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OBG MANAGEMENT

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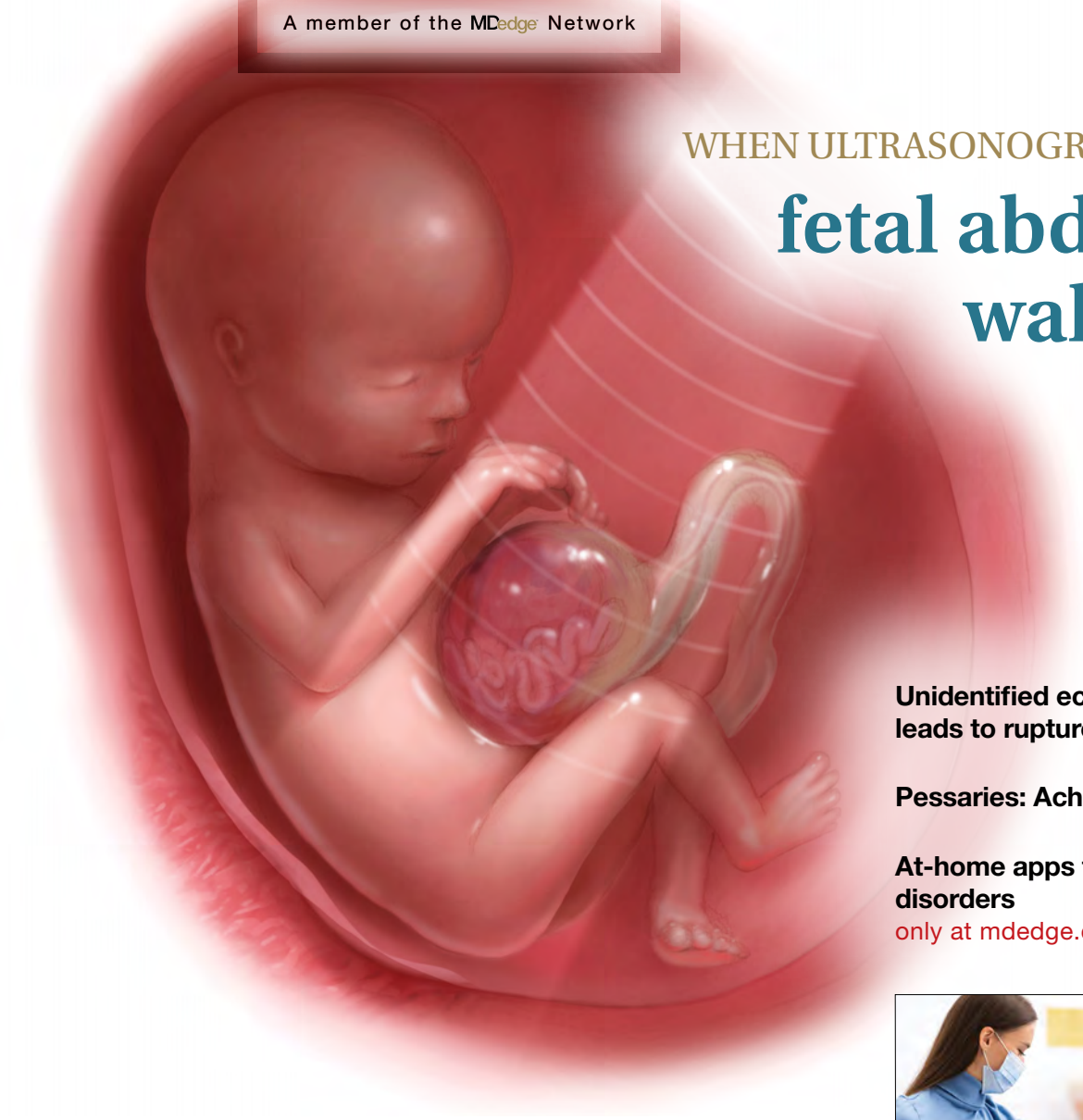
Optimal oxytocin use in L&D
Robert L. Barbieri, MD

Return to fertility after contraception

New FGR workup, plus more obstetrics updates



WHEN ULTRASONOGRAPHY REVEALS

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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**[1]

Empower her to be in **control of her fertility and menstruation** with a **predictable bleeding profile**[1,2*†]

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[1,3**]

97.3% effective and **high patient satisfaction:** ~90% of women in the clinical trial were satisfied with ANNOVERA[4‡]

* For each cycle, ANNOVERA is inserted for 21 continuous days and then removed for 7 days for 13 cycles.
† 5-10% of females experienced unscheduled bleeding and/or spotting for ~1 day or less per 28-day cycle.
** Based on pharmacological studies in animals and in vitro studies. The clinical significance of these data is not known.
‡ In an ANNOVERA Phase 3 study, a product acceptability questionnaire was administered and completed at the end of Cycle 3 (n=1036). Results based on data from 905 subjects in the areas of ease-of-use, expulsion, side effects, and sex/intercourse.

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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.

WARNINGS 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

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(segesterone acetate and ethinyl estradiol vaginal system)

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One ANNOVERA, One Prescription, One Full Year of CONTRACEPTION*

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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/m^2.

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.

References: 1. Annovera® [Full Prescribing Information]. Boca Raton, FL: TherapeuticsMD, Inc; 2020. **2.** Vieira CS, Fraser IS, Plagianos MG, et al. Bleeding profile associated with 1-year use of the segesterone acetate/ethinyl estradiol contraceptive vaginal system: pooled analysis from Phase 3 trials. *Contraception*. 2019;100(6):438-444. doi: 10.1016/j.contraception.2019.07.145. **3.** Kumar N, Koide SS, Tsong YY, Sundaram K. Nestorone®: a progestin with a unique pharmacological profile. *Steroids*. 2000;65:629–636. **4.** Merkatz RB, Plagianos M, Hoskin E, et al. Acceptability of the Nestorone®/ethinyl estradiol contraceptive vaginal ring: development of a model; implications for introduction. *Contraception*. 2014;90(5):514–521. doi:10.1016/j.contraception.2014.05.015.

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ANVA-20142.3 12/2020

ANNOVERA® (segesterone acetate and ethinyl estradiol vaginal system)

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use ANNOVERA safely and effectively. Please visit **ANNOVERA.com/pi.pdf** for Full Prescribing Information (PI).

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptive (CHC) use. This risk increases with age, particularly in females over 35 years of age, and with the number of cigarettes smoked. For this reason, CHCs should not be used by females who are over 35 years of age and smoke.

INDICATIONS AND USAGE

ANNOVERA is indicated for use by females of reproductive potential to prevent pregnancy.

Limitations of Use: ANNOVERA has not been adequately studied in females with a BMI >29 kg/m^2.

DOSAGE AND ADMINISTRATION

One ANNOVERA is inserted in the vagina. The vaginal system must remain in place continuously for 3 weeks (21 days) followed by a 1-week (7-day) vaginal system-free interval. One vaginal system provides contraception for thirteen 28-day cycles (1 year). Follow instructions for starting ANNOVERA, including switching from other contraceptive methods, and use after abortion, miscarriage, or childbirth *[see How to Start ANNOVERA (2.2) in PI]*.

Contraceptive efficacy of ANNOVERA may be reduced if a woman deviates from the recommended use. If ANNOVERA is out of the vagina for more than 2 continuous hours or more than 2 cumulative hours during the 21 days of continuous use, then back-up contraception, such as male condoms or spermicide, should be used until the vaginal system has been in the vagina for 7 consecutive days.

CONTRAINDICATIONS

ANNOVERA is contraindicated in females who are known to have the following conditions: • A high risk of arterial or venous thrombotic diseases. Examples include females who are known to: smoke, if over age 35; have current or history of deep vein thrombosis or pulmonary embolism; have cerebrovascular disease; have coronary artery disease; have thrombogenic valvular or thrombogenic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation); have inherited or acquired hypercoagulopathies; have uncontrolled hypertension or hypertension with vascular disease; have diabetes mellitus and are over age 35, diabetes mellitus with hypertension or vascular disease, or other end-organ damage, or diabetes mellitus of >20 years duration; have headaches with focal neurological symptoms, migraine headaches with aura, or are over age 35 with any migraine headaches. • 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. Hypersensitivity reactions reported include: throat constriction, facial edema, urticaria, hives, and wheezing. • Use of Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to the potential for alanine transaminase (ALT) elevations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Other Vascular Conditions

Females are at increased risk for a venous thrombotic event (VTE) when using ANNOVERA.

Stop ANNOVERA if a thrombotic or thromboembolic event occurs, or unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately. Stop ANNOVERA 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. Before starting ANNOVERA, consider history and risk factors of thrombotic or thromboembolic disorders. ANNOVERA is contraindicated in females with a high risk of arterial or venous thrombotic/thromboembolic diseases.

Arterial Events

Consider cardiovascular risk factors before initiating in all females, particularly those over 35 years. CHCs increase the risk 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.

Venous Events

The use of CHCs increases the risk of VTE, such as deep vein thrombosis and pulmonary embolism. Risk factors for VTEs include smoking, obesity, and family history of VTE, in addition to other factors that contraindicate use of CHCs. The rates of VTE are even greater during pregnancy, and especially during the postpartum period. The risk of VTE is highest during the first year of CHC use and when restarting hormonal contraception following a break of 4 weeks or longer. The risk of VTE due to CHCs gradually disappears after use is discontinued.

Liver Disease

Impaired Liver Function

ANNOVERA is contraindicated in females with acute hepatitis or severe (decompensated) cirrhosis of the liver. Discontinue ANNOVERA if jaundice develops. Acute liver test abnormalities may necessitate the discontinuation of ANNOVERA use until the liver tests return to normal and ANNOVERA causation has been excluded.

Liver Tumors

ANNOVERA is contraindicated in females with benign or malignant liver tumors. Hepatic adenomas are associated with CHC use (estimated 3.3 cases/100,000 CHC users). Rupture of hepatic adenomas may cause death through intra-abdominal hemorrhage.

Risk of Liver Enzyme Elevations with Concomitant Hepatitis C Treatment

Stop ANNOVERA prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir. ANNOVERA can be restarted 2 weeks following completion of treatment with the Hepatitis C combination drug regimen.

Hypertension

ANNOVERA is contraindicated in females with uncontrolled hypertension or hypertension with vascular disease. For all females, including those with well-controlled hypertension, monitor blood pressure at routine visits and stop ANNOVERA if blood pressure rises significantly.

Age-Related Considerations

The risk for cardiovascular disease and prevalence of risk factors for cardiovascular disease increase with age. Certain conditions, such as smoking and migraine headache without aura, that do not contraindicate CHC use in younger females, are contraindications to use in women over 35 years of age. Consider the presence of underlying risk factors that may increase the risk of cardiovascular disease or VTE, 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, other vascular disease, or females with diabetes of >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 hypertriglyceridemia, 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 indicated.

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 diaries from the 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 use due to menstrual disorders including metrorrhagia, menorrhagia, and abnormal withdrawal bleeding. Females who are not pregnant and use ANNOVERA may experience amenorrhea. Based on subject diary 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

Some studies suggest that CHCs are associated with an increase in the risk of cervical cancer or intraepithelial neoplasia.

Effect on Binding Globulins

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

Hereditary Angioedema

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

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 Use

Some females are aware of the vaginal system on occasion during the 21 days of use or during coitus, and partners may feel the vaginal system during coitus. ANNOVERA may not 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 by ≥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 (10.0%); breast pain/tenderness/discomfort (9.5%); metrorrhagia/menstrual disorder (7.5%); diarrhea (7.2%); and genital 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/vulvovaginal mycotic infections (1.3%); nausea/vomiting (1.2%). 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); psychiatric events; 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 HCV 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 causation has been excluded.

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/m^2 have not been adequately evaluated because this subpopulation was excluded from the clinical trials after 2 VTEs occurred in females with a BMI > 29 kg/m^2. Higher body weight is associated with lower systemic exposure of SA and EE.

Manufactured for: TherapeuticsMD, Inc.
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Based on ANVA-LAB-20001.2 01/2020

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Enhancing the quality of women's health care and the professional development of ObGyns and all women's health care clinicians†

*Source: Kantar Media, Medical Surgical Study June 2020, Obstetrics/Gynecology Combined Office & Hospital Readers.
†OBG MANAGEMENT recognizes the importance of addressing the reproductive health of gender-diverse individuals.

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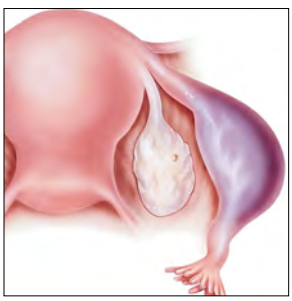
Contraception and fertility **10**



What's the Verdict? **45**

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Reference:
1. Rafalko et al. Impact of mosaicism ratio on positive predictive value of cfDNA screening. *Prenatal Diagnosis*, 2020.

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Two at-home apps for patients with pelvic floor disorders
KATHERINE T. CHEN, MD, MPH

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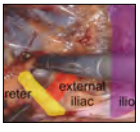

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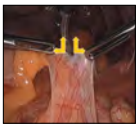

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Optimizing the use of oxytocin on labor and delivery

Oxytocin is the most common hormone administered in obstetrics. Reducing variation in the use of this agent will improve patient safety.

Robert L. Barbieri, MD
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Oxytocin is the hormone most commonly administered to women on labor and delivery. It is used for induction of labor, augmentation of labor, and to reduce the risk of postpartum hemorrhage. Licensed independent prescribers, including physicians and nurse midwives, order oxytocin, and licensed professional nurses execute the order by administering the hormone. Optimal management of oxytocin infusion requires effective interprofessional communication and collaboration. During labor it is common for disagreements to arise between the professionals ordering and the professionals administering oxytocin. The disagreements are usually caused by differing perspectives on the appropriate oxytocin dose. Standardized protocols and checklists reduce practice variation and improve patient safety.

Oxytocin hormone

Oxytocin is a cyclic nonapeptide synthesized in the hypothalamus and secreted into the circulation from axonal terminals in the posterior pituitary. In the myometrium, oxytocin activates a membrane G protein-coupled receptor, increasing phospholipase C and intracellular calcium. Following several intracellular chemical cascades, oxytocin stimulation results in myosin and actin filaments sliding over each other initiating shortening of the smooth muscle cell. Myometrial smooth muscle cells are connected by gap junctions, facilitating the coordinated contraction of the uterus.[1]

Oxytocin pulse frequency and uterine oxytocin receptor concentration both increase during pregnancy and labor, facilitating the birth process. Oxytocin pulse frequency increases from 2.4 pulses per hour before labor to 13.4 pulses per hour in the second stage.[2] In addition, uterine oxytocin receptor concentration increases 12-fold from the early second trimester of pregnancy to term.[3]

Oxytocin has a half-life of approximately 10 to 15 minutes. Many pharmacologists believe that for a given dose of a drug, it takes 4 to 5 half-lives for a stabilized

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circulating concentration to be achieved. Therefore, during an oxytocin infusion, when the dose is increased it may take 40 to 50 minutes to achieve a new higher, stabile circulating concentration.[4]

Low-dose vs high-dose oxytocin protocols

Oxytocin is often used in a premixed solution of 30 units of oxytocin in 500 mL of lactated Ringer's solution. With this mixture, an infusion of 1 mL/hour results in the administration of 1 mU of oxytocin per minute (1 mU/min). There is no national consensus on an optimal oxytocin infusion regimen for induction or augmentation of labor. A commonly used low-dose regimen is an initial dose of 1 to 2 mU/min, with a dose increase of 1 to 2 mU/min every 30 to 40 minutes until regular uterine contractions occur every 2 to 3 minutes.[5] An example of a high-dose oxytocin regimen is an initial dose of 6 mU/min with an increase of 3 to 6 mU/min every 30 to 40 minutes (induction of labor).[6]

A randomized trial reported that, compared with a low-dose oxytocin regimen, a high-dose regimen increased the risk of tachysystole without a significant change in cesarean birth rate.[7] A Cochrane review concluded that, compared with low-dose regimens, high-dose oxytocin regimens were more likely to be associated with tachysystole.[8] Based on these reports, **I would suggest avoiding the use of a high-dose oxytocin regimen**. Experts have reported that an oxytocin dose of approximately 6 mU/min achieves a circulating oxytocin concentration similar to that observed in normal spontaneous labor.[9]

Maximum dose of oxytocin infusion

There is no national consensus on the maximum safe dose of oxytocin for induction or augmentation of labor. Many labor and delivery units have a protocol where the maximum dose of oxytocin is 20 mU/min for women in the following clinical situations: previous vaginal delivery, prior cesarean delivery, multiple gestation, and nulliparous women in the second stage of labor. A maximum oxytocin dose of 30 mU/min may be appropriate for nulliparous women in the first stage of labor. Some units permit an oxytocin dose of 40 mU/min. Many labor nurses are concerned that an oxytocin dose that high may be associated with an increased frequency of adverse effects.

Management of the oxytocin dose when tachysystole is diagnosed

Tachysystole is defined as more than 5 uterine contractions in 10 minutes averaged over 30 minutes.[5,6] Because uterine contractions cause a reduction in oxygen delivery to the fetus, tachysystole, prolonged uterine contractions, and sustained elevated intrauterine pressure can result in fetal hypoxia and an abnormal fetal heart rate (FHR) pattern. If tachysystole is detected and the FHR pattern is Category 1, the oxytocin dose should be reduced. If tachysystole is detected and the FHR pattern is a concerning Category 2 or Category 3 pattern, the oxytocin infusion should be discontinued until the concerning FHR pattern resolves. If tachysystole is diagnosed, changing the maternal position (ensuring a lateral maternal position) and administering an intravenous bolus of 500 mL of lactated Ringer's solution may help resolve an abnormal FHR. Terbutaline 0.25 mg, administered by subcutaneous injection, may be given to reduce myometrial contractility. Following resolution of an episode of tachysystole with a concerning FHR tracing, the oxytocin infusion can be restarted at a dose less than the dose that was associated with the tachysystole.

Inadvertent excess oxytocin administration

Oxytocin only should be administered using a computerized medication infusion pump with the oxytocin line piggybacked into a main infusion line.[5] Occasionally, an excessively large bolus of oxytocin is administered inadvertently because the oxytocin line was mistakenly thought to be the main line or because of an infusion pump failure. These situations usually result in a tetanic contraction that will need to be treated by the immediate discontinuation of the oxytocin infusion, a fluid bolus, and one or more doses of terbutaline.

Reduction in oxytocin dose as labor progresses

Many investigators have reported that once rapid cervical dilation is occurring, or in the second stage of labor, the dose of exogenous oxytocin often can be reduced without stalling the progress of labor. Dilation of the vagina and pelvic floor, which occurs late in the process of labor, is a powerful stimulus for the release of oxytocin from the posterior pituitary.[10,11] The marked increase in endogenous secretion of oxytocin during the second stage of labor may be the reason that the exogenous oxytocin infusion can be reduced or discontinued.

In a systematic review and meta-analysis, discontinuation of oxytocin after 5 cm of cervical dilation was associated with a reduced rate of uterine tachysystole and no increase in cesarean delivery.[12] A Cochrane evidence-based review

also concluded that once rapid cervical dilation is occurring, the dose of oxytocin can be reduced with a decrease in the rate of tachysystole with an abnormal FHR and without an increase in the rate of cesarean delivery.[13]

Management of the oxytocin dose is a common cause of clinical disagreement

As noted in two recent research studies, experienced independent professional labor nurses often feel pressured by obstetricians to increase the dose of oxytocin. One nurse reported that physicians "like the pit pushed and you'd better push it and go, go, go, otherwise they'll be…really mad if it is not going." Many obstetricians favor working with a labor nurse who will actively manage labor by aggressively increasing the oxytocin dose. One obstetrician reported, "When I hear I've got a nurse who will go up on the pit, I know it's going to be a good day."[14]

Obstetricians and labor nurses with a good relationship can openly discuss differing perspectives and find a compromise solution. However, if the relationship is not good, the conflict may not be resolved, and the labor nurse may use a passive-aggressive approach to the situation. As one nurse reported, "It actually depends on the doctor and his personality. I know that there were times when I had a doc who would throw a fit if I didn't up the pitocin, so I would pacify him by agreeing to, but never would."[15]

An oxytocin checklist may help to reduce conflict over the optimal management of oxytocin infusion and improve patient safety.[16] Practice variation among nurses, obstetricians, and nurse midwives may contribute to difficulty in achieving a consensus on how to manage oxytocin. One approach to reducing practice variation is to use checklists to improve collaboration and uniformity on a clinical team. Clark and colleagues describe the beneficial effect of both a pre-oxytocin checklist and an oxytocin in-use checklist.[16] Their in-use checklist, which is completed every 30 minutes by the labor nurse, recommended decreasing the dose of oxytocin unless the FHR is reassuring and no tachysystole has occurred. In one retrospective study, when compared against outcomes prior to the use of a checklist, the use of the checklist resulted in a lower maximum dose of oxytocin (11.4 vs 13.8 mU/min; P = .003), a greater 1-minute Apgar score at birth (7.9 vs 7.6; P = .048), and no increase in time to delivery (8.2 vs 8.5 hours) or cesarean delivery rate (13% vs 15%).[16] When nurses and obstetricians collaborate using an oxytocin in-use checklist, both clinical variation and probability of conflict are reduced.

Consider use of a checklist to reduce conflict

Oxytocin infusion for induction or augmentation of labor is one of the most common and most important interventions on labor and delivery units. Oxytocin infusion practices vary widely among labor and delivery units. In addition to the lack of a consensus national standard, within any one labor unit the perspectives of obstetricians and labor nurses regarding the management of oxytocin infusions often differ, leading to conflict. The use of an oxytocin in-use checklist may help to reduce variability and improve patient outcomes. ●

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References

1. Blanks AM, Shmygol A, Thornton S. Regulation of oxytocin receptors and oxytocin receptor signaling. *Semin Reprod Med*. 2007;25:52-59.
2. Fuchs AM, Romero R, Keefe D, et al. Oxytocin secretion and human parturition: pulse frequency and duration increase during spontaneous labor in women. *Am J Obstet Gynecol*. 1991;165:1515-1523.
3. Fuchs AR, Fuchs F, Husslein P, et al. Oxytocin receptors in the human uterus during pregnancy and parturition. *Am J Obstet Gynecol*. 1984;150:734-741.
4. Seitchik J, Amico J, Robinson AG, et al. Oxytocin augmentation of dysfunctional labor. IV. Oxytocin pharmacokinetics *Am J Obstet Gynecol*. 1984;150:225-228.
5. Simpson KR. Cervical ripening, labor induction and labor augmentation, 5th edition. *Nurs Womens Health*. 2020;24:S1-S43.
6. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 107: induction of labor. *Obstet Gynecol*. 2009;114:386-397.
7. Selin L, Wennerholm UB, Jonsson M, et al. High-dose versus low-dose of oxytocin for labor augmentation: a randomized controlled trial. *Women Birth*. 2019;32:356-363.
8. Budden A, Chen LJ, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labor at term. *Cochrane Database Syst Rev*. 2014;CD00970.
9. Cuppett CD, Caritis SN. Uterine contraction agents and tocolytics. In: Mattison DR (Ed.) *Clinical Pharmacology During Pregnancy*. London, United Kingdom: Elsevier;2013:307-330.
10. Ferguson JK. A study of the motility of the intact uterus at term. *Surg Gynecol Obstet*. 1941;73:359-366.
11. Fisher DA. Maternal-fetal neurohypophyseal system. *Clin Perinatol*. 1983;10:695-707.
12. Saccone G, Ciadulli A, Baxter JK, et al. Discontinuing oxytocin in the active phase of labor: a systematic review and meta-analysis. *Obstet Gynecol*. 2017;130:1090-1096.
13. Boie S, Glavind J, Velu AV, et al. Discontinuation of oxytocin in the active phase of induced labour. *Cochrane Database Syst Rev*. 2018;CD012274.
14. Simpson KR, James DC, Knox GE. Nurse-physician communication during labor and birth: implications for patient safety. *J Obstet Gynecol Neonatal Nursing*. 2006;35:547-566.
15. Simpson KR, Lyndon A. Clinical disagreements during labor and birth: how does real life compare to best practice? *MCN Am J Matern Child Nurs*. 2009;34:31-39.
16. Clark S, Belfort M, Saade G, et al. Implementation of a conservative checklist-based protocol for oxytocin administration: maternal and newborn outcomes. *Am J Obstet Gynecol*. 2007;197:480.e1-e5.
17. Gawande A. *The Checklist Manifesto*. New York, NY: Henry Holt and Co; 2009.

Does last contraceptive method used impact the return of normal fertility?

Yes, according to a prospective observational study of more than 17,000 women that evaluated fecundability after stopping contraception. The authors found hormonal intrauterine device (IUD) users had slightly increased fecundability compared with users of barrier methods. There was no difference in fecundability for users of copper IUDs, implant, oral contraception, patches, rings, or natural methods compared with barrier methods. Users of injectable contraceptives experienced the longest delay in return of normal fertility, about 5 to 8 menstrual cycles.

FAST TRACK

While the efficacy and safety of contraception have been established, few studies have examined the effect of recent contraceptive use on fertility

Yland JJ, Bresnick KA, Hatch EE, et al. Pregravid contraceptive use and fecundability: prospective cohort study. BMJ. 2020;371:m3966.

EXPERT COMMENTARY

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Most US women aged 15 to 49 currently use contraception, with long-acting reversible contraception (LARC)—IUDs and the contraceptive implant—increasing in popularity over the last decade.[1] Oral contraceptive pills, male condoms, and LARC are the most common reversible methods used.[1] While the efficacy and safety of contraception have been established, few studies have examined the effect of recent contraceptive use on fertility.

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Fecundability is the probability of pregnancy during a single menstrual cycle for a couple engaging in regular intercourse and not using contraception.[2] Small studies have found short-term reductions in fecundability after discontinuing combined oral contraceptives and larger reductions after stopping injectable contraceptives, with no long-term differences among methods.[3,4]

Data are limited regarding the effects of other forms of contraception on fecundability, particularly LARC methods. A recent study was designed to evaluate the association between the last contraceptive method used and subsequent fecundability.[2]

Details of the study

Yland and colleagues pooled data from 3 prospective cohort studies of 17,954 women planning pregnancies in Denmark, Canada, and the United States. Participants reported the contraceptive method used most recently before trying to conceive. They completed questionnaires every 2 months for 12 months or until they reported a pregnancy. Women were excluded if they tried to conceive for more than 6 menstrual cycles at study entry.

CONTINUED ON PAGE 13

FOR THE TREATMENT OF WOMEN WITH MODERATE TO SEVERE DYSPAREUNIA, A SYMPTOM OF VULVAR AND VAGINAL ATROPHY, DUE TO MENOPAUSE

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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 Progestin Therapy

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

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 hemangiomas 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 (≥3%) was headache.

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

References: 1. Imvexxy [package insert]. Boca Raton, FL: TherapeuticsMD, Inc; 2019. **2.** Data on file. Vaginal Estrogen PIs. **3.** Constantine GD, Simon JA, Pickar JH, et al. The REJOICE trial: a phase 3 randomized, controlled trial evaluating the safety and efficacy of a novel vaginal estradiol soft-gel capsule for symptomatic vulvar and vaginal atrophy. *Menopause*. 2017;24(4):409-416. **4.** Constantine GD, Millheiser LS, Kaunitz AM, et al. Early onset of action with a 17ß-estradiol, softgel, vaginal insert for treating vulvar and vaginal atrophy and moderate to severe dyspareunia. *Menopause*. 2019;26(11):1259-1264. **5.** Simon JA, Pickar JH, Shadiack AM, et al. Physical characteristics and properties of estradiol softgel vaginal inserts. *Menopause*. 2020;27(2):150-155. **6.** Data on file. IMVEXXY MMIT Formulary Coverage Analysis January 2020.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use **IMVEXXY** safely and effectively. Please visit www.IMVEXXYHCP.com for Full Prescribing Information.

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

Estrogen-Alone Therapy

Endometrial Cancer

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding *[see Warnings and Precautions (5.3) in full prescribing information].*

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, 5.4), and Clinical Studies (14.2, 14.3) in full prescribing information].*

The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE) [0.625 mg]-alone, relative to placebo *[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 CE (0.625 mg)-alone, 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.

Estrogen Plus Progestin Therapy

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, 5.4), 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 the WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age of 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].*

Breast Cancer

The WHI estrogen plus progestin substudy also demonstrated an increased risk of invasive breast cancer *[see Warnings and Precautions (5.3), 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 MPA, and other combinations and dosage forms of estrogens and progestins.

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

DOSAGE 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, hysterectomized 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 arterial thromboembolic disease (e.g., stroke and 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 vaginal 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.

Malignant Neoplasms

Endometrial Cancer

An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in a woman with a uterus. The reported endometrial cancer risk among unopposed estrogen users is about 2 to 12 times greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with use of estrogens for less than 1 year. The greatest risk appears associated with prolonged use, with an increased risk of 15- to 24-fold for 5 to 10 years or more and this risk has been shown to persist for at least 8 to 15 years after estrogen therapy is discontinued.

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

There is no evidence that the use of natural estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen dose. Adding a progestin to estrogen therapy in postmenopausal women has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.

Breast Cancer

In the WHI estrogen-alone substudy, after an average follow-up of 7.1 years, daily CE-alone was not associated with an increased risk of invasive breast cancer [relative risk (RR) 0.80][5] *[see Clinical Studies (14.2) in full prescribing information].*

The WHI estrogen plus progestin substudy demonstrated an increased risk of invasive breast cancer. Consistent with the WHI clinical trial, observational studies have also reported an increased risk of breast cancer for estrogen plus progestin therapy, and a smaller increased risk for estrogen-alone therapy, after several years of use. The use of estrogen-alone and estrogen plus progestin therapy has been reported to result in an increase in abnormal mammograms requiring further evaluation. All women should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations.

Ovarian Cancer

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.

Probable Dementia

In the WHIMS estrogen-alone ancillary study of WHI, a population of 2,947 hysterectomized women 65 to 79 years of age was randomized to daily CE (0.625 mg)-alone or placebo.

After an average follow-up of 5.2 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE-alone versus placebo was 1.49 (95 percent CI, 0.83-2.66). The absolute risk of probable dementia for CE-alone versus placebo was 37 versus 25 cases per 10,000 women-years[8] *[see Use in Specific Populations (8.5), and Clinical Studies (14.3) in full prescribing information].*

In the WHIMS estrogen plus progestin ancillary study of WHI, a population of 4,532 postmenopausal women 65 to 79 years of age was randomized to daily CE (0.625 mg) plus MPA (2.5 mg) or placebo. After an average follow-up of 4 years, 40 women in the CE plus MPA group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE plus MPA versus placebo was 2.05 (95 percent CI, 1.21-3.48). The absolute risk of probable dementia for CE plus MPA versus placebo was 45 versus 22 cases per 10,000 women-years[8] *[see Use in Specific Populations (8.5), and Clinical Studies (14.3) in full prescribing information].*

When data from the two populations in the WHIMS estrogen-alone and estrogen plus progestin ancillary studies were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.76 (95 percent CI, 1.19-2.60). Since both ancillary studies were conducted in women 65 to 79 years of age, it is unknown whether these findings apply to younger postmenopausal women[8] *[see Use in Specific Populations (8.5), and Clinical Studies (14.3) in full prescribing information].*

Other Warnings and Precautions include:

Gallbladder disease; severe hypercalcemia; visual abnormalities; elevated blood pressure; hypertriglyceridemia; hepatic impairment and/or past history of cholestati jaundice; hypothyroidism (women on thyroid replacement therapy may require higher doses of thyroid hormone); fluid retention; hypocalcemia; exacerbation of endometriosis; hereditary angioedema; exacerbation of other conditions (asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas).

ADVERSE REACTIONS

Clinical Trials Experience: In a single, prospective, randomized, placebo-controlled, double-blind trial, the most common adverse reaction with IMVEXXY (incidence ≥ 3 percent) and greater than placebo was headache.

Post Marketing Experience: The following adverse reactions have been identified during post-approval use of IMVEXXY 4 and 10 mcg: *Genitourinary System*: vaginal discharge.

DRUG INTERACTIONS

Inducers and inhibitors of CYP3A4 may affect estrogen drug metabolism and decrease or increase the estrogen plasma concentration.

USE IN SPECIFIC POPULATIONS

IMVEXXY is not indicated for use in pregnancy, in females of reproductive potential, or in children.

Geriatric Use

An increased risk of probable dementia in women over 65 years of age was reported in the Women's Health Initiative Memory ancillary studies of the Women's Health Initiative.

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CONTINUED FROM PAGE 10

The authors calculated the fecundability ratio—the average probability of conception per cycle for a specific contraceptive method compared with a reference method—using proportional probability models adjusted for potential confounders. They also calculated pregnancy attempt time using participant-reported menstrual cycle length and date of last menstrual period during follow-up questionnaires.

Injectable contraceptives associated with longest delayed fertility return

After adjusting for personal factors, medical history, lifestyle characteristics, and indicators of underlying fertility, the authors found that injectable contraceptive use was associated with decreased fecundability compared with barrier method use (fecundability ratio [FR], 0.65; 95% confidence interval [CI], 0.47–0.89). Hormonal IUD use was associated with slight increases in fecundability compared with barrier method use (FR, 1.14; 95% CI, 1.07–1.22) and copper IUD use (FR, 1.18; 95% CI, 1.05–1.33). All other contraceptive methods were not significantly different from barrier methods.

LARC method use was associated with the shortest delay in return of normal fertility (2 cycles), followed by oral and ring contraceptives (3 cycles) and patch (4 cycles). Women using injectable contraceptives experienced the longest delay (5–8 menstrual cycles). Lifetime duration of contraceptive use did not impact fecundability in the North American cohort.

Study strengths and limitations

This large, prospective study contributes useful information about fecundability after stopping contraceptive methods. It confirms earlier studies' findings that showed decreased fecundability after stopping injectable contraceptives. Study participants' most recent method used was similar to overall US method distribution.[1]

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This is the largest study to date to evaluate fecundability after stopping different contraceptive methods among women planning pregnancies. The study confirms previous research that associated injectable contraceptives with delayed return of normal fertility. It provides reassurance for counseling users of IUDs, implants, oral contraception, ring, and patch: those methods were not associated with reduced fecundability compared with barrier methods. The study also suggests long-term contraceptive use does not decrease fecundability.

Women may ask when to stop their contraceptive method to optimally time a pregnancy. In this study, measurements of return to normal fertility were imprecise. Individualized counseling, accounting for personal circumstances, is still best when advising when to stop contraception for couples planning pregnancy.

LISA HOFLER, MD, MPH, MBA, AND LINDSAY DALE, MD

Study limitations include online recruitment of self-selecting participants, which introduces selection bias. The study population was overwhelmingly white (92%) and highly educated (70% with college degrees), quite different from the US population. These findings may therefore have limited generalizability. Additionally, injectable contraceptive users had higher body mass index and were more likely to smoke and have diabetes, infertility, or irregular menstrual cycles. IUD users were more likely to be parous and have a history of unplanned pregnancy, indicating possible higher baseline fertility. Even after adjusting, possible unmeasured factors could impact study results. ●

FAST TRACK

Injectable contraceptive use was associated with decreased fecundability compared with barrier method use; hormonal IUD use was associated with slight increases in fecundability compared with barrier method use and copper IUD use

References

1. Daniels K, Abma JC. Current contraceptive status among women aged 15–49: United States, 2017–2019. NCHS Data Brief, no. 388. Hyattsville, MD: National Center for Health Statistics; 2020.
2. Yland JJ, Bresnick KA, Hatch EE, et al. Pregravid contraceptive use and fecundability: prospective cohort study. *BMJ*. 2020;371:m3966.
3. Hassan MA, Killick SR. Is previous use of hormonal contraception associated with a detrimental effect on subsequent fecundity? *Hum Reprod*. 2004;19:344-351.
4. Mansour D, Gemzell-Danielsson K, Inki P, et al. Fertility after discontinuation of contraception: a comprehensive review of the literature. *Contraception*. 2011;84:465-477.

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Essential updated guidance on FGR workup and timing of delivery; term and preterm PROM management strategies based on gestational age; and approaches to VTE prophylaxis, including for patients with COVID-19 infection

While 2020 was a challenge to say the least, obstetrician-gynecologists remained on the frontline caring for women through it all. Life continued despite the COVID-19 pandemic: prenatal care was delivered, albeit at times in different ways; babies were born; and our role in improving outcomes for women and their children became even more important. This year's Update focuses on clinical guidelines centered on safety and optimal outcomes for women and children.

IN THIS ARTICLE

ACOG and SMFM update guidance on FGR management

American College of Obstetricians and Gynecologists. Practice advisory: Updated guidance regarding fetal growth restriction. September 2020. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/09/updated-guidance-regarding-fetal-growth-restriction. Accessed December 18, 2020.

Fetal growth restriction (FGR) affects up to 10% of pregnancies and is a leading cause of infant morbidity and mortality. Suboptimal fetal growth can have lasting negative effects on development into early childhood and, some hypothesize, even into adulthood.[1,2] Antenatal detection of fetuses with FGR is critical so that antenatal testing can be implemented in an attempt to deliver improved clinical outcomes. FGR is defined by several different diagnostic criteria, and many studies have been conducted to determine how best to diagnose this condition.

In September 2020, the American College of Obstetricians and Gynecologists (ACOG) released a Practice Advisory regarding guidance on FGR in an effort to align the ACOG Practice Bulletin No. 204, ACOG Committee Opinion No. 764, and SMFM (Society for Maternal-Fetal Medicine) Consult Series No. 52.[3-5] This guidance updates and replaces prior guidelines, with an emphasis on 3 notable changes.

FGR definition, workup have changed

While the original definition of FGR was an

estimated fetal weight (EFW) of less than the 10th percentile for gestational age, a similar level of accuracy in prediction of subsequent small for gestational age (SGA) at birth has been shown when this or an abdominal circumference (AC) of less than the 10th percentile is used. Based on these findings, SMFM now recommends that FGR be defined as an EFW or AC of less than the 10th percentile for gestational age.

Recent studies have done head-to-head comparisons of different methods of estimating fetal weight to determine the best detection and pregnancy outcome improvement in FGR. In all instances, the Hadlock formula has continued to more accurately estimate fetal weight, prediction of SGA, and composite neonatal morbidity. As such, new guidelines recommend that population-based fetal growth references (that is, the Hadlock formula) should be used to determine ultrasonography-derived fetal weight percentiles.

The new guidance also suggests classification of FGR based on gestational age at onset, with early FGR at less than 32 weeks and late FGR at 32 or more weeks. The definition of severe FGR is reserved for fetuses with an EFW of less than the 3rd percentile. A diagnosis of FGR should prompt the recommendation for a detailed obstetric ultrasonography. Diagnostic genetic testing should be offered in cases of early-onset FGR, concomitant sonographic abnormalities, and/or polyhydramnios. Routine serum screening for toxoplasmosis, rubella, herpes, or cytomegalovirus (CMV) should not be done unless there are risk factors for infection. If amniocentesis is performed for genetic diagnostic testing, consideration can be made for polymerase chain reaction for CMV in the amniotic fluid.

Timing of delivery in isolated FGR

A complicating factor in diagnosing FGR is distinguishing between the pathologically growth-restricted fetus and the constitutionally small fetus. Antenatal testing and serial umbilical artery Doppler assessment should be done following diagnosis of FGR to monitor for evidence of fetal compromise until delivery is planned.

The current ACOG Practice Bulletin No. 204 and Committee Opinion No. 764 recommend delivery between 38 0/7 and 39 6/7 weeks in the setting of isolated FGR with reassuring fetal testing and umbilical artery Doppler assessment. To further refine this, the new recommendations use the growth percentiles. In cases of isolated FGR with EFW between the 3rd and 10th percentile in the setting of normal umbilical artery Doppler, delivery is recommended between 38 and 39 weeks' gestation. In cases of isolated FGR with EFW of less than the 3rd percentile (severe FGR) in the setting of normal umbilical artery Doppler, delivery is recommended at 37 weeks.

Timing of delivery in complicated FGR

A normal umbilical artery Doppler reflects the low impedance that is necessary for continuous forward flow of blood to the fetus. Abnormal umbilical artery Doppler signifies aberrations of this low-pressure system that affect the amount of continuous forward flow during diastole of the cardiac cycle. With continued compromise, there is progression to absent end-diastolic velocity (AEDV) and, most concerning, reversed end-diastolic velocity (REDV).

Serial umbilical artery Doppler assessment should be done following diagnosis of FGR to monitor for progression that is associated

WHAT THIS EVIDENCE MEANS FOR PRACTICE

- Fetal growth restriction is now defined as EFW of less than the 10th percentile or AC of less than the 10th percentile.
- Evaluation of FGR includes detailed anatomic survey and consideration of genetic evaluation, but infection screening should be done only if the patient is at risk for infection.
- With reassuring antenatal testing and normal umbilical artery Doppler studies, delivery is recommended at 38 to 39 weeks for isolated FGR with EFW in the 3rd to 10th percentile and at 37 weeks for FGR with EFW of less than the 3rd percentile.
- Umbilical artery Doppler studies are used to decrease the risk of perinatal mortality and further guide timing of delivery.

with perinatal mortality, since intervention can be initiated in the form of delivery. Delivery at 37 weeks is recommended for FGR with elevated umbilical artery Doppler of greater than the 95th percentile for gestational age. For FGR with AEDV, delivery is recommended between 33 and 34 weeks of gestation and for FGR with REDV between 30 and 32 weeks, as the neonatal morbidity and mortality associated with continuing the pregnancy outweighs the risks of prematurity in this setting. Because of the abnormal placental-fetal circulation in FGR complicated by AEDV/REDV, there may be a higher likelihood of fetal intolerance of labor and cesarean delivery (CD) may be considered.

New recommendations for PROM management

American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstetrics. ACOG practice bulletin no. 217: Prelabor rupture of membranes. Obstet Gynecol. 2020;135:e80-e97.

FAST TRACK

Once reassuring fetal testing, infection evaluation, and no other contraindications to expectant management have been established, the most important determinant of PROM management is gestational age

Rupture of membranes prior to the onset of labor occurs at term in 8% of pregnancies and in the preterm period in 2% to 3% of pregnancies.[6] Accurate diagnosis, gestational age, evidence of infection, and discussion of the risks and benefits to the mother and fetus/neonate are necessary to optimize outcomes. In the absence of other indications for delivery, a gestational age of 34 or more weeks traditionally has been the cutoff to proceed with delivery, although this has not been globally agreed on and/or practiced.

ACOG has published a comprehensive update that incorporates the results of the PPROMT trial and other recommendations for the diagnosis and management of both term and preterm prelabor rupture of membranes (PROM).[6,7]

Making the diagnosis

Diagnosis of PROM usually can be made clinically via history and the classic triad of physical exam findings—pooling of fluid, basic pH, and ferning; some institutions also use commercially available tests that detect placental-derived proteins. Both ACOG and the US Food and Drug Administration caution against using these tests alone without clinical evaluation due to concern for false-positives and false-negatives that lead to adverse maternal and fetal/neonatal outcomes. For equivocal cases, ultrasonography for amniotic fluid evaluation and ultrasonography-guided dye tests can be used to assist in accurate diagnosis, especially in the preterm period in which there are significant implications for pregnancy management.

PROM management depends on gestational age

All management recommendations require reassuring fetal testing, evaluation for infection, and no other contraindications to expectant management. Once these are established, the most important determinant of PROM management then becomes gestational age.

Previable PROM

Previable PROM (usually defined as less than 23–24 weeks) has high risks of both maternal and fetal/neonatal morbidity and mortality from infection, hemorrhage, pulmonary hypoplasia, and extreme prematurity. These very difficult cases benefit from a multidisciplinary approach to patient counseling regarding expectant management versus immediate delivery.

If expectant management is chosen, outpatient management with close monitoring

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Mindy H.
Cervical cancer survivor
See Mindy's story:
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for signs of maternal infection may be done until an agreed on gestational age of viability. Then inpatient management with fetal monitoring, corticosteroids, tocolysis, magnesium for neuroprotection, and group B streptococcus (GBS) prophylaxis may be considered as appropriate.

Preterm PROM at less than 34 weeks

If the mother and fetus are otherwise stable, PROM at less than 34 weeks warrants inpatient expectant management with close maternal and fetal monitoring for signs of infection and labor. Management includes latency antibiotics, antenatal corticosteroids, magnesium for neuroprotection if less than 32 weeks' gestation and at risk for imminent delivery, and GBS prophylaxis. While tocolysis may increase latency and help with steroid course completion, it should be used cautiously and avoided in cases of abruption or chorioamnionitis. Although there is no definitive recommendation published, a rescue course of steroids may be considered as appropriate but should not delay an indicated delivery.

Late preterm PROM

The biggest change to clinical management in this ACOG Practice Bulletin is for late preterm (34–36 6/7 weeks) PROM, with the recommendation for either immediate delivery or expectant management up to 37 weeks stemming from the PPROMPT study by Morris and colleagues.[7]

From the neonatal perspective, no difference has been demonstrated between immediate delivery and expectant management for neonatal sepsis or a composite neonatal morbidity and mortality. Expectant management may be preferred from the neonatal point of view as immediate delivery was associated with an increased rate of neonatal respiratory distress, mechanical ventilation, and length of stay in the neonatal intensive care unit. The potential for long-term neurodevelopmental outcomes of delivery at 34 versus 37 weeks also should be considered.

From the maternal perspective, expectant management has an increased risk of antepartum and postpartum hemorrhage, fever, antibiotic use, and maternal length of stay, but a decreased risk of CD.

A late preterm steroid course can be considered if delivery is planned in *no less than 24 hours* and likely to occur in the next 7 days and if the patient has not already received a course of steroids. A rescue course of steroids is **not** indicated if the patient received a steroid course prior in the pregnancy. While appropriate GBS prophylaxis is recommended, latency antibiotics and tocolysis are **not,** and delivery should not be delayed if chorioamnionitis is diagnosed.

Ultimately, preterm PROM management with a stable mother and fetus at or beyond 34 weeks requires comprehensive counseling of the risks and benefits for both mother and fetus/neonate. A multidisciplinary team that together counsels the patient also may help with this shared decision making.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

- Accurate diagnosis is necessary for appropriate counseling and management of PROM.
- Delivery is recommended for term PROM, chorioamnionitis, and for patients with previable PROM who do not desire expectant management.
- If the mother and fetus are otherwise stable, expectant management of preterm PROM until 34 to 37 weeks is recommended.
- The decision of when to deliver between 34 and 37 weeks is best made with multidisciplinary counseling and shared decision making with the patient.

Term PROM

For patients with term PROM, delivery is recommended. Although a short period of expectant management for 12 to 24 hours is reported as "reasonable," the risk of infection increases with the length of rupture of membranes. Therefore, induction of labor or CD soon after rupture of membranes is recommended for patients who are GBS positive and is preferred for all others.

VTE prophylaxis in pregnancy: Regimen adjustments, CD strategies, and COVID-19 considerations

Birsner ML, Turrentine M, Pettker CM, et al. ACOG practice advisory: Options for peripartum anticoagulation in areas affected by shortage of unfractionated heparin. March 2020. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/options-for-peripartum-anticoagulation-in-areas-affected-by-shortage-of-unfractionated-heparin. Accessed December 8, 2020.

Pacheco LD, Saade G, Metz TD. Society for Maternal-Fetal Medicine Consult Series No. 51: Thromboembolism prophylaxis for cesarean delivery. Am J Obstet Gynecol. 2020;223:B11-B17.

Venous thromboembolism (VTE) prophylaxis is a timely topic for a number of reasons. First, a shortage of unfractionated heparin prompted an ACOG Practice Advisory, endorsed by SMFM and the Society for Obstetric Anesthesia and Perinatology, regarding use of low molecular weight heparin (LMWH) in the peripartum period.[8] In addition, SMFM released updated recommendations for VTE prophylaxis for CD as part of the SMFM Consult Series.[9] Finally, there is evidence that COVID-19 infection may increase the risk of coagulopathy, leading to consideration of additional VTE prophylaxis for pregnant and postpartum women with COVID-19.

Candidates for prophylaxis

As recommended by the ACOG Practice Bulletin on thromboembolism in pregnancy, women who may require VTE prophylaxis during pregnancy and/or the postpartum period include those with[10]:

- VTE diagnosed during pregnancy
- a history of VTE, including during pregnancy or with use of hormonal contraception
- a history of thrombophilia with or without a personal or family history of VTE.

For these patients, LMWH has many advantages over unfractionated heparin, including ease of use and reliability of dosing. It generally is preferred in pregnancy and postpartum (for both prophylactic and therapeutic anticoagulation) by patients and providers.

The Practice Bulletin references a strategy that describes converting LMWH to unfractionated heparin at around 36 weeks' gestation in preparation for delivery because unfractionated heparin has the advantage of a shorter half-life and the option for anticoagulation reversal with protamine sulfate. In the Practice Advisory, a global shortage of unfractionated heparin and an argument that the above conversion was less about concern for maternal hemorrhage and more about avoiding spinal and epidural hematomas led to the following recommendations for continued use of LMWH through delivery:

- LMWH heparin can be discontinued in a planned fashion prior to scheduled induction of labor or CD (generally 12 hours for prophylactic dosing and 24 hours for intermediate dosing).
- Patients in spontaneous labor may receive neuraxial anesthesia 12 hours after the last prophylactic dose and 24 hours after the last intermediate dose of LMWH.
- Patients who require anticoagulation during pregnancy should be counseled that if they have vaginal bleeding, leakage of fluid, or regular contractions they should be evaluated prior to taking their next dose of anticoagulant.
- In the absence of other complications, delivery should not be before 39 weeks for the indication of anticoagulation requirement alone.

Managing VTE risk in CD

Recognizing that VTE is a major cause of maternal morbidity and mortality, as well

FAST TRACK

Women who may require VTE prophylaxis during pregnancy and/or postpartum include those with VTE diagnosed during pregnancy, a history of VTE, or a history of thrombophilia with or without a personal or family history of VTE

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PART 2

Pessaries for POP and SUI: Their fitting, care, and effectiveness in various disorders

A refresher on how to fit a pessary, instructions for patients, goals for pessary aftercare visits, and the various conditions for which pessaries may or may not be effective

Henry M. Lerner, MD

IN THIS ARTICLE

In Part 1 of this article in the December 2020 issue of *OBG Management,* I discussed the reasons that pessaries are an effective treatment option for many women with pelvic organ prolapse (POP) and stress urinary incontinence (SUI) and provided details on the types of pessaries available.

In this article, I highlight the steps in fitting a pessary, pessary aftercare, and potential complications associated with pessary use. In addition, I discuss the effectiveness of pessary treatment for POP and SUI as well as for preterm labor prevention and defecatory disorders.

The pessary fitting process

For a given patient, the best size pessary is the smallest one that will not fall out. The only "rule" for fitting a pessary is that a woman's internal vaginal caliber should be wider than her introitus.

When fitting a pessary, goals include that the selected pessary:

- should be comfortable for the patient to wear
- is not easily expelled
- does not interfere with urination or defecation
- does not cause vaginal irritation.

The presence or absence of a cervix or uterus does not affect pessary choice.

Most experts agree that the process for fitting the right size pessary is one of trial and error. As with fitting a contraceptive diaphragm, the clinician should perform a manual examination to estimate the integrity and width of the perineum and the depth of the vagina to roughly approximate the pessary size that might best fit. Using a set of "fitting pessaries," a pessary of the estimated size should be placed into the vagina and the fit evaluated as to whether the device is too big, too small, or appropriate. If the pessary is easily expelled, larger sizes should be tried until the pessary remains in place or the patient is uncomfortable. Once the pessary is in place, the clinician should be able to run his or her finger around the entire pessary; if this is not possible, the pessary is too tight. In addition, the pessary should remain more than one finger breadth above the introitus when the patient is standing or bearing down.

Since many patients who require a pessary are elderly, their perineal skin and

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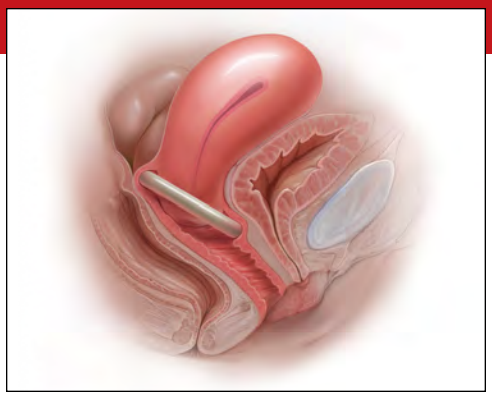

vaginal mucosa may be atrophic and fragile. Inserting a pessary can be uncomfortable and can cause abrasions or tears. Successfully fitting a pessary may require extra care under these circumstances. The following steps may help alleviate these difficulties:

- Explain the fitting process to the patient in detail.
- Employ lubrication liberally.
- Enlarge the introitus by applying gentle digital pressure on the posterior fourchette.
- Apply 2% lidocaine ointment several minutes prior to pessary fitting to help decrease patient discomfort.
- Treat the patient for several weeks with vaginal estrogen cream before attempting to fit a pessary if severe vulvovaginal atrophy is present.

Once the type and size of the pessary are selected and a pessary is inserted, evaluate the patient with the pessary in place. Assess for the following:

Discomfort. Ask the patient if she feels discomfort with the pessary in position. A patient with a properly fitting pessary should not feel that it is in place. If she does feel discomfort initially, the discomfort will only increase with time and the issue should be addressed at that time.

Expulsion. Test to make certain that the pessary is not easily expelled from the vagina. Have the patient walk, cough, squat, and even jump if possible.

Urination. Have the patient urinate with the pessary in place. This tests for her ability to void while wearing the pessary and shows whether the contraction of pelvic muscles during voiding results in expulsion of the pessary. (Experience shows that it is best to do this with a plastic "hat" over the toilet so that if the pessary is expelled, it does not drop into the bowl.)

Re-examination. After these provocative tests, examine the patient again to ensure that the pessary has not slid out of place.

Depending on whether or not your office stocks pessaries, at this point the patient is either given the correct type and size of pessary or it is ordered for her. If the former, the patient should try placing it herself; if she is unable to, the clinician should place it for her. In either event, its position should be checked. If the pessary has to be ordered, the patient must schedule an appointment to return for pessary insertion.

Whether the pessary is supplied by the office or ordered, instruct the patient on how to insert and remove the pessary, how frequently to remove it for cleansing (see below), and signs to watch for, such as vaginal bleeding, inability to void or defecate, or pelvic pain.

It is advisable to schedule a subsequent visit for 2 to 3 weeks after initial pessary placement to assess how the patient is doing and to address any issues that have developed.

Special circumstances

It is safe for a patient with a pessary in place to undergo magnetic resonance imaging.[1] Patients should be informed, however, that full body scans, such as at airports, will detect pessaries. Patients may need to obtain a physician's note to document that the pessary is a medical device.

Finally, several factors may prevent successful pessary fitting. These include prior pelvic surgery, obesity, short vaginal length (less than 6–7 cm), and a vaginal introitus width of greater than 4 finger breadths.

FAST TRACK

Evaluate the patient with the pessary in place for discomfort, expulsion, and urination, and then re-examine to ensure that the pessary has not slid out of place

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ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

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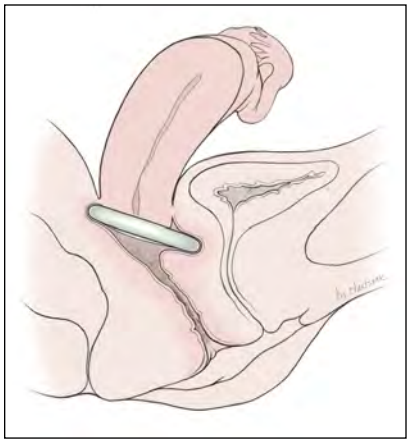
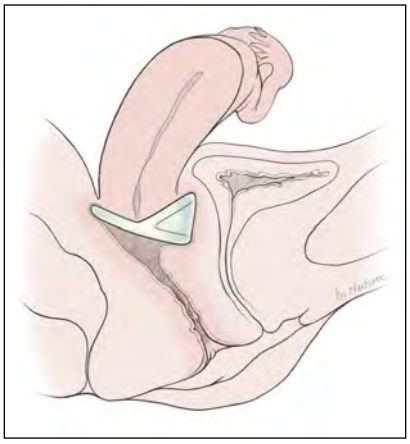
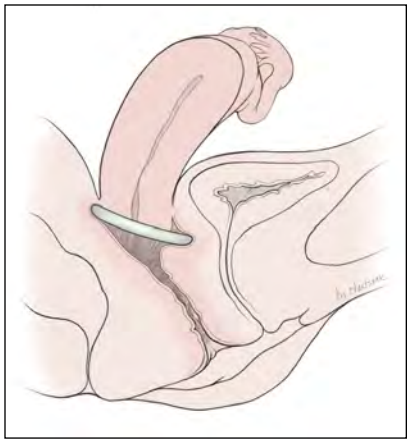
Ring pessary



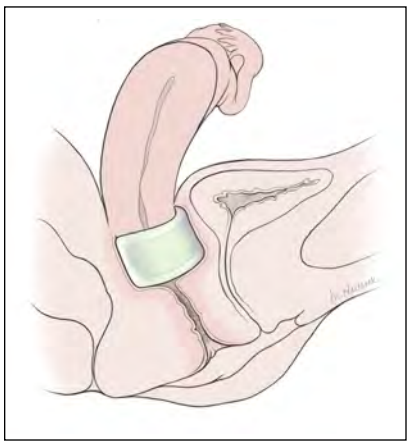
Marland pessary



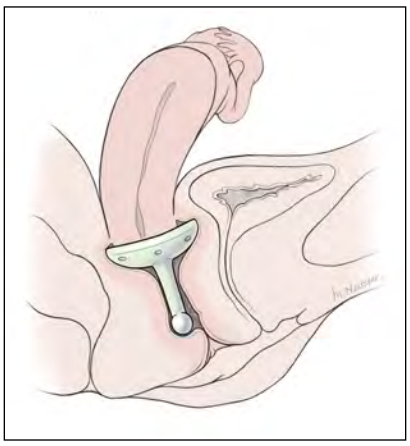
Shaatz pessary



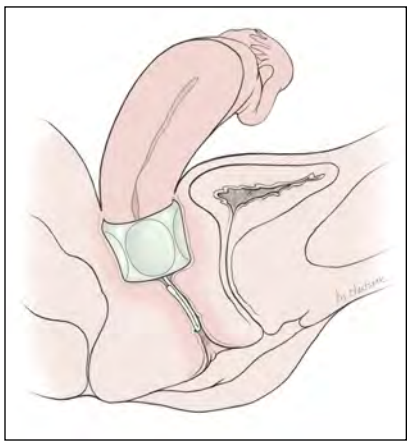
Gehrung pessary



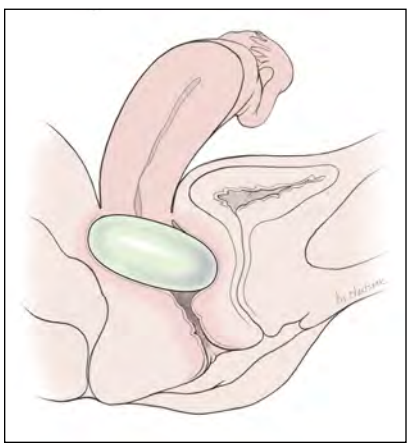
Gellhorn pessary



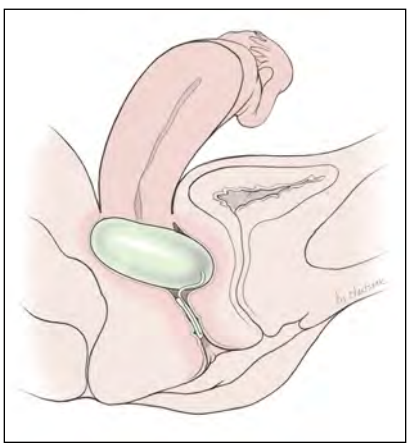
Cube pessary



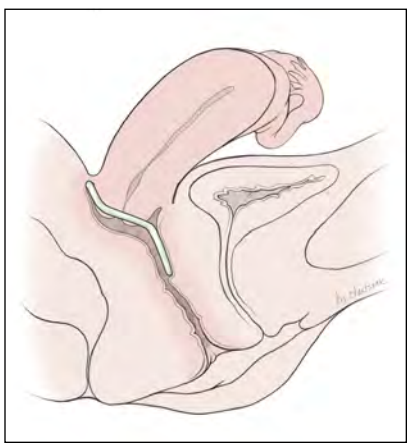
Donut pessary



Inflatable pessary



Lever pessary



ILLUSTRATIONS: MARCIA HARTSOCK FOR OBG MANAGEMENT

Necessary pessary aftercare

Once a pessary is in place and the patient is comfortable with it, the only maintenance necessary is the pessary's intermittent removal for cleansing and for evaluation of the vaginal mucosa for erosion and ulcerations. How frequently this should be done varies based on the type of pessary, the amount of discharge that a woman produces, whether or not an odor develops after prolonged wearing of the pessary, and whether or not the patient's vaginal mucosa has been abraded.

The question of timing for pessary cleaning

Although there are many opinions about how often pessaries should be removed and cleaned, no data in the literature support any specific interval. Pessaries that are easily removed by women themselves can be cleaned as frequently as desired, often on a weekly basis. The patient simply removes the pessary, washes it with soap and water, and reinserts it. For pessaries that are difficult to remove (such as the Gellhorn, cube, or donut) or for women who are physically unable to remove their own ring pessary, the clinician should remove and clean the pessary in the office every 3 to 6 months. It has been shown that there is no difference in complications from pessary use with either of these intervals.[2]

Prior to any vaginal surgical procedure, patients must be instructed to remove their pessary 10 to 14 days beforehand so that the surgeon can see the full extent of prolapse when making decisions about reconstruction and so that any vaginal mucosal erosions or abrasions have time to heal.

Office visits for follow-up care

The pessary "cleaning visit" has several goals, including to:

- see if the pessary is meeting the patient's needs in terms of resolving symptoms of prolapse and/or restoring urinary continence
- discuss with the patient any problems she may be having, such as pelvic discomfort or pressure, difficulty voiding or defecating, excessive vaginal discharge, or vaginal odor
- check for vaginal mucosal erosion or ulceration; such vaginal lesions often can be prevented by the prophylactic use of either estrogen vaginal cream twice weekly or the continuous use of an estradiol vaginal ring in addition to the pessary
- evaluate the condition of the pessary itself and clean it with soap and water.

Potential complications of pessary use

The most common complications experienced by pessary users are:

Odor or excessive discharge. Bacterial vaginosis (BV) occurs more frequently in women who use pessaries. The symptoms of BV can be minimized—but unfortunately not totally eliminated—by the prophylactic use of antiseptic vaginal creams or gels, such as metronidazole, clindamycin, Trimo-San (oxyquinoline sulfate and sodium lauryl sulfate), and others. Inserting the gel vaginally once a week can significantly reduce discharge and odor.[3]

Vaginal mucosal erosion and ulceration. These are treated by removing the pessary for 2 weeks during which time estrogen cream is applied daily or an estradiol vaginal ring is put in place. If no resolution occurs after 2 weeks, the nonhealing vaginal mucosa should be biopsied.

Pressure on the rectum or bladder. If the pessary causes significant discomfort or interferes with voiding function, then either a different size or a different type pessary should be tried

Patients may discontinue pessary use for a variety of reasons. Among these are:

- discomfort
- inadequate improvement of POP or incontinence symptoms
- expulsion of the pessary during daily activities
- the patient's desire for surgery instead
- worsening of urine leakage
- difficulty inserting or removing the pessary
- damage to the vaginal mucosa
- pain during removal of the pessary in the office.

FAST TRACK

For difficult-to-remove pessaries or for women physically unable to remove their own ring pessary, the clinician should remove and clean the pessary in the office every 3 to 6 months

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TABLE 1 Percentage of women with relief of POP symptoms with pessary use[4-13]

Study	No. of women	Outcome	Percentage
Wu, 1997[4]	81	Continued pessary use 12 months	66
Bai, 2005[5]	104	"Satisfied" with pessary use	70
Clemons, 2004[6]	72	"Satisfaction" after pessary use for 2 months	92
Hanson, 2006[7]	661	Relief of POP symptoms	83
Fernando, 2006[8]	97	Success maintaining pessary for 4 months	48
Cundiff, 2007[9]	134	Relief of symptoms of protrusion and voiding dysfunction at 6 months	57
Komesu, 2007[10]	64	Continued use 6–12 months	56
Yang, 2018[11]	162	"Satisfied" after pessary use for 1 year	79
Mao, 2018[12]	142	Successful use of pessary 17 months	69
Duenas, 2018[13]	94	Continuous use, average 27 months	80.8

Abbreviation: POP, pelvic organ prolapse.

TABLE 2 Percentage of women with relief of SUI symptoms with pessary use[6,8,14-17]

Study	No. of women	Outcome	Percentage
Clemons, 2004[6]	73	SUI improvement after 2 months	45
Farrell, 2004[14]	97	Complete or partial decrease in SUI symptoms at 11 months	61
Donnelly, 2004[15]	101	SUI improvement after 6 months	50
Fernando, 2006[8]	97	SUI improvement after 4 months	77
Richter, 2010[16]	149	SUI improvement after 3 months	40
Ding, 2016[17]	31	SUI improvement after 3 months	58

Abbreviation: SUI, stress urinary incontinence.

Pessary effectiveness for POP and SUI symptoms

As might be expected with a device that is available in so many forms and is used to treat varied types of POP and SUI, the data concerning the success rates of pessary use vary considerably. These rates depend on the definition of success, that is, complete or partial control of prolapse and/or incontinence; which devices are being evaluated; and the nature and severity of the POP and/or SUI being treated.

That being said, a review of the literature reveals that the rates of prolapse symptom relief vary from 48% to 92% (**TABLE 1**).[4-13]

As for success in relieving symptoms of incontinence, studies show improvements in from 40% to 77% of patients (**TABLE 2**).[6,8,14-17]

In addition, some studies show a 50% improvement in bowel symptoms (urgency, obstruction, and anal incontinence) with the use of a pessary.[9,18]

How pessaries compare with surgery

While surgery has the advantage of being a one-time fix with a very high rate of initial success in correcting both POP and incontinence, surgery also has potential drawbacks:

- It is an invasive procedure with the discomfort and risk of complications any surgery entails.
- There is a relatively high rate of prolapse recurrence.
- It exposes the patient to the possibility of mesh erosion if mesh is employed either for POP support or incontinence treatment.

Pessaries, on the other hand, are inexpensive, nonsurgical, removable, and allow for immediate correction of symptoms. Moreover, if the pessary is tried and is found to be unsatisfactory, surgery always can be performed subsequently.

Drawbacks of pessary treatment compared with surgery include the:

- ongoing need to wear an artificial internal device
- need for intermittent pessary removal and cleansing
- inability to have sexual intercourse with certain kinds of pessaries in place
- possible accumulation of vaginal discharge and odor.

Sexual activity and pessaries

Studies by Fernando, Meriwether, and Kuhn concur that for a substantial number of pessary users who are sexually active, both frequency and satisfaction with sexual intercourse are increased.[8,19,20] Kuhn further showed that desire, orgasm, and lubrication improved with the use of pessaries.[20] While some types of pessaries do require removal for intercourse, Clemons reported that issues involving sexual activity are not associated with pessary discontinuation.[21]

Using a pessary to predict a surgical outcome

Because a pessary elevates the pelvic organs, supports the vaginal walls, and lifts the bladder and urethra into a position that simulates the results of surgical repair, trial placement of a pessary can be used as a fairly accurate predictive tool to model what pelvic support and continence status will be after a proposed surgical procedure.[22,23] This is especially important because a significant number of patients with POP will have their occult stress incontinence unmasked following a reparative procedure.[24] A brief pessary trial prior to surgery, therefore, can be a useful tool for both patient and surgeon.

Pessaries for prevention of preterm labor

Almost 1 in 10 births in the United States occurs before 37 completed weeks of gestation.[25] Obstetricians have long thought that in women at risk for preterm delivery, the use of a pessary might help reduce the pressure of the growing uterus on the cervix and thus help prevent premature cervical dilation. It also has been thought that use of a pessary would be a safer and less invasive alternative to cervical cerclage. Many studies have evaluated the use of pessaries for the prevention of preterm labor with a mixture of positive (**TABLE 3**, page 26)[26-29] and negative results (**TABLE 4**, page 26).[30-33]

From these data, it is reasonable to conclude that:

- The final answer concerning the effectiveness or lack thereof of pessary use in preventing preterm delivery is not yet in.
- Any advantage there might be to using pessaries to prevent preterm delivery cannot be too significant if multiple studies show as many negative outcomes as positive ones.

Pessary effectiveness in defecatory disorders

Vaginal birth has the potential to create multiple anatomic injuries in the anus, lower pelvis, and perineum that can affect defecation and bowel control. Tears of the anal sphincter, whether obvious or occult, may heal incompletely or be repaired inadequately.[34] Nerve innervation of the perianal and perineal areas can be interrupted or damaged by stretching, tearing, or prolonged compression. Of healthy parous adult women, 7% to 16% admit incontinence of gas or feces.[35,36]

In addition, when a rectocele is present,

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Trial placement of a pessary can be used as a fairly accurate predictive tool to model what pelvic support and continence status will be after a proposed surgical procedure

TABLE 3 Effectiveness of pessaries to prevent preterm labor[26-29]

Study	No. of women	Effectiveness
Goya, 2012[26]	385	4.5-fold lower rate of preterm delivery with pessary use (6%) vs expectant management (27%)
Di Tommaso, 2016[27]	40	30% less likely to deliver before 36 weeks with use of pessary in twins, cervical length <2.5 cm between 21 and 31 weeks
Saccone, 2017[28]	300	2-fold lower preterm delivery rate with pessary use and progesterone (7.3%) vs progesterone alone (15%)
Perez-Lopez, 2019[29]	1,612	Reduced the rate of spontaneous preterm birth both at 34 and at 37 weeks (risk ratio, 0.33)

TABLE 4 Lack of effectiveness of pessaries to prevent preterm labor[30-33]

Study	No. of women	Effectiveness
Hui, 2013[30]	108	Higher rate of preterm delivery in the pessary group (9.4%) than in the control group (5.5%)
Nicolaides, 2016[31]	931	No difference in preventing preterm labor: use of the pessary (12%) vs expectant management (10.8%)
Saccone, 2017[32]	1,420	Use of a vaginal pessary did not reduce the rate of spontaneous preterm delivery or improve perinatal outcomes
Conde-Agudelo, 2020[33]	4,687 (12 studies)	No significant differences between the pessary and no-pessary groups in the risk of spontaneous preterm birth <34 weeks

TABLE 5 Pessary CPT codes[38]

Diagnosis	CPT code	Notes
Pessary fitting	57160	Fitting and insertion of pessary
Pessary device	A4562	
Evaluation, management–Existing patient	99211-99215	Depending on complexity and length of visit
Evaluation, management–New patient	99201-99205	Depending on complexity and length of visit
Return visit for follow-up/cleaning	99213	E & M only

Abbreviations: CPT, Current Procedural Terminology; E & M, evaluation and management.

stool in the lower rectum may cause bulging of the anterior rectal wall into the vagina, preventing stool from passing out of the anus. This sometimes requires women to digitally press their posterior vaginal walls during defecation to evacuate stool successfully. The question thus arises as to whether or not pessary placement and subsequent relief of rectoceles might facilitate bowel movements and decrease or eliminate defecatory dysfunction.

As with the issue of pessary use for prevention of preterm delivery, the answer is mixed. For instance, while Brazell[18] showed that there was an overall improvement in bowel symptoms in pessary users, a study by Komesu[10] did not demonstrate improvement.

There is, however, a relatively new device specifically designed to control defecatory problems: the vaginal bowel control system (Eclipse; Pelvalon). The silicon device is placed intravaginally as one does a pessary. After insertion, it is inflated via a valve and syringe. It works by putting pressure on and reversibly closing the lower rectum, thus blocking the uncontrolled passage of stool and gas. It can be worn continuously or intermittently, but it does need to be deflated for normal bowel movements. One trial of this device demonstrated a 50% reduction in incontinence episodes with a patient satisfaction rate of 84% at 3 months.[37] This device may well prove to be a valuable nonsurgical approach to the treatment of fecal incontinence. Unfortunately, the device is relatively expensive and usually is not covered by insurance as third-party payers do not consider it to be a pessary (which generally is covered).

Practice management particulars

Useful information on Current Procedural Terminology codes for pessaries, diagnostic codes, and the cost of various pessaries is provided in **TABLE 5**,[38] **TABLE 6**,[39] and **TABLE 7**.[40-42]

TABLE 6 **Diagnostic codes supporting medical necessity for pessary**[39]

Diagnosis	CPT codes
Complete uterovaginal prolapse	N81.3
Cystocele	N81.10
Rectocele	N81.6
Stress incontinence	N39.3
Enterocele	N81.5
Other female genital prolapse	N81.9

Abbreviation: CPT, Current Procedural Terminology.

TABLE 7 **Cost of various pessaries**[40-42]

Type of pessary	Source	Cost
Ring	Milex	$131
Ring	CooperSurgical	$123
Ring	Online	$30
Inflatable	Milex	$129
Cube	Milex	$116
Cube	CooperSurgical	$166
Cube	Online	$45–$60
Gellhorn	CooperSurgical/Milex	$152
Gellhorn	Online	$30–$55

A contemporary device used since antiquity

Pessaries, considered "old-fashioned" by many gynecologists, are actually a very cost-effective and useful tool for the correction of POP and SUI. It behooves all who provide medical care to women to be familiar with them, to know when they might be useful, and to know how to fit and prescribe them. ●

References

1. O'Dell K, Atnip S. Pessary care: follow up and management of complications. *Urol Nurs.* 2012;32:126-136, 145.
2. Gorti M, Hudelist G, Simons A. Evaluation of vaginal pessary management: a UK-based survey. *J Obstet Gynaecol.* 2009;29:129-131.
3. Meriwether KV, Rogers RG, Craig E, et al. The effect of hydroxyquinoline-based gel on pessary-associated bacterial vaginosis: a multicenter randomized controlled trial. *Am J Obstet Gynecol.* 2015;213:729.e1-9.
4. Wu V, Farrell SA, Baskett TF, et al. A simplified protocol for pessary management. *Obstet Gynecol.* 1997;90:990-994.
5. Bai SW, Yoon BS, Kwon JY, et al. Survey of the characteristics and satisfaction degree of the patients using a pessary. *Int Urogynecol J Pelvic Floor Dysfunct.* 2005;16:182-186.
6. Clemons JL, Aguilar VC, Tillinghast TA, et al. Patient satisfaction and changes in prolapse and urinary symptoms in women who were fitted successfully with a pessary for pelvic organ prolapse. *Am J Obstet Gynecol.* 2004;190:1025-1029.
7. Hanson LM, Schulz JA, Flood CG, et al. Vaginal pessaries in managing women with pelvic organ prolapse and urinary incontinence: patient characteristics and factors contributing to success. *Int Urogynecol J Pelvic Floor Dysfunct.* 2006;17:155-159.
8. Fernando RJ, Thakar R, Sultan AH, et al. Effect of vaginal pessaries on symptoms associated with pelvic organ prolapse. *Obstet Gynecol.* 2006;108:93-99.
9. Cundiff GW, Amundsen CL, Bent AE, et al. The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries. *Am J Obstet Gynecol.* 2007;196:405.e1-405e.8.
10. Komesu YM Rogers RG, Rode MA, et al. Pelvic floor symptom changes in pessary users. *Am J Obstet Gynecol.* 2007;197:620.e1-6.
11. Yang J, Han J, Zhu F, et al. Ring and Gellhorn pessaries used in

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Is it safe to be pregnant during the COVID-19 pandemic?

Expert answers to 8 of your most pressing questions about coronavirus disease 2019 and pregnancy, including vaccination

Malavika Prabhu, MD

IN THIS ARTICLE

Pregnant women, or women considering pregnancy, want to know—is pregnancy safe in the midst of the coronavirus disease 2019 (COVID-19) pandemic? In this article, I tackle common questions facing reproductive-aged or pregnant women and their providers.

1. What are the risks of COVID-19 in pregnancy?

A large, national prospective cohort study of outpatient pregnant and recently postpartum women with the diagnosis of suspected or confirmed COVID-19 demonstrated that many affected women have mild illnesses, with typical symptoms including cough, sore throat, body aches, fever, and headache.[1] Although symptoms were most common within the first 3 weeks of presentation, approximately 25% of women had a protracted course of symptoms (8 or more weeks). As this cohort disproportionately enrolled outpatients, it is important to note that many women had mild illnesses, which is the most likely course of infection in otherwise healthy, young women.

Data on the impact of COVID-19 on rates of miscarriage and birth defects are limited, yet the published reports are reassuring, with no increased risks of miscarriage, and no clear signal for birth defects.[2]

In a prospective cohort study across 3 New York City institutions when universal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing was recommended upon admission for delivery, approximately 80% of women who were positive were asymptomatic.[3] Maternal outcomes generally were reassuring, with no patients experiencing severe or critical illness. There were no differences in preterm delivery rates by SARS-CoV-2 status, but the rate of cesarean delivery was higher among women with COVID-19, for unclear reasons. Most notably, the rate of postpartum complications was 13% among women with COVID-19, versus 2.5% among women without COVID-19. These complications included readmission for worsening COVID-19, postpartum hypoxia, and postpartum fever.

A recent prospective cohort study from 1 institution in Texas similarly demonstrated favorable maternal outcomes with COVID-19, with 95% of women with asymptomatic or mild illness, and no differences in adverse pregnancy outcomes between COVID-19–positive and COVID-19–negative women, including cesarean delivery rate.[4]

Finally, certain characteristics increase the risk of COVID-19 among pregnant

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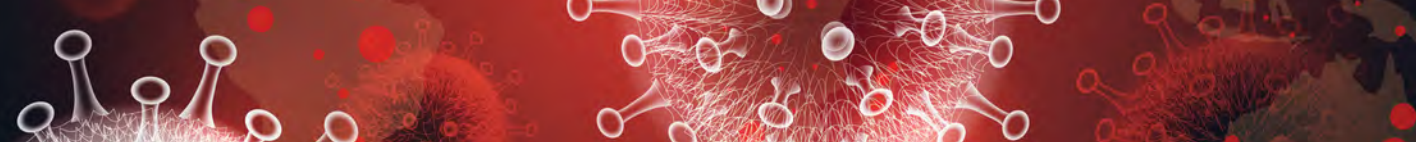

women and nonpregnant individuals alike. In a nationwide prospective cohort from the United Kingdom, medical comorbidities including obesity, diabetes (gestational or pregestational), hypertension, as well as Black or other minority ethnicities are associated with COVID-19.[5] This is particularly notable given universal health insurance in the United Kingdom. Other data have also confirmed that women with comorbidities, women of Black or Hispanic ethnicity, and women with lower socioeconomic status, are at increased risk of COVID-19.[3,6,7]

2. Is COVID-19 worse in pregnancy?

Given the well-documented risks of COVID-19 outside of pregnancy, is COVID-19 worse in a pregnant woman than in a nonpregnant woman? The most recent guidance from the Centers for Disease Control and Prevention (CDC) from November 2020 suggests that pregnant women are at increased risk for severe illness.[8] However, it is important to understand the design of this study in order to appreciate its implications. Laboratory confirmed SARS-CoV-2 in the United States is systematically reported to the CDC. Among women aged 15–44 years with such confirmation, data on pregnancy status were available for 35.5%, almost 90% of whom were symptomatic. Within this cohort of largely symptomatic pregnant women, risks of intensive care unit (ICU) admission, invasive ventilation, and use of extracorporeal membrane oxygenation (ECMO) were approximately 2 to 3 times higher for pregnant women than for nonpregnant women. The absolute risks, however, were low. The risk of ICU admission for symptomatic pregnant women was approximately 1%; the risk of invasive ventilation, 0.3%; and the risk of ECMO, 0.1%.

Moreover, the lack of uniform data capture on pregnancy status for all women ages 15–44 years may skew the population with known pregnancy status to be sicker and, thus, may bias the results toward increased risks. Nevertheless, there is consistency in several publications with different data

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sources, all of which suggest pregnancy is an independent risk factor for increased severity of COVID-19.[9-11] Additionally, women with medical comorbidities (such as pregestational or gestational diabetes or obesity) are more likely to have severe COVID-19.

3. What are newborn outcomes if COVID-19 is diagnosed during pregnancy?

Two large cohorts of newborns, disproportionately term infants, from the first wave of the pandemic in New York City, have reassuring news. In one cohort of 101 infants born at 2 New York City institutions to SARS-CoV-2–positive mothers, 2 neonates were diagnosed with SARS-CoV-2 during the immediate postnatal period.[12] Neither infant demonstrated clinical COVID-19. In another cohort of 120 infants born at 3 other New York City institutions to SARS-CoV-2–positive mothers and tested systematically within 24 hours of life, 5–7 days of life, and 14 days of life, there were no neonates who tested positive for SARS-CoV-2 at the initial time point. Among the 79 infants who had testing at 5–7 days of life and the 72 tested at 14 days of life, there were no infants positive for SARS-CoV-2.[13] It is important to note that case reports and

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Overwhelming evidence suggests that the risk of vertical transmission of SARS-CoV-2 is very low

small case series have demonstrated some convincing evidence of vertical transmission. However, the overwhelming evidence suggests this risk is very low.

4. What is a reasonable outpatient setting–approach to managing COVID-19 in a pregnant woman?

Women should be counseled to quarantine for 10 to 14 days from symptom onset or, if asymptomatic, from positive polymerase chain reaction (PCR) test. Warning signs of worsening COVID-19 disease should be reviewed. Serial telemedicine follow-up for 10 to 14 days is recommended to ensure clinical stability and continued management as an outpatient. A home pulse oximeter is also recommended. Women should be advised to check their oxygen saturation daily and to call if oxygen saturation becomes less than 93%. Supportive care is recommended.

If delay in obstetric care may result in adverse pregnancy outcomes (for instance, postponing indicated fetal surveillance), obstetric care should be delivered, with appropriate personal protective equipment for health care workers and minimization of exposure of other pregnant women to the infected patient. Appointments should be scheduled at the end of the day.

During influenza season, women should receive empiric oseltamivir treatment (75 mg twice a day) per CDC guidelines for symptoms that may also be consistent with influenza, regardless of testing.

Prophylactic anticoagulation is not indicated for pregnant antepartum women who do not require inpatient care.

If inpatient care is required, management is individualized.

The approach to prenatal care after resolution of COVID-19 is not evidence-based. At my institution, all patients have a detailed mid-trimester anatomic evaluation, but if this is not routine, a detailed anatomic ultrasound (Current Procedural Terminology code 76811) may be considered. Additionally, for women with COVID-19 we perform one third-trimester growth ultrasound to screen for fetal growth restriction, on the basis of several placental studies demonstrating clots on the fetal or maternal side of the placenta.[3,14] Routine antenatal testing in the absence of growth restriction, or other comorbid conditions for which testing occurs, is not recommended.

5. What if asymptomatic or mild COVID-19 is diagnosed at the time of delivery? What is reasonable management?

Asymptomatic or mildly symptomatic COVID-19 should not alter obstetric management, beyond appropriate use of personal protective equipment. Delayed cord clamping is also reasonable, if there are no other contraindications, as there is no documented harm associated with this practice among women with COVID-19.

Women with COVID-19 may be at higher risk for venous thromboembolic events in the postpartum period. At my institution, prophylactic postpartum anticoagulation is recommended for 2 weeks after vaginal delivery, and 6 weeks after cesarean delivery.

During the postpartum hospitalization, given reassuring data about vertical transmission and postnatal horizontal transmission risks, babies may room in with mothers in a single private room, if rooming-in is the current standard of care—as long as the mother and newborn do not require higher levels of care. Mothers should wear a mask and use hand hygiene when in contact with the baby. Skin-to-skin and breastfeeding or infant feeding of breast milk are appropriate practices to continue. There is no evidence to suggest that transmission of COVID-19 can occur via breastmilk; however, given the close contact inherent in breastfeeding, transmission through direct contact or maternal respiratory droplets is possible, and thus maternal use of masks and hand hygiene is recommended. When not feeding, the infant should be 6 feet away, and if possible, in an isolette.

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As postpartum VTE is a risk for women with COVID-19, prophylactic anticoagulation is recommended for 2 weeks after vaginal and 6 weeks after cesarean delivery

6. When can individuals with COVID-19 discontinue transmission precautions or "home quarantine"?

For women with mildly symptomatic COVID-19 and without immunocompromise, home quarantine can be discontinued 10 days after onset of symptoms as long as there has been symptom improvement and no fever for at least 24 hours without the use of antipyretics. For immunocompetent women with incidentally diagnosed asymptomatic COVID-19, home quarantine can be discontinued 10 days after the positive test was obtained. Pregnancy in and of itself is not an immunocompromising condition.[15,16]

For women with severe or critical COVID-19, who were hospitalized due to their clinical status, home quarantine can be discontinued when at least 10 days, and up to 20 days, after onset of symptoms *and* with symptom improvement *and* with no fever for at least 24 hours, without the use of antipyretics. Local hospital infection control experts may be able to guide the recommended practice for your site better, based on local information.[15,16]

Repeating a PCR test to discontinue home quarantine is not recommended in most circumstances, as individuals may have prolonged shedding of noninfectious particles in their nasopharynx. Immunocompromise may be one exception to this general guidance, but consultation with local hospital infection control experts will help guide management.[15,16]

7. Should women get pregnant during the COVID-19 pandemic?

Every pandemic has its own set of implications for the health of the mother, fetus, or both, and COVID-19 is no exception. While there are risks, described above, to mother and fetus, these risks are not so catastrophic as to strongly and directively recommend a patient not become pregnant.[17] Moreover, the last several months of the pandemic have demonstrated that consistent mask usage, social distancing, and hand hygiene, are effective methods of preventing the acquisition of COVID-19. All of these risk-reducing strategies are available to pregnant women. Finally, accessing care during a pandemic in a hospital setting does not also pose a risk for acquisition of SARS-CoV-2.[18]

8. Is the COVID-19 vaccine safe for pregnant or postpartum/lactating women?

On December 11, 2020, the US Food and Drug Administration (FDA) issued emergency use authorization (EUA) for the Pfizer-BioNtech mRNA vaccine (BNT 162b2) against COVID-19, for individuals aged 16 and older as a 2-dose series given 21 days apart. Among the more than 40,000 individuals in the trial that led to this EUA, vaccine efficacy was 95%.[19] Adverse effects included fatigue and headache most commonly, with 16% of vaccine recipients experiencing fever after the second dose. Follow-up regarding safety is planned for 2 years by the manufacturer, in addition to safety monitoring by pre-existing national systems.

On December 18, 2020, the FDA announced EUA for Moderna's mRNA-based vaccine, mRNA-1273, in men and women aged 18 and older. This is a 2-dose series given 28 days apart. The vaccine efficacy has been reported at 94.5%, with the most common adverse effects being injection site pain, tiredness, headache, muscle pain, chills, joint pain, swollen lymph nodes in the same arm as the injection, nausea and vomiting, and fever.[20,21] The phase 3 trial is ongoing.

Despite the speed with which these effective vaccines were developed, it is important to note that all regulatory and safety steps mandated for the development of any vaccine were met for these two, as well as for other COVID-19 vaccinations that will similarly receive EUA from the FDA.

In the EUA for BNT 162b2, the specific language regarding pregnant and lactating women recommends that patients and

FAST TRACK

Two mRNA vaccines are currently authorized for EUA use, with efficacy rates reported as 95% and 94.5% with each 2-dose series

providers have an individualized conversation about vaccination. In the data presented to the FDA for the Pfizer-BioNtech mRNA vaccine, a limited number of pregnant women received either the vaccine (12 women) or placebo (11 women), with no long-term follow-up data available to characterize either maternal or fetal benefits and risks. The mechanism of action of an mRNA vaccine is to induce the cytoplasmic machinery within cells to create the coronavirus spike protein, which then allows the body's immune system to create antibodies against this protein and confer protection accordingly. While the above mechanism is not theorized to result in different outcomes or different efficacy, the safety for the pregnant woman and fetus are unknown. It is not believed that vaccination during lactation would cause any adverse outcomes to a neonate, and lactating women do not need to interrupt or discontinue breast milk production in order to receive the vaccine.

The American College of Obstetricians and Gynecologists (ACOG) released a Practice Advisory on December 13, 2020, regarding their recommendations.[22] ACOG recommends that vaccines against COVID-19 not be withheld from pregnant or lactating women, if they might otherwise meet criteria for and have access to vaccination. Currently, the CDC's Advisory Committee on Immunization Practices (ACIP) stated that health care workers and long-term care facility residents represent priority groups to vaccinate in the initial phases of vaccination, given limitations in supply.[23] This recommendation is likely to be updated frequently as additional vaccines become available. Shared decision-making between patient and provider may help the patient to make the best decision for herself, but provider input is not required prior to a pregnant woman being vaccinated.

Additional animal data evaluating adverse effects on the reproductive system from developmental and reproductive toxicity (DART) studies for both mRNA vaccines should be available in the coming weeks, which may aid in the counseling of reproductive-aged women.

Vaccine trials to specifically enroll pregnant women are set to begin in early 2021, and more data will certainly inform the conversation between patient and provider regarding risks and benefits.

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ACOG recommends that COVID-19 vaccines not be withheld from pregnant or lactating women. Trials specific to pregnant women will begin in early 2021 and will offer more information in this patient group.

Conclusions

While the absolute risks of COVID-19 to mothers, fetuses, and neonates is low, pregnancy is a risk factor for severe disease. Many pregnant women with COVID-19 can be safely followed as outpatients via telemedicine, and supportive care is recommended. Inpatient care should be individualized. Pregnancy during the COVID-19 pandemic should be not be absolutely discouraged; instead, a conversation about risk mitigation should be undertaken. The COVID-19 vaccine is available to pregnant and lactating women, and the decision to choose vaccination in pregnancy is in the purview of the patient, in consultation with her physician. ●

References

1. Afshar Y, Gaw SL, Flaherman VJ, et al. Clinical presentation of coronavirus disease 2019 (COVID-19) in pregnant and recently pregnant people. *Obstet Gynecol.* 2020;128:1117-1125.
2. Cosma S, Carosso AR, Cusato J, et al. Coronavirus disease 2019 and first-trimester spontaneous abortion: a case-control study of 225 pregnant patients. *Am J Obstet Gynecol.* 2020;S0002-9378:31177-7. doi: 10.1016/j.ajog.2020.10.005.
3. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. *BJOG.* 2020;127:1548-1556.
4. Adhikari E, Moreno W, Zofkie AC, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. *JAMA Netw Open.* 2020;3:e2029256.
5. Knight M, Bunch K, Vousden B, et al; UK Obstetric Suveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ.* 2020;369:m2107.
6. Emeruwa UN, Ona S, Shaman JL, et al. Associations between built environment, neighborhood socioeconomic status, and SARS-CoV-2 infection among pregnant women in New York City. *JAMA.* 2020;324:390-392.
7. Emeruwa UN, Spiegelman J, Ona S, et al. Influence of race and ethnicity on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection rates and clinical outcomes in pregnancy. *Obstet Gynecol.* 2020;126:1040-1043.
8. Zambrano LD, Ellington S, Strid P, et al; CDC COVID-19

response pregnancy and infant linked outcomes team. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status–United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1641-1647.
9. Badr DA, Mattern J, Carlin A, et al. Are clinical outcomes worse for pregnant women at ≥20 weeks' gestation infected with coronavirus disease 2019? A multicenter case control study with propensity score matching. *Am J Obstet Gynecol*. 2020;223:764-768.
10. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical COVID-19 have increased composite morbidity compared with nonpregnant matched controls. *Am J Obstet Gynecol*. 2020;S0002-9378:31312-0.
11. Collin J, Byström E, Carnahan A, et al. Public Health Agency of Sweden's Brief Report: pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. *Acta Obstet Gynecol Scand*. 2020;99:819-822.
12. Dumitriu D, Emeruwa UN, Hanft E, et al. Outcomes of neonates born to mothers with severe acute respiratory syndrome coronavirus 2 infection at a large medical center in New York City. *JAMA Pediatr*. 2020;e204298.
13. Salvatore CM, Han JY, Acker KP, et al. Neonatal management and outcomes during the COVID-19 pandemic: an observational cohort study. *Lancet Child Adolesc Health*. 2020;4:721-727.
14. Shanes ED, Mithal LB, Otero S, et al. Placental pathology in COVID-19. *Am J Clin Path*. 2020;154:23-32.
15. Centers for Disease Control and Prevention. Duration of isolation and precautions for adults with COVID-19. Updated October 19, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcommunity%2Fstrategy-discontinue-isolation.html. Accessed December 15, 2020.
16. Centers for Disease Control and Prevention. Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings. Updated August 10, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html. Accessed December 15, 2020.
17. Rasmussen SA, Lyerly AD, Jamieson DJ. Delaying pregnancy during a public health crisis–examining public health recommendations for COVID-19 and beyond. *N Engl J Med*. 2020;383:2097-2099.
18. Reale SC, Field KG, Lumbreras-Marquez MI, et al. Association between number of in-person health care visits and SARS-CoV-2 infection in obstetrical patients. *JAMA*. 2020;324:1210-1212.
19. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT 162b2 mRNA Covid-19 vaccine. *N Engl J Med*. December 10, 2020. doi: 10.1056/NEJMoa2034577.
20. Widge AT, Rouphael NG, Jackson LA, et al. Durability of responses after SARS-CoV-2 mRNA-1273 vaccination. December 3, 2020. doi: 10.1056/NEJMc2032195.
21. US Food and Drug Administration. FDA takes additional action in fight against COVID-19 by issuing emergency use authorization for second COVID-19 vaccine. December 18, 2020. https://www.fda.gov/news-events/press-announcements/fda-takes-additional-action-fight-against-covid-19-issuing-emergency-use-authorization-second-covid. Accessed December 22, 2020.
22. American College of Obstetricians and Gynecologists. Practice advisory: vaccinating pregnancy and lactating patients against COVID-19. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19. Last updated December 21, 2020. Accessed December 21, 2020.
23. Dooling K, McClung N, Chamberland M, et al. The Advisory Committee on Immunization Practices' interim recommendation for allocating initial supplies of COVID-19 vaccine–United States, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1857-1859.

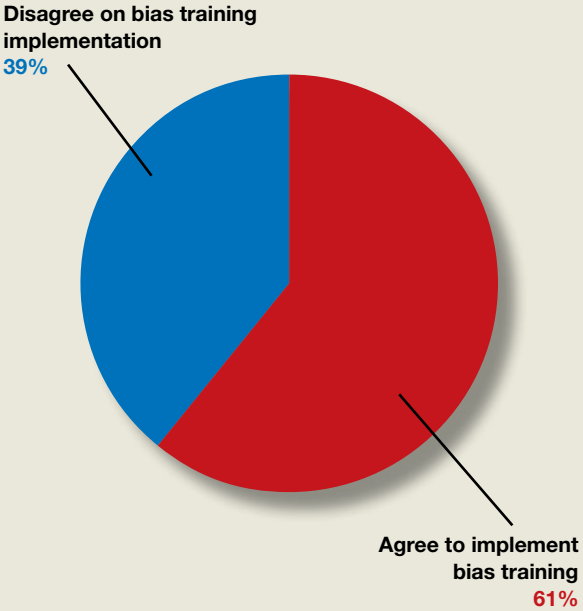
Do ObGyns agree that bias training and inclusion and diversity policies should be implemented?

In their column, "Physician leadership: Racial disparities and racism. Where do we go from here?" (August 2020), Biftu Mengesha, MD, MAS; Kavita Shah Arora, MD, MBE, MS; and Barbara Levy, MD, stated that, "The COVID-19 pandemic…has highlighted the continued poor outcomes our health and health care systems create for Black, Indigenous, and Latinx communities." They implored readers to "advocate as physicians and leaders in our settings for every policy, practice, and procedure to be scrutinized using an antiracist lens" and set out action items for doing so. OBG MANAGEMENT followed up with a poll for readers: "Should institutions implement implicit bias training and policies for inclusion and diversity to address health care inequities?"

Poll results

A total of 89 readers cast their vote:

- **61% (54 readers)** said yes
- **39% (35 readers)** said no



When ultrasonography reveals a fetal abdominal wall defect

Although these fetal defects are rare, be alert to their potential presence when early ultrasonography indicates structural abnormalities. Here, surveillance, planning, and appropriate patient counseling are reviewed.

Alexander L. Juusela, MD, MPH, and Martin Gimovsky, MD

IN THIS ARTICLE

CASE Fetal anomalies detected on ultrasonography

A 34-year-old woman (G2P1) at 19 weeks' gestation presented for fetal anatomy ultrasonography evaluation. Ultrasonography demonstrated fetal demise with fetal size less than dates, oligohydramnios, and what appeared to be a full-thickness herniation of the thoracic and abdominal contents. Due to the positioning of the fetus and the oligohydramnios, the fetus appeared to have ectopia cordis and herniated liver and bowel; the bladder was not visualized. The patient was counseled regarding the findings and the suspected diagnosis of pentalogy of Cantrell. After counseling, the patient expressed desire to bury the fetus intact according to her religious custom. She underwent a successful uterine evacuation with misoprostol administration and delivered a nonviable fetus that had a closed thoracic cage without ectopia cordis. Key findings were a very short 2-vessel umbilical cord without coiling that was tethered to the intra-abdominal organs, "pulling" the internal organs out of the abdomen, and lack of an anterior abdominal wall (**FIGURE 1**). Given these findings, a final diagnosis of body-stalk anomaly was made.

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Fetal abdominal wall defects (AWDs) encompass a wide array of congenital defects, although they all involve herniation of 1 or more intra-abdominal content through a ventral abdominal defect.[1] Overall, the estimated incidence of AWDs is approximately 6 per 10,000 births.[1] Gastroschisis and omphalocele are the most common of these defect types.[2]

The majority of AWDs can be diagnosed during the first trimester of pregnancy via ultrasonography; however, during the first trimester the physiologic midgut herniation resolves by 12 weeks of gestation. It is therefore important to repeat imaging at a later gestational age to confirm the suspicion. Furthermore, the differential diagnosis should include the relatively benign condition of umbilical hernia.

While many AWDs share similarities, they differ significantly in prognosis and management. Early detection is therefore

crucial for fetal surveillance, prenatal testing, perinatal planning, and patient counseling (**TABLE**, page 36). In this article, we outline antenatal surveillance and management of AWDs based on recommendations from the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine as well as on our experience and practice.

Gastroschisis is an increasingly prevalent AWD

Gastroschisis is a full-thickness, ventral wall defect that results in bowel evisceration; it typically occurs to the right of the umbilical cord insertion.[3] It is one of the most common AWDs and its prevalence has increased in the past few decades, from 2 to 3 cases per 10,000 live births in 1995 to as high as 6 cases per 10,000 live births in 2011.[2,4,5]

The cause of gastroschisis remains unclear. The main theory is that there is an ischemic disruption of the closure of the abdominal wall at or near the omphalomesenteric artery or the right umbilical vein.[6,7] In addition, investigators have reported an increased incidence of gastroschisis in mothers exposed to cigarette smoking and certain medications, such as pseudoephedrine, salicylates, ibuprofen, and acetaminophen.[8,9]

Making the diagnosis

Prenatal diagnosis using ultrasonography is possible at around 10 weeks of gestation. As previously mentioned, however, physiologic herniation of the midgut must be excluded by performing follow-up imaging at a later gestational age. In our practice, we typically do this at around 16 weeks of gestation.

Ultrasonographic features of gastroschisis include loops of bowel herniating through a small paraumbilical wall defect (usually 2–3 cm) floating in amniotic fluid without a covering membrane[4] (**FIGURE 2**, page 38). Direct exposure to amniotic fluid causes small bowel inflammation and fibrin deposition, leading to a thickened, echogenic appearance. Polyhydramnios and intra-abdominal bowel dilation have been associated with the presence of intestinal atresia.[10]

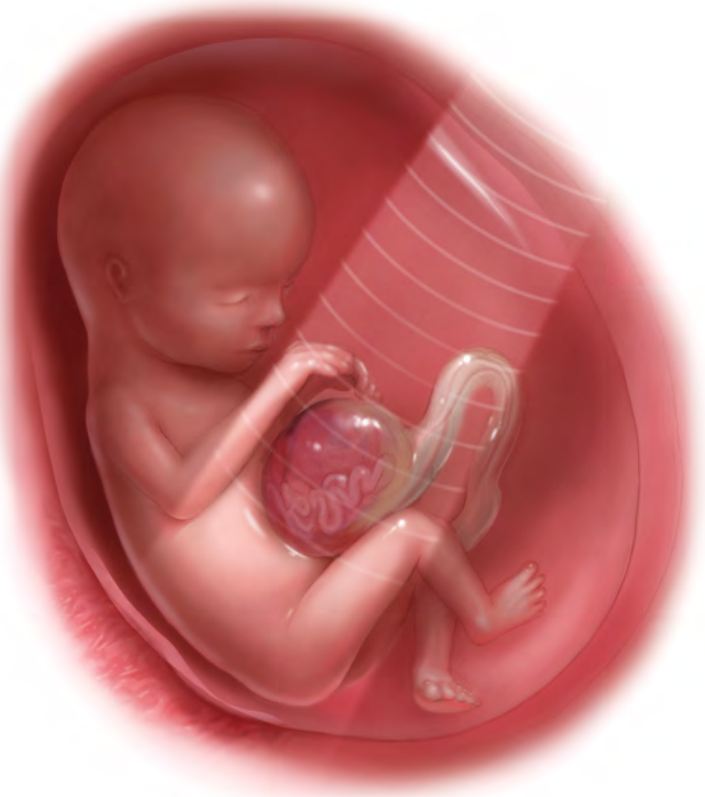
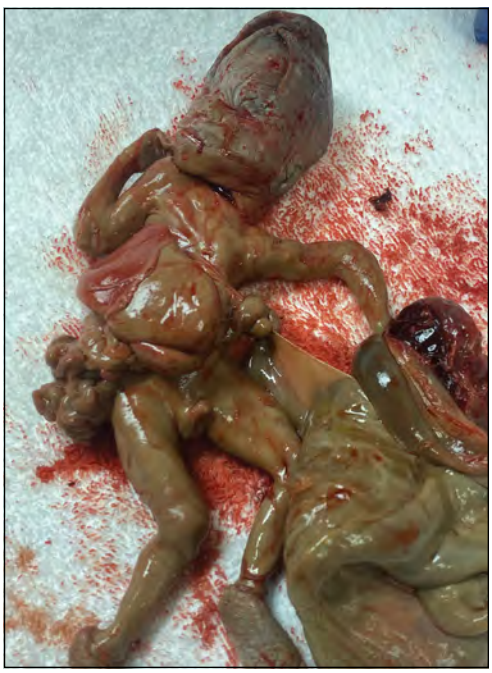


FIGURE 1 Fetus with body-stalk anomaly



This fetus had a very short 2-vessel umbilical cord without coiling tethered to the intra-abdominal organs and lacked an anterior abdominal wall. The final diagnosis was body-stalk anomaly.

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ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

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TABLE Overview of antenatal surveillance and management of fetal abdominal wall defects

Abdominal wall defect	Imaging findings	Associated structural abnormalities	Associated chromosomal abnormalities	Fetal evaluation	Delivery timing/method	Survival rate
Gastroschisis	Full thickness ventral wall defect Typically to the right of the umbilicus No membrane covering herniated contents May contain the liver	Increased incidence of IUGR (25%) Intestinal atresia (10%–15%)	Usually none	Genetic testing Fetal echocardiography Serial fetal growth ultrasonography NST/BPP weekly starting at 32 weeks	No consensus: vaginal versus cesarean delivery If significant liver involvement, some pediatric surgeons recommend cesarean delivery due to the risk of hepatic rupture	91%–94%
Omphalocele	Midline abdominal herniation through the base of the umbilical cord Covered by a membrane May contain liver (80% of cases)	Cardiac defects Gastrointestinal defects Genitourinary defects Neural tube defects Diaphragmatic defects Orofacial clefts Polyhydramnios is common Associated with IUGR	30% have chromosomal abnormalities (trisomy 13, 18, 21) Small (<5 cm) lesions without hepatic involvement are associated with a fetal aneuploidy Large (≥5 cm) liver containing lesions are associated with euploid fetuses Associated with Beckwith-Wiedemann syndrome	Genetic testing Fetal echocardiography Beckwith-Wiedemann syndrome testing Serial fetal growth ultrasonography NST/BPP weekly starting at 32 weeks	Timing: individualized expectant management until spontaneous labor, other indication for delivery, or at least 39 weeks Method: no evidence-based guidelines for term fetuses Large defects are at risk of rupture Preterm induction of labor not advised as approximately 50% neonatal mortality rate	Isolated defects 50%–90% Presence of aneuploidy and/or other anomalies is strongly associated with a poor prognosis
Body-stalk anomaly	2 of the 3: Exencephaly or encephalocele with facial clefts Large anterior abdominal wall defect Limb defects	A short or absent umbilical cord Severe kyphosis or scoliosis Oligohydramnios Increased nuchal translucency	None	Genetic testing Fetal complete anatomical evaluation	Elective termination of pregnancy often is advised Women who continue pregnancy are at increased risk of preterm labor and gestational hypertension	Nearly incompatible with life Only case reports of surviving neonates

TABLE Overview of antenatal surveillance and management of fetal abdominal wall defects *(continued)*

Abdominal wall defect	Imaging findings	Associated structural abnormalities	Associated chromosomal abnormalities	Fetal evaluation	Delivery timing/method	Survival rate
Pentalogy of Cantrell	Anterior chest wall, cardiac, pericardial, and midline abdominal defects	Abnormalities to anterior diaphragm Ectopia cordis	Majority are idiopathic Possible X-linked inheritance on Xq25-q26.1	Genetic testing Fetal echocardiography Fetal MRI	Individualized based on severity of the case Elective termination of pregnancy often is advised	Depends on the type and severity of the cardiac and extracardiac manifestations Severe ectopia cordis cases have a 5%–10% survival rate
OEIS complex	Omphalocele Exstrophy of the cloaca Imperforate anus Spinal defects	Absent bladder	None Multifactorial	Genetic testing Fetal echocardiography Fetal MRI Beckwith-Wiedemann syndrome testing Serial fetal growth ultrasonography NST/BPP weekly starting at 32 weeks	Individualized based on severity of the case	Depends on the type and severity of the defects Neonates who are candidates for surgical repair have a near 100% survival rate

Abbreviations: BPP, biophysical profile; IUGR, intrauterine growth restriction; MRI, magnetic resonance imaging; NST, nonstress testing; OEIS, omphalocele-exstrophy-imperforate anus-spinal defects.

Management

There is no expert consensus regarding optimal prenatal management of gastroschisis.[11-17] Prenatal care, patient counseling, and delivery planning should be individualized based on the defect and should be determined in a multidisciplinary discussion with specialists in maternal-fetal medicine, neonatology, and pediatric surgery, as necessary. In our practice, if the gastroschisis is isolated and uncomplicated, our generalist obstetricians manage the patient with maternal-fetal medicine consultation, increased fetal surveillance as described below, and delivery at our tertiary care institution.

Our standard practice is to use the initial ultrasonography imaging to evaluate the size and contents of the defect, measure the nuchal translucency, and evaluate for additional abnormalities. Serial ultrasonography monitoring of the fetus is required to assess the size and quality of the herniated intestine, amount of amniotic fluid, and fetal growth.[10]

As gastroschisis is a full-thickness defect of the anterior abdominal wall, the abdominal contents are exposed to amniotic fluid. This exposure causes progressive intestinal damage, which can be identified on ultrasonography as bowel thickening and dilation.[12-14] Currently, intestinal thickening and dilation is not considered an indication for delivery as it is assumed that the intestinal damage has already occurred. It is debatable whether delivery around 37 weeks compared with delayed delivery beyond 37 weeks improves outcomes and decreases the stillbirth rate.[11,13] Studies show that neonates delivered prior to 37 weeks have worse outcomes compared with those delivered after 37 weeks.[14,15]

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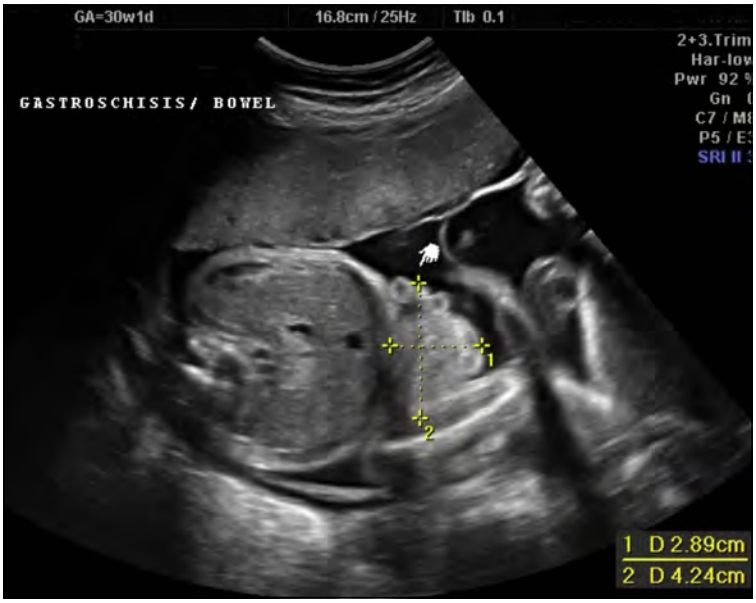
FIGURE 2 Ultrasound scan demonstrating gastroschisis



Ultrasonography reveals loops of bowel herniating through a paraumbilical wall defect and floating in amniotic fluid without a covering membrane, features of gastroschisis.

Fetal surveillance. As standard practice, we evaluate the fetus at around 16 weeks and then again at around 20 weeks. In the absence of fetal growth restriction, which is associated with 25% of cases,[16,17] our standard practice includes performing serial growth ultrasonography every 3 to 4 weeks starting at 28 weeks and biophysical profiles and nonstress testing weekly starting at 32 weeks. Fetal echocardiography can be offered. However, unlike with omphalocele, which has a high incidence of associated cardiac structural anomalies, gastroschisis has a low incidence of congenital cardiac anomalies, estimated to be between 2.5% and 4%.[18,19]

Delivery considerations. Little agreement exists regarding when and how to deliver pregnancies complicated by fetal gastroschisis. While some advocate for induction of labor at 36 to 38 weeks, most infants with gastroschisis can be delivered safely at term via either vaginal or cesarean delivery.[14,15]

Delivery timing should consider the clinical picture and incorporate performance on antenatal testing, fetal growth, the size and contents of the gastroschisis, and consultation with maternal-fetal medicine. Fetuses with gastroschisis often have non-reassuring antenatal testing. This can necessitate early delivery, although cesarean delivery should be reserved for obstetric indications, with the caveat that if there is large liver involvement, some pediatric surgeons recommend cesarean delivery due to the risk of hepatic rupture.

Neonate management. The survival rate of gastroschisis is reported to be as high as 91% to 94%.[2] Morbidity is related to intestinal complications, such as strictures, adhesions, and volvulus.

In the case of simple gastroschisis, when the bowel is in good condition, the treatment method of choice is primary reduction.[20] If performed in the operating room, an immediate sutured closure of the defect can be done. The benefits of primary repair include decreased length of stay, fewer intensive care bed days, and less time to achieve full feeds.[20,21] Primary reduction has a reported success rate of 50% to 83%.[22] A reduction with a delayed spontaneous closure also can be performed at bedside in the neonatal intensive care unit.[22]

For complex gastroschisis, characterized by bowel complications such as inflammation, perforation, ischemia, atresia, necrosis, or volvulus, primary closure may not be possible and reduction may need to be achieved through silo application.[22-25] Additionally, further bowel surgery, such as stoma formation and bowel resection, may be required.[25]

Omphalocele often is associated with abnormal karyotype

Also known as exomphalos, omphalocele is a relatively common defect, with an estimated prevalence of 2 to 3 cases per 10,000 live births.[2] In this condition, there is a midline defect in which intra-abdominal contents herniate through the base of the umbilical cord. Omphaloceles are covered by amniotic membranes, making them distinguishable from gastroschisis, which has no covering, and congenital umbilical hernias, which are covered by intact skin and subcutaneous tissue.[26-33]

Additionally, in omphalocele the umbilical cord insertion site varies, whereas in gastroschisis the umbilical cord insertion is usually to the right of midline. An omphalocele is often categorized based on whether or not it contains the liver (extracorporeal liver) or only the bowel (intracorporeal liver).

Genetic studies

Approximately 67% to 88% of all pregnancies with omphalocele have an abnormal karyotype and/or associated malformations, including Beckwith-Wiedemann syndrome.[31] Of the aneuploidies, trisomy 18 is the one most commonly associated with omphalocele, accounting for approximately 62% to 75%, while trisomy 13 accounts for approximately 11% to 24%.[32,33] The presence of other anomalies is strongly associated with poor prognosis, and increased defect size is an independent predictor of neonatal morbidity and mortality, as neonates with large omphaloceles with extracorporeal livers can develop respiratory insufficiency and require more complex surgical repairs. It is interesting, however, that the absence of an extracorporeal liver is associated with a higher risk of aneuploidy than are cases with an intracorporeal liver.[33]

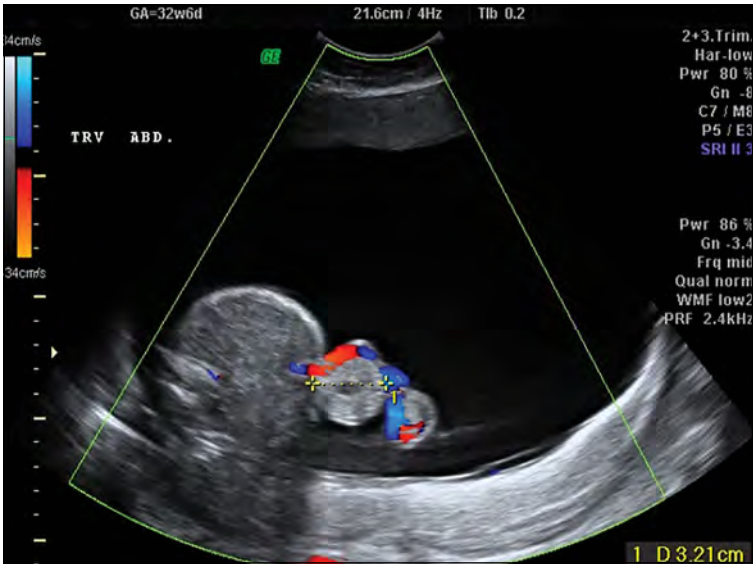
We offer chorionic villus sampling or amniocentesis to all patients with omphalocele. If the patient undergoes invasive diagnostic testing, the sample then undergoes karyotyping, chromosomal microarray, and testing for Beckwith-Wiedemann syndrome. If the patient declines diagnostic sampling, we perform a cell-free DNA screening to rule out aneuploidy.

Making the diagnosis

Omphaloceles can be diagnosed via prenatal ultrasonography as early as 11 to 14 weeks' gestation.[26] They are classified based on size, location, and contents of the sac.[26,27] A small omphalocele is defined as a defect less than 5 cm with a sac that may contain a few loops of intestines (**FIGURE 3**).[27] A giant omphalocele is a defect with more than 75% of the liver contained in the sac.[29]

Location can be epigastric, umbilical, or hypogastric, and both small and giant omphaloceles may have ruptured membranes that will result in exposure of the contained viscera.[27] Omphaloceles are associated with such structural anomalies as cardiac, gastrointestinal, genitourinary, diaphragmatic, and neural tube defects. We do not routinely perform magnetic resonance imaging (MRI) for evaluation of omphaloceles, but MRI may be used to help predict postnatal outcomes in the case of giant omphaloceles.[26]

FIGURE 3 **Ultrasound scan showing omphalocele**



Ultrasonography shows a small omphalocele (<5 cm), with intra-abdominal contents covered by amniotic membranes herniating through the base of the umbilical cord.

Management

Our standard practice is to use the initial ultrasonography imaging to evaluate the size and contents of defect, measure the nuchal translucency, and evaluate for additional abnormalities. As in cases of gastroschisis, serial ultrasonography monitoring of the fetus is required to assess the size and quality of the herniated intestine, amount of amniotic fluid, and fetal growth. We typically evaluate the fetus at around 16 weeks and then again at around 20 weeks. In the absence of fetal growth restriction, we recommend serial growth ultrasonography every 3 to 4 weeks starting at 28 weeks and biophysical profiles and nonstress testing weekly starting

Clinical pearls: Management of fetal abdominal wall defects

- Patients with fetuses with anterior wall defects should be referred to a maternal-fetal medicine specialist for co-management and advanced fetal imaging.
- The American College of Obstetricians and Gynecologists recommends microarray for all major fetal structural abnormalities, with the qualifier that karyotype can be offered if a specific aneuploidy is suspected based on the abnormality or prior genetic screening tests.
- If confirmatory testing is performed (amniocentesis or chorionic villus sampling), the sample should undergo karyotyping, chromosomal microarray, and if indicated, testing for Beckwith-Wiedemann syndrome. If the patient declines confirmatory sampling, performing cell-free DNA screening to rule out aneuploidy is recommended.
- Fetal echocardiography is recommended.
- Fetal magnetic resonance imaging should be considered in complex cases.
- Management should be individualized based on the type and severity of defect(s).
- Delivery timing and method should be individualized based on the defect(s) and determined in a multidisciplinary discussion with maternal-fetal medicine, neonatology, pediatric surgery, and pediatric cardiology, as necessary.
- The most common fetal abdominal wall defect is omphalocele, followed by gastroschisis.
- Maternal serum α-fetoprotein is usually elevated in all of the disorders.

at 32 weeks. Additionally, we routinely obtain a fetal echocardiogram to rule out cardiac structural abnormalities.

Delivery considerations. Fetuses that do not undergo spontaneous abortion or medical termination of pregnancy often are born at term.[26] We recommend expectant management until spontaneous labor, another indication for delivery arises, or at least 39 weeks' estimated gestational age. There are no evidence-based guidelines for the optimal mode of delivery in fetuses with omphalocele, although we recommend cesarean delivery for fetuses with large defects to avoid postnatal sac rupture and liver damage. Preterm induction of labor is not indicated as infants born preterm have about a 50% mortality rate.[26,27]

Children born with isolated omphalocele typically have a good prognosis, with an estimated survival rate of 50% to 90%.[32,33] However, compared to gastroschisis, omphaloceles are often associated with other anomalies.[32,33]

Management of omphaloceles depends on the size of the defect. In our institution, our generalist obstetricians manage the standard prenatal care with the addition of increased fetal surveillance and testing, interdisciplinary patient counseling with maternal-fetal medicine, pediatric surgeons, and neonatologists for delivery planning, and delivery is performed at our tertiary care center.

Neonate management. Small omphaloceles are amenable to primary early fascial closure.[26-30] However, attempted primary closure of giant omphaloceles carries significant risks, including abdominal compartment syndrome and postoperative herniation.[29,30] Instead, several options exist for staged surgical closure, in which there are multiple operations prior to final fascial closure, as well as nonoperative delayed closure for management of giant omphaloceles.[29,30]

Conservative management of giant omphaloceles has certain benefits, such as earlier first feeds, decreased risk of abdominal compartment syndrome, and lower risk of infection.[30] Ruptured omphaloceles can be repaired through primary repair, employment of a synthetic or biologic mesh fascial bridge, or silo placement with delayed closure.[28]

Body-stalk anomaly: Multiple defects and poor prognosis

Also known as limb body wall complex, body-stalk anomaly is a rare malformation that has a reported prevalence of approximately 0.12 cases per 10,000 births (both live and stillbirths).[34] Body-stalk anomaly is characterized by multiple defects, including severe kyphosis or scoliosis, a short or absent umbilical cord, and a large anterior abdominal wall defect.[34-36] This malformation is almost entirely incompatible with life, resulting in abortion or stillbirth.[35] Survival is extremely rare and limited to case reports.

While the exact etiology of body-stalk anomaly is unknown, 3 possible causes have been hypothesized: early amnion rupture, vascular compromise, and embryonic dysgenesis.[37-40]

Making the diagnosis

Body-stalk anomaly typically can be diagnosed by 10 to 14 weeks' gestation via ultrasonography.[34-41] We currently follow the

diagnostic criteria proposed by Van Allen and colleagues, which requires 2 of the following 3 anomalies[34]:

- exencephaly/encephalocele with facial clefts
- thoraco- and/or abdominoschisis (midline defect)
- limb defect.

Additional ultrasonographic findings can include the identification of evisceration of the abdominal contents, a short umbilical cord, and increased nuchal thickness.[36,42] During the second and third trimesters, oligohydramnios may be seen.[2]

Management

Body-stalk anomaly is considered a fatal condition without specific therapeutic interventions. Maternal risks include an increased risk of preterm labor and gestational hypertension.[35] Research on body-stalk anomaly has not shown any correlation with patients' age, fetal sex, or abnormal karyotype, and the reported risk of recurrence for this anomaly is very low.[42,43] Early diagnosis therefore is essential to provide families with information and counseling. Given the poor fetal prognosis, increased maternal risk, and low recurrence rates, mothers can be advised toward elective termination of pregnancy.

Should a patient desire expectant management, care can be provided by generalist obstetricians or care can be transferred to maternal-fetal medicine, with the addition of increased fetal surveillance and testing, interdisciplinary patient counseling with maternal-fetal medicine, pediatric surgeons, and neonatologists for delivery planning; delivery should be performed at a tertiary care center.

Multidisciplinary team strategy is essential

Based on our experience, when faced with an anterior AWD in utero, prenatal imaging, genetic testing, increased fetal surveillance, and a multidisciplinary team approach improves outcomes. We must emphasize that careful patient counseling is paramount in our practice. ●

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To read about more types of fetal abdominal wall defects, see the online version of this article at mdedge.com/obgyn.

References

1. Victoria T, Andronikou S, Bowen D, et al. Fetal anterior abdominal wall defects: prenatal imaging by magnetic resonance imaging. *Pediatr Radiol.* 2018;48:499-512.
2. Pakdaman R, Woodward PJ, Kennedy A. Complex abdominal wall defects: appearances at prenatal imaging. *Radiographics.* 2015;35:636-649.
3. Oakes MC, Porto M, Chung JH. Advances in prenatal and perinatal diagnosis and management of gastroschisis. *Semin Pediatr Surg.* 2018;27:289-299.
4. Mastroiacovo P, Lisi A, Castilla EE. The incidence of gastroschisis: research urgently needs resources. *BMJ.* 2006;332:423-424.
5. Boyd PA, Haeusler M, Barisic I. EUROCAT report 9: surveillance of congenital anomalies in Europe 1980-2008. *Birth Defects Res A Clin Mol Teratol.* 2011;91(suppl 1):S1.
6. Gamba P, Midrio P. Abdominal wall defects: prenatal diagnosis, newborn management, and long-term outcomes. *Semin Pediatr Surg.* 2014;23:283-290.
7. Beaudoin S. Insights into the etiology and embryology of gastroschisis. *Semin Pediatr Surg.* 2018;27:283-288.
8. Yazdy MM, Mitchell AA, Werler MM. Maternal genitourinary infections and the risk of gastroschisis. *Am J Epidemiol.* 2014;180:518-525.
9. Werler MM, Sheehan JE, Mitchell AA. Maternal medication use and risks of gastroschisis and small intestinal atresia. *Am J Epidemiol.* 2002;155:26-31.
10. D'Antonio F, Virgone C, Rizzo G, et al. Prenatal risk factors and outcomes in gastroschisis: a meta-analysis. *Pediatrics.* 2015;136:e159-e169.
11. Baud D, Lausman A, Alfaraj MA, et al. Expectant management compared with elective delivery at 37 weeks for gastroschisis. *Obstet Gynecol.* 2013;121:990-998.
12. Goetzinger KR, Tuuli MG, Longman RE, et al. Sonographic predictors of postnatal bowel atresia in fetal gastroschisis. *Ultrasound Obstet Gynecol.* 2014;43:420-425.
13. Overton TG, Pierce MR, Gao H, et al. Antenatal management and outcomes of gastroschisis in the UK. *Prenat Diagn.* 2012;32:1256-1262.
14. Ergün O, Barksdale E, Ergün FS, et al. The timing of delivery of infants with gastroschisis influences outcome. *J Pediatr Surg.* 2005;40:424-428.
15. Overcash RT, DeUgarte DA, Stephenson ML, et al; University of California Fetal Consortium. Factors associated with gastroschisis outcomes. *Obstet Gynecol.* 2014;124:551-557.
16. Wissanji H, Puligandla PS. Risk stratification and outcome determinants in gastroschisis. *Semin Pediatr Surg.* 2018;27:300-303.
17. Raynor BD, Richards D. Growth retardation in fetuses with gastroschisis. *J Ultrasound Med.* 1997;16:13-16.
18. Mastroiacovo P, Lisi A, Castilla EE, et al. Gastroschisis and associated defects: an international study. *Am J Med Genet A.* 2007;143A:660-671.
19. Kunz LH, Gilbert WM, Towner DR. Increased incidence of cardiac anomalies in pregnancies complicated by gastroschisis. *Am J Obstet Gynecol.* 2005;193(3 pt 2):1248-1252.
20. Lakshminarayanan B, Lakhoo K. Abdominal wall defects. *Early Hum Dev.* 2014;90:917-920.
21. Prefumo F, Izzi C. Fetal abdominal wall defects. *Best Pract Res Clin Obstet Gynaecol.* 2014;28:391-402.
22. Petrosyan M, Sandler AD. Closure methods in gastroschisis. *Semin Pediatr Surg.* 2018;27:304-308.

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23. Skarsgard ED. Management of gastroschisis. *Curr Opin Pediatr.* 2016;28:363-369.
24. Bergholz R, Boettcher M, Reinshagen K, et al. Complex gastroschisis is a different entity to simple gastroschisis affecting morbidity and mortality—a systematic review and meta-analysis. *J Pediatr Surg.* 2014;49:1527-1532.
25. Emil S. Surgical strategies in complex gastroschisis. *Semin Pediatr Surg.* 2018;27:309-315.
26. Verla MA, Style CC, Olutoye OO. Prenatal diagnosis and management of omphalocele. *Semin Pediatr Surg.* 2019;28:84-88.
27. Gonzalez KW, Chandler NM. Ruptured omphalocele: diagnosis and management. *Semin Pediatr Surg.* 2019;28:101-105.
28. Sugandhi N, Saha M, Bhatnagar V, et al. Repair of ruptured omphalocele sac in the neonatal period and beyond. *J Indian Assoc Pediatr Surg.* 2020;25:46-48.
29. Bauman B, Stephens D, Gershone H, et al. Management of giant omphaloceles: a systematic review of methods of staged surgical vs nonoperative delayed closure. *J Pediatr Surg.* 2016;51:1725-1730.
30. Kogut KA, Fiore NF. Nonoperative management of giant omphalocele leading to early fascial closure. *J Pediatr Surg.* 2018;53:2404-2408.
31. Conner P, Vejde JH, Burgos CM. Accuracy and impact of prenatal diagnosis in infants with omphalocele. *Pediatr Surg Int.* 2018;34:629-633.
32. Iacovella C, Contro E, Ghi T, et al. The effect of the contents of exomphalos and nuchal translucency at 11-14 weeks on the likelihood of associated chromosomal abnormality. *Prenat Diagn.* 2012;32:1066-1070.
33. Getachew MM, Goldstein RB, Edge V, et al. Correlation between omphalocele contents and karyotypic abnormalities: sonographic study in 37 cases. *AJR Am J Roentgenol.* 1992;158:133-136.
34. Singh A, Singh J, Gupta K. Body stalk anomaly: antenatal sonographic diagnosis of this rare entity with review of literature. *J Ultrason.* 2017;17:133-135.
35. Lazaroni TL, Cruzeiro PC, Piçarro C, et al. Body stalk anomaly: Three months of survival. Case report and literature review. *J Pediatr Surg Case Rep.* 2016;14:22-25.
36. Gajzer DC, Hirzel AC, Saigal G, et al. Possible genetic origin of limb-body wall complex. *Fetal Pediatr Pathol.* 2015;34:257–270.
37. Maruyama H, Inagaki T, Nakata Y, et al. Minimally conjoined omphalopagus twins with a body stalk anomaly. *AJP Rep.* 2015;5:e124-e128.
38. Bhat A, Ilyas M, Dev G. Prenatal sonographic diagnosis of limb-body wall complex: case series of a rare congenital anomaly. *Radiol Case Rep.* 2016;11:116-120.
39. Quijano FE, Rey MM, Echeverry M, et al. Body stalk anomaly in a 9-week pregnancy. *Case Rep Obstet Gynecol.* 2014;2014:357285.
40. Kocherla K, Kumari V, Kocherla PR. Prenatal diagnosis of body stalk complex: a rare entity and review of literature. *Indian J Radiol Imaging.* 2015;25:67-70.
41. Panaitescu AM, Ushakov F, Kalaskar A, et al. Ultrasound features and management of body stalk anomaly. *Fetal Diagn Ther.* 2016;40:285-290.
42. Routhu M, Thakkallapelli S, Mohan P, et al. Role of ultrasound in body stalk anomaly and amniotic band syndrome. *Int J Reprod Med.* 2016;2016:3974139.
43. Costa ML, Couto E, Furlan E, et al. Body stalk anomaly: adverse maternal outcomes in a series of 21 cases. *Prenat Diagn.* 2012;32:264-267.

Home pregnancy tests—Is ectopic always on your mind?

When a patient presents to the ED reporting early pregnancy and intermittent vaginal bleeding, failure to evaluate for ectopic pregnancy can expose clinicians to liability

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

CASE Unidentified ectopic pregnancy leads to rupture*

A 33-year-old woman (G1 P0010) with 2 positive home pregnancy tests presents to the emergency department (ED) reporting intermittent vaginal bleeding for 3 days. Her last menstrual period was 10 weeks ago, but she reports that her menses are always irregular. She has a history of asymptomatic chlamydia, as well as spontaneous abortion 2 years prior. At present, she denies abdominal pain or vaginal discharge.

Upon examination her vital signs are: temperature, 98.3 °F; pulse, 112 bpm, with a resting rate of 16 bpm; blood pressure (BP), 142/91 mm Hg; pulse O2, 99%; height, 4' 3"; weight, 115 lb. Her labs are: hemoglobin, 12.1 g/dL; hematocrit, 38%; serum human chorionic gonadotropin (hCG) 236 mIU/mL. Upon pelvic examination, no active bleeding is noted. She agrees to be followed up by her gynecologist and is given a prescription for serum hCG in 2 days. She is instructed to return to the ED should she have pain or increased vaginal bleeding.

Three days later, the patient follows up with her gynecologist reporting mild cramping. She notes having had an episode of heavy vaginal bleeding and a "weakly positive" home pregnancy test. Transvaginal ultrasonography notes endometrial thickness 0.59 mm and unremarkable adnexa. A urine pregnancy test performed in the office is positive; urinalysis is positive for nitrites. With the bleeding slowed, the gynecologist's overall impression is that the patient has undergone complete spontaneous abortion. She prescribes Macrobid for the urinary tract infection. She does not obtain the ED-prescribed serum HCG levels, as she feels, since complete spontaneous abortion has occurred there is no need to obtain a follow-up serum HCG.

Five days later, the patient returns to the ED reporting abdominal pain after eating. Fever and productive cough of 2 days are noted. The patient states that she had a recent miscarriage. The overall impression of the patient's condition is bronchitis, and it is noted on the patient's record, "unlikely ectopic pregnancy and pregnancy test may be false positive," hence a pregnancy test is not ordered. Examination

*The "facts" of this case are a composite, drawn from several cases to illustrate medical and legal issues. The statement of facts should be considered hypothetical.

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IN THIS ARTICLE

reveals mild suprapubic tenderness with no rebound; no pelvic exam is performed. The patient is instructed to follow up with a health care clinic within a week, and to return to the ED with severe abdominal pain, higher fever, or any new concerning symptoms. A Zithromax Z-pak is prescribed.

Four days later, the patient is brought by ambulance to the ED of the local major medical center with severe abdominal pain involving the right lower quadrant. She states that she had a miscarriage 3 weeks prior and was recently treated for bronchitis. She has dizziness when standing. Her vital signs are: temperature, 97.8 °F; heart rate, 95 bpm; BP, 72/48 mm Hg; pulse O2, 100%. She reports her abdominal pain to be 6/10.

The patient is given a Lactated Ringer's bolus of 1,000 mL for a hypotensive episode. Computed tomography is obtained and notes, "low attenuation in the left adnexa with a dilated fallopian tube." A large heterogeneous collection of fluid in the pelvis is noted with active extravasation, consistent with an "acute bleed."

The patient is brought to the operating room with a diagnosis of probable ruptured ectopic pregnancy. Intraoperatively she is noted to have a right ruptured ectopic and left tubo-ovarian abscess. The surgeon proceeds with right salpingectomy and left salpingo-oophorectomy. Three liters of hemoperitoneum is found.

She is followed postoperatively with serum hCG until levels are negative. Her postoperative course is uneventful. Her only future option for pregnancy is through assisted reproductive technology (ART) with in vitro fertilization (IVF). The patient sues the gynecologist and second ED physician for presumed inappropriate assessment for ectopic pregnancy.

WHAT'S THE VERDICT?

A defense verdict is returned.

Medical considerations

The incidence of ectopic pregnancy is 2% of all pregnancies, with a higher incidence (about 4%) among infertility patients.[1] Up to 10% of ectopic pregnancies have no symptoms.[2]

FAST TRACK

Ectopic pregnancy is the most common cause of maternal mortality in the first trimester, with an incidence of up to 10% of all first-trimester deaths

Clinical presentations. Classic signs of ectopic pregnancy include:

- abdominal pain
- vaginal bleeding
- late menses (often noted).

A recent case of ectopic pregnancy presenting with chest pain was reported.[3] Clinicians must never lose site of the fact that ectopic pregnancy is the most common cause of maternal mortality in the first trimester, with an incidence of 1% to 10% of all first-trimester deaths.[4]

Risk factors include pelvic inflammatory disease, as demonstrated in the opening case. "The silent epidemic of chlamydia" comes to mind, and tobacco smoking can adversely affect tubal cilia, as can pelvic adhesions and/or prior tubal surgery. All of these factors can predispose a patient to ectopic pregnancy; in addition, intrauterine devices, endometriosis, tubal ligation (or ligation reversal), all can set the stage for an ectopic pregnancy.[5] Appropriate serum hCG monitoring during early pregnancy can assist in sorting out pregnancies of unknown location (PUL; **FIGURE**, page 47). First trimester ultrasonography, at 5 weeks gestation, usually identifies early intrauterine gestation.

Imaging. With regard to pelvic sonography, the earliest sign of an intrauterine pregnancy (IUP) is a sac eccentrically located in the decidua.[6] As the IUP progresses, it becomes equated with a "double decidual sign," with double rings of tissue around the sac.[6] If the pregnancy is located in an adnexal mass, it is frequently inhomogeneous or noncystic in appearance (ie, "the blob" sign); the positive predictive value (PPV) is 96%.[2] The PPV of transvaginal ultrasound is 80%, as paratubal, paraovarian, ovarian cyst, and hydrosalpinx can affect the interpretation.[7]

Heterotopic pregnancy includes an intrauterine gestation and an ectopic pregnancy. This presentation includes the presence of a "pseudosac" in the endometrial cavity plus an extrauterine gestation. Heterotopic pregnancies have become somewhat more common as ART/IVF has unfolded, especially prior to the predominance of single embryo transfer.

Managing ectopic pregnancy

For cases of early pregnancy complicated

by intermittent bleeding and/or pain, monitoring with serum hCG levels at 48-hour intervals to distinguish a viable IUP from an abnormal IUP or an ectopic is appropriate. The "discriminatory zone" collates serum hCG levels with findings on ultrasonography. Specific lower limits of serum hCG levels are not clear cut, with recommendations of 3,500 mIU/mL to provide sonographic evidence of an intrauterine gestation "to avoid misdiagnosis and possible interruption of intrauterine pregnancy," as conveyed in the American College of Obstetricians and Gynecologists 2018 practice bulletin.[8] Serum progesterone levels also have been suggested to complement hCG levels; a progesterone level of <20 nmol/L is consistent with an abnormal pregnancy, whereas levels >25 nmol/L are suggestive of a viable pregnancy.[2] Inhibin A levels also have been suggested to be helpful, but they are not an ideal monitoring tool.

While most ectopic pregnancies are located in the fallopian tube, other locations also can be abdominal or ovarian. In addition, cesarean scar ectopic pregnancy can occur and often is associated with delay in diagnosis and greater morbidity due to such delay.[9] With regard to ovarian ectopic, Spiegelberg criteria are established for diagnosis (**TABLE 1**).[10]

Appropriate management of an ectopic pregnancy is dependent upon the gestational age, serum hCG levels, and imaging findings, as well as the patient's symptoms and exam findings. Treatment is established in large part on a case-by-case basis and includes, for early pregnancy, expectant management and use of methotrexate (**TABLE 2**).[11] Dilation and curettage may be used to identify the pregnancy's location when the serum hCG level is below 2,000 mIU/mL and there is no evidence of an IUP on ultrasound. Surgical treatment can include minimally invasive salpingostomy or salpingectomy and, depending on circumstance, laparotomy may be indicated.

Fertility following ectopic pregnancy varies and is affected by location, treatment, predisposing factors, total number of ectopic pregnancies, and other factors. Ectopic pregnancy, although rare, also can occur with use of IVF.

TABLE 1 **Spiegelberg criteria for ovarian pregnancy**[10]

- The gestational sac is located in the region of the ovary
- The ectopic pregnancy is attached to the uterus by the ovarian ligament
- Ovarian tissue in the wall of the gestational sac is proved histologically
- The tube on the involved side is intact

TABLE 2 **Indications and contraindications to methotrexate therapy for ectopic pregnancy**[11]

Candidates for methotrexate
1. Confirmed ectopic pregnancy (or clinically high suspicion)
2. Hemodynamically stable
3. Ectopic mass is not ruptured
4. Patients who will be able to have follow-up visits and lab testing
Absolute contraindications to methotrexate therapy
1. Liver disease including alcoholism
2. Peptic ulcer disease
3. Blood dyscrasias
4. Immunodeficiency
5. Breastfeeding
6. Active pulmonary disease
7. Liver, kidney, or hematologic dysfunction
8. Hypersensitivity to methotrexate
9. Heterotopic pregnancy
10. Unable or unwilling to complete protocol
Relative contraindications to methotrexate therapy[a]
1. Mass greater than 3.5 cm
2. Fetal heart motion
3. Peritoneal fluid
Necessary lab testing prior to methotrexate therapy
1. Serum creatinine level
2. Liver transaminases
3. Complete blood count
4. Quantitative human chorionic gonadotropin level

[a]Women with high baseline human chorionic gonadotropin concentration (greater than 5,000 mIU/mL) are more likely to require multiple courses of medical therapy or experience treatment failure.

Humans are not unique with regard to ectopic pregnancies, as they also occur in sheep.[12]

Legal perspective

Lawsuits related to ectopic pregnancy are not a new phenomenon. In fact, in 1897,

a physician in Ohio who misdiagnosed an "extrauterine pregnancy" as appendicitis was the center of a malpractice lawsuit.[13] Unrecognized or mishandled ectopic pregnancy can result in serious injuries—in the range of 1% to 10% (see above) of maternal deaths are related to ectopic pregnancy.[14] Ectopic pregnancy cases, therefore, have been the subject of substantial litigation over the years. An informal, noncomprehensive review of malpractice lawsuits brought from 2000 to 2019, found more than 300 ectopic pregnancy cases. Given the large number of malpractice claims against ObGyns,[15] ectopic pregnancy cases are only a small portion of all ObGyn malpractice cases.[16]

A common claim: negligent diagnosis or treatment

The most common basis for lawsuits in cases of ectopic pregnancy is the clinician's negligent failure to properly diagnose the ectopic nature of the pregnancy. There are also a number of cases claiming negligent treatment of an identified ectopic pregnancy. Not every missed diagnosis, or unsuccessful treatment, leads to liability, of course. It is only when a diagnosis or treatment fails to meet the standard of care within the profession that there should be liability. That standard of care is generally defined by what a reasonably prudent physician would do under the circumstances. Expert witnesses, who are familiar with the standard of practice within the specialty, are usually necessary to establish what that practice is. Both the plaintiff and the defense obtain experts, the former to prove what the standard of care is and that the standard was not met in the case at hand. The defense experts are usually arguing that the standard of care was met.[17] Inadequate diagnosis of ectopic pregnancy or other condition may arise from a failure to take a sufficient history, conduct an appropriately thorough physical examination, recognize any of the symptoms that would suggest it is present, use and conduct ultrasound correctly, or follow-up appropriately with additional testing.[18]

A malpractice claim of negligent treatment can involve any the following circumstances[19]:

- failure to establish an appropriate treatment plan
- prescribing inappropriate medications for the patient (eg, methotrexate, when it is contraindicated)
- delivering the wrong medication or the wrong amount of the right medication
- performing a procedure badly
- undertaking a new treatment without adequate instruction and preparation.

Given the nature and risks of ectopic pregnancy, ongoing, frequent contact with the patient is essential from the point at which the condition is suspected. The greater the risk of harm (probability or consequence), the more careful any professional ought to be. Because ectopic pregnancy is not an uncommon occurrence, and because it can have devastating effects, including death, a reasonably prudent practitioner would be especially aware of the clinical presentations discussed above.[20] In the opening case, the treatment plan was not well documented.

Negligence must lead to patient harm. In addition to negligence (proving that the physician did not act in accordance with the standard of care), to prevail in a malpractice case, the plaintiff-patient must prove that the negligence *caused* the injury, or worsened it. If the failure to make a diagnosis would not have made any difference in a harm the patient suffered, there are no damages and no liability. Suppose, for example, that a physician negligently failed to diagnose ectopic pregnancy, but performed surgery expecting to find the misdiagnosed condition. In the course of the surgery, however, the surgeon discovered and appropriately treated the ectopic pregnancy. (A version of this happened in the old 19th century case mentioned above.) The negligence of the physician did not *cause* harm, so there are no damages and no liability.

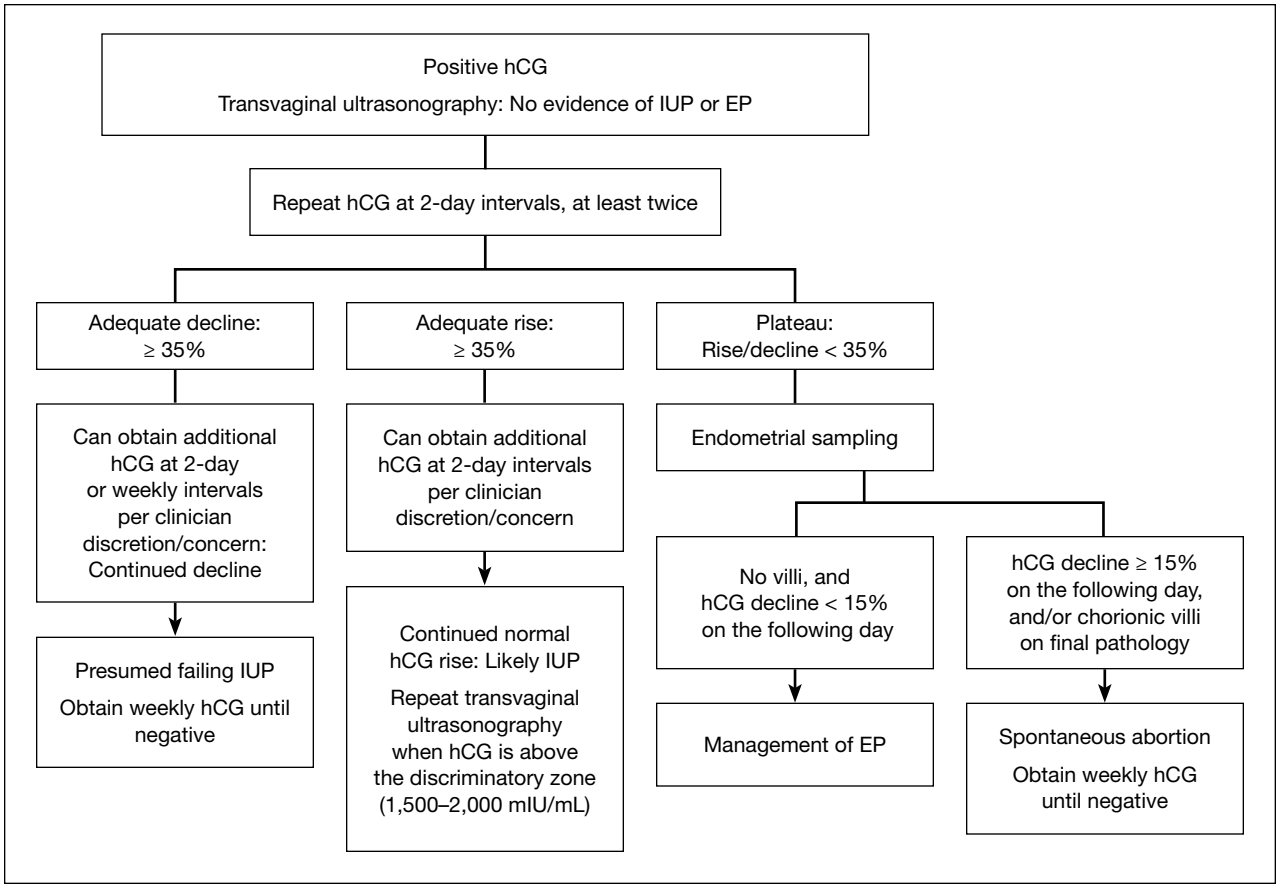
Informed consent is vital

A part of malpractice is informed consent (or the absence of it)—issues that can arise in any medical care.[21] It is wise to pay particular attention in cases where the nature of the illness is unknown, and where there are

FAST TRACK

Physician liability depends on whether or not there was diagnosis or treatment negligence that led to patient harm

FIGURE Suggested algorithm for assessment of pregnancy of unknown location



Abbreviations: EP, ectopic pregnancy; hCG, human chorionic gonadotropin; IUP, intrauterine pregnancy.

Source: Insogna I, Brady P. Pregnancy of unknown location: evidence-based evaluation and management. *OBG Manag*. 2020;32:42-48.

significant uncertainties and the nature of testing and treatment may change substantially over a period of a few days or few weeks. As always, informed consent should include a discussion of what process or procedure is proposed, its risks and benefits, alternative approaches that might be available, and the risk of doing nothing. Frequently, the uncertainty of ectopic pregnancy complicates the informed consent process.[22]

Because communication with the patient is an essential function of informed consent, the consent process should productively be used in PUL and similar cases to inform the patient about the uncertainty, and the testing and (nonsurgical) treatment that will occur. This is an opportunity to reinforce the message that the patient must maintain ongoing communication with the physician's office about changes in her condition, and appear for each appointment scheduled. If more invasive procedures—notably surgery—become required, a separate consent process should be completed, because the risks and considerations are now meaningfully different than when treatment began. As a general matter, any possible treatment that may result in infertility or reduced reproductive capacity should specifically be included in the consent process.

In the hypothetical case, the gynecologist failed to obtain a follow-up serum hCG level. In addition, the record did not reflect ectopic pregnancy in the differential

diagnosis. As noted above, the patient had predisposing factors for an ectopic pregnancy. The physician should have acknowledged the history of sexually transmitted disease predisposing her to an ectopic pregnancy. Monitoring of serum hCG levels until they are negative is appropriate with ectopic, or presumed ectopic, pregnancy management. Appropriate monitoring did not occur in this case. Each of these errors (following up on serum hCG levels and the inadequacy of notations about the possibility of ectopic pregnancy) seem inconsistent with the usual standard of care. Furthermore, as a result of the outcome, the only future option for the patient to pursue pregnancy was IVF.

Other legal issues

There are a number of other legal issues that are associated with the topic of ectopic pregnancy. There is evidence, for example, that Catholic and non-Catholic hospitals treat ectopic pregnancies differently,[23] which may reflect different views on taking a life or the use of methotrexate and its association with abortion.[24] In addition, the possibility of an increase in future ectopic pregnancies is one of the "risks" of abortion that pro-life organizations have pushed to see included in abortion informed consent.[25] This has led some commentators to conclude that some Catholic hospitals violate federal law in managing ectopic pregnancy. There is also evidence of "overwhelming rates of medical misinformation on pregnancy center websites, including a link between abortion and ectopic pregnancy."[26]

The fact that cesarean deliveries are related to an increased risk for ectopic pregnancy (because of the risk of cesarean scar ectopic pregnancy) also has been cited as information that should play a role in the consent process for cesarean delivery.[27] In terms of liability, failed tubal ligation leads to a 33% risk of ectopic pregnancy.[28] The risk of ectopic pregnancy is also commonly included in surrogacy contracts.[29]

Why the outcome was for the defense

The opening hypothetical case illustrates some of the uncertainties of medical malpractice cases. As noted, there appeared a deviation from the usual standard of care, particularly the failure to follow up on the serum hCG level. The weakness in the medical record, failing to note the possibility of ectopic pregnancy, also was probably an error but, apparently, the court felt that this did not result in any harm to the patient.

The question arises of how there would be a defense verdict in light of the failure to track consecutive serum hCG levels. A speculative explanation is that there are many uncertainties in most lawsuits. Procedural problems may result in a case being limited, expert witnesses are essential to both the plaintiff and defense, with the quality of their review and testimony possibly uneven. Judges and juries may rely on one expert witness rather than another, juries vary, and the quality of advocacy differs. Any of these situations can contribute to the unpredictability of the outcome of a case. In the case above, the liability was somewhat uncertain, and the various other factors tipped in favor of a defense verdict. ●

FAST TRACK

Despite the apparent lack of standard of care (including inadequate follow-up on serum hCG levels), many variables factor in to case outcomes, and this one ended in a defense verdict

References

1. Centers for Disease Control and Prevention. Ectopic pregnancy—United States, 1990-1992. *MMWR Morb Mortal Wkly Rep*. 1995;44:46-48.
2. Kirk E, Bottomley C, Bourne T. Diagnosing ectopic pregnancy and current concepts in the management of pregnancy of unknown location. *Hum Reprod Update*. 2012;20:250-261.
3. Dichter E, Espinosa J, Baird J, Lucerna A. An unusual emergency department case: ruptured ectopic pregnancy presenting as chest pain. *World J Emerg Med*. 2017;8:71-73.
4. Cecchino GN, Araujo E, Elito J. Methotrexate for ectopic pregnancy: when and how. *Arch Gynecol Obstet*. 2014;290:417-423.
5. Barnhart KT, Sammel MD, Cracia CR, et al. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. *Fertil Steril*. 2006;86:36-43.
6. Carusi D. Pregnancy of unknown location: evaluation and management. *Semin Perinatol*. 2019;43:95-100.
7. Barnhart KT, Fay CA, Suescum M, et al. Clinical factors affecting the accuracy of ultrasonography in symptomatic first-trimester pregnancy. *Obstet Gynecol*. 2011;117:299-306.
8. American College of Obstetricians and Gynecologists Practice Bulletin No. 193: tubal ectopic pregnancy. *Obstet Gynecol*. 2018;131:e91-e103.
9. Bouyer J, Coste J, Fernandez H, et al. Sites of ectopic pregnancy: a 10-year population-based study of 1800 cases. *Hum Reprod*. 2002;17:3224-3230.

10. Spiegelberg O. Zur casuistic der ovarial schwangerschaft. *Arch Gynecol*. 1978;13:73.
11. OB Hospitalist Group. Methotrexate use for ectopic pregnancies guidelines. https://www.obhg.com/wp-content/uploads/2020/01/Methotrexate-Use-for-Ectopic-Pregnancies_2016-updates.pdf. Accessed December 10, 2020.
12. Brozos C, Kargiannis I, Kiossis E, et al. Ectopic pregnancy through a caesarean scar in a ewe. *N Z Vet J*. 2013;61:373-375.
13. Tucker v. Gillette, 12 Ohio Cir. Dec. 401 (Cir. Ct. 1901).
14. Creanga AA, Syverson C, Seed K, et al. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol*. 2017;130:366-373.
15. Matthews LR, Alvi FA, Milad MP. Reproductive surgery malpractice patterns. *Fertil Steril*. 2016;106:e42-e43.
16. Kim B. The impact of malpractice risk on the use of obstetrics procedures. *J Legal Studies*. 2006;36:S79-S120.
17. Abinader R, Warsof S. Complications involving obstetrical ultrasound. In: Warsof S, Shwayder JM, eds. *Legal Concepts and Best Practices in Obstetrics: The Nuts and Bolts Guide to Mitigating Risk*. 2019;45-48.
18. Creanga AA, Shapiro-Mendoza CK, Bish CL, et al. Trends in ectopic pregnancy mortality in the United States: 1980-2007. *Obstet Gynecol*. 2011;117:837-843.
19. Shwayder JM. IUP diagnosed and treated as ectopic: How bad can it get? *Contemporary OB/GYN*. 2019;64:49-46.
20. Kaplan AI. Should this ectopic pregnancy have been diagnosed earlier? *Contemporary OB/GYN*. 2017;62:53.
21. American College of Obstetricians and Gynecologists Committee on Ethics. Committee opinion 439: informed consent. Reaffirmed 2015. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2009/08/informed-consent. Accessed December 9, 2020.
22. Shwayder JM. Liability in ob/gyn ultrasound. *Contemporary OB/GYN*. 2017;62:32-49.
23. Fisher LN. Institutional religious exemptions: a balancing approach. *BYU Law Review*. 2014;415-444.
24. Makdisi J. Aquinas's prohibition of killing reconsidered. *J Catholic Legal Stud*. 2019:57:67-128.
25. Franzonello A. Remarks of Anna Franzonello. *Alb Law J Sci Tech*. 2012;23:519-530.
26. Malcolm HE. Pregnancy centers and the limits of mandated disclosure. *Columbia Law Rev*. 2019;119:1133-1168.
27. Kukura E. Contested care: the limitations of evidence-based maternity care reform. *Berkeley J Gender Law Justice*. 2016;31:241-298.
28. Donley G. Contraceptive equity: curing the sex discrimination in the ACA's mandate. *Alabama Law Rev*. 2019;71:499-560.
29. Berk H. Savvy surrogates and rock star parents: compensation provisions, contracting practices, and the value of womb work. *Law Social Inquiry*. 2020;45:398-431.

UPDATE

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as the variety of the published guidelines for VTE prophylaxis after CD, the SMFM Consult Series provides recommendations to assist clinicians caring for postpartum women after CD. As reviewed in the ACOG Practice Bulletin, there are good data to support pharmacologic prophylaxis during pregnancy and the postpartum period for women with a history of VTE or a thrombophilia. Solid evidence is lacking, however, for what to do for women who have a CD without this history but may have other potential risk factors for VTE, such as obesity, preeclampsia, and transfusion requirement. Universal pharmacologic prophylaxis also is not yet supported by evidence. SMFM supports LMWH as the preferred medication in pregnancy and postpartum and provides these additional recommendations:

- All women who have a CD should have sequential compression devices (SCDs) placed prior to surgery and continued until they are ambulatory.
- Women with a history of VTE or thrombophilia without history of VTE should have SCDs and pharmacologic VTE prophylaxis for 6 weeks postpartum.
- Intermediate dosing of LMWH is recommended for patients with class III obesity.
- Institutions should develop patient safety bundles for VTE prophylaxis to identify

WHAT THIS EVIDENCE MEANS FOR PRACTICE

- Pregnant patients with a history of VTE or a thrombophilia may be candidates for pharmacologic anticoagulation during pregnancy and/or postpartum.
- LMWH is the preferred method of pharmacologic VTE prophylaxis during pregnancy and postpartum.
- For most patients, CD and neuraxial anesthesia safely can be performed 12 to 24 hours after the last dose of prophylactic or intermediate LMWH, respectively.
- All patients undergoing CD should have at least mechanical VTE prophylaxis with SCDs.
- All women who have a CD should be evaluated via institutional patient safety bundles for VTE prophylaxis for additional risk factors that potentially warrant postpartum pharmacologic VTE prophylaxis.
- More data are needed to determine recommendations for universal/near universal pharmacologic VTE prophylaxis in the postpartum period.
- Pregnant or postpartum patients with moderate to severe COVID-19 infection may be at increased risk for VTE, warranting consideration of additional pharmacologic prophylaxis.

additional risk factors that may warrant pharmacologic prophylaxis after CD in select patients.

Our approach to patients with COVID-19 infection

At our institution, we recently incorporated a VTE prophylaxis protocol into our electronic medical record that provides risk stratification for each patient. In addition to the above recommendations, our patients may qualify for short-term in-house or longer postpartum prophylaxis depending on risk factors.

A new risk factor in recent months is COVID-19 infection, which appears to increase the risk of coagulopathy, especially in patients with disease severe enough to warrant hospitalization. Given the potential for additive risk in pregnancy, in consult with our medicine colleagues, we have placed some of our more ill hospitalized pregnant patients on a course of prophylactic LMWH both in the hospital and after discharge independent of delivery status or mode of delivery. ●

References

1. Baschat AA, Gembruch U, Harman CR. The sequence of changes in Doppler and biophysical parameters as severe fetal growth restriction worsens. *Ultrasound Obstet Gynecol*. 2001;18:571-577.
2. Almond D, Currie J. Killing me softly: the fetal origins hypothesis. *J Econ Perspect*. 2011;25:153-172.
3. American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstetrics and Society for Maternal-Fetal Medicine. ACOG practice bulletin no. 204: Fetal growth restriction. *Obstet Gynecol*. 2019;133:e97-e109.
4. American College of Obstetricians and Gynecologists Committee on Obstetric Practice and Society for Maternal-Fetal Medicine. ACOG committee opinion no. 764: Medically indicated late-preterm and early-term deliveries. *Obstet Gynecol*. 2019;133:e151-e155.
5. Society for Maternal-Fetal Medicine; Martins JG, Biggio FR, Abuhamad A. SMFM consult series no. 52: diagnosis and management of fetal growth restriction. *Am J Obstet Gynecol*. 2020;223:B2-B17.
6. American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstetrics. ACOG practice bulletin no. 217: Prelabor rupture of membranes. *Obstet Gynecol*. 2020;135:e80-e97.
7. Morris JM, Roberts CL, Bowen JR, et al; PPROMT Collaboration. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. *Lancet*. 2016;387:444-452.
8. Birsner ML, Turrentine M, Pettker CM, et al. ACOG practice advisory: Options for peripartum anticoagulation in areas affected by shortage of unfractionated heparin. March 2020. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/options-for-peripartum-anticoagulation-in-areas-affected-by-shortage-of-unfractionated-heparin. Accessed December 8, 2020.
9. Pacheco LD, Saade G, Metz TD. Society for Maternal-Fetal Medicine consult series no. 51: Thromboembolism prophylaxis for cesarean delivery. *Am J Obstet Gynecol*. 2020;223:B11-B17.
10. American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstetrics. ACOG practice bulletin no. 196: Thromboembolism in pregnancy. *Obstet Gynecol*. 2018;132:e1-e17.

CONTINUED FROM PAGE 27

patients with pelvic organ prolapse: a retrospective study of 8 years. *Arch Gynecol Obstet*. 2018;298:623-629.
12. Mao M, Ai F, Zhang Y, et al. Changes in the symptoms and quality of life of women with symptomatic pelvic organ prolapse fitted with a ring with support pessary. *Maturitas*. 2018;117:51-56.
13. Duenas JL, Miceli A. Effectiveness of a continuous-use ring-shaped vaginal pessary without support for advanced pelvic organ prolapse in postmenopausal women. *Int Urogynecol J*. 2018;29:1629-1636.
14. Farrell S, Singh B, Aldakhil L. Continence pessaries in the management of urinary incontinence in women. *J Obstet Gynaecol Canada*. 2004;26:113-117.
15. Donnelly MJ, Powell-Morgan SP, Olsen AL, et al. Vaginal pessaries for the management of stress and mixed urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct*. 2004;15:302-307.
16. Richter HE, Burgio KL, Brubaker L, et al; Pelvic Floor Disorders Network. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. *Obstet Gynecol*. 2010;115:609-617.
17. Ding J, Chen C, Song XC, et al. Changes in prolapse and urinary symptoms after successful fitting of a ring pessary with support in women with advanced pelvic organ prolapse: a prospective study. *Urology*. 2016;87:70-75.
18. Brazell HD, Patel M, O'Sullivan DM, et al. The impact of pessary use on bowel symptoms: one-year outcomes. *Female Pelvic Med Reconstr Surg*. 2014;20:95-98.
19. Meriwether KV, Komesu YM, Craig C, et al. Sexual function and pessary management among women using a pessary for pelvic floor disorders. *J Sex Med*. 2015;12:2339-2349.
20. Kuhn A, Bapst D, Stadlmayr W, et al. Sexual and organ function in patients with symptomatic prolapse: are pessaries helpful? *Fertil Steril*. 2009;91:1914-1918.
21. Clemons JL, Aguilar VC, Sokol ER, et al. Patient characteristics that are associated with continued pessary use versus surgery after 1 year. *Am J Obstet Gynecol*. 2004;191:159-164.
22. Liang CC, Chang YL, Chang SD, et al. Pessary test to predict postoperative urinary incontinence in women undergoing hysterectomy for prolapse. *Obstet Gynecol*. 2004;104:795-800.
23. Liapis A, Bakas P, Georgantopoulou C, et al. The use of the pessary test in preoperative assessment of women with severe genital prolapse. *Eur J Obstet Gynecol Reprod Biol*. 2011; 155:110-113.
24. Wei JT, Nygaard I, Richter HE, et al; Pelvic Floor Disorders Network. A midurethral sling to reduce incontinence after vaginal prolapse repair. *N Engl J Med*. 2012;366:2358-2367.
25. March of Dimes. Quick facts: preterm birth. https://www.marchofdimes.org/Peristats/ViewTopic.aspx?reg=99&top=3&lev=0&slev=1&gclid=EAIaIQobChMI4r. Accessed December 10, 2020.
26. Goya M, Pratcorona L, Merced C, et al; PECEP Trial Group. Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomized controlled trial. *Lancet*. 2012;379:1800-1806.
27. Di Tommaso M, Seravalli V, Arduino S, et al. Arabin cervical pessary to prevent preterm birth in twin pregnancies with short cervix. *J Obstet Gynaecol*. 2016;36:715-718.
28. Saccone G, Maruotti GM, Giudicepietro A, et al; Italian Preterm Birth Prevention (IPP) Working Group. Effect of cervical pessary on spontaneous preterm birth in women with singleton pregnancies and short cervical length: a randomized clinical trial. *JAMA*. 2017;318:2317-2324.
29. Perez-Lopez FR, Chedraui P, Perez-Roncero GR, et al; Health Outcomes and Systematic Analyses (HOUSSAY) Project. Effectiveness of the cervical pessary for the prevention of preterm birth in singleton pregnancies with a short cervix: a meta-analysis of randomized trials. *Arch Gynecol Obstet*. 2019;299:1215-1231.
30. Hui SYA, Chor CM, Lau TK, et al. Cerclage pessary for preventing preterm birth in women with a singleton pregnancy and a short cervix at 20 to 24 weeks: a randomized controlled trial. *Am J Perinatol*. 2013;30:283-288.
31. Nicolaides KH, Syngelaki A, Poon LC, et al. A randomized trial of a cervical pessary to prevent preterm singleton birth. *N Engl J Med*. 2016;374:1044-1052.
32. Saccone G, Ciardulli A, Xodo S, et al. Cervical pessary for preventing preterm birth in singleton pregnancies with short cervical length: a systematic review and meta-analyses. *J Ultrasound Med*. 2017;36:1535-1543.
33. Conde-Agudelo A, Romero R, Nicolaides KH. Cervical pessary to prevent preterm birth in asymptomatic high-risk women: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2020;223:42-65.e2.
34. Sultan AH, Kamm MA, Hudson CN, et al. Anal-sphincter disruption during vaginal delivery. *N Engl J Med*. 1993;329: 1905-1911.
35. Talley NJ, O'Keefe EA, Zinsmeister AR, et al. Prevalence of gastrointestinal symptoms in the elderly: a population-based study. *Gastroenterology*. 1992;102:895-901.
36. Denis P, Bercoff E, Bizien MF, et al. Prevalence of anal incontinence in adults [in French]. *Gastroenterol Clin Biol*. 1992;16:344-350.
37. Richter HE, Matthew CA, Muir T, et al. A vaginal bowel-control system for the treatment of fecal incontinence. *Obstet Gynecol*. 2015;125:540-547.
38. *2019 Current Procedural Coding Expert*. Optum360; 2018.
39. *ICD-10-CM Expert for Physicians*. Optum360; 2019.
40. MDS Medical Department Store website. http://www.medicaldepartmentstore.com/Pessary-Vaginal-Pessaries-/3788.htm?gclid=CjwKCAiAlNf-BRB_EiwA2osbxdqln8fQg-AxOUEMphM9aYlTIftSkwy0xXLT0PrcpIZnb5gBhiLc1RoCsbMQAvD_BwE. Accessed December 15, 2020.
41. Monarch Medical Products website. https://www.monarchmedicalproducts.com/index.php?route=product/category&path=99_67. Accessed December 15, 2020.
42. CooperSurgical Medical Devices website. https://www.coopersurgical.com/our-brands/milex/. Accessed December 15, 2020.

A ROUNDTABLE DISCUSSION

CERVICAL CANCER PREVENTION: ADDRESSING HEALTH DISPARITIES

01.26.21 6:00PM CST

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.

DR. HAYWOOD BROWN MD

Professor of Obstetrics and Gynecology, Associate Dean for Diversity, Morsani College of Medicine, University of South Florida

DR. JANE DELGADO PHD, MS

President and CEO, National Alliance for Hispanic Health

DR. E. BLAIR HOLLADAY PHD, MASCP, SCT (ASCP) CM

CEO, American Society for Clinical Pathology

DR. JESSICA SHEPHERD MD, MBA

OB/GYN, Baylor University Medical Center

DR. TARA HAYES CONSTANT PHD, MPH, MSN, ARNP

Nurse Practitioner, Sea Mar Community Health Centers

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