Lesions in close proximity to the interureteric ridge may require ureteroneocystostomy. Follow-up after excisional procedures involves monitoring the patient for signs and symptoms of disease recurrence, especially in cases of ureteral involvement, to avoid the devastating consequences of silent kidney loss. ●

FAST TRACK

Regular history and physical exam, renal function testing, and pelvic ultrasonography have a role in surveillance for recurrent uretic disease

See "Pathophysiology of endometriosis" discussion in the online version of this article at **www.mdedge.com/obgyn.**

CONTINUED ON PAGE 38

References

1. Veeraswamy A, Lewis M, Mann A, et al. Extragenital endometriosis. *Clin Obstet Gynecol.* 2010;53:449-466.
2. Nezhat C, Crowgey SR, Garrison GP. Surgical treatment of endometriosis via laser laparoscopy. *Fertil Steril.* 1986;45:778-783.
3. Bosev D, Nicoll LM, Bhagan L, et al. Laparoscopic management of ureteral endometriosis: the Stanford University hospital experience with 96 consecutive cases. *J Urol.* 2009;182:2748-2752.
4. Nezhat C, Falik R, McKinney S, et al. Pathophysiology and management of urinary tract endometriosis. *Nat Rev Urol.* 2017;14:359-372.
5. Shook TE, Nyberg LM. Endometriosis of the urinary tract. *Urology.* 1988;31:1-6.

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CONTINUED FROM PAGE 37

6. Nezhat C, Modest AM, King LP. The role of the robot in treating urinary tract endometriosis. *Curr Opin Obstet Gynecol.* 2013;25:308-311.
7. Comiter CV. Endometriosis of the urinary tract. *Urol Clin North Am.* 2002;29:625-635.
8. Gustilo-Ashby AM, Paraiso MF. Treatment of urinary tract endometriosis. *J Minim Invasive Gynecol.* 2006;13:559-565.
9. Berlanda N, Somigliana E, Frattaruolo MP, et al. Surgery versus hormonal therapy for deep endometriosis: is it a choice of the physician? *Eur J Obstet Gyneocol Reprod Biol.* 2017;209:67-71.
10. Cavaco-Gomes J, Martinho M, Gilabert-Aguilar J, et al. Laparoscopic management of ureteral endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol.* 2017;210:94-101.
11. Nezhat C, Nezhat F, Green B. Laparoscopic treatment of obstructed ureter due to endometriosis by resection and ureteroureterostomy: a case report. *J Urol.* 1992;148:865-868.
12. Nezhat C, Paka C, Gomaa M, et al. Silent loss of kidney secondary to ureteral endometriosis. *JSLS.* 2012;16:451-455.
13. Iosca S, Lumia D, Bracchi E, et al. Multislice computed tomography with colon water distention (MSCT-c) in the study of intestinal and ureteral endometriosis. *Clin Imaging.* 2013;37(6):1061-1068.
14. Medeiros LR, Rosa MI, Silva BR, et al. Accuracy of magnetic resonance in deeply infiltrating endometriosis: a systematic review and meta-analysis. *Arch Gynecol Obstet.* 2015;291:611-621.
15. Pateman K, Mavrelos D, Hoo WL, et al. Visualization of ureters on standard gynecological transvaginal scan: a feasibility study. *Ultrasound Obstet Gynecol.* 2013;41:696-701.
16. Guerriero S, Condous G, van den Bosch T, et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol.* 2016;48:318-332.
17. Sillou S, Poirée S, Millischer AE, et al. Urinary endometriosis: MR imaging appearance with surgical and histological correlations. *Diagn Interv Imaging.* 2015;96:373-381.
18. Nisenblat V, Bossuyt PM, Farquhar C, et al. Imaging modalities for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev.* 2016;2:CD009591.
19. Nezhat CH, Malik S, Osias J, et al. Laparoscopic management of 15 patients with infiltrating endometriosis of the bladder and a case of primary intravesical endometrioid adenosarcoma. *Fertil Steril.* 2002;78:872-875.
20. Kolodziej A, Krajewski W, Dołowy L, et al. Urinary tract endometriosis. *Urol J.* 2015;12:2213-2217.
21. Nezhat C, Buescher E, Paka C, et al. Video-assisted laparoscopic treatment of endometriosis. In: Nezhat C, Nezhat F, Nezhat C, eds. *Nezhat's Video-Assisted and Robotic-Assisted Laparoscopy and Hysteroscopy.* 4th ed. New York, NY: Cambridge University Press; 2013;265.
22. Al-Fozan H, Tulandi T. Left lateral predisposition of endometriosis and endometrioma. *Obstet Gynecol.* 2003;101:164-166.
23. Hastings JC, Van Winkle W, Barker E, et al. The effect of suture materials on healing wounds of the bladder. *Surg Gynecol Obstet.* 1975;140:933-937.
24. Cornell KK. Cystotomy, partial cystectomy, and tube cystostomy. *Clin Tech Small Anim Pract.* 2000;15:11-16.
25. Nezhat C, Nezhat F, Nezhat C, eds. *Nezhat's Video-Assisted and Robotic-Assisted Laparoscopy and Hysteroscopy.* 4th ed. New York, NY: Cambridge University Press; 2013.
26. Uccella S, Cromi A, Casarin J, et al. Laparoscopy for ureteral endometriosis: surgical details, long-term follow-up, and fertility outcomes. *Fertil Steril.* 2014;102:160-166.e2.
27. Knabben L, Imboden S, Fellmann B, et al. Urinary tract endometriosis in patients with deep infiltrating endometriosis: prevalence, symptoms, management, and proposal for a new clinical classification. *Fertil Steril.* 2015;103:147-152.
28. Nezhat C, Nezhat F, Nezhat CH, et al. Urinary tract endometriosis treated by laparoscopy. *Fertil Steril.* 1996;66:920-924.
29. Nezhat CH, Nezhat F, Seidman D, et al. Laparoscopic ureteroureterostomy: a prospective follow-up of 9 patients. *Prim Care Update Ob Gyns.* 1998;5:200.
30. Nezhat CH, Bracale U, Scala A, et al. Laparoscopic ureteroneocystostomy and vesicopsoas hitch for infiltrative endometriosis. *JSLS.* 2004;8:3-7.
31. Nezhat C, Lewis M, Kotikela S, et al. Robotic versus standard laparoscopy for the treatment of endometriosis. *Fertil Steril.* 2010;94:2758-2760.
32. Isac W, Kaouk J, Altunrende F, et al. Robotic-assisted ureteroneocytostomy: techniques and comparative outcomes. *J Endourol.* 2013;27:318-323.
33. Nezhat C, Nezhat F. Laparoscopic repair of ureter resected during operative laparoscopy. *Obstet Gynecol.* 1992;80(3 pt 2):543-544.
34. De Cicco C, Ussia A, Koninckx PR. Laparoscopic ureteral repair in gynaecological surgery. *Curr Opin Obstet Gynecol.* 2011;23:296-300.
35. Nezhat C, Hajhosseini B, King LP. Robotic-assisted laparoscopic treatment of bowel, bladder, and ureteral endometriosis. *JSLS.* 2011;15:387-392.
36. Fadhlaoui A, Gillon T, Lebbi I, et al. Endometriosis and vesico-sphincteral disorders. *Front Surg.* 2015;2:23.
37. Nezhat C, Nezhat FR. Safe laser endoscopic excision or vaporization of peritoneal endometriosis. *Fertil Steril.* 1989;52:149-151.
38. Nezhat C, Winer W, Nezhat FA. Comparison of the CO2, argon, and KTP/532 lasers in the videolaseroscopic treatment of endometriosis. *J Gynecol Surg.* 2009;41-47.
39. Azioni G, Bracale U, Scala A, et al. Laparoscopic ureteroneocytostomy and vesicopsoas hitch for infiltrative ureteral endometriosis. *Minim Invasive Ther Allied Technol.* 2010;19:292-297.
40. Stepniewska A, Grosso G, Molon A, et al. Ureteral endometriosis: clinical and radiological follow-up after laparoscopic ureterocystoneostomy. *Hum Reprod.* 2011;26:112-116.
41. Nezhat CH, Nezhat FR, Freiha F, et al. Laparoscopic vesicopsoas hitch for infiltrative ureteral endometriosis. *Fertil Steril.* 1999;71:376-379.
42. Scioscia M, Molon A, Grosso G, et al. Laparoscopic management of ureteral endometriosis. *Curr Opin Obstet Gynecol.* 2009;21:325-328.
43. Antonelli A. Urinary tract endometriosis. *Urologia.* 2012;79:167-170.
44. Camanni M, Bonino L, Delpiano EM, et al. Laparoscopic conservative management of ureteral endometriosis: a survey of eighty patients submitted to ureterolysis. *Reprod Biol Endocrinol.* 2009;7:109.
45. Chapron C, Bourret A, Chopin N, et al. Surgery for bladder endometriosis: long-term results and concomitant management of associated posterior deep lesions. *Hum Reprod.* 2010;25:884-889.
46. Nezhat CR, Nezhat FR. Laparoscopic segmental bladder resection for endometriosis: a report of two cases. *Obstet Gynecol.* 1993;81(5 pt 2):882-884.
47. Bourdel N, Cognet S, Canis M, et al. Laparoscopic ureteroneocystostomy: be prepared! *J Minim Invasive Gynecol.* 2015;22:827-833.
48. Page B. Camran Nezhat and the Advent of Advanced Operative Video-laparoscopy. In: Nezhat C, ed. *Nezhat's History of Endoscopy.* Tuttlingen, Germany: Endo Press; 2011:159-187.
49. Podratz K. *Degrees of Freedom: Advances in Gynecological and Obstetrical Surgery. Remembering Milestones and Achievements in Surgery: Inspiring Quality for a Hundred Years 1913–2012.* Published by American College of Surgeons 2012. Tampa, FL: Faircount Media Group; 2013.
50. Kelley WE. The evolution of laparoscopy and the revolution in surgery in the decade of the 1990s. *JSLS: J Soc Laparoendoscopic Surgeons.* 2008;12:351-357.

Your 15-year-old patient requests an IUD without parental knowledge

The dilemmas of adolescent consent

Joseph S. Sanfilippo, MD, MBA, and Steven R. Smith, MS, JD

CASE Adolescent seeks care without parent

A 15-year-old patient (G0) presents to the gynecology clinic requesting birth control. She reports being sexually active over the past 6 months and having several male partners over the past 2 years. She and her current male partner use condoms inconsistently. She reports being active in school sports, and her academic performance has been noteworthy. Her peers have encouraged her to seek out birth control; one of her good friends recently became pregnant and dropped out of school. She states that her best friend went to a similar clinic and received a "gynecologic encounter" that included information regarding safe sex and contraception, with no pelvic exam required for her to receive birth control pills.

The patient insists that her parents are not to know of her request for contraception due to sexual activity or that she is a patient at the clinic. The gynecologist covering the clinic is aware of the American College of Obstetricians and Gynecologists Committee on Adolescent Health Care and their many publications. The patient is counseled regarding human papillomavirus (HPV) vaccination and screened for sexually transmitted infections. In addition, the gynecologist discusses contraceptive options with the patient, ranging from oral contraceptives, vaginal rings, subdermal implants, depomedroxyprogesterone acetate, as well as intrauterine devices (IUDs). The gynecologist emphasizes safe sex and advises that her partner consider use of condoms independent of her method of birth control. The patient asks for oral contraceptives and is given information about their use and risks, and she indicates that she understands.

A few months later the patient requests an IUD, as she would like to have lighter menses and not have to remember to take a pill every day. The provider obtains informed consent for the insertion procedure; the patient signs the appropriate forms.

The IUD is inserted, with difficulty, by a resident physician in the clinic. The patient

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Instant Poll

Do/Have you consulted with a health care attorney related to a case of adolescent consent and/or treatment disclosure in your state?

❍ Yes ❍ No

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IN THIS ARTICLE

experiences severe pelvic pain during and immediately following the insertion. She is sent home and told to contact the clinic or another health care provider or proceed to the local emergency department should pain persist or if fever develops.

The patient returns 72 hours later in pain. Pelvic ultrasonography shows the IUD out of place and at risk of perforating the fundus of the uterus. Later that day the patient's mother calls the clinic, saying that she found a statement of service with the clinic's number on it in her daughter's bedroom. She wants to know if her daughter is there, what is going on, and what services have been or are being provided. In passing she remarks that she has no intention of paying (or allowing her insurance to pay for) any care that was provided.

What are the provider's obligations at this point, both medically and legally?

FAST TRACK

No circumstances involving adolescent consent and treatment have been more contentious than abortion and contraception. Clinicians must focus on their state laws.

Medical and legal considerations

One of the most difficult and important health law questions in adolescent medicine is the ability of minors to consent to treatment and to control the health care information resulting from treatment. ("Minor" describes a child or adolescent who has not obtained the age of legal consent, generally 18 years old, to lawfully enter into a legal transaction.)

The consent of minor patients

The traditional legal rule is that parents or guardians ("parent" refers to both) must consent to medical treatment for minor children. There is an exception for emergency situations but generally minors do not provide consent for medical care, a parent does.[1] The parent typically is obliged to provide payment (often through insurance) for those services.

This traditional rule has some exceptions—the emergency exception already noted and the case of emancipated minors, notably an adolescent who is living almost entirely independent of her parents (for example, she is married or not relying on parents in a meaningful way). In recent times there has been increasing authority for "mature minors" to make some medical decisions.[2] A mature minor is one who has sufficient understanding and judgment to appreciate the consequences, benefits, and risks of accepting proposed medical intervention.

No circumstance involving adolescent treatment has been more contentious than services related to abortion and, to a lesser degree, contraception.[3] Both the law of consent to services and the rights of parents to obtain information about contraceptive and abortion services have been a matter of strong, continuing debate. The law in these areas varies greatly from state-to-state, and includes a mix of state law (statutes and court decisions) with an overlay of federal constitutional law related to reproduction-related decisions of adolescents. In addition, the law in this area of consent and information changes relatively frequently.[4] Clinicians, of course, must focus on the consent laws of the state in which they practice.

STI counseling and treatment

All states permit a minor patient to consent to treatment for an STI (**TABLE 1**).[5] A number of states expressly permit, but do not require, health care providers to inform parents of treatment when a physician determines it would be in the best interest of the minor. Thus, the clinic would not be required to provide proactively the information to our case patient's mother (regarding any STI issues) when she called.[6]

Contraception

Consent for contraception is more complicated. About half the states allow minors who have reached a certain age (12, 14, or 16 years) to consent to contraception. About 20 other states allow some minors to consent to contraceptive services, but the "allowed group" may be fairly narrow (eg, be married, have a health issue, or be "mature"). In 4 states there is currently no clear legal authority to provide contraceptive services to minors, yet those states do not specifically prohibit it. The US Supreme Court has held that a state cannot

TABLE 1 **State by state minor consent to contraceptive, sexually transmitted infection (STI), and abortion services**[a,5]

State	Contraceptive services	STI services	Abortion services
Alabama	All[b]	All[c]	Parental Consent
Alaska	All	All	(Parental Notice)[e]
Arizona	All	All	Parental Consent
Arkansas	All	All[c]	Parental Consent
California	All	All	(Parental Consent)[e]
Colorado	All	All	Parental Notice
Connecticut	Some	All	All
Delaware	All[c]	All[c]	Parental Notice[f]
Dist. of Columbia	All	All	All
Florida	Some	All	Parental Notice
Georgia	All	All[c]	Parental Notice
Hawaii	All[b,c]	All[b,c]	
Idaho	All	All[b]	Parental Consent
Illinois	Some	All[c]	Parental Notice
Indiana	Some	All	Parental Consent
Iowa	All	All	Parental Notice
Kansas	Some	All[c]	Parental Consent
Kentucky	All[c]	All[c]	Parental Consent
Louisiana	Some	All[c]	Parental Consent
Maine	Some	All[c]	All
Maryland	All[c]	All[c]	Parental Notice
Massachusetts	All	All	Parental Consent
Michigan	Some	All[c]	Parental Consent
Minnesota	All[c]	All[c]	Parental Notice
Mississippi	Some	All	Parental Consent
Missouri	Some	All[c]	Parental Consent
Montana	All[c]	All[c]	(Parental Consent)[e]
Nebraska	Some	All	Parental Consent
Nevada	Some	All	(Parental Notice)[e]
New Hampshire	Some	All[b]	Parental Notice
New Jersey	Some	All[c]	(Parental Notice)[e]
New Mexico	All	All	(Parental Consent)[e]
New York	All	All	
North Carolina	All	All	Parental Consent
North Dakota		All[b]	Parental Consent
Ohio		All	Parental Consent
Oklahoma	Some	All[c]	Parental Consent and Notice
Oregon	All[c]	All	
Pennsylvania	All[b]	All	Parental Consent
Rhode Island		All	Parental Consent
South Carolina	All[d]	All[d]	Parental Consent[f]
South Dakota	Some	All	Parental Notice
Tennessee	All	All	Parental Consent
Texas	Some	All[c]	Parental Consent and Notice
Utah	Some	All	Parental Consent and Notice
Vermont	Some	All	
Virginia	All	All	Parental Consent and Notice
Washington	All	All[b]	
West Virginia	Some	All	Parental Notice
Wisconsin		All	Parental Consent
Wyoming	All	All	Parental Consent and Notice
TOTAL	**26+DC**	**50+DC**	**2+DC**

[a]"All" applies to those aged 17 and younger or to minors of at least a specified age such as 12 or 14. "Some" applies to specified categories of minors (those who have a health issue, or are married, pregnant, mature, etc.) The totals include only those states that allow all minors to consent.
[b]Applies to minors 14 and older.
[c]Physicians may, but are not required to, inform the minor's parents.
[d]Applies to mature minors 15 and younger and to all minors 16 and older.
[e]Enforcement permanently or temporarily enjoined by a court order; policy not in effect.
[f]Delaware's abortion law applies to women younger than 16. South Carolina's abortion law applies to those younger than 17.

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TABLE 2 Joint Commission components of informed consent[4,13]

Discussion of the following elements is required:
• Nature of proposed care/treatment/services/medications/interventions or procedures
• Potential benefits/risks or adverse effects, including recuperation/potential problems
• Likelihood of achieving care/treatment and service goals
• Relevant risks/benefits/adverse effects of alternatives
• Risks of refusal of treatment
• Any limitations on confidentiality of information learned from the patient
• Documentation of elements of informed consent

completely prohibit the availability of contraception to minors.[7] The reach of that decision, however, is not clear and may not extend beyond what the states currently permit.

The ability of minors to consent to contraception services does not mean that there is a right to consent to all contraceptive options. As contraception becomes more irreversible, permanent, or risky, it is more problematic. For example, consent to sterilization would not ordinarily be within a minor's recognized ability to consent. Standard, low risk, reversible contraception generally is covered by these state laws.[8]

In our case here, the patient likely was able to consent to contraception—initially to the oral contraception and later to the IUD. The risks and reversibility of both are probably within her ability to consent.[9,10] Of course, if the care was provided in a state that does not include the patient within the groups that can give consent to contraception, it is possible that she might not have the legal authority to consent.

FAST TRACK

The general requirements of consent pertain to adolescent care: the patient must have capacity and be appropriately informed and consent must be voluntary and free of manipulation

General requirements of consent

Even when adolescent consent is permitted for treatment, including in cases of contraception, it is essential that all of the legal and ethical requirements related to informed consent are met.

1. The adolescent has the capacity to consent. This means not only that the state-mandated requirements are met (age, for example) but also that the patient can and does understand the various elements of consent, and can make a sensible, informed decision.

The bottom line is "adolescent capacity is a complex process dependent upon the development of maturity of the adolescent, degree of intervention, expected benefit of the medical procedure, and the sociocultural context surrounding the decision."[11] Other items of interest include the "evolving capacity" of the child,[12] which is the concept of increasing ability of the teen to process information and provide more appropriate informed consent. Central nervous system (CNS) maturation allows the adolescent to become increasingly more capable of decision making and has awareness of consequences of such decisions. Abstract thinking capabilities is a reflection of this CNS maturing process. If this competency is not established, the adolescent patient cannot give legitimate consent.

2. The patient must be given appropriate information (be "informed"). The discussion should include information relevant to the condition being treated (and the disease process if relevant). In addition, information about the treatment or intervention proposed and its risks and alternatives must be provided to the patient and in a way that is understandable.

3. As with all patients, consent must be voluntary and free of coercion or manipulation. These elements of informed consent are expanded on by the Joint Commission, which has established a number of components of informed consent (**TABLE 2**).[4,13]

Confidentiality and release of information to parents and others

Similar to consent, parents historically have had the authority to obtain medical information about their minor children. This right generally continues today, with some limitations. The right to give consent generally carries with it the right to medical information.

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Abortion consent is a complex, and separate, issue

It is important to emphasize that the issues of consent to abortion are much different than those for contraception and sexually transmitted infections. As our case presentation does not deal with abortion, we will address this complex but important discussion in the future—as there are an estimated 90,000 abortions in adolescent girls annually.[1]

Given that abortion consent and notification laws are often complex, any physician providing abortion services to any minor should have sound legal advice on the requirements of the pertinent state law. In earlier publications of this section in OBG MANAGEMENT we have discussed the importance of practitioners having an ongoing relationship with a health law attorney. We make this point again, as this person can provide advice on consent and the rights of parents to have information about their minor children.

Reference

1. Henshaw SK. U.S. teenage pregnancy statistics with comparative statistics for women age 20-24. New York, New York: Alan Guttmacher Institute; May 2003.

There are some times when parents may access medical information even if they have not given consent.

This right adds complexity to minor consent and is an important treatment issue and legal consideration because confidentiality for adolescents affects quality of care. Adolescents report that "confidentiality is an important factor in their decision to seek [medical] care."[14] Many parents are under the assumption that the health care provider will automatically inform them independent of whether or not the adolescent expressed precise instruction not to inform.[15,16]

Of course if a minor patient authorizes the physician to provide information to her parents, that is consent and the health care provider may then provide the information. If the patient instructs the provider to convey the information, the practitioner would ordinarily be expected to be proactive in providing the information to the parent. The issue of "voluntariness" of the waiver of confidentiality can be a question, and the physician may discuss that question with the patient. Ordinarily, however, once a minor has authorized disclosure to the parent, the clinician has the authority to disclose the information to the parent, but not to others.

All of the usual considerations of confidentiality in health care apply to adolescent ObGyn services and care. This includes the general obligation not to disclose information without consent and to ensure that health care information is protected from accidental release as required by the Health Insurance Portability and Accountability Act (HIPAA) and other health information privacy laws.[17]

How and when to protect minor confidentiality

A clinician cannot assure minors of absolute confidentiality and should not agree to do so or imply that they are doing so.[18] In our hypothetical case, when the patient told the physician that her parents were not to know of any of her treatment or communications, the provider should not have acquiesced by silence. He/she might have responded along these lines: "I have a strong commitment to confidentiality of your information, and we take many steps to protect that information. The law also allows some special protection of health care information. Despite the commitment to privacy, there are circumstances in which the law requires disclosure of information—and that might even be to parents. In addition, if you want any of your care covered by insurance, we would have to disclose that. While I expect that we can do as you ask about maintaining your confidentiality, no health care provider can absolutely guarantee it."

Proactive vs reactive disclosure. There is "proactive" disclosure of information and "reactive" disclosure. Proactive is when the provider (without being asked) contacts a parent or others and provides information. Some states require proactive information about specific kinds of treatment (especially abortion services). For the most part, in states where a minor can legally consent to treatment, health care providers are not required to proactively disclose information.[19]

Clinicians may be required to respond to parental requests for information, which is reactive disclosure and is reflected in our

case presentation. Even in such circumstances, however, the individual providing care may seek to avoid disclosure. In many states, the law would not require the release of this information (but would permit it if it is in the best interest of the patient). In addition, there are practical ways of avoiding the release of information. For example, the health care provider might acknowledge the interest and desire of the parent to have the information, but might humbly explain that in the experience of many clinicians protecting the confidentiality of patients is very important to successful treatment and it is the policy of the office/clinic not to breach the expectation of patient confidentiality except where that is clearly in the best interest of the patient or required by law.

In response to the likely question, "Well, isn't that required by law?" the clinician can honestly reply, "I don't know. There are many complex factors in the law regarding disclosure of medical information and as I am not an attorney I do not know how they all apply in this instance." In some cases the parent may push the matter or take some kind of legal action. It is in this type of situation that an attorney familiar with health law and the clinician's practice can be invaluable.

When parents are involved in the minor's treatment (bringing the patient to the office/clinic, for example), there is an opportunity for an understanding, or agreement, among the patient, provider, and parent about what information the parent will receive. Ordinarily the agreement should not create the expectation of detailed information for the parent. Perhaps, for example, the physician will provide information only when he or she believes that doing so will be in the best interest of the patient. Even with parental agreement, complete confidentiality cannot be assured for minor patients. There may, for example, be another parent who will not feel bound by the established understanding, and the law requires some disclosures (in the case of child abuse or a court order).[20]

Accidental disclosure. Health care providers also should make sure that office procedures do not unnecessarily or accidentally disclose information about patients. For example, routinely gathering information about insurance coverage may well trigger the release of information to the policy holder (often a parent). Thus, there should be clear understandings about billing, insurance, and related issues before information is divulged by the patient. This should be part of the process of obtaining informed consent to treatment. It should be up front and honest. Developing a clear understanding of the legal requirements of the state is essential, so that assurance of confidentiality is on legal, solid ground.

Additional resources and guidance

As the pediatric and adolescent segment of gynecologic care continues to evolve, it is noteworthy that the American Board of Obstetrics and Gynecology recently has established a "Focused Practice" designation in pediatric adolescent gynecology. This allows ObGyns to have an ongoing level of professional education in this specialized area. Additional information can be obtained at www.abog.org or info@abog.org.

More resources for adolescent contraceptive care include:

- The American College of Obstetricians and Gynecologists (ACOG) "Birth Control (Especially for Teens)" frequently asked questions information series (https://www.acog.org/Patients/FAQs/Birth-Control-Especially-for-Teens)
- ACOG's Adolescent Healthcare Committee Opinions address adolescent pregnancy, contraception, and sexual activity (https://www.acog.org/-/media/List-of-Titles/COListOfTitles.pdf)
- ACOG statement on teen pregnancy and contraception, April 7, 2015 (https://www.acog.org/About-ACOG/News-Room/Statements/2015/ACOG-Statement-on-Teen-Pregnancy-and-Contraception?IsMobileSet=false)
- North American Society for Pediatric and Adolescent Gynecology resources for patients (https://www.naspag.org/page/patienttools)
- Society for Adolescent Health and Medicine statement regarding contraceptive access policies (https://www.adolescenthealth.org)
- The Guttmacher Institute's overview of state laws relevant to minor consent, as of January 1, 2019 (https://www.guttmacher.org/state-policy/explore/overview-minors-consent-law). It is updated frequently.

Abuse reporting obligations

All states have mandatory child abuse reporting laws. These laws require medical professionals (and others) to report known, and often suspected, abuse of children. Abuse

includes physical, sexual, or emotional, and generally also includes neglect that is harming a child. When there is apparent sexual or physical abuse, the health care provider is obligated to report it to designated state authorities, generally child protective services. Reporting laws vary from state to state based on the relationship between the suspected abuser and the minor, the nature of the harm, and how strong the suspicion of abuse needs to be. The failure to make required reports is a crime in most states and also may result in civil liability or licensure discipline. Criminal charges seldom result from the failure to report, but in some cases the failure to report may have serious consequences for the professional.

An ObGyn example of the complexity of reporting laws, and variation from state to state, is in the area of "statutory rape" reporting. Those state laws, which define serious criminal offenses, set out the age below which an individual is not legally capable of consenting to sexual activity. It varies among states, but may be an absolute age of consent, the age differential between the parties, or some combination of age and age differential.[21] The question of reporting is further complicated by the issue of when statutory rape must be reported—for example, the circumstances when the harm to the underage person is sufficient to require reporting.[22]

Laws are complex, as is practice navigation

It is apparent that navigating these issues makes it essential for an ObGyn practice to have clear policies and practices regarding reporting, yet the overall complexity is also why it is so difficult to develop those policies in the first place. Of course, they must be tailored to the state in which the practice resides. Once again, the need is clear for health care professionals to have an ongoing relationship with a health attorney who can help navigate ongoing questions. ●

References

1. Benjamin L, Ishimine P, Joseph M, et al. Evaluation and treatment of minors. *Ann Emerg Med*. 2018;71(2):225-232.
2. Coleman D, Rosoff P. The legal authority of mature minors to consent to general medical treatment. *Pediatrics*. 2013;13:786-793.
3. American College of Obstetricians and Gynecologists. Committee Opinion No. 699. Adolescent pregnancy, contraception, and sexual activity. *Obstet Gynecol*. 2017;129:e142-e149.
4. Tillett J. Adolescents and informed consent. *J Perinat Neonat Nurs*. 2005;19:112-121.
5. An overview of minor's consent law. Guttmacher Institute's website. https://www.guttmacher.org/state-policy/explore/overview-minors-consent-law. Accessed February 14, 2019.
6. Chelmow D, Karjane N, Ricciotti HA, et al, eds. A 16-year-old adolescent requesting confidential treatment for chlamydia exposure (understanding state laws regarding minors and resources). *Office Gynecology: A Case-Based Approach*. Cambridge, United Kingdom: Cambridge University Press; January 31, 2019:39.
7. Carey v Population Services, 431 US 678 (1977).
8. Williams RL, Meredith AH, Ott MA. Expanding adolescent access to hormonal contraception: an update on over-the-counter, pharmacist prescribing, and web-based telehealth approaches. *Curr Opin Obstet Gynecol*. 2018;30:458-464.
9. McClellan K, Temples H, Miller L. The latest in teen pregnancy prevention: long-acting reversible contraception. *J Pediatr Health Care*. 2018;32:e91-e97.
10. Behmer Hansen RT, Arora KS. Consenting to invasive contraceptives: an ethical analysis of adolescent decision-making authority for long-acting reversible contraception. *J Med Ethics*. 2018;44:585-588.
11. Robertson D. Opinions in pediatric and adolescent gynecology. *J Pediatr Adolesc Gynecol*. 2008:21:47-51.
12. Lansdown G. The evolving capacities of the child. Florence, Italy: UNICEF Innocenti Research Centre, Innocenti Insight; 2005. https://www.unicef-irc.org/publications/384-the-evolving-capacities-of-the-child.html. Accessed February 15, 2019.
13. Clapp JT, Fleisher LA. What is the realistic scope of informed consent? *Jt Comm J Qual Patient Saf*. 2018;44(6):341-342.
14. Berlan E, Bravender T. Confidentiality, consent and caring for the adolescent. Curr Opin Pediatr. 2009;21:450-456.
15. Schantz K. Who Needs to Know? Confidentiality in Adolescent Sexual Health Care. Act for Youth website. http://www.actforyouth.net/resources/rf/rf_confidentiality_1118.pdf. Accessed February 14, 2019.
16. Lynn A, Kodish E, Lazebnik R, et al. Understanding confidentiality: perspectives of African American adolescents and their parents. *J Adolesc Health*. 2006;39:261-265.
17. English A, Ford CA. The HIPAA privacy rule and adolescents: legal questions and clinical challenges. *Perspect Sex Reprod Health*. 2004;36:80-86.
18. Schapiro NA, Mejia J. Adolescent confidentiality and women's health: history, rationale, and current threats. *Nurs Clin North Am*. 2018;53:145-156.
19. Scott NL, Alderman EM, 2018. Case of a girl with a secret. In: *Adolescent Gynecology: A Clinical Casebook*. New York, New York: Springer International; 2017:3-11.
20. Cullitan CM. Please don't tell my mom—a minor's right to informational privacy. *JL & Educ*. 2011;40:417–460.
21. Bierie DM, Budd KM. Romeo, Juliet, and statutory rape. *Sex Abuse*. 2018;30:296-321.
22. Mathews B. A taxonomy of duties to report child sexual abuse: legal developments offer new ways to facilitate disclosure. *Child Abuse Negl*. 2019;88:337-347.

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caused by the persistent OP position will be minimized.

CASE Resolved

The consulting obstetrician performed a transabdominal ultrasound and observed the fetal orbits were facing the transducer, confirming an OP position. On physical examination, the station was +3/5, and the fetal weight was confirmed to be approximately 8 lb. The obstetrician recommended a direct forceps delivery from the OP position. The patient and CNM agreed with the plan.

The obstetrician applied Simpson forceps and performed a mediolateral episiotomy just prior to delivery of the head. Following delivery, the rectal sphincter and anal mucosa were intact and the episiotomy was repaired. The newborn, safely delivered, and the mother, having avoided a CD, were transferred to the postpartum floor later in the day. ●

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References

1. Cheng YW, Hubbard A, Caughey AB, et al. The association between persistent fetal occiput posterior position and perinatal outcomes: An example of propensity score and covariate distance matching. *Am J Epidemiol*. 2010;171:656-663.
2. Cheng YW, Shaffer BL, Caughey AB. Associated factors and outcomes of persistent occiput posterior position: a retrospective cohort study from 1976 to 2001. *J Matern Fetal Neonatal Med*. 2006;19:563-568.
3. Ponkey SE, Cohen AP, Heffner LJ, et al. Persistent fetal occiput posterior position: obstetric outcomes. *Obstet Gynecol*. 2003;101:915-920.
4. Barth WH Jr. Persistent occiput posterior. *Obstet Gynecol*. 2015;125:695-709.
5. Cheng YW, Shaffer BL, Caughey AB. The association between persistent occiput posterior position and neonatal outcomes. *Obstet Gynecol*. 2006;107:837-844.
6. Ghi T, Dall'Asta A, Masturzo B, et al. Randomised Italian sonography for occiput position trial ante vacuum. *Ultrasound Obstet Gynecol*. 2018;52:699-705.
7. Bellussi F, Ghi T, Youssef A, et al. The use of intrapartum ultrasound to diagnose malpositions and cephalic malpresentations. *Am J Obstet Gynecol*. 2017;217:633-641.
8. Ramphul M, Ooi PV, Burke G, et al. Instrumental delivery and ultrasound: a multicenter randomised controlled trial of ultrasound assessment of the fetal head position versus standard of care as an approach to prevent morbidity at instrumental delivery. *BJOG*. 2014;121:1029-1038.
9. Malvasi A, Tinelli A, Barbera A, et al. Occiput posterior position diagnosis: vaginal examination or intrapartum sonography? A clinical review. *J Matern Fetal Neonatal Med*. 2014;27:520-526.
10. Akmal S, Tsoi E, Kaemtas N, et al. Intrapartum sonography to determine fetal head position. *J Matern Fetal Neonatal Med*. 2002;12:172-177.
11. Ghi T, Eggebo T, Lees C, et al. ISUOG practice guidelines: intrapartum ultrasound. *Ultrasound Obstet Gynecol*. 2018;52:128-139.
12. Phipps H, de Vries B, Hyett J, et al. Prophylactic manual rotation for fetal malposition to reduce operative delivery. *Cochrane Database Syst Rev*. 2014;CD009298.
13. Le Ray C, Serres P, Schmitz T, et al. Manual rotation in occiput posterior or transverse positions. *Obstet Gynecol*. 2007;110:873-879.
14. Shaffer BL, Cheng YW, Vargas JE, et al. Manual rotation to reduce caesarean delivery in persistent occiput posterior or transverse position. *J Matern Fetal Neonatal Med*. 2011;24:65-72.
15. Bertholdt C, Gauchotte E, Dap M, et al. Predictors of successful manual rotation for occiput posterior positions. *Int J Gynaecol Obstet*. 2019;144:210–215.
16. Irving FC. *A Textbook of Obstetrics*. New York, NY: Macmillan, NY; 1936:426-428.
17. Merriam AA, Ananth CV, Wright JD, et al. Trends in operative vaginal delivery, 2005–2013: a population-based study. *BJOG*. 2017;124:1365-1372.
18. Verhoeven CJ, Nuij C, Janssen-Rolf CR, et al. Predictors of failure of vacuum-assisted vaginal delivery: a case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2016;200:29-34.

Neuraxial analgesia use in labor across the US

Where is the epidural most prevalent?

Understanding geographic variability of neuraxial analgesia (epidural) use is important to improve the quality of obstetric anesthesia care. To determine where neuraxial analgesia use was highest and lowest across US states, investigators from Stanford University School of Medicine, the University of Iowa, and the Oregon Health & Science University-Portland State University collaborated to study US birth certificate data from 2015 in a retrospective, population-based, cross-sectional analysis.[a]

Multilevel modeling (accounting for patient-level and state-level factors) was used to characterize variability in neuraxial analgesia use and to assess those factors' contribution to state-level variability.

1,920,369

Women who received neuraxial labor analgesia in 2015:
1,920,369 (**73.1%**)

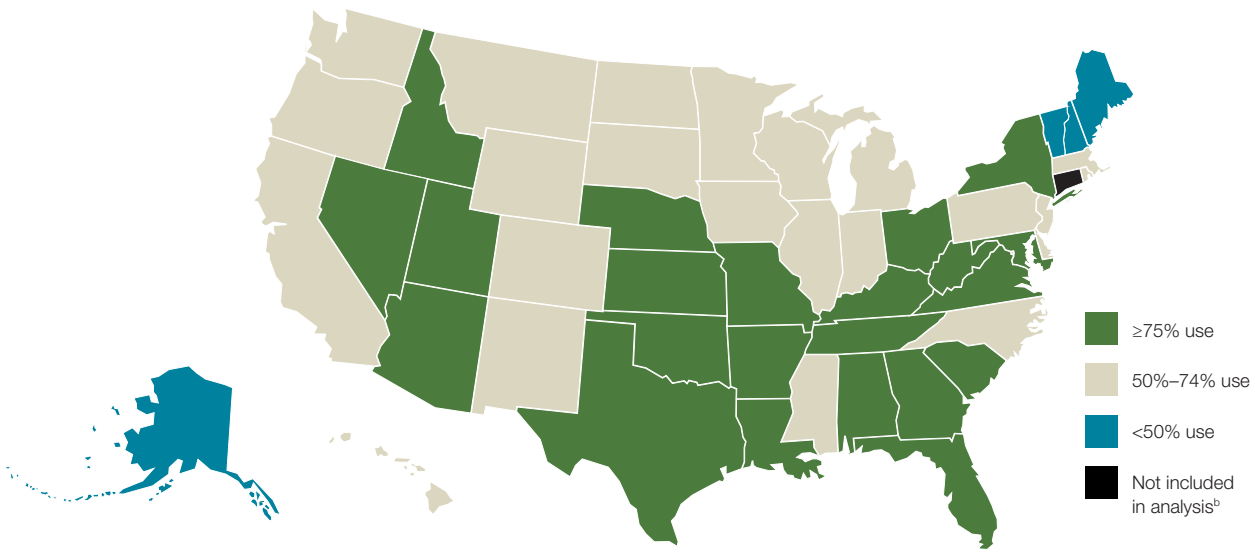
37%

80%

Variations by state: Adjusted prevalence of neuraxial analgesia use[b]

Lowest: Maine, **37%**

Highest: Nevada, **80%**



22 states had **≥75%** use of neuraxial analgesia

4 states had **<50%** use of neuraxial analgesia

CONCLUSIONS

Substantial variation exists in the prevalence of neuraxial analgesia use across the United States, with a twofold difference in the highest prevalence state (Nevada) versus the lowest prevalence state (Maine). Only 5.4% of the statewide variation, however, was attributable to the state after adjusting for patient-level factors. Other factors, such as hospital-level data and anesthesia workforce measures, may likely account for some variance between states.

Research to determine whether the prevalence variation influences outcomes for mothers and babies would be valuable, according to the study authors.

[a]Source: Butwick AJ, Bentley J, Wong CA, et al. United States state-level variation in the use of neuraxial analgesia during labor for pregnant women. *JAMA Network Open*. 2018:1(8):e186567.doi:10.1001/jamanetworkopen.2018.6567.

[b]Birth data for Connecticut was not examined because that state did not use the 2003 revised US Standard Certificate of Live Birth format.

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Minilaparotomy: Minimally invasive approach to abdominal myomectomy

Technique for removing symptomatic fibroids in a nulliparous 37-year-old patient seeking fertility

Sierra J. Seaman, MD; Patricia J. Mattingly, MD; and Arnold P. Advincula, MD

A minilaparotomy is loosely defined as a laparotomy measuring between 4 cm and 6 cm. For the appropriate surgical candidate, a minilaparotomy is a useful alternative to laparotomy or laparoscopy, especially for large pathology.[1] Benefits of minilaparotomy include improved pain management and postoperative recovery, as well as improved cosmetic outcome, with comparable blood loss and operative time.[2,3]

In this video, we illustrate the key surgical steps of a minilaparotomy for the removal of large fibroids. These steps include:

1. strategic vertical skin incision
2. use of a self-retaining retractor
3. infiltrate myometrium with dilute vasopressin
4. strategic hysterotomy
5. use of tenaculum for upward traction
6. 10# blade scalpels for the "lemon wedge" coring technique
7. layered closure.

Minilaparotomy myomectomy can be an excellent minimally invasive alternative to a traditional "full laparotomy" for women with large fibroids.

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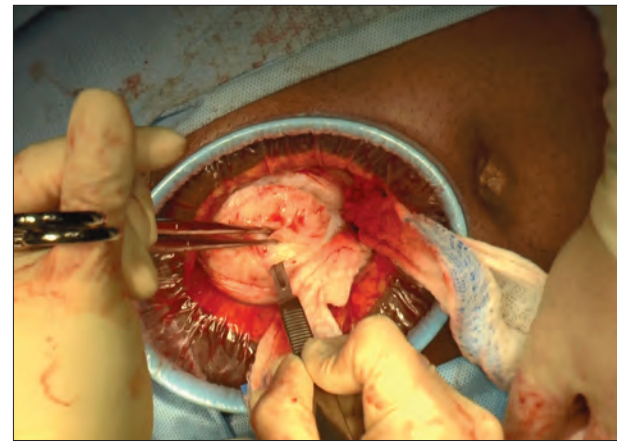
Dr. Advincula reports serving as a consultant to ConMed, CooperSurgical, Intuitive Surgical, and Titan Medical and receiving royalties from CooperSurgical. The other authors report no financial relationships relevant to this article.



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References

1. Pelosi MA 2nd, Pelosi MA 3rd. Pelosi minilaparotomy hysterectomy: a non-endoscopic minimally invasive alternative to laparoscopy and laparotomy. *Surg Technol Int.* 2004;13:157-167.
2. Fanafani F, Fagotti A, Longo R. Minilaparotomy in the management of benign gynecologic disease. *Eur J Obstet Gynecol Reprod Biol.* 2005;119:232-236.
3. Glasser MH. Minilaparotomy: a minimally invasive alternative for major gynecologic abdominal surgery. *Perm J.* 2005;9:41-45.

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