RECURRENT PREGNANCY LOSS

by Nisse V. Clark, MD, MPH

Laparoscopic Abdominal Cerclage for Cervical Insufficiency

WELL WOMAN
Cervical cancer screening on self-collected samples.

VULVOVAGINAL DISEASE
Amyloidosis of the vulva

CONTRACEPTION
Copper IUD & LNG-IUS can impact microbiota over time

LIFE TRANSITIONS
Vertigo risk factors in perimenopausal women

GYNECOLOGY
Hormonal suppression after endometriosis surgery

OBSTETRICS
Syphilis in pregnancy
REDEFINE LONG-TERM CONTRACEPTION
MEET ANNOVERA.

ANNOVERA (segesterone acetate and ethinyl estradiol vaginal system) is the only long-lasting, reversible birth control that doesn’t require a procedure.

Empower her to be in control of her fertility and menstruation with a predictable bleeding profile.

The only hormonal birth control with a non-androgenic progestin, segesterone acetate, and 13 mcg of ethinyl estradiol—making it one of the lowest dose combination hormonal contraceptives on the market.

97.3% effective and high patient satisfaction: ~90% of women in the clinical trial were satisfied with ANNOVERA.

IMPORTANT SAFETY INFORMATION

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS
See full prescribing information for complete boxed warning.

• Females over 35 years old who smoke should not use ANNOVERA.
• Cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptive use.

CONTRAINDICATIONS
ANNOVERA (segesterone acetate and ethinyl estradiol vaginal system) is contraindicated and should not be used in women with a high risk of arterial or venous thrombotic diseases; current or history of breast cancer or other estrogen- or progestin-sensitive cancer; liver tumors, acute hepatitis, or severe (decompensated) cirrhosis; undiagnosed abnormal uterine bleeding; hypersensitivity to any of the components of ANNOVERA; and use of Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir.

WARNING AND PRECAUTIONS
• Stop ANNOVERA if a thrombotic or thromboembolic event occurs, and at least 4 weeks before and through 2 weeks after major surgery. Start ANNOVERA no earlier than 4 weeks after delivery, in females who are not breastfeeding. Consider cardiovascular risk factors before initiating in all females, particularly those over 35 years.
• Discontinue if jaundice occurs.
• Stop ANNOVERA prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir: ANNOVERA can be restarted 2 weeks following completion of this regimen.
• Do not prescribe ANNOVERA for females with uncontrolled hypertension or hypertension with vascular disease. Monitor blood pressure and stop use if blood pressure rises significantly in females with well-controlled hypertension.
• Monitor glucose in pre-diabetic or diabetic females taking ANNOVERA. Consider an alternate contraceptive method for females with uncontrolled dyslipidemias.
• Patients using ANNOVERA who have a significant change in headaches or irregular bleeding or amenorrhea should be evaluated. ANNOVERA should be discontinued if indicated.
• Other warnings include: gallbladder disease; depression; cervical cancer; increased serum concentrations of binding globulins; hereditary angioedema; chloasma (females who tend
to develop chloasma should avoid exposure to the sun or UV radiation while using ANNOVERA; toxic shock syndrome (TSS) (if a patient exhibits symptoms of TSS, remove ANNOVERA, and initiate appropriate medical treatment); vaginal use (ANNOVERA may not be suitable for females with conditions that make the vagina more susceptible to vaginal irritation or ulceration).

ADVERSE REACTIONS
The most common adverse reactions reported in at least 5% of women who received ANNOVERA were: headache/migraine, nausea/vomiting, vulvovaginal mycotic infection/candidiasis, lower/upper abdominal pain, dysmenorrhea, vaginal discharge, urinary tract infection, breast pain/tenderness/discomfort, bleeding irregularities including metrorrhagia, diarrhea, and genital pruritus.

DRUG INTERACTIONS
Drugs or herbal products that induce certain enzymes, including CYP3A4, may decrease the effectiveness of ANNOVERA or increase breakthrough bleeding. Counsel patients to use a back-up or alternative method of contraception when enzyme inducers are used with ANNOVERA.

INDICATION
ANNOVERA is a progestin/estrogen combination hormonal contraceptive indicated for use by females of reproductive potential to prevent pregnancy.

Limitations of Use: ANNOVERA has not been adequately studied in females with a body mass index >29 kg/m².

Please note this information is not comprehensive. Please see Brief Summary of the Full Prescribing Information on the next page, including BOXED WARNING, or visit Annovera.com/pi.pdf.


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Limitations of Use: ANNOVERA has not been adequately studied to use ANNOVERA safely and effectively. Please visit ANNOVERA.com/pi.pdf for full prescribing information (PI).

Before starting ANNOVERA, consider history and risk factors include smoking, obesity, and family history of VTE, in addition to other factors that contraindicate use of CHCs. The rates of cardiovascular events and cerebrovascular events, such as stroke and myocardial infarction. The risk is greater among older females (≥35 years of age), smokers, and females with hypertension, dyslipidemia, diabetes, or obesity.

Cardiovascular Disease

Hypertension

ANNOVERA is contraindicated in females with uncontrolled hypertension or hypertensive disorders of pregnancy. For all females, including those with well-controlled hypertension, monitor blood pressure at routine visits and stop ANNOVERA if blood pressure rises to ≥160/100 mm Hg.

Age-Related Considerations

The risk for cardiovascular disease and prevalence of risk factors for cardiovascular disease increase with age. Certain comorbidities such as smoking and migraine headache without aura, that do not contraindicate CHC use in younger females, are contraindications to ANNOVERA use in females >20 years of age. Consider the presence of underlying risk factors that may increase the risk of cardiovascular disease or diabetes, particularly before initiating ANNOVERA for women over 35 years, such as hypertension, diabetes, dyslipidemia, and obesity.

Gallbladder Disease

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

Adverse Carbohydrate and Lipid Metabolic Effects

Hyperglycemia

ANNOVERA is contraindicated in diabetic females over age 35, or females who have diabetes with hypertension, nephropathy, retinopathy, neuropathy, or other vascular disease, or females with diabetes >20 years duration. ANNOVERA may decrease glucose tolerance. Carefully monitor prediabetic and diabetic females who are taking ANNOVERA.

Dyslipidemia

Consider alternative contraception for females with uncontrolled dyslipidemia. ANNOVERA may cause adverse lipid changes. Females with hyperlipidemia or a family history thereof, may be at an increased risk of pancreatitis when using ANNOVERA.

Headache

ANNOVERA is contraindicated in females with certain headaches, Evaluate new or significant changes in headaches, including migraines, and discontinue ANNOVERA if needed.

Bleeding Irregularities and Amenorrhea

Females using ANNOVERA may experience unscheduled breakthrough bleeding and spotting, especially during the first month of use. If unscheduled bleeding occurs or persists, check for causes such as pregnancy or malignancy.

Based on subject data from two clinical efficacy trials of ANNOVERA, 5–10% of females experienced unscheduled bleeding per 28-day cycle. A total of 41 subjects (1.7%) discontinued due to menstrual disorders including metrorrhagia, menorrhagia, and abnormal withdrawal bleeding. Females who are anemic or use ANNOVERA may experience amenorrhea. Based on subject data from two clinical trials for up to 13 cycles, amenorrhea occurred in 3–5% of females per cycle using ANNOVERA and in 0.9% of females in all 13 cycles. If scheduled bleeding does not occur, consider the possibility of pregnancy.

Depression

Carefully observe females with a history of depression and discontinue ANNOVERA if depression recurs to a serious degree.

Cervical Cancer

Effect on Birth Weight

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

Hereditary Angioid Anomaly

In females with the hereditary angioid anomaly, exogenous estrogens may induce or exacerbate symptoms of angioid. Chloasma

Chloasma may occur with ANNOVERA use, especially in females with a history of chloasma gravidarum. Advise females who tend to develop chloasma to avoid exposure to the sun or ultraviolet radiation while using ANNOVERA.

Toxic Shock Syndrome (TSS)

If a patient exhibits signs/symptoms of TSS, consider the possibility of this diagnosis, remove ANNOVERA, and initiate appropriate medical evaluation and treatment.

Vaginal Infection

Some females are aware of the vaginal system on occasion during the 21 days of use or during cohorts, and patients may feel that the vaginal system during cohorts. ANNOVERA may be suitable for females with conditions that make the vagina more susceptible to vaginal irritation or ulceration. Vaginal and cervical erosion and/or ulceration has been reported in females using other contraceptive vaginal devices. In some cases, the ring adhered to vaginal tissue, which necessitated removal by a healthcare provider.

ADVERSE REACTIONS

Clinical Trial Experience

Most Common Adverse Reactions

In clinical trials, adverse reactions reported in >5% of ANNOVERA-treated subjects include: headache, including migraine (38.6%); nausea/vomiting (25.0%); vulvovaginal mycotic infection/vaginal candidiasis (14.5%); abdominal pain/lower/upper (13.3%); dysmenorrhea (12.5%); vaginal discharge (11.8%); UTI/cystitis/pyelonephritis/genitourinary tract infection (10.9%); breast pain/boobs (9.7%); acne (4.7%); and pruritus (5.5%).

Adverse Reactions Leading to Discontinuation

Among subjects using ANNOVERA for contraception, 12% discontinued from the clinical trials due to an adverse reaction. Adverse reactions leading to discontinuation by >1% of ANNOVERA-treated subjects, include: metrorrhagia/menorrhagia (1.7%); headache, including migraine (1.3%); vaginal discharge/other mycotic infections (1.1%); rash/urticaria (1.9%); and pain of the perineum/pain/coital pain (1.1%). In addition, 1.4% of subjects discontinued ANNOVERA use due to vaginal system expulsions.

Serious Adverse Reactions

Serious adverse reactions occurring in ≤2 subjects were: VTEs (deep venous thrombosis, cerebral vein thrombosis, pulmonary embolism), drug hypersensitivity reactions; and spontaneous abortions.

DRUG INTERACTIONS

Drugs or herbal products that induce certain enzymes, including CYP3A4, may decrease the effectiveness of ANNOVERA or increase breakthrough bleeding. Counsel patients to use a backup or alternative method of contraception when enzyme inducers are used with ANNOVERA. Do not co-administer ANNOVERA with HIV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to potential for ALT elevations.

USE IN SPECIFIC POPULATIONS

Pregnancy

Discontinue ANNOVERA if pregnancy occurs. Lactation

Not recommended for nursing mothers; can decrease milk production.

Pediatric Use

Safety and efficacy of ANNOVERA have been established in women of reproductive age. Efficacy is expected to be the same for postpubertal adolescents under the age of 18 as for users 18 years and older. Use of ANNOVERA before menarche is not indicated.

Geriatric Use

ANNOVERA has not been studied in females who have reached menopause and is not indicated in this population.

Hepatic Impairment

No studies have been conducted to evaluate the effect of hepatic impairment on the disposition of ANNOVERA. Acute or chronic disturbances of liver function may necessitate the discontinuation of CHC use until markers of liver function return to normal and CHC use can be reinitiated.

Renal Impairment

No studies were conducted in subjects with renal impairment; ANNOVERA is not recommended in patients with renal impairment.

Body Mass Index (BMI)/Body Weight

The safety and efficacy of ANNOVERA in females with a BMI >29 kg/m² have not been adequately evaluated because this subpopulation was excluded from the clinical trials after 2 CHCs occurred in females with a BMI >29 kg/m². This weight is associated with lower systemic exposure of SA and EE.

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CHAIRMAN’S LETTER

Cervical Cancer Awareness Month

With this first issue of 2021, you may notice something different on the cover. This special design features a teal ribbon wrap and related content for cervical cancer content.

As women’s health care providers, you likely know that January is Cervical Cancer Awareness month. The teal ribbon is its awareness symbol. To complement the print issue, key elements on our website will turn teal for the entire month of January and we will have related articles and interviews on the topic of cervical cancer. This is a first for us and we would like to hear your feedback on it.

Under the astute guidance of Editor-in-Chief Catherine Y. Spong, MD, we also are launching a new feature in this issue called Caruside Consults that engages practitioners outside of ob/gyn with expertise in health issues that may affect pregnant women. Take a dive into dental issues in pregnancy and we would like to hear your feedback on it.

The other features in this issue focus on obstetrics, from the cover story on one method to address recurrent pregnancy loss by Nisse Clark, MD, to the article on diagnosis and management of syphilis in pregnancy by Emily Adhikari, MD, who reminds us that there are other infectious pathogens affecting our patients as we all work to get to the end of the COVID-19 pandemic.

We encourage your feedback. Please connect with us at COGeditorial@mmhgroup.com. Best wishes for a safe, healthy, and happy new year.

Mike Hennessy Sr.
Chairman and Founder, MJH Life Sciences
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Ranked #7 in the U.S. for Gynecology.
#1 in California.

At Cedars-Sinai, the dedication of our doctors and staff has made us one of the most recognized hospitals in the nation. We're proud to have earned a place on U.S. News & World Report's Best Hospitals Honor Roll. This recognition belongs to our entire team who shows up day after day, night after night, for all of Southern California.

Learn more about our gynecologic care: cedars-sinai.org/womenshealth
Vigilance is key: Syphilis spreads amidst pandemic

With the beginning of 2021, we are eager for resolution to the pandemic. Although reductions in transmission are evident with social distancing, the optimal methods to make social distancing attractive and feasible remain elusive. Research to explain the underlying mechanisms of differing rates and severity of infection in different populations is sorely needed – both for medical importance and to provide a rationale the public needs to continue social distancing. Given the duration of the SARS-CoV-2 (COVID-19) pandemic, continued isolation and social distancing coupled with different infection rates and severity of illness have stymied universal adaptation of social isolation. Although the promise of vaccines is encouraging, it will be critical to maintain our vigilance in hygiene, masking, social distancing, and infection control as vaccines are administered. Equally critical is the education about the vaccine to facilitate uptake.

Ob/gyns have a robust history treating numerous infectious diseases, from smallpox to now COVID-19 – characterized by outbreaks followed by intensive health department measures to identify new infections and trace potential exposures. Pregnancy affords

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**Figure 1. COVID-19: New cases and deaths in the U.S.**

Data from https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases
a unique time period for identification and treatment of illness. In addition, pregnancy has the unique concern of vertical transmission to the fetus, with potential concerns for fetal development. Although to date COVID-19 infection in pregnancy has not resulted in demonstrable fetal effects, vertical transmission has been documented.

In this issue of Contemporary OB/GYN®, we provide guidance on another infectious disease that has been making a comeback in recent years: syphilis. Although once truly nearing elimination in the U.S., it has again become a rising concern for obstetricians. As expertly outlined by Emily Adhikari, MD, all pregnant women should be screened, and for those at high risk, repeat screening in the third trimester and at delivery is recommended. Although there are clinical signs and symptoms in some women, typically diagnosis is initially made via serologic tests. Syphilis progresses across a course— including primary, secondary, latent, and finally, tertiary syphilis— if untreated. Importantly, vertical transmission is possible and may manifest in utero or after delivery as early or late congenital syphilis.

Importantly, the testing paradigms for syphilis have changed, and it is critical to understand the method your laboratory is using. Traditional testing—what I am most familiar with—is the initial nontreponemal test (the RPR) followed by the confirmatory treponemal-specific test. This is in contrast to the reverse sequence algorithm, which starts with a treponemal antibody test. High throughput labs are moving to this reverse screening sequence, as it affords a higher volume and more cost-effective throughput. However, the interpretation and additional studies require an understanding of whether the patient was previously diagnosed, using which test, and treated, as outlined by Adhikari.

Infectious diseases stimulate us as physicians to think broadly, identify sources, sleuth answers, and create algorithms to mitigate their spread. As we tackle COVID-19 it is imperative that we do not allow more familiar infectious conditions to take an insidious grip on our patients.

Dr. Spong, Editor in Chief, is Professor and Vice Chair in the Department of Obstetrics and Gynecology and Chief of the Division of Maternal-Fetal Medicine at UT Southwestern Medical Center in Dallas. She holds the Gillette Professorship of Obstetrics and Gynecology.

Email her at cspong@mjhlifesciences.com

FOR REFERENCES VISIT contemporaryobgyn.net/EDITsyphilis

Data from: https://www.cdc.gov/nchhstp/pregnancy/effects/syphilis.html

Figure 2. Primary and secondary syphilis in reproductive age women and congenital syphilis in the U.S.

WE WANT TO HEAR FROM YOU! Let us know what you thought of this month’s feature on recurrent pregnancy loss, or share what you have seen of STDs during the pandemic. Email our editorial staff at COGeditorial@mmhgroup.com.
Key Messages:

- Crackles or rales, systolic or diastolic murmur, or extra heart sounds such as an S3 or S4 should heighten concern for peripartum cardiomyopathy. Evaluation includes chest x-ray and an electrocardiogram. Abnormal results, or normal results on either plus an atypical history or physical exam, warrant further investigation.

- The clinical presentation of peripartum cardiomyopathy is most often that of decompensated left-sided heart failure but right-sided dysfunction also can be present.

- Common risk factors for peripartum cardiomyopathy are maternal age > 30 years, African descent, multiple gestation, and history of hypertension or preeclampsia.

- Immediate management of peripartum cardiomyopathy is focused on optimization of preload, typically with diuretics, afterload reduction, and supportive care. Cardiac telemetry, continuous fetal monitoring, and close urine output monitoring with placement of a urethral catheter are warranted.

- Delivery is recommended for patients with unstable peripartum cardiomyopathy but timing depends on the gestational age of the fetus. An attempted vaginal delivery is recommended for patients without an obstetric contraindication with consideration of cesarean delivery for causes of acute decompensated heart failure.

- With medical therapy (i.e. beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and diuretics) 50% to 80% of women with peripartum cardiomyopathy ultimately recover to an ejection fraction > 50% at 6 months. Those with a left ventricular ejection fraction < 50% should be advised against pregnancy.

Read the complete chapter from *Protocols for High-Risk Pregnancies, 7th Edition*, edited by John T. Queenan, MD, Charles J. Lockwood, MD, and Catherine Y. Spong, MD, now. CONTEMPORARYOBGYN.NET/CMPROTOCOLS

Watch an interview with Queenan and Spong here: youtube.com/watch?v=pdgpNU0txk4
FOR THE TREATMENT OF WOMEN WITH MODERATE TO SEVERE DYSPAREUNIA, A SYMPTOM OF VULVAR AND VAGINAL ATROPHY, DUE TO MENOPAUSE

DISCOVER A TREATMENT EXPERIENCE WITH

SIMPLICITY AT ITS CORE

IMVEXXY (estradiol vaginal inserts) 4 mcg - 10 mcg

THE ONLY ULTRA-LOW-DOSE VAGINAL ESTRADIOL AVAILABLE IN 4 AND 10 MCGL

PROVEN EFFICACY AT WEEK 12 WITH ONSET OF ACTION AS EARLY AS 2 WEEKSL,2

MESS-FREE ADMINISTRATION WITH NO APPLICATOR, DOSE PREPARATION, OR CLEANUP NEEDEDL,3

COVERED BY MOST INSURANCE PLANS AND, FOR THOSE WITH CO-PAY RESPONSIBILITIES, AFFORDABILITY PROGRAMS TO HELP HER GET IMVEXXY FOR AS LITTLE AS $35†

INDICATION

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

IMPORTANT SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA

See full prescribing information for complete boxed warning.

Estrogen-Alone Therapy

- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens
- Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia

The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT)

The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older

Estrogen Plus Progesterin Therapy

- Estrogen plus progesterin therapy should not be used for the prevention of cardiovascular disease or dementia
- The WHI estrogen plus progesterin substudy reported increased risks of stroke, DVT, pulmonary embolism (PE) and myocardial infarction (MI)
- The WHI estrogen plus progesterin substudy reported increased risks of invasive breast cancer
- The WHIMS estrogen plus progesterin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older

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


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TO LEARN MORE AND REQUEST SAMPLES, VISIT IMVEXXYINFO.COM

CONTRAINDICATIONS

IMVEXXY is contraindicated in women with any of the following conditions: undiagnosed abnormal genital bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active DVT, PE, or history of these conditions; active arterial thromboembolic disease or a history of these conditions; known anaphylactic reaction or angioedema to IMVEXXY; known liver impairment or disease; known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders.

WARNINGS AND PRECAUTIONS

- IMVEXXY is intended only for vaginal administration. Systemic absorption may occur with the use of IMVEXXY.
- The use of estrogen-alone and estrogen plus progestin therapy has been reported to result in an increase in abnormal mammograms requiring further evaluation.
- The WHI estrogen plus progestin substudy reported a statistically non-significant increased risk of ovarian cancer. A meta-analysis of 17 prospective and 35 retrospective epidemiology studies found that women who used hormonal therapy for menopausal symptoms had an increased risk for ovarian cancer. The exact duration of hormone therapy use associated with an increased risk of ovarian cancer, however, is unknown.
- Other warnings include: gallbladder disease; severe hypercalcemia, loss of vision, severe hypertriglyceridemia or cholestatic jaundice.
- Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomias and should be used with caution in women with these conditions.
- Women on thyroid replacement therapy should have their thyroid function monitored.

ADVERSE REACTIONS

The most common adverse reaction with IMVEXXY (≥5%) was headache.
Shortest duration consistent with treatment goals and risks for the individual woman. Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Cardiovascular Disorders and Probable Dementia

Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.3), and Clinical Studies (14.2, 14.3) in full prescribing information].

The WHI Health利出期癌影数生被同能日租柯集数和直深服记姆足（DVT）在后膜期卵巢明生60%的年份下7.1年件长数直以日光性表证数（CE）0.626 mg-单，相持到相位数（see Warnings and Precautions (5.2), and Clinical Studies (14.2) in full prescribing information).

The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily oral CE (0.625 mg), relative to placebo (see Warnings and Precautions (5.2), and Clinical Studies (14.2) in full prescribing information).

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and other dosage forms of estrogens.

Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Cardiovascular Disorders and Probable Dementia

Estrogen-plus-progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.3), and Clinical Studies (14.2, 14.3) in full prescribing information].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism (PE), stroke and myocardial infarction (MI) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625 mg) combined with medroxyprogesterone acetate (MPA) (2.5 mg) relative to placebo (see Warnings and Precautions (5.2), and Clinical Studies (14.2) in full prescribing information).

The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with daily CE (0.625 mg) combined with MPA (2.5 mg), relative to placebo. It is unknown whether this finding applies to younger postmenopausal women [see Warnings and Precautions (5.4), Use in Specific Populations (8.5), and Clinical Studies (14.3) in full prescribing information].

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and other dosage forms of estrogens. Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

INDICATIONS AND USAGE

IMVEXXY® (estradiol vaginal inserts) is an estrogen indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

DOSEAGE AND ADMINISTRATION

Generally, when estrogen is prescribed for a postmenopausal woman with a uterus, a progestin should also be considered to reduce the risk of endometrial cancer.

A woman without a uterus does not need a progestin. In some cases, however, hysterecomized women with a history of endometriosis may need a progestin [see Warnings and Precautions (5.3, 5.15) in full prescribing information].

Use of estrogen-alone, or in combination with a progestin, should be with the lowest effective dose and for the shortest duration consistent with treatment goals and risks for the individual woman.

Postmenopausal women should be re-evaluated periodically as clinically appropriate to determine if treatment is still necessary.

CONTRAINDICATIONS

Undiagnosed abnormal genital bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active DVT, PE, or history of these conditions; active hypertension; stroke or myocardial infarction (MI) or a history of these conditions; known anaphylactic reaction or angioedema with IMVEXXY®; known liver impairment or disease; known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders.

WARNINGS AND PRECAUTIONS

Risks from Systemic Absorption

IMVEXXY is intended only for local administration. Systemic absorption may occur with the use of IMVEXXY® (Pharmacokinetics [12.3]) in full prescribing information. The warnings, precautions, and adverse reactions associated with the use of systemic estrogen-alone therapy should be taken into account.

Cardiovascular Disorders

An increased risk of stroke and DVT has been reported with estrogen-alone therapy. An increased risk of PE, DVT, stroke, and MI has been reported with estrogen plus progestin therapy. Should these occur or be suspected, estrogen with or without progestin therapy should be discontinued immediately.

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

I read the article about robotic surgery (The state of gynecologic robotic surgery, Contemporary OB/GYN, November 2020) and I am dismayed that the American College of Obstetricians and Gynecologists and the ob/gyn world has embraced the robot despite the evidence for hysterectomy that transvaginal hysterectomy (THV) is safer. We are justifying less safe surgical options because the robots are available? Why are we not training based on evidence-based medicine? No trainee in ob/gyn residency should be allowed to use a robot unless it is for surgery that is enhanced by robot technology, such as endometrial cancer and lymph node dissection. I have never been able to understand this disconnect from evidence-based care.

We promote TVH as the surgery of choice for hysterectomy, yet we bemoan the fact that trainees are not being trained in TVH skills. WHY? Have we lost our sense of direction and all focused on the bright lights of the robots?

I personally forced myself to develop my TVH skills. First, I was trained to do TVH as the surgery of choice for benign conditions; that helped.

I had a 90%+ TVH rate for hysterectomies. Previous c/s did not keep me from doing a basic TVH, nulliparous cervix did not prevent me from attempting TVH and uterine size rarely prevented me from attempting and successfully completing TVH.

I even developed a new technique to complete a failed TVH. Start the TVH, enter the anterior and posterior cul-de-sac and if unable to complete the TVH I would then close the cuff vaginally and then a simple laparotomy to complete the procedure and the cuff was already closed, which made it a very simple procedure and took less than 30 minutes.

Most TVHs took less than 40 minutes and blood loss was usually less than 50 cc.

I developed our outpatient TVH program and well over 600 patients successfully went home after surgery the same day.

My complication rate was lower than the rest of our department and I was a high-volume surgeon, performing more cases than all other members of our gyn department with fewer complications and no mortalities in over 25 years.

I believe that we have sold out to the robots and we have neglected our patients in the process. Robot cases are performed because the robot is available and it is “fun.” What happened here? Fun trumps safety and evidence. No pride in developing our specialty trademark surgery?

We need to go back to basics and train our new doctors on TVH skills and then and only then should they be allowed to advance to robot surgery.

Robots need to be reserved for the specialties that use them to improve care such as gyn oncology and infertility. Stop now while we still have the surgical skills available to train the new doctors.

I feel like we have been sold out to the robot companies and they now control our patients’ care. The evidence does not support this. Let’s go back to the gold standard for benign conditions and train our new doctors.

Just my two cents. ■

Elizabeth Harmon, MD, MBA, FACOG
Gynecologist and Founder,
Salem Women’s Clinic Inc.
SALEM, OR

have a comment? SEND YOUR THOUGHTS TO COGEDITORIAL@MMHGROUP.COM
We would like to thank Dr. Harmon for the letter, and congratulate her on the skill and passion in offering a minimally invasive option to the vast majority of her patients. In skilled hands, vaginal hysterectomy is an excellent option for surgeons and patients. All surgeons strive to provide the best surgical care for their patients; however, graduating residents are not getting as much experience in vaginal hysterectomy during their training as they used to; the data on this is clear.

In addition, we now have 4 options (abdominal, vaginal, laparoscopic, robotic) for hysterectomy instead of two (abdominal and vaginal), and the goal is always to provide more minimally invasive options and avoid laparotomy. In addition to that, fewer hysterectomies are being performed annually and we have graduated over 300 fellows from Minimally Invasive Gynecologic Surgery fellowships that are taking care of a large portion of patients that require hysterectomy. Other subspecialists such as gynecologic oncologists and urogyneecologists also are doing large volumes of hysterectomies. All of these factors make it harder and harder for graduates of residency programs to develop and maintain their skills in vaginal surgery. Laparoscopic hysterectomy has become the go-to procedure and it does have its merits. The surgeon can take on any pelvic pathology, including endometriosis and ovarian cysts, and OR times in laparoscopic hysterectomy have been decreasing and are often similar to what they are for vaginal hysterectomy. With any minimally invasive approach, patient outcomes are comparable. Therefore, some have argued that the ob/gyn specialist has to ideally pick one technique in order to become proficient at it and that makes many of them pick the laparoscopic or robotic approach. In an ideal world, it would be great to have the vaginal hysterectomy expert take on most cases and refer the hard cases to the laparoscopic surgeon since this would minimize cost and reduce the number of abdominal hysterectomies even further. This, however, is not a real world situation. In the real world, the vaginal surgeon expert will take on most cases vaginally, but the really hard cases will be performed via a laparotomy. This is what reduces the reproducibility of the vaginal approach compared to laparoscopic and robotic approaches, where the laparoscopic expert can often do close to 100% of his or her cases in a minimally invasive fashion.

We agree with Dr. Harmon that robotic surgery has at times been oversold; but robotic surgery is not just in the sphere of vaginal surgery. It also provides a valuable option to a group of gynecologists who are not proficient in vaginal or straight-stick modalities, to shift their cases from laparotomy to a minimally invasive approach. High-volume, well trained robotic surgeons provide excellent care to their patients, and this technology allows more surgeons to offer a minimally invasive approach and decrease the comorbidities associated with open surgery.

Jon Einarsson, MD, MPH, PHD
Robert K. Zurawin, MD
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Effectiveness of self-collected HPV screening tests

by SANDRA FYFE

A modeled analysis concluded that women who are underscreened for human papilloma virus (HPV) still benefit from self-administered tests, despite a loss in test sensitivity.

Widely collecting self-administered HPV tests, even with lower test sensitivity, can help in the fight against cervical cancer, according to a study published in *Cancer Epidemiology, Biomarkers, and Prevention*.

Megan A Smith, MPH, PhD, a senior research fellow in the cancer research division of the Cancer Council in New South Wales, Australia, and an honorary senior research fellow at the Sydney School of Public Health at the University of Sydney, along with collaborating authors, used a proven model to compare the impact of self-collected cervical screening samples on cancer diagnoses and deaths over a woman’s lifespan. They included women with and without Australia’s restriction to women over age 30, and those 2 or more years overdue for HPV screening.

The results were compared with regular clinician-collected HPV screenings from women age 25 and older who were tested every 5 years. “We conservative-ly assumed sensitivity of HPV testing on self-collected relative to clinician-collected samples was 0.98. Outcomes were estimated either in the context of HPV vaccination ... or the absence of HPV vaccina tion,” the authors wrote.  

For unvaccinated women, the 2% worst-case loss of test sensitivity was outweighed by the health benefits, even if only 15% of women who would not ordinarily be screened used the test. In regularly vaccinated women, “population-wide self-collection could be marginally (0.2-1.0%) less effective at 15% additional uptake, but 6.2-12.4% more effective at 50% additional uptake. Most (56.6-65.0%) of the loss in effectiveness in the restricted self-collection pathway in Australia results from the requirement to be 2 or more years overdue.”

Smith told *Contemporary OB/GYN* that researchers already know that most women prefer to collect their own samples. “Some countries are now offering self-collection as an option to women who are overdue for cervical screening, but not to all women,” she said. Offering screenings in a restricted way, Smith said, prevents the process from achieving its full potential because it is too complicated for providers to know if women are eligible, and it is not widely promoted.

Following this study, Smith said that next steps were to inform women and providers about the tests’ safety and accuracy. “Clinical management path-ways need to be reviewed, and ideally there would be a triage test that could be done on the same self-collected sample for women who test positive for HPV,” Smith said. “Currently, cytology triage is used, so women still need to return for a speculum exam and clinician-collected sample.” Labs need time to prepare to process the self-collected samples, and systems that could automate the pre-analytic phase of processing would be very useful, Smith added.

“This study provides reassurance that self-collection could be offered more widely as an equal choice for women. This change would center screening around women’s preferences, making it more accessible for all.” She emphasized that self-collection is faster, does not require health facilities, and would allow screening to continue in the context of disruptions like COVID-19. “One reason it was offered in a restricted way was that, previously, it was thought that self-collection was not as good as testing on a clinician-collected sample. We now know that’s not the case.”

“Reaching these women is critical to reduce cervical cancer rates.”

Sandra Fyfe is a freelance writer for Contemporary OB/GYN®.

FOR REFERENCES VISIT contemporaryobgyn.net/HPVscreen
A ROUNDTABLE DISCUSSION

CERVICAL CANCER PREVENTION: ADDRESSING HEALTH DISPARITIES

Join us as Dr. Haywood Brown moderates a roundtable discussion about health disparities in cervical cancer prevention and how they impact the overall health and wellbeing of women.

The conversation will explore the inclusion of Black and Brown women in clinical trials, access to preventative healthcare specifically cervical cancer screening, role of medical guidelines in addressing disparities, and possible solutions looking to the future.

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Hormonal suppression after endometriosis surgery

by BOB KRONEMYER

Postoperative hormonal suppression had a statistically significant effect on reducing endometriosis recurrence and improving pain, according to a systematic review and meta-analysis published in the journal Human Reproduction Update.

“As surgeons, our primary goal is to make patients feel better and we often accomplish this by surgically treating endometriosis,” said co-author Ally Murji, MD, MPH, an associate professor of ob/gyn at the University of Toronto and Mount Sinai Hospital in Toronto, Canada.

The authors evaluated whether postoperative hormonal suppression decreases disease recurrence when compared with placebo/expectant management.

MEDLINE, Embase, Cochrane CENTRAL, and Web of Science databases were searched from inception to March 2020 for randomized clinical trials (RCTs) and prospective observational cohort studies of premenopausal women undergoing conservative surgery and initiating hormonal suppression within 6 weeks postoperatively with one of the following medical therapies: combined hormonal contraceptives, progestins, levonorgestrel-releasing intrauterine system (LNG-IUS) and gonadotropin-releasing hormone (GnRH) agonists.

The review consisted of 17 studies (13 RCTs and 4 cohort studies), totaling 2,137 patients: 1,189 receiving postoperative suppression and 948 controls.

The mean follow-up ranged from 12 to 36 months, with outcomes assessed at a median of 18 months postoperatively.

Among 14 studies (11 RCTs, 3 cohort studies; 1,766 patients total), there was a significantly decreased risk of endometriosis recurrence in patients receiving postoperative hormonal suppression compared with expectant management/placebo: relative risk (RR) 0.41; 95% confidence interval (CI): 0.26 to 0.65.

“When we limited the analysis to only RCTs, we found that the risk of postoperative endometriosis recurrence was consistently decreased with hormonal suppression,” Murji told Contemporary OB/GYN.

Among 7 studies (6 RCTs, 1 cohort study; 652 patients total), patients receiving postoperative hormonal suppression achieved significantly lower pain scores compared with controls: standard mean difference (SMD) -0.49; 95% CI: -0.91 to -0.07.

“Our review provides new evidence that postoperative hormonal suppression decreases endometriosis recurrence and pain,” Murji said. “This contradicts the last Cochrane review on the topic.”

Although there was significant heterogeneity in the studies included in the review, Murji is confident in the results.

“We found only a 4% probability that any future RCT would contradict our findings.”

“As few as eight women would need to be treated with postoperative hormonal suppression for at least 6 months to prevent one endometriosis recurrence,” Murji said, surprised by the magnitude of the effect.

It is essential for clinicians to educate patients, Murji said, as endometriosis is a chronic condition and surgery is not a panacea. “For patients not seeking to conceive immediately after surgery, I offer hormonal suppression. The plan for postsurgical prevention is formalized preoperatively.”

Due to pandemic-related surgical delays, Murji said that “there is increased opportunity to help patients find the ideal medical treatment option that aligns with their individual needs so as to bridge patients to their surgery and thereafter.”

Murji and his colleagues have found that hormonal contraceptives, progestins, the LNG-IUS and a GnRH agonists are all consistently effective in decreasing pain and disease recurrence.

DISCLOSURES Murji serves on the speakers’ bureau/advisory boards of Abbvie, Allergan, Bayer, Hologic, and Pfizer.

Bob Kronemyer is a freelance writer for Contemporary OB/GYN®.

FOR REFERENCES VISIT contemporaryobgyn.net/afterEndo
Addressing the Cervical Cancer Screening Disparities Gap

By Roland Matthews, MD

No woman should ever die of a highly preventable and treatable disease like cervical cancer. Yet, Black women are more likely to die from the disease than any other racial or ethnic group. In fact, they are twice as likely to die from cervical cancer compared to white women in the US. Despite advancements in cervical cancer screening and vaccination against high-risk human papilloma virus (HPV) that have contributed to an overall disease reduction, long-time racial, ethnic, and socioeconomic disparities are still prevalent within health care, specifically cervical cancer, and have not yet been addressed. Of concern, the American Cancer Society (ACS) recently released new cervical cancer screening guidelines that openly acknowledge Black and Latinx women have higher rates of cervical cancer, yet these guidelines will limit screening options and potentially cause the racial disparity gap to grow even further. It is imperative for the OB/GYN community to fully acknowledge this gap and work together to advance healthcare equity for all women.

Racial, Ethnic, and Socioeconomic Cervical Cancer Disparities are Prevalent

Cervical cancer incidence and mortality rates demonstrate troubling disparities when analyzed by race and ethnicity. In 2017, the cervical cancer incidence rate per 100,000 US women was:

- 7.3 for white women
- 8.3 for Black women (14% higher than white women)
- 8.9 for Hispanic women (22% higher than white women and 7% higher than Black women)

The age-adjusted cervical cancer mortality rate per 100,000 US women also demonstrated increased mortality among Black and Hispanic women when compared to white women.6

These disparities are the result of significant socioeconomic barriers that lead to differences in screening rates.2,7-10 Studies show that both Black and Hispanic women are diagnosed at a later stage and have higher resultant mortality.11,12 Black women with cervical cancer also receive less aggressive treatment and have less access to health care.12-14 A substantial widening of
the racial disparities in incidence and mortality occurs with advancing age, particularly in Black women. The incidence of cervical cancer also is higher in rural versus metropolitan communities in the US, which may reflect differences in screening rates, socioeconomic status, and access to quality health care. In fact, more than 60% of US cases occur in areas of underserved and under screened women, many of which are rural settings. These screening disparities in rural communities show up at a particularly high rate in the southern region of the US, where many women lack adequate health insurance.

Although the lack of health insurance in the US is a socioeconomic barrier contributing to inadequate access to routine cervical cancer screening, a study showed that more than half of women (56%) with long-term health insurance and access to health care were not screened for at least three years prior to their cervical cancer diagnosis. Additionally, there was failure to follow up on the testing results in an additional 13%. Poor screening frequency due to access issues was the primary factor for development of cervical cancer in a meta-analysis of 42 studies. Approximately 54% of the women with cervical cancer had inadequate screening histories and 42% had never been screened prior to their diagnosis. The main factors for explaining racial, ethnic, and socioeconomic disparities include: lack of screening, access to screening services, and follow-up of abnormal tests which can affect the overall cervical cancer incidence and stage at diagnosis.

Along with imbalances in cervical cancer screening rates, disparities in the uptake of the HPV vaccine and completion of the vaccine series by geographic region and by race or ethnicity may also contribute to continued health disparities within cervical cancer. The CDC found that less than half of adolescents in the US have completed the HPV vaccination series, including only 53% of Black adolescents and 57% of Hispanic adolescents. The HPV vaccination rates in high-risk adolescent populations need to improve to prevent a greater future increase in cervical cancer disparities. A blanket assumption of vaccine uptake across the US is detrimental to ensuring prevention and should not lead to decisions of limiting cervical cancer screening choices for women, especially in at-risk populations.

Recent Cervical Cancer Screening Guidelines May Widen the Disparities Gap

The American Cancer Society recently updated their cervical cancer screening guidelines for women at average risk. Among the notable changes was the recommendation to begin screening at 25 years of age rather than 21 years, as well as to remove the proven Pap test from frontline screening and rely on HPV-alone screening.

These new guidelines represent a significant departure from current practice and have generated responses from several professional societies. The American College of Obstetrics and Gynecologists (ACOG) released a statement about the new guidelines and reinforced their position on cotesting. Several other groups also continue to support the use of cotesting and cytology for optimal cervical cancer screening including, The American Society of Cytopathology (ASC), the College of American Pathologists (CAP), and the American Society for Clinical Pathology (ASCP). The ASCP and ASC specifically warn that if Pap testing is no longer covered by insurance companies, existing screening disparities will increase further. Additionally, cases will be missed if only high-risk HPV tests are used for screening. Up to 10% of invasive cervical cancers test negative for HPV, and up to 14% may be negative for high-risk HPV types covered by the tests. Additionally, 8.3%-14% of high grade squamous intraepithelial lesion (HSIL) cases may also be negative for high-risk HPV. The CAP recommends cytology and cotesting be retained given that there is no longitudinal data applicable to US screening populations supporting the change.

Advocacy groups and women’s health advocates are also concerned about the harmful implications of the new ACS guidelines. The Black Women’s Health Imperative released a statement saying that the new ACS guidelines “fail to preserve access to the most accurate and effective cervical cancer screening options and threatens to put lives at risk.” They emphasize that Black women are already more likely to be diagnosed with advanced cervical cancer and more likely to die from the disease. Additionally, there are concerns that adjusting the screening interval will make women visit
their healthcare provider less frequently, thus missing opportunities to counsel patients on a variety of health issues. Limiting the screening options and testing fewer women at a decreased frequency will widen the disparity gaps even further.

It’s important to note that the ACS based their guidelines strategy on data modeling that is not representative of the US screening population. In fact, the guidelines acknowledge this limitation stating, “There is disparity in the cervical cancer disease burden in the United States, with higher rates of disease among Black and Hispanic women and women of lower socioeconomic status: populations not optimally represented in the RCTs.” While the ACS acknowledges that disparities exist, they seemingly do not adequately account for these concerns within their recommendations.

The ACS guidelines suggest that clinical evidence supports the effectiveness of HPV-alone screening, a claim that directly conflicts with findings from several studies reflecting real-world data.

The national Quest Diagnostic database analysis confirmed the value of cotesting results. Their data retrospectively analyzed women over a nine-year period and found that cotesting identified cervical cancer and cervical precancers more often than cytology or HPV tests alone. HPV testing alone failed to detect twice as many cases of cervical cancer than co-testing; in fact, HPV alone missed 23% of all cervical cancer cases. Given the greater sensitivity associated with cotesting, women who receive a negative cotesting result are at lower risk for disease than women who receive a negative HPV test result.

We Must Reduce Screening Disparities by Protecting All Screening Options

Cervical cancer prevention relies heavily on adequate screening, but despite recommendations for regular cervical cancer screening, many women are inadequately screened or not screened at all. A significant driver in the disproportionate burden of cervical cancer among Black and Hispanic women is related to this lack of screening. Recommendations like those from the ACS that further limit screening options could inadvertently undermine efforts to promote preventive measures in already underserved populations. These health disparities within cervical cancer are briefly recognized but not adequately addressed in the new ACS guidelines. Their recommendations are not tailored to the current US health care system and could increase disparities rather than remove barriers to routine cervical cancer screening. Any new cervical cancer screening guidelines must adequately account for a diverse screening population and the wide range of recognized socioeconomic barriers. Additionally, the guidelines state that Pap testing is less effective in HPV-vaccinated populations; however, significant disparities in vaccine uptake also remain unaddressed. The ACS guidelines should be reconsidered for its lack of applicability to a diverse screening population and the unfortunate likelihood that they will expand pervasive cervical cancer health disparities among women across the US.

OB/GYNs and other healthcare providers must continue to advocate for all cervical cancer screening options to remain available for patients. Providing sufficient, regular preventive care is challenging enough. Any attempt to limit cervical cancer screening options will make it even more challenging to ensure women with different racial and socioeconomic backgrounds get the protection they need to prevent unnecessary disease.

Any new cervical cancer screening guidelines must adequately account for a diverse screening population and the wide range of recognized socioeconomic barriers.

References

Author Biography

Roland Matthews is professor and chairman of the Department of Obstetrics and Gynecology at the Morehouse School of Medicine, and a board-certified gynecologic oncologist and attending physician at Grady Memorial Hospital in Atlanta. He graduated from Columbia College, and earned his M.D. degree, with a distinction in research, from the State University of New York at Stony Brook. Dr. Matthews completed his residency in Obstetrics and Gynecology, then completed a fellowship in Gynecologic Oncology at the State University of New York, Downstate Medical Center. Dr. Matthews is a Georgia Cancer Coalition (GCC) Distinguished Cancer Scholar and is currently the Director of the Georgia Cancer Center for Excellence at Grady. He is Vice President of the Georgia Center for Oncology Research and Education (CORE) board, and serves on the executive committee of the Obstetrics and Gynecology Section of the National Medical Association. Throughout his career, Dr. Matthews’ research, education and clinical activities have focused on reducing disparities in underserved communities.
Copper IUD and LNG-IUS can impact microbiota

by BOB KRONEMYER

Neither the levonorgestrel-releasing intrauterine system (LNG-IUS) nor the copper intrauterine device (IUD) impact the incidence of cellular atypia, but do interfere with the microbiota over time, according to liquid-based cervical cytology and microbiological analyses.

The cross-sectional Brazilian study, published in the European Journal of Obstetrics & Gynecology and Reproductive Biology, found that the copper IUD is linked to bacterial vaginosis and the Actinomyces species infection, whereas the LNG-IUS is connected to candidiasis and cytosis.

The study, which was performed in the Northeast of Brazil between January 2012 and December 2017, divided patients into three groups: the LNG-IUS group (n = 1179), the copper IUD group (n = 519) and a control group of women not using contraception (n = 14,616).

The mean age of the LNG-IUS and IUD groups was roughly 36 years, compared to about 35 years for the control group.

The average number of previous pregnancies was low in all three groups, ranging from 1.5 to 1.6.

The mean time between dispositive placement and examination was 19 months for the LNG-IUS and 17 months for the IUD.

The most frequent complaint among all three groups was vaginal discharge: 15% among non-users, compared to 16.2% for IUD and 15.8% for LNG-IUS.

But pruritus was more prevalent in the LNG-IUS group: 31.1% vs. 1.5% for non-users and 1.2% for IUD.

Conversely, malodor and pelvic pain were more frequent in the IUD group: 3.1% and 2.3%, respectively, compared to 1.9% and 1% among non-users and 1.4% and 0.3%, respectively, among LNG-IUS users.

The frequency of epithelial atypia via cytological analysis did not differ between the three groups. However, inflammatory infiltration with no specific pathogen was significantly more frequent in the LNG-IUS and IUD groups than in the control group: 54.9%, 57.2% and 50.2%, respectively.

Cytolysis was also significantly more likely in the LNG-IUS group vs. the two other groups: 8.9% vs. 1% for non-users and 0.6% for IUD.

Candida morphotype occurred in 8.9% of non-users vs. 8.1% in LNG-IUS and 3.5% in IUD.

In addition, bacterial vaginosis and Actinomyces species were observed more frequently in the IUD group compared to the other two groups: 14.8% and 10.2%, respectively, compared to 11.1% and 0% in non-users and 9.7% and 1.3% in LNG-IUS.

Bacterial vaginosis was also significantly more common when using an IUD for more than 2 years than for less than 2 years: 21.2% vs. 9.5%, respectively.

“The association between IUDs and bacterial vaginosis, diagnosed using Nugent score and polymerase chain reaction (PCR), is described elsewhere and time of use increases the likelihood of this association,” the authors wrote.

The Actinomyces morphotype occurred at a statistically significant greater frequency after 2 years of IUD use compared to less than 2 years: 17.8% vs. 3.9%.

The authors said a better way to validate the association of dispositives to a high-grade squamous intraepithelial lesion (HSIL) and cancer would be a large cohort study with more cases containing a histologic diagnosis.

Nonetheless, the authors believe the current study’s number of cases are sufficient to assess microbiological and reactive findings with confidence.

Bob Kronemyer is a freelance writer for Contemporary OB/GYN®.

SOURCE
Laparoscopic abdominal cerclage

An effective option for refractory cervical insufficiency.

by NISSE V. CLARK, MD, MPH

Introduction
Cervical insufficiency is defined as the inability of the uterine cervix to retain a pregnancy in the second trimester in the absence of clinical contractions, labor, or both. It is an important cause of spontaneous preterm birth and is estimated to affect up to 1% of pregnancies. The most common treatment for cervical insufficiency is a vaginal cerclage, a suture placed around the cervix vaginally to provide added support during the pregnancy. In cases where a woman suffers a second trimester loss or preterm birth despite a well-timed and placed vaginal cerclage, termed refractory cervical insufficiency, an abdominal cerclage should be considered. Newer evidence indicates an abdominal cerclage improves neonatal outcomes compared to a repeat vaginal cerclage in patients who have failed one prior vaginal cerclage. This finding suggests waiting until a woman has failed two prior vaginal cerclages before placing an abdominal cerclage may be too high a threshold. Moreover, abdominal cerclages are increasingly performed using a laparoscopic approach, often prior to pregnancy. Considering the numerous advantages of laparoscopy compared to laparotomy for all gynecologic procedures, laparoscopic abdominal cerclage should be considered for refractory cervical insufficiency.

When an abdominal cerclage should be considered
The abdominal cerclage was first described by Benson and Durfee in 1965 for women with extreme cervical shortening. The most common indication for an abdominal cerclage today is at least one prior failed vaginal cerclage (despite appropriate timing and placement of the vaginal cerclage), or inability to place a vaginal cerclage. The procedure entails...

NISSE V. CLARK, MD, MPH is an ob/gyn and minimally invasive gynecologic surgeon at Massachusetts General Hospital and instructor at Harvard Medical School in Boston.
placing a suture intraperitoneally at the level of the internal os, a technique that is believed to provide greater structural integrity to the cervix and potentially avoid vaginal contamination. The two largest studies to date evaluating abdominal cerclage outcomes have demonstrated very high neonatal survival rates (defined as the percent of pregnancies with neonates surviving until hospital discharge, exclusive of first trimester losses). The first was a large retrospective study including 300 women who underwent open or laparoscopic abdominal cerclage using their prior pregnancy as a control. The neonatal survival rate was 98% and the average gestational age at delivery was 37 weeks compared to 24 weeks in the prior pregnancy. The second study included 225 women who underwent a laparoscopic abdominal cerclage and found a similarly high neonatal survival rate of 98.5%, with a mean gestational age at the time of delivery of 35 weeks. There was no comparison group in this study.

The first multicenter randomized control trial comparing abdominal and vaginal cerclage after only one prior failed vaginal cerclage was recently published. The study included 111 women with a single failed prior vaginal cerclage (defined as a loss or preterm birth between 14 and 28 weeks of gestation) randomized to either an open abdominal cerclage or repeat vaginal cerclage. The study found that preterm birth before 32 weeks of gestation was only 8% in women randomized to an abdominal cerclage compared to 38% in women randomized to a repeat vaginal cerclage (P=.008). These findings suggest an abdominal cerclage may be effective after only one prior failed vaginal cerclage. Obstetricians have often maintained a high threshold for placing an abdominal cerclage due to its perceived surgical risk and the need to perform a cesarean section for delivery when an abdominal cerclage is in place. While a cesarean section is very often necessary, surgical risk related to the cerclage itself is reduced when performed prior to pregnancy and using a laparoscopic approach.

**OBSTETRICIANS HAVE OFTEN MAINTAINED A HIGH THRESHOLD FOR PLACING AN ABDOMINAL CERCLAGE DUE TO ITS PERCEIVED SURGICAL RISK AND THE NEED TO PERFORM A CESAREAN SECTION FOR DELIVERY WHEN AN ABDOMINAL CERCLAGE IS IN PLACE.**

**Advantages of a laparoscopic approach**

Laparoscopic abdominal cerclage was first reported in 1998 by Lesser et al. and has been increasingly used since that time. Extrapolating the well-documented advantages of laparoscopy for hysterectomy and myomectomy, laparoscopic abdominal cerclage is likely to result in reduced blood loss, fewer wound complications, and a shorter recovery compared to open abdominal cerclage. In fact, one cohort study demonstrated reduced blood loss and length of stay following robotic-assisted laparoscopic abdominal cerclage compared to an open procedure. In addition to the benefit of small incisions, laparoscopy allows for careful dissection around the uterine vessels, helping to avoid vascular injury. Uterine vessel injury is a dreaded complication of abdominal cerclage, especially when performed during pregnancy. While complication rates for laparoscopic versus open abdominal cerclage have not been directly compared in the literature, reported rates are generally lower for the laparoscopic approach. Conversion to laparotomy can occur in up to 5% of laparoscopic cases and may be more likely to occur during pregnancy given the increased bleed-
ing risk, enlarged uterus, and challenges with uterine manipulation.\textsuperscript{11} Other complications are rare with single reports of suture migration, suture erosion or uterine rupture with an abdominal cerclage in place.\textsuperscript{12,13,14}

Success rates for laparoscopic abdominal cerclage are comparable to open abdominal cerclage, according to observational data. The largest systematic review was by Moawad et al. and included 1,844 women who underwent laparoscopic versus open abdominal cerclage (before or after conception) with no significant difference in neonatal survival rates between the groups (90% for the laparoscopic group and 91% for the open group, $P=.8$).\textsuperscript{15} Interestingly, when first trimester losses were excluded from the analysis (as these are unlikely to be related to the cerclage), women who underwent laparoscopic abdominal cerclage actually had a significantly greater neonatal survival rate (97% versus 90%, $P<.01$). Neonatal survival rates with laparoscopic abdominal cerclage have also tended to increase over time with improved surgical technique.\textsuperscript{16}

Simultaneous with a trend toward laparoscopic placement is a trend toward preconception abdominal cerclage placement. This shift is likely due to a couple factors: 1) a less-invasive, lower-risk laparoscopic approach may be more acceptable as a preventative measure prior to confirmation of pregnancy, and 2) laparoscopy is generally more feasible in the nongravid state when the uterus is not enlarged and a manipulator can be placed. Preconception abdominal cerclage, regardless of the surgical approach, also avoids the risk of perioperative miscarriage (estimated to occur in 1-3% of postconception abdominal cerclages).\textsuperscript{15} Literature comparing pre versus postconception abdominal cerclage is limited to observational data and often bias in that a disproportionate number of preconception abdominal cerclages are performed laparoscopically as compared to postconception abdominal cerclages which are most often performed abdominally. A systematic review by Tulandi et al. analyzed 678 women who underwent laparoscopic and open abdominal cerclage outcomes separately, showing no difference in the rate of third-trimester delivery or live birth between pre versus postconception abdominal cerclage for either method.\textsuperscript{16} A cohort study of 161 women by Dawood and Farquharson did show a greater likelihood of delivery beyond 34 weeks with pre versus postconceptional abdominal cerclage (90% versus 74%, $P=.02$).\textsuperscript{17} Most conclude that preconception abdominal cerclage placement carries lower surgical and obstetric risk.

**Laparoscopic abdominal cerclage technique**

Several techniques for laparoscopic
Abdominal cerclage are described in the literature.\textsuperscript{18,19} In general, the procedure starts with standard laparoscopic positioning and port placement using either a conventional or robotic-assisted set-up. Port placement is at the discretion of the surgeon though should consider uterine size and allow the surgeon to tie a strong knot with two hands. When the procedure is performed prior to pregnancy, a uterine manipulator is placed to aid with dissection and suture placement. The dissection begins by opening the vesicouterine peritoneum overlying the internal os (Figure 1).

This helps to reflect the bladder caudad and delineate the uterine vessels anteriorly. A nonabsorbable suture, most commonly a double-armed 5-mm Mersilene polyester tape with CTX or BP-1 needles is used. The needles can be straightened beforehand to facilitate trocar passage and ease suture placement. Each needle is then passed between the uterine vessels and the cervix either anteriorly or posteriorly, with the final knot location depending on the suture type (double-arm versus single-arm) and insertion point. For anterior knot placement, the uterosacral ligaments provide a useful reference, with the needles inserted just above the insertion of the uterosacral ligaments on either side (Figure 2).

While passing the needle with one hand, it can be helpful to control the uterine manipulator with the other hand, ensuring placement of the suture between the uterine vessels and cervical stroma while simultaneously visualizing the needle’s entry and exit point. Care should be taken not to deviate laterally which risks uterine vessel injury or deviate medially into the cervical stroma which can weaken the cerclage. Once the suture is placed and manipulator removed, the first knot is tightly secured and a total of six square knots placed (Figure 3).

Nonabsorbable suture such as silk can be secured to each suture end to aid in knot identification during future removal. The overlying peritoneum can then be closed if desired.

**How and when to remove an abdominal cerclage**

Given the risk of cervical injury or obstructed labor with an abdominal cerclage in place during labor, an elective cesarean section is typically performed at the time of delivery. The cerclage can be removed during the cesarean section or left in place for a future pregnancy. A small study of 22 women with a laparoscopic abdominal cerclage retained from a prior pregnancy found a neonatal survival rate of 86% in the second pregnancy and 100% in the third pregnancy.\textsuperscript{20} In the event of previable fetal loss, a dilation and evacuation can be performed with the abdominal cerclage in-situ. This has been performed without major complication up to 19 weeks of gestation.\textsuperscript{21} The cerclage can also be removed laparoscopically before dilation and evacuation and has been described in a single case report at 19 weeks of gestation.\textsuperscript{22} A novel technique using an anterior or posterior colpotomy and the assistance of a hysteroscope to cut and remove the stitch has been reported up to 23 weeks of gestation.\textsuperscript{23} If this is feasible at later gestational ages, a cesarean section could potentially be avoided in some viable pregnancies.

**Conclusion**

In summary, laparoscopic abdominal cerclage is a highly effective option for refractory cervical insufficiency with obstetric outcomes comparable to an open abdominal cerclage. The minimally invasive approach reduces surgical risk, especially when performed prior to conception. Given new evidence favoring an abdominal cerclage over a repeat vaginal cerclage in women who have failed one prior vaginal cerclage, laparoscopic abdominal cerclage could be strongly considered for women with refractory cervical insufficiency. Increased surgical experience and promising advances in the management of previable pregnancy loss with an abdominal cerclage in-situ, suggest that laparoscopic abdominal cerclage is a low-risk option for appropriate candidates.

**WHILE COMPLICATION RATES FOR LAPAROSCOPIC VERSUS OPEN ABDOMINAL CERCLAGE HAVE NOT BEEN DIRECTLY COMPARED IN THE LITERATURE, REPORTED RATES ARE GENERALLY LOWER FOR THE LAPAROSCOPIC APPROACH.**
Syphilis, known as the “great imitator,” is a clinical disease with myriad manifestations and stages. Clinical illness results from infection with the spirochete *Treponema pallidum*, which enters at sites of sexual contact and by transmission across the placenta during pregnancy. Maternal syphilis is associated with a 21% increased risk for stillbirth, 6% increased risk for preterm delivery, and 9% increased risk for neonatal death. Between 2014 and 2018, primary and secondary syphilis in women increased by 172% (to 3 cases per 100,000 females) in the United States. Congenital syphilis rates have paralleled this rise, increasing by 185% (to 33.1 cases per 100,000 live births) in the same years. Experts believe that recent upward trends are multifactorial, and the coronavirus disease 2019 pandemic certainly has disrupted ongoing efforts at reversing these trends, with closure of sexual health clinics and redirected public health efforts from a focus on sexually transmitted diseases to mitigating the COVID-19 crisis. As the pandemic rages on, we have yet to see how long-term effects of this generation-defining crisis will later manifest as “second waves” of other, neglected diseases such as syphilis. To prepare clinicians for what lies ahead, we review the diagnosis and management of syphilis in pregnancy.

**Prenatal screening for syphilis**

All pregnant women should be screened for syphilis at the first prenatal visit or at first presentation to care. Screening and treatment early in pregnancy is associated with decreased incidence of congenital syphilis, preterm birth, low birth weight, stillbirth, and neonatal death. Repeat screening in the early third trimester, between 28 and 32 weeks of gestation, and again at delivery is recommended in women at high risk for syphilis or who live in areas with high syphilis prevalence. State laws differ with regard to required timing and frequency of testing, and clinicians should familiarize themselves with current state prenatal screening and reporting requirements. In some states, providers who fail to abide by syphilis screening laws may be subject to civil or criminal liabilities. Testing for maternal syphilis is recommended as part of the evaluation for stillbirth. HIV and other STI screening should be offered when syphilis is diagnosed.

Although some syphilis infections may come to the attention of providers after a patient reports symptoms or lesions, the most common pathway is for clinicians to make a laboratory diagnosis first, which must be followed by patient counseling along with a thorough history and physical (including pelvic) examination to complete a clinical staging evaluation. Following all three of these elements (laboratory studies, thorough sexual history, and physical with pelvic examination), the clinical stage of syphilis is determined, any necessary fetal evaluation completed, and a treatment regimen may be prescribed. Confusion commonly arises when abnormal laboratory evaluation is detected at an initial visit prior to complete history and physical examination – just because the patient’s laboratory values are abnormal for the first time does not mean that the patient has a diagnosis of primary syphilis. Not all patients experience all symptomatic stages of syphilis, and unless physical signs of primary or second-
ary syphilis are clearly documented and supported by clinical history and laboratory studies, the assumption of recent infection should not be made.

**Clinical staging**
Primary syphilis, which occurs around 3 weeks after initial infection by the spirochete through any site of sexual contact, is characterized by a painless chancre (Table). Because the site of the chancre may be located on the cervix or vagina, lesions may be missed without a thorough pelvic examination. Women with immunosuppression may experience multiple chancres, or chancres that persist after secondary lesions appear.15 The chancre resolves within 4 to 6 weeks even without treatment (sooner if treated), although inadequate immune-mediated clearance results in

<table>
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<td>Clinical staging of primary, secondary, and latent syphilis</td>
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<th>Clinical stage</th>
<th>Sexual history</th>
<th>Physical examination</th>
<th>Laboratory (serologic) tests*</th>
<th>Treatment in pregnancy</th>
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| Primary | ▪ Frequent co-infection with other STI  
▪ Frequent partner history of genital lesion or recent STI  
▪ New, multiple or unknown partners in past 3 months | ▪ Painless chancre (possibly with painful lesions if co-infection)  
▪ Localized lymphadenopathy | ▪ Usually reactive nontreponemal (RPR, VDRL)  
▪ Reactive nontreponemal (FTA-ABS, MHA-TP, TP-PA, CIA, EIA)  
▪ One of these tests may be nonreactive if early in the course of infection | ▪ 2.4 million units IM benzathine penicillin G  
▪ Some experts recommend 2 weekly doses in pregnancy |
| Secondary | ▪ Frequent co-infection with other STI  
▪ Frequent partner history of genital lesion or recent STI  
▪ New, multiple or unknown partners in past 3 months | ▪ Maculopapular or annular rash typically involving palms and soles  
▪ Mucous patches (oral), genital condyloma lata  
▪ Flu-like illness, alopecia, generalized lymphadenopathy | ▪ Reactive nontreponemal (RPR, VDRL)  
▪ Reactive nontreponemal (FTA-ABS, MHA-TP, TP-PA, CIA, EIA) | ▪ 2.4 million units IM benzathine penicillin G  
▪ Some experts recommend 2 weekly doses in pregnancy |
| Early latent (early nonprimary nonsecondary) | ▪ Reported history of resolved primary or secondary lesions for patient or partner is helpful but not diagnostic;  
▪ Documented laboratory serocconversion using the same test (with or without clinical lesions) within past year is required | No significant findings | ▪ Reactive nontreponemal (RPR, VDRL)  
▪ Reactive nontreponemal (FTA-ABS, MHA-TP, TP-PA, CIA, EIA) | ▪ 2.4 million units IM  
▪ benzathine penicillin  
▪ G in 3 weekly doses |
| Late Latent (unknown duration or late syphilis) | Frequently not specific or unknown | No significant findings | ▪ Reactive nontreponemal (RPR, VDRL)  
▪ Reactive nontreponemal (FTA-ABS, MHA-TP, TP-PA, CIA, EIA) | ▪ 2.4 million units IM  
▪ benzathine penicillin  
▪ G in 3 weekly doses |

* RPR, Rapid Plasma Reagin; VDRL, Venereal Disease Research Laboratory; FTA-ABS, Indirect fluorescent-antibody; MHA-TP, Microhemagglutination assay; TP-PA, Treponema pallidum particle agglutination assay; CIA, Chemiluminescence immunoassay; EIA, Enzyme immunoassay. Refer to Figure for sequential interpretation of treponemal and nontreponemal tests in traditional and reverse sequence screening algorithms.
systemic dissemination of organisms and later secondary manifestations of disease around 6 to 8 weeks later. Classic symptoms of secondary syphilis are diffuse maculopapular skin rash (in up to 90%), generalized lymphadenopathy, and highly-contagious mucosal lesions including oral mucous patches and genital condyloma lata. Some women may describe systemic symptoms such as malaise, arthralgias, and fevers. Manifestations of secondary syphilis resolve after approximately 1 to 6 months regardless of treatment, and typically resolve within a few weeks after adequate syphilotherapy.

Latent syphilis is characterized by positive diagnostic testing in a patient without objective findings. Clinically, latent syphilis is divided into early and late (or unknown duration) latent stages, depending on the timing of initial infection based on a detailed history of exposure and reported symptoms. In 2018, the Centers for Disease Control and Prevention (CDC) began using the surveillance term “syphilis, early non-primary non-secondary” rather than “early latent syphilis” to clarify that some clinical manifestations such as neurosyphilis may occur during any stage. From a clinical perspective, however, either name represents asymptomatic infection, which is clearly documented based on laboratory seroconversion to have occurred within the previous 12 months.

Figure. Traditional and reverse sequence syphilis screening algorithms

### TRADITIONAL SCREENING ALGORITHM

- **Nontreponemal test (Quantitative RPR or VDRL)**
  - Nonreactive
    - No syphilis
  - Reactive
    - Treponemal test (FTA-ABS, TP-PA, MHA-TP)
    - Reactive
      - Past or current syphilis
    - Nonreactive
      - False positive RPR VDRL

### REVERSE SEQUENCE SCREENING ALGORITHM

- **Treponemal immunoassay (EIA or CIA)**
  - Reactive
    - Reflex TP-PA
    - Reactive
      - Probable false positive immunoassay
        - Repeat CIA or EIA in 4 weeks
    - Nonreactive
      - No syphilis
  - Nonreactive
    - No syphilis
months. In a woman with early latent syphilis, secondary lesions may recur in 25% of patients. In late latent syphilis, now known as “unknown duration or late syphilis” from a surveillance perspective, infection duration is either unknown or greater than one year. Late latent syphilis is relatively less contagious to sexual partners but still transmissible to the fetus in pregnancy, with an approximate 10% risk of fetal infection.26

Tertiary syphilis, which occurs in up to 40% of individuals with untreated syphilis, refers to benign gummas and cardiovascular syphilis, but not to neurosyphilis. It is rare in a reproductive-aged population.

Neurosyphilis is clinically described as early or late neurosyphilis, as manifestations may occur at any time during the course of infection. Early neurologic involvement may include meningitis, uveitis or retinitis, or stroke-like symptoms, and occurs in approximately 1% of patients with secondary syphilis.19 Late neurosyphilis occurs a decade or more after initial diagnosis, and may occur along with other manifestations of tertiary syphilis.

**Vertical transmission**

Congenital syphilis may result from maternal syphilis infection prior to or during pregnancy, or when maternal syphilis is diagnosed at delivery.

Diagnosis of congenital syphilis following delivery is challenging, and involves assessment of maternal history and laboratory studies, complete physical, laboratory and radiologic evaluation of a neonate, and may include pathologic evaluation of the placenta. Risk of congenital infection is related to the stage of maternal infection, and occurs in approximately 50–80% of women with untreated primary, secondary, or early latent syphilis, and up to 10% of women with late latent syphilis. Syphilitic stillbirths also are included as cases of congenital syphilis for national reporting purposes.2

Neonatal manifestations of congenital syphilis are divided into two characteristic syndromes. Early congenital syphilis is diagnosed in the first two years of life, and may involve clinical symptoms similar to those in adult secondary syphilis. Classically, hepatosplenomegaly, desquamating skin rash, rhinitis (“snuffles”), anemia, thrombocytopenia, and osteochondritis may be observed.20 Late congenital syphilis manifests after two years of life, and may be characterized by notched teeth (Hutchinson’s teeth), deafness, and interstitial keratitis of the eye; together, these are known as Hutchinson’s Triad. Central nervous system involvement with developmental delay, hydrocephalus, seizures, and nerve palsies, as well as bone deformities, may occur.

At delivery, the placenta itself may have gross and histopathologic characteristics of *T. pallidum* infection. On gross examination, the placenta appears large, pale, and hydropic. On microscopic examination, terminal villi appear enlarged and densely cellular, with evidence of chronic villitis.21 Umbilical cord sections demonstrate necrotizing funisitis, characterized by perivascular rings of necrotic debris surrounding the large vessels. These findings are not specific to syphilis infection, however. In some laboratories, *T. pallidum* may be directly detected by immunohistochemistry in either placenta or umbilical cord specimens in a woman with untreated or inadequately treated syphilis. This evaluation should be encouraged when feasible, as the direct detection of *T. pallidum* facilitates accurate reporting and optimal maternal and neonatal care.

**Diagnosis**

*T. pallidum* is difficult to visualize or directly detect with common methods available in most laboratories (such as culture or polymerase chain reaction [PCR]). Clinicians usually rely on serologic testing, which allows only indirect diagnosis of infection, and must be combined with complete history and physical (with pelvic) examination. Two algorithms are used, and require slightly different interpretation (Figure). In a traditional screening algorithm, presumptive serologic diagnosis of syphilis requires two tests: an initial nontreponemal test followed by a confirmatory treponemal-specific test.8 The rapid plasma reagin is the most commonly used nontreponemal antibody in the United States. This test measures antibody to cardiolipin, which is thought to be contained within *T. pallidum*, as well as in the damaged host cell membrane.22 A confirmatory test is required because false positive nontreponemal tests occur, and the false-positive rate for a rapid plasma reagin is about 1% in pregnant women.23 When reactive, the nontreponemal test...
is quantified as a titer, which typically correlates with disease activity and is used to follow treatment response. The reverse sequence algorithm begins with a treponemal antibody test, typically an automated enzyme or chemiluminescent immunoassays (EIA or CIA). The advantage to this test is in the laboratory through-put: for high-volume laboratories, the ability to perform automated testing has proposed cost advantages. The sensitivity of available treponemal immunoassays ranges between 97% and 100%, depending on clinical stage and the specific assay used. However, false-positive rates are as high as 40 to 80%, and thus reflex testing is still required. When reactive, a treponemal immunoassay is reflexed to a nontreponemal test, which then (if reactive) must be interpreted as presumptive active syphilis or (if non-reactive) reflexed to a second treponemal test (typically Treponema pallidum particle agglutination test, or TP-PA). With either algorithm, a detailed clinical history and physical exam are needed to establish risk factors for syphilis, confirm previous treatment regimens, and document any physical evidence of early-stage infection. If no previous treatment can be confirmed in an asymptomatic patient with laboratory evidence of syphilis, initiation of a full course of treatment for latent syphilis is recommended following consultation with a specialist and fetal evaluation, if indicated.

Ultrasound findings
Congenital infection is presumed in all cases of maternal syphilis infection during pregnancy. When present, sonographic findings consistent with congenital infection represent severely infected fetuses. Ultrasound findings of congenital infection typically are not manifest until after approximately 18 to 20 weeks of gestation due to relative immaturity of the fetal immune response. Findings may include placentalomegaly (thickness exceeding 4cm), hepatomegaly, polyhydramnios, ascites, and non-immune hydrops. Detailed sonography is indicated with performance of middle cerebral artery Doppler studies to evaluate for fetal anemia when maternal syphilis is diagnosed. When ultrasound findings of congenital syphilis are identified after fetal viability, initial treatment in an inpatient setting with monitoring of the mother and fetus are recommended to detect possible fetal distress or preterm labor.

Treatment in pregnancy
Optimal treatment of syphilis during pregnancy is estimated to reduce the risk of congenital syphilis by 97%, stillbirth by 82%, preterm birth by 64%, and neonatal mortality by 80%. Long-acting parenteral penicillin G is the only currently recommended treatment for syphilis in pregnancy. For early-stage syphilis, including primary, secondary, and early latent (early non-primary non-secondary), a single intramuscular dose of 2.4 million units of benzathine penicillin G is necessary. Some experts recommend two weekly doses of 2.4 million units of benzathine penicillin G for women diagnosed with early clinical stage infection, because congenital syphilis may still occur despite treatment with a single dose, particularly with high nontreponemal titers common to early maternal stage syphilis. Our practice is to routinely administer two doses of 2.4 million units intramuscular benzathine penicillin G over 2 consecutive weeks to all women with early-stage syphilis, with an interval of no more than 10 days between injections.

Treatment with three weekly doses of 2.4 million units intramuscular benzathine penicillin G is necessary for late latent (unknown duration or late syphilis) in pregnancy. Currently the CDC acknowledges that an interval of 7-9 days between doses may be optimal based on pharmacokinetic studies, but

JUST BECAUSE THE PATIENT’S LABORATORY VALUES ARE ABNORMAL FOR THE FIRST TIME DOES NOT MEAN THAT THE PATIENT HAS A DIAGNOSIS OF PRIMARY SYPHILIS.

Have you been witnessing a rise in syphilis cases among your patients? How do you think increasing telehealth appointments could benefit your patients? Let us know what you think by sending an email to COGeditorial@mmhgroup.com or via Twitter @ContempOBGYN.
clinical experience suggests that an interval of 10-14 days between doses may be acceptable. A conservative practice is to allow an interval of up to 10 days between intramuscular injections for treatment of late latent syphilis in pregnancy. If a patient misses a scheduled dose, the treatment course is restarted.

**Penicillin allergy**
For pregnant women reporting a penicillin allergy, a thorough clinical history should be taken to determine whether the reported reaction is *moderate to high risk* for anaphylaxis or other life-threatening drug reaction. In women with a clinical history consistent with a moderate to high risk allergic reaction, formal evaluation for possible penicillin allergy testing in a setting with clinicians trained in recognition and treatment of hypersensitivity reactions is recommended. For women with verified IgE-mediated hypersensitivity reactions, penicillin desensitization is indicated. Fortunately, this is rarely necessary. Importantly, in women with IgE-mediated allergy who undergo desensitization and treatment with penicillin and are later reinfected, repeat allergy testing and desensitization is necessary because IgE antibodies may reform.

**Clinical response to treatment**
Symptoms of primary or secondary syphilis should resolve within a few weeks after treatment is initiated. In the first 24 hours following initial treatment, some women may experience a Jarisch-Herxheimer reaction, an acute febrile reaction characterized by myalgia, fever, headache, and potentially preterm labor and fetal heart rate tracing abnormalities in pregnant women. Before treatment, women should be counseled about the potential for these symptoms, as well as on appropriate management with antipyretics. Because fetal heart rate tracing abnormalities may occur in a severely affected fetus, initial treatment at a center with the capability for emergent delivery and neonatal stabilization is recommended for women with ultrasound evidence of congenital infection in a potentially viable fetus. Subsequent doses are administered in the outpatient setting as appropriate for the clinical stage of infection.

**Serologic response to treatment**
In general, a nontreponemal titer may be repeated if maternal re-exposure to an untreated partner is suspected, although the decision to retreat is a clinical one. There is little evidence supporting the benefit of repeating monthly nontreponemal titers following adequate therapy. In all women, we inquire about partner treatment and potential for re-exposure at each prenatal visit after maternal diagnosis, and repeat a rapid plasma reagin test at 28-32 weeks or sooner if the clinical history suggests re-exposure or reinfection. If clinical symptoms persist or recur, or when nontreponemal titer increases by fourfold (2-dilution) or greater for more than 2 weeks, reinfection should be considered and retreatment initiated.

Some patients may have a persistent low nontreponemal titer known as “serofast” despite complete treatment (typically <1:8). A serofast rapid plasma reagin is more common with lower initial rapid plasma reagin titers and latent syphilis at the time of diagnosis. When past treatment has been confirmed and there is no suspicion of re-exposure in a patient with serofast rapid plasma reagin or venereal disease research laboratory test, no additional treatment is indicated. A final nontreponemal titer is repeated at the time of delivery for all women diagnosed with syphilis during pregnancy, and for all women in some states. This confirms maternal treatment response (or lack thereof) and allows for a direct comparison of the neonatal nontreponemal titer, which may reflect maternal antibody levels or neonatal response to congenital infection.

### Conclusion
Despite near elimination of syphilis in the United States only two decades ago, maternal and congenital syphilis have made an unwelcome return, even as we face new challenges with the COVID-19 pandemic. Ob/gyns should be well-informed about current guidelines for syphilis screening and management in pregnancy. Ultimately, virtual collaboration among physicians, scientists, public health facilities, and political leaders will be needed to increase public and physician awareness, facilitate access to early prenatal care in underserved communities, and reverse the current epidemic.
Vertigo risk factors in perimenopausal women

by BOB KRONEMYER

It has yet to be fully elucidated why postmenopausal women have a higher prevalence of benign paroxysmal positional vertigo (BPPV); however, the sudden decrease in estrogen during menopause can cause a rapid decrease in estrogen receptors, which may disturb otoconial metabolism and thus, increase the prevalence of BPPV.

Likewise, hormone replacement therapy can reverse low otoconin levels, thus reducing the incidence of BPPV.

These are two findings published in the journal Frontiers in Neuroscience from a review of BPPV risk factors unique to perimenopausal women.1

“Adoption of a customized approach considering the neurochemical changes in perimenopause will be extremely helpful for the management of BPPV in women,” wrote sole author Seon-Hae Jeong, MD, PhD, of the Department of Neurology at Chungnam National University Hospital and School of Medicine in Deajeon, South Korea. “Cooperative management among neurologists, endocrinologists, and gynecologists is also important as a focus for neurotological disorders, including BPPV, in women.”

BPPV is the most common cause of recurrent vertigo, affecting more than 420 million adults worldwide and a lifetime prevalence of 10%. The disorder also increases with age, especially during menopause.2

The review highlights the current state of knowledge about BPPV risk factors specific to women. Older age, head and neck trauma, inactivity, and ear problems are some of the common factors that may increase the susceptibility of women to BPPV.

Recurrent BPPV might also be caused by oral contraceptives because they may induce disturbances in the water and electrolyte balance, variances in endolymph pH, and abnormalities in carbohydrate or lipid metabolism. These occurrences could cause otoconial degeneration and subsequent otoconial detachment and BPPV.

In addition, some women are initially diagnosed with BPPV during pregnancy.

Decreased bone mineral density is also linked to the occurrence and/or recurrence of BPPV. In women undergoing rapid bone loss after menopause, bone resorption and urinary calcium ion excretion are increased; these changes are reversed by estrogen replacement therapy.

Because estrogen loss is a causal factor for bone loss during perimenopause, a specific estrogen replacement modulator could be used to treat postmenopausal BPPV patients.

One prospective study found that women taking postmenopausal hormone replacement therapy achieved better scores than the placebo group on the Kupperman scale for sweating, hot flushes, myalgia and vertigo.3

“The hormonal fluctuation of ovarian neurosteroids might trigger the occurrence/recurrence of BPPV during the perimenopausal period,” Jeong wrote.

Another study concluded that the incidence of BPPV was significantly lower in patients taking estrogen for menopausal syndrome in two age groups: ages 45 to 65 and ages 65 and over.4

A potential mechanism that allows for the efficacy of estrogen supplementation to decrease the occurrence of BPPV in women with menopause is estrogen blood levels that are more complete and more reliable, thus inducing protective effects, estrogen effects on autophagy and possible epigenetic modulation.

The chronic use of hormone replacement therapy increases the risk of breast cancer, stroke, and venous thrombosis, and many postmenopausal women rely on alternative nonsteroidal estrogen mimetics or natural remedies.

Phytoestrogens, including soy isoflavones, could be an option, but so far there have been no reports on the efficacy of phytoestrogens on BPPV recurrence.

Bob Kronemyer is a freelance writer for Contemporary OB/GYN®.

FOR REFERENCES VISIT contemporaryobgyn.net/vertigo
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Vulvar amyloidosis

A case study on diagnosis and management. Could you recognize this rare condition?

by NATALIE A. SAUNDERS, MD, KATHRYN C. WELCH, MD, EBONY C. PARKER-FEATHERSTONE, MD, ROSALYN E. MABEN-FEASTER, HOPE K. HAEFNER, MD, & ASHLEY M. HESSON, MD

Presentation
A 51-year-old patient presents for evaluation of possible vulvar lichen sclerosus. The patient describes a 12-month history of vulvar discomfort. The pain was initially intermittent but is now continuous. She describes “pinching and stretching” extending from the perineum spreading to the anus. She notes “ripping” with intercourse. She describes “raised clear blisters” on her inferior vulva. A biopsy done at the referring hospital demonstrated “stromal sclerosis, favor lichen sclerosis over amyloidosis.” Patient had no improvement with topical clobetasol ointment 0.05% for 1 month and therefore was referred to Michigan Medicine Center for Vulvar Diseases for further evaluation.

Diagnosis
Repeat vulvar biopsies were performed. Pathology showed amyloidosis (evaluated with Congo red histochemistry). Mass spectrometry for amyloid typing was performed at the Mayo Clinic, which revealed AL (kappa)-type amyloid deposition. This type of amyloid is usually associated with systemic disease due to an underlying clonal plasma cell proliferative disorder or a B-cell lymphoma.

Management
The patient was referred to Michigan Medicine Hematology/Oncology clinic for further evaluation and management of the underlying disease. Bone marrow biopsy showed Kappa light chain myeloma with t(11;14). She was initially treated with cyclophosphamide, bortezomib, dexamethasone, followed by ixazomib and lenalidomide. She again presented to Michigan Medicine Center for Vulvar Diseases 6 months after initial presentation. She was still suffering from vulvar discomfort. Examination of the vulva was unchanged. After extensive review of the literature, she was offered laser ablation of the amyloidosis of the vulva. Risk of recurrence, pain after surgery, prolonged recovery time with healing, and inability to remove all of the affected tissue were reviewed. At that time, the amyloidosis extended to the anus but did not appear to go into the anus. Risk of injury to surrounding tissue, especially anus/rectum given proximity of disease was reviewed. We reviewed concern for hemostasis given the friable nature of the tissue.

The patient was taken to the operating room for laser ablation of amyloidosis of the vulva. The area of concern was carefully demarcated with a 0.5 cm border using a marking pen. We first followed the border outlined preoperatively using a CO2 silk touch laser. We then filled in our outline working to create a surgical plane. As expected, the tissue was highly friable and bled...
The lesions required multiple cautious passes with laser and subsequent cautery. We varied between a 4 mm and 6 mm spot size and power of 20-25 watts. Despite our efforts with the laser, mechanical dissection was ultimately needed in order to separate the planes of disease and normal tissue. We used gentle scraping with the Bovie cautery in order to separate the planes. A tactical difference could be appreciated between the abnormal and normal tissue. We repeated our mixed method approach through the entire affected area. We eventually cleared all grossly visible disease and achieved excellent hemostasis.

Ultimately, the patient underwent bone marrow transplant for treatment of her systemic disease with excellent results. At 9 months post-operative evaluation there was no evidence of recurrence of amyloidosis on the vulva.

**Discussion**

Amyloidosis is a term used to describe fibril deposition of proteins. AL amyloidosis is due to deposition of protein from immunoglobulin light chain fragments. A monoclonal protein is detected in the urine and or blood of more than 95% of patients with amyloidosis. Amyloidosis can be present by itself or associated with underlying systemic disease such as plasma cell dyscrasias (multiple myeloma, Waldenström macroglobulinemia). These are malignant disorders of plasma cells or lymphoplasmacytic cells.

Since AL amyloidosis is a clonal cell disorder, it is treated with chemotherapy to destroy the underlying clone. In our patient, diagnosis of AL amyloidosis (deriving from a light chain fragment) was confirmed by mass spectrometry. This differentiates AL from other types of amyloidosis such as AA amyloidosis, ATTRmt amyloidosis, and ATTRwt amyloidosis. These types are not neoplasms and therefore not susceptible to chemotherapy.

AL amyloidosis is a very rare disease. It is estimated that in the United States the incidence is 9 to 14 cases per million person-years. Patients present in a variety of ways.
Since AL amyloidosis is often associated with plasma cell dyscrasias such as multiple myeloma, it can present as a myeloma defining event such as bone pain that is shown to be an osteolytic bone lesion. Some common symptoms on presentation include unintentional weight loss and fatigue. It can also present in a variety of organ systems. Common presentations include nephrotic syndrome, cardiomyopathy, peripheral neuropathy, hepatosplenomegaly, and bleeding diathesis. It can also present with skin manifestations such as thickening of the skin, easy bruising, and infiltration of subcutaneous fat.

Diagnosis is made through biopsy that demonstrates amyloid fibrils. It can be confirmed with Congo Red staining that demonstrate green birefringence under polarized light. The amyloid is then typed using a variety of techniques (in our patient’s case using mass spectrometry). This can identify the amyloid type with 100% specificity.

The Mayo Clinic and the International Myeloma Working Group have established diagnostic criteria for AL amyloidosis. All 4 must be met to confirm diagnosis.

These include:
1. An amyloid related systemic syndrome. Organ damage must be confirmed to be related to amyloid protein deposition;
2. Amyloid that is Congo red positive;
3. Confirmation that amyloid is light chain (mass spectometry);

For treatment of our patient’s vulvar amyloidosis she was offered laser ablation to the affected areas. Case reports suggest CO₂ laser is successful in managing nodular disease, satisfactory cosmetic results and no recurrences at follow-up. There is no consensus on particular settings/technique, especially with gynecologic lesions.

It is imperative that AL amyloidosis is differentiated from other forms because treatment and prognosis is markedly different. Our patient ultimately underwent bone marrow transplant to cure her underlying multiple myeloma. She continues to do well without evidence of recurrence of multiple myeloma and with no recurrence of vulvar amyloidosis.

In conclusion, systemic AL amyloidosis can manifest as atypical nodular lesions on the vulva. Extensive amyloid deposits can cause significant discomfort, warranting surgical management. A combination of ablative therapy and mechanical dissection may be needed to create the necessary surgical plane for successful treatment. Maintenance of hemostasis and avoidance of sensitive structures are key operative concern. Vulvar amyloidosis is a rare, but important clinical entity. Its diagnosis can facilitate the recognition of a potentially life-threatening systemic condition. Proper treatment provides symptomatic relief without significant disfigurement or loss of function.
The Value of Hysteroscopy in the Diagnosis of Endometrial Cancer

For patients at risk for developing endometrial cancer, timely biopsy is essential toward diagnosis and identifying optimal treatment regimens. “Blind” biopsies are commonly utilized as a means of sampling for the diagnosis of complex atypical hyperplasia and endometrial cancer. Recent research suggests that hysteroscopy is effective as a diagnostic tool for focal intrauterine lesions.1-5

To elucidate the benefits of hysteroscopic procedures, board-certified gynecologists Yelena Havryliuk, MD, of Weill Cornell Medicine in New York, NY, and Samar Nahas, MD, MPH, of UCR Health in Riverside, CA, reflect on the findings and implications of several key articles that have been published in recent years, each demonstrating the unique utility of hysteroscopy.

STUDY BRIEF

STUDY TITLE: Sampling in Atypical Endometrial Hyperplasia: Which Method Results in the Lowest Underestimation of Endometrial Cancer? A Systematic Review and Meta-analysis

JOURNAL: The Journal of Minimally Invasive Gynecology

KEY TAKEAWAY: Hysteroscopic resection reduces the risk of underdiagnosed endometrial cancer, thereby reducing the risk of inappropriate surgical procedures.

Havryliuk: There has been a lot of evidence that patients with gynecologic cancers who are treated by trained specialists have an improved prognosis. Involvement of the gynecologic oncologist early in the process can streamline pre-operative assessments, focus intraoperative management and the need for additional therapies. Underdiagnosis of cancer and having suboptimal follow up surgeries is a problem. Having a proper diagnosis preoperatively is imperative to channel those patients to a specialist so they can get correct treatment.

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NAHAS: If the tumor is an early stage, and early size, you have a higher chance of missing it with a blind biopsy. The best approach in those types is to do hysteroscopy and direct biopsy. The problem is that when we see patients, we don’t know which have complex hyperplasia and which don’t. If they do [have complex hyperplasia]: Is it small? Is it big? Has it been there for a long time? We really don’t know, because it depends on when the patient started developing the pathology. Abnormal uterine bleeding is common, but not all abnormal bleeding is related to the time when the abnormalities started. If the complex hyperplasia or cancer is in early stages, and the abnormality is small, we have a higher chance of missing it with blind biopsy. That’s why we tell the patients to come back again for repetitive endometrial biopsies every 3 to 6 months if they continue to have abnormal bleeding.

If you’re doing a direct hysteroscopic biopsy, even if it’s a small abnormality, [you can see it and directly biopsy it] from the abnormal area with less of a chance of missing it, because you’re visualizing it and [biopsying] directly based on the area sampling. Using an advanced tissue extraction system like the TruClear™ hysteroscopic tissue removal system enables you to visualize that pathology and directly resect it.

5.8%
The mean risk of finding endometrial cancer at hysterectomy following hysteroscopic resection in patients diagnosed with atypical endometrial hyperplasia, compared with 32.7% and 45.3% for uterine curettage and hysteroscopically guided biopsy, respectively.¹

STUDY BRIEF

STUDY TITLE: Does Hysteroscopy Worsen Prognosis in Women With Type II Endometrial Carcinoma?²

JOURNAL: PLoS One

KEY TAKEAWAY: Despite increased rates of positive peritoneal cytology in patients following hysteroscopy, there was no difference in prognosis between hysteroscopy and dilation and curettage.

NAHAS: Some studies show that hysteroscopy increases the chance of positive washing, but it does not impact prognosis in type 1 or type 2 endometrial cancer. Positive washing doesn’t have any impact on prognosis and it’s not part of the staging anymore. In a patient with [suspected] endometrial cancer who doesn’t want to preserve their fertility, you [may] want to proceed with hysterectomy and full surgical staging.

HAVRYLIUK: Endometrial cancers are classified into 2 major types based on their histology. Type 1 endometrial cancers account for 75% of all endometrial cancers. Frequently those tumors are low-grade, confined to the uterus at the time of diagnosis and carry more favorable prognosis. Endometrial intraepithelial hyperplasia can transform into Type 1 endometrial cancer.

Type 2 tumors are considered more aggressive and they are associated with worse prognosis due to the increased risk of extraterine spread. These tumors might be more difficult to diagnose, [because] patients may lack the classical signs and symptoms, such as postmenopausal bleeding and endometrial thickening on the pelvic ultrasound. If, however, a patient has a negative initial assessment and even benign in-office endometrial biopsy, and she has persistent abnormal uterine bleeding or postmenopausal bleeding, it is important to pursue further work-up. Hysteroscopic assessment is imperative in those situations and is a gold standard of diagnosis of patients who have persistent abnormal bleeding.

30%
The percentage of patients in which positive peritoneal cytology was found following diagnostic hysteroscopy in patients with type II endometrial cancer, as compared with 12% following dilation and curettage.²
HAVRYLIUK: Hysteroscopic procedures are associated with a less than 1% rate of complications. Although patients who underwent hysteroscopic procedures had higher rates of positive peritoneal cytology, this finding did not correlate with overall prognosis and survival rates. Conclusions in this study are consistent with the results from the past studies. In addition, peritoneal cytology is no longer included in the official surgical staging of endometrial cancers. It is still frequently obtained, recorded, and, sometimes, it can be used to plan for more specific treatments. Hysteroscopy, overall, is a safe procedure, and it does not affect prognosis and survival of women with early-stage endometrial cancer, despite higher rates of positive peritoneal cytology found during definite surgery.

NAHAS: When it comes to long-term survival and management of patients with endometrial cancer [of women who do not want to preserve their fertility], the standard of care is to do a biopsy. Once cancer is diagnosed, [you can] then proceed with hysterectomy, bilateral salpingoopherectomy, and staging. In most cases, it’s sufficient to do endometrial biopsies in the office; you don’t necessarily need to do the hysteroscopy unless the biopsy came back inconclusive or negative despite the patient having recurrent abnormal bleeding.

In a woman with post-menopausal bleeding with negative endometrial biopsy, you have to counsel that result is negative, but if they continue to bleed they should come back for hysteroscopy directed biopsy to rule out cancer, because the tumor might be small and was not detected or sampled by the blind endometrial biopsy. In summary, for post-menopausal [patients] that have negative biopsy and continue to bleed, we need [perform a] hysteroscopy to explore and examine for a visual diagnosis and do a direct biopsy if there’s anything abnormal, instead of repeating the blind biopsy that will likely lead to a false negative result. In those scenarios, the next appropriate thing is to proceed with the hysteroscopy and do a direct biopsy.

Significant work needs to be done in the field to increase the adoption of hysteroscopy. I highly recommend that we start by showing those studies showing that it has a big influence and impact on patient care, we need to increase awareness and more research on that topic. Performing large, multicenter trials may be a good way to cause a significant impact nationally and internationally, to be able to collect enough and show enough evidence about the safety of that approach.

STUDY BRIEF

STUDY TITLE: The Oncological Safety of Hysteroscopy in the Diagnosis of Early-stage Endometrial Cancer: An Israel Gynecologic Oncology Group Study

JOURNAL: European Journal of Obstetrics & Gynecology and Reproductive Biology

KEY TAKEAWAY: In patients with early-stage endometrial cancer, hysteroscopy does not compromise the survival.

90.2%
The rate of 5-year recurrence-free survival in patients with early stage endometrial cancer who underwent hysteroscopy as a diagnostic procedure, as compared with 88.2% in who underwent another means of diagnosis.

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NAHAS: Hysteroscopy should be utilized more widely, especially in patients with a smaller pathology, such as those in whom you already did a biopsy [that] came back negative. It becomes crucial that the first step is to do a diagnostic hysteroscopy. In this study, hysteroscopic evaluation and resection of focal lesions was more likely to completely remove the lesion as compared with blind dilation and curettage. This means that hysteroscopic evaluation could improve diagnostic sensitivity, allowing for the preservation of the patient’s uterus and giving them a chance to have similar opportunities that other patients have. The beauty is you can actually do it and retrieve the sample in the office, which is very convenient for clinicians and patients.

HAVRYLIUK: This study demonstrated that blind endometrial testing procedures, such as endometrial biopsies or dilation and curettage, do not adequately sample uterine cavities. The authors showed that dilation and curettage with aspiration treated only 20% of the lesions and correctly diagnosed 55% of the pathology leading to conclusion that hysteroscopy is a superior tool in identifying and removing endometrial lesions. Hysteroscopy is probably underutilized in the day-to-day clinical practice for the treatment of patients who have abnormal uterine bleeding or post-menopausal bleeding. Using hysteroscopy earlier in the work up of those patients can identify patients with focal endometrial lesions that possibly could of been missed by blind endometrial sampling. Hysteroscopy leads to increased identification of the lesions, more accurate diagnosis and channeling patients to receive more suitable treatments.

REFERENCES
Dental dilemmas in pregnancy

Curbside Consults delivers expert perspectives from physicians outside of the ob/gyn specialty to provide insight into various health issues affecting pregnant women, about which they are experts. This new section is the brainchild of Editorial Advisory Board member Christine Isaacs, MD.

By Sarah H. Glass, DDS, an assistant professor in Oral Diagnostic Sciences at Virginia Commonwealth University’s School of Dentistry.

Scenario 1: The Terrible Toothache

A 30-year-old patient presents to labor and delivery at 3 a.m. in tears. She is 32 weeks pregnant and complains of a “terrible toothache” refractory to acetaminophen and ice packs. She has no obstetric complaints. All vital signs and fetal surveillance are reassuring. You see the following (Figure 1):

WHAT SHOULD YOU DO?

In this scenario, the source of the pain is a cavity that has progressed to the innermost portion of the tooth (pulp) where nerves and blood vessels reside. Clinically, this is illustrated by the dark cavitation noted on the image. The pressure from the swelling can be excruciating and even involve the bone surrounding the tooth root. Definitive treatment likely requires extracting the tooth or cleaning the infection with a root canal if the tooth can be restored.

Initial management by an obstetrician can include:

1. Comfort measures and referral to a dental provider for definitive treatment.

   - Direct pain relief can be achieved with “dental balls” by prescribing lidocaine 2% mucous membrane solution to be mixed with equal parts of over-the-counter aluminum hydroxide/magnesium hydroxide and liquid diphenhydramine. Patients can be instructed to soak cotton balls in this mixture and apply them to the site of dental pain every 4 hours, as needed. The cotton balls should be refrigerated and discarded after 5 days.

2. Antibiotics may be considered when the patient has facial swelling.

3. To avoid any delay in dental treatment, proactively provide a medical clearance form stating that dental procedures with lidocaine with epinephrine are permissible.

Scenario 2: Puffy, Bleeding Gums

A 19-year-old patient presents for her routine prenatal care appointment at 14 weeks gestation and mentions her gums feel puffy, tender and swollen. Her gums bleed more frequently, and her exam appears in the image (Figure 2).

WHAT SHOULD YOU DO?

Patients who are pregnant can be at risk for the gum disease gingivitis, as illustrated in Figure 2. It’s theorized that changes in hormones can result in an exaggerated inflammatory response to bacteria, and thus, the inflamed gingiva. Clinicians should stress the importance of maintaining
good oral hygiene by brushing and flossing twice a day and seeing a dentist for routine care. Establishing a dental home early in pregnancy can help reduce the risk of dental emergencies in the future.

**Scenario 3: Sensitive Teeth**
Your 35-year-old patient with hyperemesis gravidarum complains that her teeth are becoming more sensitive. You note the following on her exam. (Figure 3).

**WHAT SHOULD YOU DO?**
Acid from gastric secretions can cause erosions of the outermost layer of tooth structure (enamel) and expose the sensitive underlying yellow tooth structure (dentin), as illustrated in Figure 3. The mouth relies on a healthy pH balance, so you can recommend a baking soda rinse for use after an emesis episode to help neutralize the acid. This is made by combining 8 oz. of water with 1 tsp. of baking soda to rinse in the oral cavity. Although counterintuitive, patients should be instructed to wait at least 1 hour after vomiting to brush their teeth and avoid gritty/abrasive toothpastes so as to not further erode the tooth enamel.

**Scenario 4: A New Growth**
A 28-year-old patient in her second trimester is concerned about a rapidly growing red bump in her mouth. You note the following lesion on her gums (Figure 4):

**WHAT SHOULD YOU DO?**
This patient has a pyogenic granuloma, a finding so infamous associated with pregnancy that some call it the "pregnancy tumor." This lesion is not a true granuloma or a tumor but rather a tumor-like growth associated with an exuberant response to local irritation of the gums (gingiva). It can appear worrisome clinically due to its rapid growth and propensity to bleed. Because pyogenic granuloma has a high recurrence rate during pregnancy, dental providers will often defer treatment with surgical removal until after delivery, unless there are functional or aesthetic concerns at the time of diagnosis.
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54% OPIOID-SPARED* Women took ≤10 mg of oxycodone with no bother or stress from ORAEs through 72 hours (P=0.0015).‖

OPIA*  opioids-related adverse events (such as vomiting, itching, sweating, freezing, and dizziness).

The clinical benefit of this decrease in opioid consumption was not demonstrated in the pivotal trials.

A prospective, multicenter, randomized, double-blind clinical trial of 186 patients who underwent an elective C-section with a multimodal pain management protocol, including a transversus abdominis plane (TAP) block using either 20 mL EXPAREL 266 mg, 30 mL 0.25% bupivacaine HCl, and 20 mL normal saline for a total volume of 80 mL (30 mL volume on each side), or 20 mL 0.25% bupivacaine HCl and 40 mL normal saline for a total volume of 80 mL (30 mL volume on each side).

‡Single-center retrospective chart review of 201 patients ≥18 years of age who underwent C-section with either a multimodal pain management protocol including a TAP block with 20 mL EXPAREL 266 mg, 30 mL 0.25% bupivacaine HCl, and 30 mL normal saline for a total volume of 80 mL (40 mL volume on each side); or a multimodal pain management protocol alone. Mean hospital length of stay was 2.9 days with EXPAREL (n=87) vs 3.9 days without EXPAREL (n=88). Time to ambulation was 16.7 hours with EXPAREL (n=87) and 30.7 hours without EXPAREL (n=82).‖

†Defined as patients who took no more than 10 mg of oxycodone (15 mg of morphine or equivalent) with no bother or stress from vomiting, itching, sweating, freezing, or dizziness through 72 hours.

Important Safety Information

EXPAREL is contraindicated in obstetrical paracervical block anesthesia. Adverse reactions reported with an incidence greater than or equal to 1% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via interscalene brachial plexus nerve block were nausea, pyrexia, and constipation. If EXPAREL and other non-bupivacaine local anesthetics, including lidocaine, are administered at the same site, there may be an immediate release of bupivacaine from EXPAREL. Therefore, EXPAREL may be administered to the same site 20 minutes after injecting lidocaine. EXPAREL is not recommended to be used in the following patient population: patients ≤18 years old and/or pregnant patients.

Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease.

Warnings and Precautions Specific to EXPAREL

Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL. EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks (other than interscalene brachial plexus nerve block), or intravenous or intra-articular use. The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.

Warnings and Precautions for Bupivacaine-Containing Products

Central Nervous System (CNS) Reactions: There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesia. CNS reactions are characterized by excitation.

Please refer to brief summary of Prescribing Information on adjacent page.

For more information, please visit www.EXPAREL.com or call 1-855-793-9727.

References:

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Navigating the Annual Pregnancy Meeting

The Society for Maternal-Fetal Medicine’s (SMFM) 2021 Annual Pregnancy Meeting will be held virtually throughout the month of January, with core meeting activities taking place Jan. 25-30. SMFM’s President, Judette Louis, MD, MPH, and Program Committee Chair, Cynthia Gyamfi-Bannerman, MD, MSc, tell readers what they can expect in the new online format.

While it will certainly be different than the 40 meetings before it, SMFM’s 41st Annual Meeting will provide the same cutting-edge science, postgraduate courses, poster sessions, and networking events that you have experienced in the past. Here is a bit more about how it will work.

President’s Workshop
On Jan. 25-26, SMFM and the Preeclampsia Foundation will co-host the 2021 President’s Workshop on Preeclampsia, bringing together the world’s leading researchers, clinicians, and patients for an in-depth look at how to better predict, prevent, and manage preeclampsia. Participate in the President’s Workshop at no cost and join the Twitter chat on Jan. 26 at 3:00 pm ET by posting and following the hashtag #MyPreeclampsiaStory.

Postgraduate Courses and CME
As we’ve done in the past for live meetings, we will kick off the 2021 Annual Meeting with a series of 15 half-day and full day Postgraduate Courses. Interact live with the course faculty and course directors on Jan. 25, 26 and 27 or watch the recorded version of the courses at your leisure. This year, we are offering up to 74 hours of CME via these courses.

If you want to register for multiple Postgraduate Courses on the same day, you can do that in 2021. The courses will be offered via Zoom and you can bounce between courses or watch the recorded version on another day. Because of the Zoom’s limitations, however, it will not be possible to be logged into multiple courses at the same time.

Scientific Sessions
We will offer a new and timely course on Jan. 27 at 1:30 p.m. with an event jointly sponsored by SMFM and the American College of Obstetricians and Gynecologists called “Racism, Equity and Respectful Care: A Primer for MFMs.” This keynote panel presentation will feature Dr. Joia Crear-Perry, Prof. Dorothy Roberts, and Dr. Elizabeth Howell who will focus on three main messages: racism, not race, is the root of maternal health disparities; we must provide respectful care; and there is no quality without equity.

Following the keynote panel, there will be 15 Scientific Forums on Jan. 27. As we’ve always done, this will lead into the oral plenary sessions at 10:30 a.m. on Jan. 28 and 29, and the poster presentations at various times on Jan. 28, 29, and 30. This year, we will have 101 oral presentations that will be shown live in real time with live Q+A. Recordings will be available after the meeting. For more information and extended Q&A on this meeting, visit: contemporaryobgyn.net/SMFM-apm

For more information and extended Q&A on this meeting, visit: contemporaryobgyn.net/SMFM-apm
A look back at our top cases

General surgeons and ob/gyns are the most likely physicians to get sued, according to data from the American Medical Association’s 2016 Physician Practice Benchmark Survey. Malpractice claims are not a rare occurrence. In fact, 50% of ob/gyns are likely to get sued at least once before they turn 55. An average of 162 claims were filed for every 100 ob/gyns, which may be due to the high-risk nature of the practice.

Being named in a lawsuit, however, does not always mean a medical error was made. Most claims are dropped, dismissed, or withdrawn, and trials are often won by the physician. Take a look back at the year’s top cases and see how each one unfolded.

1. Major vascular injury incurred at laparoscopy (Vol 65 No 09)

An LVAH case underscores the importance of continuing education.

This case highlights the importance of remaining cognizant of current literature and surgical practices. All too often, physicians fail to remain current in the various areas of their practices.

One would assume that maintenance of certification would allow physicians to stay current in their practice. However, ongoing education in specific practice areas may be required. Ultrasound, a valuable adjunct to our care of patients, is rapidly changing.

2. Was loss of ovary in this pediatric case avoidable? (Vol 65 No 08)

This case involves an eight-year-old patient who originally presented with a chief complaint of right-sided abdominal pain and one episode of vomiting.

Sometimes medicolegal cases have so many moving parts that until they are all fleshed out, as it were, one cannot be certain as to where the focused allegations and defenses will lie. While this started out as a misdiagnosis and delay case as to all defendants, through the discovery process and expert evaluation, we were able to determine that the pathologic findings rendered any delay argument, at least as to our client, moot.

Thank you to our Legally Speaking experts, Andrew Kaplan, ESQ and James Shwayder, MD, JD, for great legal insights in all of our 2020 articles.
Was this a failure to diagnose ovarian failure? (Vol 65, No 10)

The outcome in this case underscores the need for solid documentation, especially when one of the defendants has passed.

Putting aside the opportunity to resolve this case for less than the cost of trying it, the matter settled primarily for two reasons.

The first reason was the absence of any documentation by the defendants of awareness or follow-up with the patient for the elevated FSH. Whether or not the die was cast, as it were, documenting acknowledgment of the abnormal results and discussion with the patient still was required.

Shoulder dystocia: The unpredictable nightmare (Vol 65 No 07)

This case involves induction of labor for a suspected large for gestational age (LGA) baby in a mother with a normal antepartum course.

This case was defensible, except for two major issues: the lack of a pre-induction estimated fetal weight and the resulting nerve avulsion. The lack of an estimated fetal weight is not uncommon in shoulder dystocia cases resulting in litigation. Even though inaccurate, a clinical or ultrasound-based estimated fetal weight should be included in the initial assessment of all patients, whether for induction or in labor. Documentation of an estimated fetal weight, even if inaccurate, renders cases more defensible.

Cesarean delivery leads to unexpected outcome (Vol 65 No 11)

This case presents a unique dynamic involving certified nurse midwives; following protocols enhanced defensibility.

This case presented a unique dynamic, with CNMs providing the primary management of the patient. In contrast to a separate birthing center, this hospital had established a birthing unit in Labor and Delivery, allowing CNMs to manage patients with immediate physician consultation if needed.

Have you missed a legally speaking case? Catch up now at CONTEMPORARYOBGYN.NET/LEGALLY-SPEAKING
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fFN testing can help rule out
~80% of patients with symptoms of preterm labor.

~80% Patients receive a negative result
~20% Patients receive a positive result

Benefits of a Negative Result
A negative fFN result means the patient has a <1% chance of delivery in the next 14 days.

High NPV:
NPV for delivery within:

- 7 days = 99.5%
- 14 days = 99.2%

Benefits of a Positive Result
A positive result can help clinicians identify patients that may benefit from interventions, such as steroids or maternal transfer.

Useful PPV:
PPV for delivery within:

- 7 days = 12.7%
- 14 days = 16.7%


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Open for Pages 3 and 4
ACOG guidelines state that pain may also be effectively managed following surgery and to optimize recovery. The multimodal analgesia approach followed in ERAS can include either systemic opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), or acetaminophen; a local anesthetic; epidural or spinal anesthesia with morphine and bupivacaine. The infiltration indication includes regional field or interfascial injection to provide postsurgical local analgesia and as an intercostal block before surgery. EXPAREL is indicated for single-dose infiltration of the intercostal space in adults to produce postsurgical local analgesia and as an intercostal block before surgery. It may be beneficial to implant enhanced recovery protocols for cesarean delivery that involve reduced or no opioid use and discuss nonopioid options available to women having surgery. Enhanced Recovery after Surgery and Multimodal Pain Management

The study published that ENBD ELAXV%L boundaries for cesarean delivery have approached safe limits on improving and standardizing perioperative care for the patient population.7 EXPAREL involves patient-centered evidence-based multimodal care to help reduce the adverse response following surgery and to optimize recovery. The multimodal analgesia approaches followed in ENBD ELAXV%L can include opioid use, nonopioid anti-inflammatory drugs (NSAIDs), or acetaminophen; a local anesthetic; epidural or spinal anesthesia with morphine and bupivacaine; and a nonopioid approach such as the EXPAREL protocol. The infiltration indication includes regional field or interfascial injection to provide postsurgical local analgesia and as an intercostal block before surgery. It may be beneficial to implant enhanced recovery protocols for cesarean delivery that involve reduced or no opioid use and discuss nonopioid options available to women having surgery. EXPAREL® (bupivacaine liposome injectable suspension) has been shown to be safe and efficacious in adult patients undergoing cesarean delivery management following cesarean delivery. In addition, EXPAREL® has been shown to improve in-hospital, outpatient, and after discharge settings across a variety of women’s health procedures.6

EXPAREL® (bupivacaine liposome injectable suspension) has been shown to be safe and efficacious in adult patients undergoing cesarean delivery management following cesarean delivery. In addition, EXPAREL® has been shown to improve in-hospital, outpatient, and after discharge settings across a variety of women’s health procedures.6

The multimodal analgesia approach is supported by guideline recommendations for postpartum pain management. ACOG guidelines state that ENBD ELAXV%L can provide substantial analgesia following cesarean delivery. This trend effects women having cesarean delivery. In addition to recommending standard and parenteral opioid analgesia, the Multimodal Pain Management guidelines state that ENBD ELAXV%L may play an effective role in local anesthetic administration via an interscalene brachial plexus nerve block to produce postsurgical local analgesia and as an intercostal block before surgery. EXPAREL is indicated for single-dose infiltration of the intercostal space in adults to produce postsurgical local analgesia and as an intercostal block before surgery. It may be beneficial to implant enhanced recovery protocols for cesarean delivery that involve reduced or no opioid use and discuss nonopioid options available to women having surgery.