PART 1

PREGNATAL ULTRASOUND

FOCUS ON ANOMALIES

Stephen T Chase, MD and Daniel W Skupski, MD

Microbiome in prematurity

Bleeding disorders
When to worry and how to help

ACOG GUIDELINES
Prenatal diagnostic testing

LEGALLY SPEAKING
Failure to determine fetal abnormalities

PRACTICE MANAGEMENT
Choosing the right malpractice insurance
PATIENTS WANT TO KNOW.
RESULTS YOU CAN TRUST.

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- Validated in the average and high-risk population\(^1\)^\(^3\)
- ACOG/SMFM state any patient may choose cell-free DNA (cfDNA) analysis as a screening strategy for common aneuploidies regardless of her risk status\(^2\)
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The Harmony Prenatal Test was developed by Ariosa Diagnostics, a CLIA-certified laboratory. As with other lab-developed tests, it has not been cleared or approved by the FDA and is not available for sale as an IVD in the US. Non-invasive prenatal testing (NIPT) based on cell-free DNA analysis is not diagnostic; results should be confirmed by diagnostic testing.


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Severe maternal morbidity affects over 60,000 women each year¹
Every 10 minutes a woman in the US nearly dies of pregnancy-related complications¹

Start with IM and transition to Oral Tablets*
Ensure your patients are protected from Hospital to Home
*In appropriate patients who are at risk of PPH.

INDICATIONS
Methergine® (methylergonovine maleate) is indicated for routine management of uterine atony, hemorrhage and subinvolution of the uterus following delivery of placenta and for control of uterine hemorrhage in the second stage of labor following delivery of the anterior shoulder.

IMPORTANT SAFETY INFORMATION
Methergine Tablets are contraindicated for patients with the following conditions: hypertension, toxemia, pregnancy, and hypersensitivity.

WARNINGS
General: This drug should not be administered I.V. routinely because of the possibility of inducing sudden hypertensive and cerebrovascular accidents. If I.V. administration is considered essential as a lifesaving measure, Methergine (methylergonovine maleate) should be given slowly over a period of no less than 60 seconds with careful monitoring of blood pressure. Intra-arterial or periarterial injection should be strictly avoided. Caution should be exercised in presence of impaired hepatic or renal function.

Breast-Feeding: Mothers should not breast-feed during treatment with Methergine. Milk secreted during this period should be discarded. Methergine may produce adverse effects in the breast-feeding infant. Methergine may also reduce the yield of breast milk. Mothers should wait at least 12 hours after administration of the last dose of Methergine before initiating or resuming breast feeding.

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

Medication Errors: Inadvertent administration of Methergine to newborn infants has been reported. In these cases of inadvertent neonatal exposure, symptoms such as respiratory depression, convulsions, cyanosis and oliguria have been reported. Usual treatment is symptomatic. However, in severe cases, respiratory and cardiovascular support is required. Methergine has been administered instead of vitamin K and Hepatitis B vaccine, medications which are routinely administered to the newborn. Due to the potential for accidental neonatal exposure, Methergine injection should be stored separately from medications intended for neonatal administration.

ADVERSE REACTIONS
The most common adverse reaction is hypertension associated in several cases with seizure and/or headache. Hypotension and anaphylaxis has also been reported. Cerebrovascular accident, paraesthesia, ventricular fibrillation, ventricular tachycardia, angina pectoris, atrioventricular block were also reported post-marketing.

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

Drug Interactions: There have been rare reports of serious adverse events in connection with the coadministration of certain ergot alkaloid drugs (e.g. dihydroergotamine and ergotamine) and potent CYP 3A4 inhibitors, resulting in vasospasm leading to cerebral ischemia and/or ischemia of the extremities. Caution should be exercised when Methergine® Tablets are used concurrently with beta-blockers. Concomitant administration with beta-blockers may enhance the vasoconstrictive action of ergot alkaloids.

ADVERSE REACTIONS
The most common adverse reaction is hypertension associated in several cases with seizure and/or headache. Hypotension and anaphylaxis has also been reported. Cerebrovascular accident, paraesthesia, ventricular fibrillation, ventricular tachycardia, angina pectoris, atrioventricular block were also reported post-marketing. Safety and effectiveness in pediatric patients have not been established.

Please note that this information is not comprehensive. See the full Prescribing Information at www.methergine.com

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088, or contact Lupin Pharmaceuticals, Inc. at 1-800-399-2561.

References:

Please see Brief Summary of Prescribing Information on the next page.
INDICATIONS AND USAGES

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

CONTRAINDICATIONS

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

WARNINGS

General: This drug should not be administered intravenously routinely because of the possibility of inducing sudden hypertensive and cerebrovascular accidents. If intravenous administration is considered essential as a lifesaving measure, methylergonovine maleate should be given slowly over a period of no less than 60 seconds with careful monitoring of blood pressure. Intra-arterial or periarterial injection should be strictly avoided. Caution should be exercised in presence of impaired hepatic or renal function.

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

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

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

PRECAUTIONS

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

Drug Interactions

CYP3A4 Inhibitors (e.g., Macrolide Antibiotics and Protease Inhibitors): There have been rare reports of serious adverse events in connection with the coadministration of certain ergot alkaloid drugs (e.g., dihydroergotamine and ergotamine) and potent CYP3A4 inhibitors, resulting in vasospasm leading to cerebral ischemia and/or ischemia of the extremities. Although there have been no reports of such interactions with methylergonovine alone, potent CYP3A4 inhibitors should not be coadministered with methylergonovine. Examples of some of the more potent CYP3A4 inhibitors include macrolide antibiotics (e.g., erythromycin, troleandomycin, clarithromycin), HIV protease or reverse transcriptase inhibitors (e.g., ritonavir, indinavir, nelfinavir, delavirdine) or azole antifungals (e.g., ketoconazole, voriconazole). Less potent CYP3A4 inhibitors should be administered with caution. Less potent inhibitors include saquinavir, nefazodone, fluconazole, grapefruit juice, fluoxetine, fluvoxamine, zileuton, and clotrimazole. These lists are not exhaustive, and the prescriber should consider the effects on CYP3A4 of other agents being considered for concomitant use with methylergonovine.

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

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

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

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

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

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

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

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

ADVERSE REACTIONS

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

Nervous System Disorders: Cerebrovascular accident, paraesthesia.

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

DRUG ABUSE AND DEPENDENCE

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

OVERDOSAGE

Symptoms of acute overdose may include: nausea, vomiting, abdominal pain, numbness, tingling of the extremities, rise in blood pressure, in severe cases followed by hypotension, respiratory depression, hypothermia, convulsions, and coma.

Because reports of overdosage with methylergonovine maleate are infrequent, the lethal dose in humans has not been established. The oral LD50 (in mg/kg) for the mouse is 187, the rat 93, and the rabbit 4.5. Several cases of accidental methylergonovine maleate injection in newborn infants have been reported, and in such cases 0.2 mg represents an overdose of great magnitude. However, recovery occurred in all but one case following a period of respiratory depression, hypothermia, hypotonicity with jerking movements, and convulsions.

Also, several children 1-3 years of age have accidentally ingested up to 10 tablets (2 mg) with no apparent ill effects. A postpartum patient took 4 tablets at one time in error and reported paresthesias and clamminess as her only symptoms.

Treatment of acute overdose is symptomatic and includes the usual procedures of: 1. Removal of offending drug by inducing emesis, gastric lavage, catharsis, and supportive diuresis. 2. Maintenance of adequate pulmonary ventilation, especially if convulsions or coma develop. 3. Correction of hypotension with pressor drugs as needed. 4. Control of convulsions with standard anticonvulsant agents. 5. Control of peripheral vasospasm with warmth to the extremities if needed.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088, or call Lupin Pharmaceuticals, Inc. at 1-800-399-2561.

Please note that this information is not comprehensive. Please see the full Prescribing Information at www.methergine.com.

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Pharmaceuticals, Inc.

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Is federal medical liability reform possible?

With passage by the House of a bill capping noneconomic damages, there may be potential for meaningful tort reform from Washington.

Over the past few years, progress has clearly been made with regard to the professional liability crisis. Between 2002 and 2013 the rate of paid claims per 1000 physicians fell from 18.6 to 9.9, an average decrease of 6.3% per year. Moreover, since 2007 median indemnity amounts paid have fallen and high-end awards have plateaued. Overall professional liability insurance rates have stabilized. This salutary state primarily reflects the improving economy and stock market valuations coupled with modest state-based reforms, but implementation of a wide range of patient safety programs has likely also had an impact. The Agency for Healthcare Research and Quality (AHRQ) Patient Safety and Medical Liability Demonstration Program has suggested such a linkage, particularly in obstetrical claims. Pettker and associates compared obstetrical liability claims at a single tertiary-care teaching hospital during 2 5-year periods (1998 to 2002 and 2003 to 2007), before and after implementing a rigorous patient safety program. Despite a stable statewide malpractice insurance market, this patient safety initiative resulted in a decline in median annual claims (1.31 to 0.64; P = 0.02), median annual payments per 1000 deliveries ($1,141,638 to $63,470; P < 0.01) and the median payout per case ($632,262 vs $216,815; P < 0.05).

Ob/gyns still feeling the pain

While these overall trends are reassuring, for ob/gyns professional liability insurance premiums costs continue to climb, albeit more modestly than a decade ago. But even more concerning, our medical liability crisis continues to contribute to burnout and adverse practice patterns. The 2015 American Congress of Obstetricians and Gynecologists (ACOG) Survey on Professional Liability noted multiple disturbing trends. Of the survey’s nearly 4300 respondents, 23.8% reported that fear of malpractice litigation had forced them to reduce numbers of high-risk obstetrical patients; 17.0% posited that it had increased their cesarean delivery rate; 13.6% had stopped offering trials of labor for vaginal birth after cesarean (VBAC); and 5.1% had stopped their obstetrics practice altogether. An astonishing 73.6% of ob/gyn respondents (average age 51.4 years) had experienced at least 1 liability claim during their career and the group averaged 2.59 claims per physician. Since the last ACOG liability climate survey in 2012, 40.5% had experienced 1 or more claims, two-thirds being obstetrical in origin, most often for neurological injury. While survey data can be subject to selection bias, there is strong empiri-
Indeed, 35 states have now capping non-economic damages, and alleviating expert witness standards, and dating certificates of merit, strength-Branstad recently signed a law man-

For example, Iowa’s Governor Terry implemented tort reform including such caps on non-economic damage. Driven by cost concerns and pressure from organized medicine, and commensurate with Republicans gaining control of the majority of state legislatures and governorships, a growing number of states have implemented tort reform including such caps on non-economic damage. For example, Iowa’s Governor Terry Branstad recently signed a law mandating certificates of merit, strengthening expert witness standards, and capping non-economic damages at $250,000. Indeed, 35 states have now implemented some form of cap on non-economic damages.

These wins at the state level, however, can be ephemeral as recently demonstrated in my home state of Florida. There, the Supreme Court recently ruled unconstitutional a law limiting non-economic damages in medical malpractice cases. Sadly this law, passed in 2003 while Jeb Bush was governor, had greatly helped stabilized what was one of the severest professional liability insurance crises in the nation. Ironically, it was the law’s very success that led to the judges’ decision. The majority opinion read in part, “We further conclude that because there is no evidence of a continuing medical malpractice insurance crisis justifying the arbitrary and invidious discrimination between medical malpractice victims, there is no rational relationship between the personal injury noneconomic damage caps … and alleviating this purported crisis.”

The limits of state-based reforms, ascendency of the GOP over all 3 branches of the federal government and the pressing need to contain costs in the Republican healthcare reform plan have all led to renewed hopes for a federal solution to our long twilight struggle against a patently unjust, inequitable, and fundamentally flawed tort system.

Renewed federal efforts at liability reform

Many ob/gyns in particular and physicians in general have justifiable concerns about the potential for reduced access to care, contraction of Medicaid eligibility and decreased support for maternal, child, and reproductive healthcare accompany-ing the US House of Representatives American Health Care Act (AHCA).

Yet the focus of the AHCA on the economic sustainability of our healthcare enterprise is much needed and long overdue and helps make the case for federal medical liability reform.

As I have written in this column on what seems like countless occasions, US public and private expenditures for healthcare are wholly unsustain-able. There are many reasons for our excessive medical costs including overutilization of technology, underutilization of primary care, aging and overweight populations, unrestrained medication costs, and bloated administrative expenses fed by burdensome regulations and reciprocal “gaming” of medical bills by both providers and payors. Moreover, defensive medicine adds at least $55 billion to our collective healthcare bill and perhaps much more; thus, it is a prime target for reform.

Led by Health and Human Services Secretary and orthopedic surgeon Dr. Tom Price (R-GA), tort reform has suddenly become the focus of multiple House bills.

THE MAJOR AIMS OF THESE BILLS ARE:

1. Creation of “safe harbors” for physicians who adhere to accepted practice guidelines. Any malpractice claim would be adjudicated by a panel of medical experts if the defendant claimed care fell within such an established pathway;

2. Establishment of administrative health “tribunals” presided over by judges with requisite expertise. Plaintiffs would be required to prove a physician’s behavior was reckless to receive payment;

3. A $250,000 cap on non-economic damages; and

Limits of state-based reforms

Driven by cost concerns and pressure from organized medicine, and commensurate with Republicans gaining control of the majority of state legislatures and governorships, a growing number of states have implemented tort reform including such caps on non-economic damage. For example, Iowa’s Governor Terry Branstad recently signed a law mandating certificates of merit, strengthening expert witness standards, and capping non-economic damages at $250,000. Indeed, 35 states have now implemented some form of cap on non-economic damages.

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The limits of state based-reforms, ascendency of the GOP over all 3 branches of the federal government and the pressing need to contain costs in the Republican healthcare reform plan have all led to renewed hopes for a federal solution to our long twilight struggle against a patently unjust, inequitable, and fundamentally flawed tort system.

Renewed federal efforts at liability reform

Many ob/gyns in particular and physicians in general have justifiable concerns about the potential for reduced access to care, contraction of Medicaid eligibility and decreased support for maternal, child, and reproductive healthcare accompanying the US House of Representatives American Health Care Act (AHCA).
A host of other provisions long favored by organized medicine (eg, joint-and-several liability reform, reduced statutes of limitations, limits on attorney fees, periodic payments, and exposure of a plaintiff’s collateral sources of coverage, such as health insurance).

To be fair, there is a limited “evidentiary base” and in some cases no evidence in support of several of these reforms (eg, limiting attorney fees, and collateral source rules). There are simply no data on the potential benefits of safe harbors, and many claims may be for care not covered by current, established guidelines. However, as evidence-based guidelines proliferate, such an approach has enormous potential for better care, lower costs, and greater fairness. Moreover, as noted above, there is strong evidence for the benefits of tight caps on non-economic damage such as the “Protecting Access to Care Act” which was recently passed by the House 218-210.

Thus, we should strongly support bills containing these provisions.

**Take-home message**

For the first time in a long time there is at least the potential for truly meaningful medical liability reform from Washington. Unfortunately, there are many hurdles to be overcome, not the least of which is the expected deluge in trial lawyer lobby money targeting bills containing any limits on recovery or attorneys’ fees. In addition, beyond the rancor, partisanship and general ill will that exist between the major political parties, there are also serious policy conflicts emerging between the 2 Houses of Congress and within the GOP itself, which has experienced an unprecedented degree of internal division over healthcare policy—all of which could stymie medical liability and patient safety reform efforts. So, while such federal reform is possible it is not probable, and while we wait, let’s all redouble our efforts to ensure that all our patients are safe.

**FOR REFERENCES VISIT**
contemporaryobgyn.net/editorial-201707,
PART 1
Using ultrasound to recognize fetal anomalies

First- and second-trimester ultrasounds are key prenatal tools for revealing structural anomalies that may point to genetic conditions.

by Stephen T. Chase, MD, and Daniel W. Skupski, MD

Like much of medicine, ultrasound diagnosis of fetal anomalies is both a science and an art. Part 1 of this article will detail, within the text and with images, the anomalies that should not be missed when performing ultrasound during the first and second trimesters of pregnancy. Part 2, in a future issue, will deal with multifetal gestations. This series will discuss and show the appearance of anomalies in the first and second trimesters, and in multifetal gestations (anomalies unique to multiples) to enhance the ob/gyn’s knowledge of pitfalls that can lead to errors in diagnosis.

Ultrasound and prenatal diagnosis of structural fetal anomalies

Ultrasound can identify the majority of major structural fetal abnormalities. Prenatal diagnosis can lead to improved outcomes by ensuring that delivery occurs in a hospital with the necessary personnel to manage newborns who may require surgery or other specialized care. In rare cases, prenatal diagnosis can lead to fetal intervention, although most anomalies do not require any treatment in utero. Some structural anomalies are associated with genetic conditions, and recognition can lead to prenatal genetic diagnosis. In cases in which prenatal diagnosis reveals a major structural abnormality, some patients may choose to terminate the pregnancy.

Patients who present early for pre-
natal care typically undergo 2 ultrasound fetal assessments. At 11 to 14 weeks, when nuchal translucency (NT) is measured as a component of Down syndrome screening, a brief fetal anatomic scan is performed. A first-trimester ultrasound is a valuable tool to confirm viability, rule out multiple pregnancy, and evaluate anatomy, even if genetic screening is not desired. The main ultrasound used to screen for structural anomalies is in the second trimester, generally at 18 to 20 weeks.

In the first trimester, some major anomalies can be diagnosed or excluded. In other cases, there may be findings that are not diagnostic but that may suggest a structural anomaly. In these patients, second-trimester ultrasound before 18 weeks can lead to earlier prenatal diagnosis. Abnormal NT in a fetus with a normal karyotype is associated with a higher rate of structural abnormalities. When NT is abnormal, it is reasonable to assess fetal anatomy early in the second trimester, as some structural anomalies can be identified prior to 18 weeks' gestation.

**First trimester**

**Fetal brain**

Late in the first trimester, the brain can be imaged in the transverse plane, identifying both hemispheres and midline structures. Major anomalies that can be identified include anencephaly (absent skull and brain; Figure 1), acrania (absent skull), and holoprosencephaly (no division into separate hemispheres, with absence of midline structures; Figure 2). If a transverse view through the fetal brain identifies a normal midline, representing the falx cerebri, and lateral ventricles, these 3 conditions can be excluded. A large skull defect (cephalocele; Figure 3) can be identified as well.

**Face**

In the same image used to assess NT, the profile can be evaluated. A profile view can identify a small mandible, or micrognathia (Figure 4). Large median or bilateral cleft lip can also be suspected based on profile views. Coronal imaging can identify the orbits, and large clefts may be visible. Rarely, facial masses representing teratomas or lymphangiomas may be visible.
Neck
NT measurements require proper fetal position, image magnification, and caliper placement. All individuals measuring NT as a component of screening for genetic abnormalities must undergo the requisite training, credentialing and quality review. An extreme variant of abnormal NT is the cystic hygroma, characterized by midline septations and edema extending to the fetal thorax. While studies looking at outcomes of this condition have identified high rates of genetic and structural abnormalities, it is not clear that the prognosis is poorer compared to fetuses with comparable NT measurements not categorized as cystic hygroma.

Chest
Evaluation of the chest is very limited in the first trimester. The heart should be visible in the midline, and lung tissue should be present on both sides. Mediastinal shift can represent evidence of a chest mass or diaphragmatic hernia, although those are uncommon diagnoses early in pregnancy. Late in the first trimester, it should be possible to distinguish the left from the right side of the heart, and normal situs can be verified. While structural cardiac anomalies rarely can be suspected, diagnosis before the second trimester is uncommon.
An abnormal-appearing cardiac axis may reflect underlying structural abnormalities.3

Abdomen
In the first trimester, visible structures include the ventral wall, umbilical cord insertion, stomach bubble, and urinary bladder. The most common abnormalities identified are the ventral wall defects omphalocele (Figure 5), gastroschisis (Figure 6 and discussed in detail in our February 2017 issue), and more extensive defects including body-stalk anomaly and limb-body-wall complex. Physiologic midgut herniation is common prior to 12 weeks’ gestation and should not be confused with an omphalocele. An enlarged urinary bladder (megacystis; Figure 7) can represent early evidence of bladder outlet obstruction. Kidneys are generally not imaged at < 14 weeks, and because amniotic fluid does not consist primarily of fetal urine until the second trimester, absent or dysfunctional kidneys will not result in oligohydramnios earlier in pregnancy.

Spine
The spine is not easy to evaluate in the first trimester, and most abnormalities will go undetected. Spina bifida involving multiple levels can be suspected in rare cases, as can large masses such as sacrococcygeal teratoma.

Limbs
At a minimum, all limbs should be documented, including proximal long bones (humerus and femur) and distal long bones (radius/ulna and tibia/fibula). Severe skeletal dysplasias, such as thanatophoric dysplasia, can have features such as small limbs and narrow chest even in the first trimester. Hands and feet can also be imaged, although abnormalities of the digits cannot always be identified. In some cases, polydactyly (Figure 8) may be suspected.

Risk factors for structural abnormalities
Abnormal NT is associated with a higher rate of structural abnormalities in fetuses with normal and abnormal karyotypes. Abnormal NT at 11-14 weeks is an indication for genetic counseling, and early second trimester ultrasound at 14-16 weeks should be considered. Abnormal NT is also an indication for fetal echocardiography in the second trimester.

In some cases, first-trimester ultrasound findings may be suspicious, but not diagnostic, for abnormalities of certain structures. In these cases, early second-trimester ultrasound can lead to prenatal diagnosis prior to the routine 18- to 20-week scan. In our experience, early second-trimester ultrasound in such cases contributed to lower gestational age

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at abortion in women undergoing ultrasound at 11 to 14 weeks.  

### Second trimester

At 18 to 20 weeks, detailed ultrasound can evaluate most anatomic structures. Earlier second-trimester anatomic evaluation at <18 weeks should be limited to high-risk patients and/or specialized centers.

#### Fetal brain/skull

Imaging in the transverse plane at the level where the biparietal diameter (BPD) and head circumference (HC) are measured allows identification of the cavum septum pellucidum, third ventricle, and thalami. An oblique/transverse view will image structures in the posterior fossa. Finally, a transverse view superior to the midbrain can identify the lateral ventricles. Real-time scanning should evaluate the integrity of the calvarium. Anomalies that should not be missed in the first trimester should not be missed in the second trimester, such as holoprosencephaly (Figure 9), cephalocele (Figure 10), and anencephaly (Figure 11).

Enlarged ventricles, or ventriculomegaly can indicate several conditions (Figure 12). As an isolated finding, ventriculomegaly can represent obstruction of the flow of cerebrospinal fluid (CSF), and can indicate hydrocephalus. Abnormal cortical development can result in ventricular enlargement in the absence of obstruction.

Ventriculomegaly is also present in the Dandy-Walker malformation (Figure 13), a malformation characterized by absence of the middle portion of the cerebellum, known as the vermis, with cystic dilation of the fourth ventricle visible in the posterior fossa.

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**Continued on page 38**

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**TABLE 2**  
**Second trimester (18-20 weeks)**

<table>
<thead>
<tr>
<th>Don’t miss*</th>
<th>You might miss</th>
<th>You will miss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRAIN/SKULL</strong></td>
<td>• Ventriculomegaly</td>
<td>• Partial agenesis of the corpus callosum</td>
</tr>
<tr>
<td></td>
<td>• Dandy-Walker malformation</td>
<td>• Vascular malformations</td>
</tr>
<tr>
<td></td>
<td>• Arnold-Chiari II malformation</td>
<td>• Destructive lesions</td>
</tr>
<tr>
<td><strong>FACE</strong></td>
<td>• Cleft lip</td>
<td>• Superficial cleft lip</td>
</tr>
<tr>
<td></td>
<td>• Micrognathia</td>
<td>• Mild micrognathia</td>
</tr>
<tr>
<td></td>
<td>• Large masses</td>
<td>• Retrornathia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ear abnormalities</td>
</tr>
<tr>
<td><strong>NECK</strong></td>
<td>• Nuchal edema/cystic hygroma</td>
<td>• Small neck mass</td>
</tr>
<tr>
<td></td>
<td>• Large neck mass</td>
<td></td>
</tr>
<tr>
<td><strong>CHEST</strong></td>
<td>• Diaphragmatic hernia</td>
<td>• Small chest masses</td>
</tr>
<tr>
<td></td>
<td>• Large chest mass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pleural effusion</td>
<td></td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>• Ventricular disproportion</td>
<td>• Smaller ventriculo-septal defects</td>
</tr>
<tr>
<td></td>
<td>• Large ventricular septal defect</td>
<td>• Aortic coarctation/stenosis</td>
</tr>
<tr>
<td></td>
<td>• Tricuspid/mitral valve atresia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Arrhythmia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tetralogy of Fallot</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Truncus arteriosus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Transposition of great vessels</td>
<td></td>
</tr>
<tr>
<td><strong>ABDOMEN</strong></td>
<td>• Gastrochisis</td>
<td>• Esophageal atresia</td>
</tr>
<tr>
<td></td>
<td>• Omphalocele</td>
<td>• Extrapulmonary bronchopulmonary sequestration</td>
</tr>
<tr>
<td></td>
<td>• Choledochal cyst</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ascesis</td>
<td></td>
</tr>
<tr>
<td><strong>GENITOURINARY</strong></td>
<td>• Single umbilical artery</td>
<td>• Unilateral renal agenesis</td>
</tr>
<tr>
<td></td>
<td>• Renal agenesis</td>
<td>• Ectopic kidney</td>
</tr>
<tr>
<td></td>
<td>• Multicystic/dysplastic kidneys</td>
<td>• Ambiguous genitalia</td>
</tr>
<tr>
<td></td>
<td>• Hydronephrosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Megacystis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bladder extrophy</td>
<td></td>
</tr>
<tr>
<td><strong>SPINE</strong></td>
<td>• Spina bifida</td>
<td>• Hemivertebra</td>
</tr>
<tr>
<td></td>
<td>• Sacrococcygeal teratoma</td>
<td>• Spina bifida occulta</td>
</tr>
<tr>
<td><strong>EXTREMITIES</strong></td>
<td>• Limb reduction defects</td>
<td>• Polydactyly</td>
</tr>
<tr>
<td></td>
<td>• Micromelia (short limbs)</td>
<td>• Syndactyly</td>
</tr>
<tr>
<td></td>
<td>• Fractures/bowing</td>
<td>• Soft-tissue abnormalities</td>
</tr>
<tr>
<td></td>
<td>• Joint contractures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Absent thumb</td>
<td></td>
</tr>
</tbody>
</table>

*In addition to everything that should not be missed in the first trimester.
Bleeding disorders
When to worry, how to help
Ob/gyns play a key role in diagnosing and managing these under-recognized conditions

A 16-year-old girl presents to your office complaining of heavy menstrual cycles since menarche. Her cycles last 15 days on average and she changes her pads every hour on the heaviest days. She often passes large clots and misses at least 1 day of school per cycle. Should you be concerned?

Studies have shown that 1 in 5 women who consult their doctor for heavy or prolonged bleeding during their periods actually have an underlying bleeding disorder. The proportion is postulated to be even higher for adolescents. A study that looks at all admissions to a children’s hospital over a 9-year time period for acute menorrhagia in adolescence found a primary coagulation disorder in almost 20% of 59 adolescent patients and in 50% of those who presented at menarche. In this study, 25% of the adolescents had a hemoglobin of less than 10 g/100ml on admission, and one-third required a transfusion.

Bleeding disorders can have major downstream health consequences, including iron deficiency anemia, the need for blood transfusions, increased bleeding during and after surgeries, postpartum bleeding, poor wound healing, and an increased risk of hysterectomy. A survey from the Centers for Disease Control and Prevention (CDC) reported that women with bleeding disorders are also more likely to have 1 or more of several other gynecologic conditions, including hemorrhagic ovarian cysts, endometriosis, polyps, and fibroids.

Early recognition of a bleeding disorder can have a major impact on a patient’s quality of life. Because ob/gyns are often the first to evaluate menstrual bleeding concerns it is extremely important that they have a comprehensive understanding of appropriate screening measures and treatment options for patients with suspected bleeding disorders.

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Inherited bleeding disorders

Von Willebrand disease

In a 2002 CDC survey of 376 ob/gyns across the United States, only 4% of respondents claimed that they would consider von Willebrand disease (vWD) as the cause of heavy menstrual bleeding (HMB) in a woman of reproductive age, and only 6% of respondents would consider it in a girl near menarche. The responses substantially improved in a similar survey conducted in 2012, when 39% reported that they would consider a bleeding disorder as causing HMB in women of reproductive age and 77% would consider this an option in adolescents.

vWD is the most common inherited bleeding disorder, with an overall prevalence of 0.6% to 1.3%. It has an autosomal-dominant inheritance pattern and is caused by a missing or defective von Willebrand factor (vWF), a clotting protein. vWF binds to both factor VIII, a key clotting protein, and to platelets, to form a platelet plug during the clotting process. There are 3 types of vWD, which vary in severity. Type 1 is the most common (60% to 80% of cases) and is relatively mild. The disease is diagnosed more often in females because of the presentation of HMB - according to a systematic review of 11 studies involving 988 women, the prevalence of vWD in women presenting with HMB was reported to be as high as 13% to 24%. Research has suggested that as many as 9 of 10 individuals with vWD remain undiagnosed. (For a full discussion of vWD, see the May 2017 issue of Contemporary OB/GYN.)

Platelet function defects

Platelet dysfunction leads to impaired clot formation and includes disorders of platelet adhesion, aggregation, secretion, or procoagulant activity. Acquired platelet dysfunction is common with use of certain medications, such as aspirin. Data on the prevalence of platelet dysfunction in women presenting with HMB are very limited, as it is very difficult to diagnose due to the need for highly complex and specialized testing. Some studies, however, have shown a prevalence upwards of 47% in women with HMB and a higher incidence among African-American women than Caucasians.

Coagulation factor deficiencies

Women with coagulation factor deficiencies have low levels of a specific blood protein, such as factors I (fibrinogen), II, V, VII, X, XI, and XIII. The exact prevalence of these disorders is unknown, but deficiencies of this type are relatively rare and are estimated to occur in approximately 1 out of 500,000 individuals. The most common factor deficiencies involve factors VIII (Hemophilia A) and IX (Hemophilia B).

Hemophilia

Hemophilic disorders represent the most common severe inherited bleeding conditions. Hemophilia largely affects males, as it is an X linked genetic condition. Females are carriers, but may also exhibit mild to severe bleeding symptoms as carriers. Hemophilia A (a deficiency in clotting factor VIII) affects approximately 1 in 10,000 individuals, and Hemophilia B (a deficiency in clotting factor IX) affects approximately one in 50,000. An estimated 10% to 57% of women with HMB are hemophilia carriers.

Screening for and diagnosing bleeding disorders

As previously noted, gynecologists are often tasked with screening for bleeding disorders due to the complaint of HMB. According to the American College of Obstetricians and Gynecologists (ACOG), an adolescent who reports even 1 of the following should be further evaluated for a bleeding disorder: menses greater than 7 days with a flooding/gushing sensation or bleeding through a pad/tampon in 2 hours; history of anemia; family history of a bleeding disorder; or history of a bleeding disorder after a monostatic challenge (tooth extraction, surgery, delivery). (Figures 1 and 2)

Several qualitative and quantitative methods can be used to screen for...
MONSEL'S

INDICATIONS: Used as a styptic in its undiluted form. Helps to control bleeding during biopsy, LLETZ and laser procedures. INGREDIENTS: Ferrous Sulfate, Sulfuric Acid, Nitric Acid, and Purified Water.
DESCRIPTION: A reddish-brown odorless liquid, widely known as Ferric Subsulfate Solution. Classified as an astringent, used as a styptic.
PHARMACOLOGY: Less irritating than Ferric Sulfate Solution, owing to the smaller proportion of Sulfuric Acid. It is soluble with water or alcohol, and is affected by light.
CONTRAINDICATIONS/WARNINGS: It should not be used in vesicular, bullous, or exudative (oozing) dermatoses because it may then cause permanent pigmentation on the skin. May be harmful if swallowed. Restricted use by or on order of a licensed physician. For external use only. Keep out of reach of children.
DIRECTIONS: Apply to affected area.
HOW SUPPLIED: Box of 12 x 8 mL amber glass bottles with applicators.

LUGOL'S

INDICATIONS: Topical anti-infective agent. INGREDIENTS: Iodine, Potassium Iodide, Purified water. DESCRIPTION: A dark red-black solution with a sharp irritating odor. PHARMACOLOGY: Aqueous solutions of Iodine have the advantage of being less painful or irritating than alcoholic solutions when applied to cuts. The Potassium Iodide is added to increase the solubility of the Iodine. CONTRAINDICATIONS/WARNINGS: May cause eye irritation. In case of eye contact, flush with water for at least 15 minutes and seek medical assistance. May be harmful if swallowed. Restricted use by or on order of a licensed physician. For external use only. Keep out of reach of children.
DIRECTIONS: Apply to affected area.
HOW SUPPLIED: Box of 12 x 8 mL amber glass bottles with applicators.
HMB to accurately diagnose an underlying bleeding disorder. Although the alkaline hematin test is considered the gold standard for measuring menstrual blood loss (MBL), it is complex and used, primarily, in research settings. The method involves pummeling used feminine hygiene products in a solution and measuring the resulting hematin absorbance against calibration curves. The Pictorial Blood Assessment Chart (PBAC) uses diagrams with light, moderate, and heavily soaked pads and tampons to evaluate how much bleeding a patient is experiencing during her cycle. (Figure 3) A total score of more than 100 per cycle correlates to HMB.¹³

A 2014 European study of 165 women demonstrated a more practical method for estimating MBL through use of a calculated questionnaire score that compares to a baseline of healthy women of childbearing age. Like the PBAC, the MBL score calculates a numerical value based on the number of pads or tampons used, which is then used to estimate blood loss.¹⁴ The menstrual cup, a device that catches menstrual flow inside the vagina and is used by women as a hygiene product, can also be used as a quick and fairly reliable method of assessing blood loss by describing how full the cup is and how many times it is changed per day. Each cup can hold 30 mL of blood, and it is a product used by many adolescents. Questionnaires may also be used as screening tools to estimate blood loss. (Figure 4)

In both adolescents and adults, once a positive bleeding screen has been confirmed, initial tests to order include a complete blood count (CBC), platelet count, prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen. If bleeding history is strong or anemia is present in the absence of fibroids, specific tests for vWD disease may be ordered, including von Willebrand-ristocetin cofactor activity, vWF antigen, and factor VIII (often ordered as a von Willebrand panel).¹⁵ It should be noted that no single test alone can reliably diagnose vWD. A hematologist usually interprets test results in conjunction with a gynecologist. Iron studies can also be considered with heavy bleeding, even in the absence of anemia.

Some of the hematological test results may be affected by several variables, including stress, systemic inflammation, anemia, pregnancy, oral contraceptives (OC), time of the menstrual cycle, sample processing, and quality of the laboratory. Ideally, any vWD tests should be performed before starting hormonal management and, because of potential confounders...
repeat testing may be necessary to establish a definitive diagnosis. Because of these and other factors, the mean time to diagnose a bleeding disorder is on the order of 9 years.

**Treatment of acute bleeding**

Treatment of acute bleeding can certainly overlap in patients with and without bleeding disorders. Figure 5 lists common medications used, both hormonal and non-hormonal, as well as surgeries available for management of acute bleeding.16,17

In women with vWD, the recommendation for first-line treatment of acute abnormal uterine bleeding is desmopressin (DDAVP) and tranexamic acid (TA) together for 2 to 3 days, followed by TA alone for 3 to 4 days.16 DDAVP is a synthetic derivative of the antidiuretic hormone vasopressin and works by stimulating the release of vWF from endothelial cells. It can be given intravenously, subcutaneously, intranasally or orally. Antifibrinolytics such as TA inhibit conversion of plasminogen to plasmin, which then inhibits fibrinolysis and helps to stabilize clots. TA was approved for oral treatment of HMB by the US Food and Drug Administration (FDA) in 2009. Of note, there are theoretical risks of increased VTE if taking TA while on hormonal contraception.

Exogenous coagulation factors in the form of vWF concentrate or a factor VIII–vWF concentrate (HUMATE P) can also be infused to normalize vWF and factor VIII levels in the blood.16

Treatment for acute abnormal uter-
ine bleeding in patients with a platelet function disorder should include platelet transfusion as first-line therapy. These patients should also avoid nonsteroidal anti-inflammatory drugs and other drugs that affect platelet aggregation. In the setting of factor deficiencies, factors that are missing or diminished should first be infused and consideration given to use of fibrinogen as an adjunct option. For hemophilia A carriers, DDAVP can be used. Infusions of clotting factor concentrates may also be necessary for both hemophilia A and B. Lastly, TA can be useful for treatment of acute bleeding with platelet dysfunction (Figure 6).16,17

Maintenance therapy
Maintenance therapy for women with bleeding disorders includes evaluation of several factors, such as patient compliance, preference, cost, results of prior therapy (if applicable), insurance coverage, current medication use, and existence of any preexisting medical conditions. Both hormonal and non-hormonal options are available and are often used together. A 2010 study looked at the Mirena IUD for management of heavy menstrual bleeding in women with inherited bleeding disorders and found significant benefit in its use as a long-term treatment.18 Initiating or adding TA to a hormonal treatment regimen has also been shown to reduce HMB by 34% to 65% in patients with bleeding disorders.19 If using a combined hormonal treatment, such as OCs, the patch, or the ring, continuous or extended use is recommended to reduce menstrual bleeding.

Obstetrical considerations
In obstetrics, women with bleeding disorders may actually benefit from the hypercoagulable state of pregnancy, which increases concentrations of several coagulation factors and fibrinogen. Nevertheless, women with bleeding disorders remain at increased risk of multiple complications as they often do not achieve the same level of clotting factors as others.20 (Figure 7)

With respect to preconception counseling women suspected of having a bleeding disorder, or of being carriers, should undergo diagnostic testing prior to pregnancy to optimize pregnancy management. If a woman is a carrier of a certain disorder, pre-implantation genetic testing can be considered and in vitro fertilization may be used to implant only those embryos without the disorder. Another aspect of preconception care includes immunization against hepatitis A and B for those likely to require a blood transfusion.

CONTINUED ON PAGE 23
Does she know what she wants from her birth control?

Consider PARAGARD® (intrauterine copper contraceptive)—the only highly effective, reversible birth control that is hormone free.1,2

High patient satisfaction

~94% of women reported that they were satisfied with PARAGARD when considering their bleeding and cramping at 3 and 6 months post-placement3*

100% hormone free1,2
Patient satisfaction with bleeding and cramping3*
Removable whenever she decides—for up to 10 years1†
>99% effective1

INDICATION
PARAGARD is indicated for intrauterine contraception for up to 10 years.

IMPORTANT SAFETY INFORMATION

• PARAGARD does not protect against HIV/AIDS or other sexually transmitted infections (STI).

• PARAGARD must not be used by women who are pregnant or may be pregnant as this can be life threatening and may result in loss of pregnancy or fertility.

• PARAGARD must not be used by women who have acute pelvic inflammatory disease (PID) or current behavior suggesting a high risk of PID; have had a postpregnancy or postabortal uterine infection in the past 3 months; have cancer of the uterus or cervix; have an infection of the cervix; have an allergy to any component; or have Wilson's disease.

• The most common side effects of PARAGARD are heavier and longer periods and spotting between periods; for most women, these typically subside after 2 to 3 months.

• If a woman misses her period, she must be promptly evaluated for pregnancy.

• Some possible serious complications that have been associated with intrauterine contraceptives, including PARAGARD, are PID, embedment, perforation of the uterus, and expulsion.

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

*Data are from the Contraceptive CHOICE Project. The study evaluated 3- and 6-month self-reported bleeding and cramping patterns in 5011 long-acting reversible contraceptive (LARC) users (n=826, PARAGARD), and the association of these symptoms with method satisfaction. Study participants rated satisfaction with their LARC method as “very satisfied,” “somewhat satisfied,” or “not satisfied.” For the data analyses, “satisfied” and “very satisfied” were grouped together as “satisfied.”3

†PARAGARD must be removed by a healthcare professional.1


PARAGARD is a registered trademark of Teva Women’s Health, Inc.
©2017 Teva Women’s Health, Inc. PAR-41088 January 2017
ParaGard® T 380A Intrauterine Copper Contraceptive

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

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

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

2. Insertion precautions, continuing care, and removal.

3. Vaginal bleeding
In the 2 largest clinical trials with ParaGard®, menstrual changes were the most common medical reason for discontinuation of ParaGard®. Discontinuation rates for pain and bleeding combined are highest in the first year of use and diminish thereafter. The percentage of women who discontinued ParaGard® because of bleeding problems or pain during these studies ranged from 11.5% in the first year to 2.2% in year 9. Women complaining of heavy vaginal bleeding should be evaluated and treated, and may need to discontinue ParaGard®.

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

5. Expulsion following placement after a birth or abortion
ParaGard® has been placed immediately after delivery, although risk of expulsion may be higher than when ParaGard® is placed at times unrelated to delivery. However, expulsion does not necessarily result. Expulsion should be delayed to the second postpartum month because insertion during the first postpartum month (except for after immediately after delivery) has been associated with increased risk of perforation. ParaGard® can be placed immediately after abortion, although immediate placement has a slightly higher risk of expulsion than placement at other times. Placement after second trimester abortion is associated with a higher risk of expulsion than placement after the first trimester abortion.

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

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

8. Pregnancy
ParaGard® is contraindicated during pregnancy.

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

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

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

<table>
<thead>
<tr>
<th>Intrauterine pregnancy</th>
<th>Pelvic infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic abortion</td>
<td>Perforation</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>Embolism</td>
</tr>
</tbody>
</table>

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

- Anemia
- Backache
- Dysmenorrhea
- Dyspareunia
- Dysuria
- Expulsion, complete or partial
- Leukorrhea
- Menstrual flow, prolonged
- Menstrual spotting
- Pain and cramping
- Urinary allergy skin reaction
- Vaginitis

Teva Women’s Health, Inc.
A Subsidiary of Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454

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

PAR-41071 10/16
Regarding early pregnancy, there are several case reports and series documenting an increased risk of miscarriage and placental abruption in women with certain bleeding disorders, such as a Factor XIII or fibrinogen deficiency, and during labor there is an increased risk of spinal/epidural hematomas. A fetus can also potentially be at a substantial risk of bleeding complications during birth. Invasive intrapartum monitoring techniques (e.g., fetal scalp electrode) should be avoided in pregnancies with a potentially affected fetus as intracranial hemorrhage may occur.

Most experts agree that women with bleeding disorders can have a safe vaginal delivery and that a cesarean delivery should be reserved for standard reasons. A recent study on babies with hemophilia found no difference in the rate of fetral intracranial hemorrhage based on mode of delivery. Vacuum and forceps deliveries, however, should be avoided due to the higher risk of intracranial hemorrhage.

Women with bleeding disorders are at increased risk of both antepartum and postpartum hemorrhage. Risk of postpartum hemorrhage in women with vWD is 50% higher than in those without a bleeding disorder. Because women with bleeding disorders are known to present with delayed hemorrhage once estrogen levels decrease in the postpartum period, some physicians will offer prophylactic therapy to cover the immediate postpartum period. DDAVP, for example, can be used to raise vWF levels for this purpose.

**Conclusion**

Bleeding disorders are both prevalent and serious enough in obstetrical and gynecologic practice that the generalist ob/gyn should be fully aware of their existence, potential downstream consequences, and treatment options. These disorders can significantly impact quality of life, but unfortunately, many women remain undiagnosed and untreated due to a lack of familiarity on the part of both patients and the health care professionals they rely on. Ob/gyns should heighten their understanding and appreciation of the importance and implications of bleeding disorders to consistently deliver the best care possible for their patients.

**DISCLOSURES** The authors do not report any conflicts of interest with respect to this article.

**FOR REFERENCES VISIT** contemporaryobgyn.net/bleeding-disorders
Inexpensive generic prevents bleeding deaths after childbirth

An inexpensive generic drug has been found to prevent hemorrhaging in women after childbirth. The WOMAN Trial, involving more than 20,000 women in 21 countries, found that tranexamic acid “could save the lives of mothers who would otherwise bleed to death after childbirth,” according to the trial’s website. Tranexamic acid is an antifibrinolytic agent. It is on the WHO’s List of Essential Medicines.

In the United States, tranexamic acid is sold under the brand name Lysteda and Cyklokapron, with an indication for treating severe menstrual bleeding. The generic form of the drug costs about $2 per dose.

The study, conducted by the London School of Hygiene and Tropical Medicine, was published in the April 26 issue of The Lancet.

In the trial, death due to bleeding was reduced by about a third when tranexamic acid treatment was given within 3 hours. Tranexamic acid reduced the need for laparotomy to control bleeding by more than a third.

There were no side effects observed from the drug for either mothers or babies.

“We now have important evidence that the early use of tranexamic acid can save women’s lives and ensure more children grow up with a mother,” the website stated.

Postpartum hemorrhage is the leading cause of maternal death worldwide. In the randomized, double-blind, placebo-controlled trial, researchers recruited women aged 16 years and older with a clinical diagnosis of postpartum hemorrhage after a vaginal birth or cesarean delivery from 193 hospitals in 21 countries.

They randomly assigned women to receive either 1 (10 mg/mL) dose of intravenous tranexamic acid or matching placebo, in addition to usual care. If bleeding continued after 30 minutes, or stopped and restarted within 24 hours of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given.

The researchers found that death due to bleeding was significantly reduced in women given tranexamic acid (155 of 10,036 patients vs 191 of 9985 patients in the placebo group). In women given treatment within 3 hours of giving birth, death was reduced most significantly (89 in the tranexamic acid group vs 127 in the placebo group).

“Tranexamic acid reduces death due to bleeding in women with postpartum hemorrhage with no adverse effects,” the researchers wrote in The Lancet. “When used as a treatment for postpartum hemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.”

REFERENCE

WHI data shed light on risks of long-term bisphosphonate use

Analysis of data from the Women’s Health Initiative study adds to concerns about potential risks of long-term use of bisphosphonates in elderly women. The findings, published in The Journal of the American Geriatrics Society, reflect outcomes in a large group of patients at high risk of fracture, many of whom had taken the drugs for at least 10 years.
Women in the retrospective cohort had an average age of 80 years and had used bisphosphonates for at least 2 years, as self-reported on a 2008-2009 medication inventory. The 2-year mark was chosen as a reference because that duration of use has been associated with lower fracture risk. Follow-up on the group was from 3.7 ± 1.2 years. Women who had used other medications that affect bone metabolism, including calcitonin, selective estrogen reuptake inhibitors, parathyroid hormone, and aromatase inhibitors, were excluded. The cohort also did not include patients who reported using estrogen within 5 years before the medication inventory or those who had discontinued bisphosphonates but resumed them.

For outcomes, the researchers looked at annual rates of hip, clinical vertebral, wrist or forearm fracture, and any clinical fracture. They also used multivariate Cox proportional hazards models to determine whether there was an association between use of bisphosphonates for 3 to 5; 6 to 9; or 10 to 13 years and fracture, compared with use for 2 years.

The multivariate-adjusted analysis showed that using bisphosphonates for 10 to 13 years was associated with higher risk of clinical fracture than 2 years of use (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.07 to 1.57). The risk persisted when the analysis was limited to women who had a prior fracture (HR = 1.30, 95% CI = 1.01-1.67) and those with no history of cancer (HR = 1.36, 95% CI = 1.10-1.68). Among patients on bisphosphonates for 10 to 13 years, risk was higher for hip (HR = 1.66, 95% CI = 0.81-3.40) and clinical vertebral fractures (HR = 1.65, 95% CI = 0.99-2.76) although the associations for this dosage duration were not statistically significant for any site-specific fracture.

The researchers noted that their study looked at the association between fracture risk and bisphosphonate use “in more high-risk, older female long-term bisphosphonate users than any previous study.” They theorized that the findings may be explained by “biological changes in bone during long-term bisphosphonate use...including oversuppression of the bone remodeling process, which may damage bone.”

The study’s strengths include the large sample, which incorporated long-term users of the drugs and women who had taken them for up to 13 years. The authors also adjusted for 5-year hip fracture risk score and for many participant characteristics predictive of fracture risk.

REFERENCE
ACOG GUIDELINES AT A GLANCE

EXPERT PERSPECTIVES ON PRACTICE BULLETINS

COMMITTEE ON PRACTICE BULLETINS—Obstetrics, Committee On Genetics, And Society For Maternal-Fetal Medicine


PREGNANT DIAGNOSTIC TESTING FOR GENETIC DISORDERS

Prenatal genetic diagnostic testing is intended to determine, with as much certainty as possible, whether a specific genetic disorder or condition is present in the fetus. In contrast, prenatal genetic screening is designed to assess whether a patient is at increased risk of having a fetus affected by a genetic disorder. Originally, prenatal genetic testing focused primarily on Down syndrome (trisomy 21), but now it is able to detect a broad range of genetic disorders. Although it is necessary to perform amniocentesis or chorionic villus sampling (CVS) to definitively diagnose most genetic disorders, in some circumstances, fetal imaging with ultrasonography, echocardiography, or magnetic resonance imaging may be diagnostic of a particular structural fetal abnormality that is suggestive of an underlying genetic condition.

The objective of prenatal genetic testing is to detect health problems that could affect the woman, fetus, or newborn and provide the patient and her obstetrician–gynecologist or other obstetric care provider with enough information to allow a fully informed decision about pregnancy management. Prenatal genetic testing cannot identify all abnormalities or problems in a fetus, and any testing should be focused on the individual patient’s risks, reproductive goals, and preferences. It is important that patients understand the benefits and limitations of all prenatal screening and diagnostic testing, including the conditions for which tests are available and the conditions that will not be detected by testing. It also is important that patients realize that there is a broad range of clinical presentations, or phenotypes, for many genetic disorders and that results of genetic testing cannot predict all outcomes. Prenatal genetic testing has many benefits, including reassuring patients when results are normal, identifying disorders for which prenatal treatment may provide benefit, optimizing neonatal outcomes by ensuring the appropriate location for delivery and the necessary personnel to care for affected infants, and allowing the opportunity for pregnancy termination.

The purpose of this Practice Bulletin is to review the current status of prenatal genetic diagnostic testing and the evidence supporting its use. For information regarding screening for fetal aneuploidy, refer to Practice Bulletin No. 163, Screening for Fetal Aneuploidy.

COMMENTARY

A welcome review of current evidence on prenatal diagnostic testing

by JOE LEIGH SIMPSON, MD

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have recently revisited and updated clinical information and recommendations on several related documents: Practice Bulletin 162, which will be reviewed in this communication; Screening for Fetal Aneuploidies (Practice Bulletin 163); Microarrays and Next Generation Sequencing Technology (Committee Opinion 682); and Carrier Screening for Genetic Conditions (Committee Opinion 691).
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In Practice Bulletin 162, Drs. Mary Norton and Marc Jackson are the acknowledged authors on behalf of the ACOG Committee on Genetics and SMFM. Practice Bulletin 162 should be applauded for recommendations and conclusions that previous ACOG bulletins could be accused of obviating in deference to tradition.

Invasive prenatal diagnostic techniques

In 2007, ACOG boldly stated in Practice Bulletin 77 that all pregnant women should have the option of an invasive procedure (chorionic villus sampling [CVS] or amniocentesis). This statement still holds and reflects sensitivity of detecting fetal abnormalities being greatest with diagnostic tests possible only using tissue obtained from an invasive procedure. New in Practice Bulletin 162 are updated risks for CVS and amniocenteses. The hackneyed and outdated allusions to a loss rate of up to 1% for CVS or 0.5% (“1 in 200”) for amniocenteses are no longer applicable. Pregnancy loss rate following CVS ≥ 10 weeks is now cited as 0.22% (1 in 455).1 The risk of limb reduction defects with CVS is stated to be 6 per 10,000, not significantly different from the general population and as concluded by the World Health Organization in 1994.2

The loss rate following traditional amniocenteses is now stated to be 0.13% (1 in 769) in experienced hands. Practice Bulletin 162 does cite a 1% to 2% rate of amniotic membrane rupture, which seems unduly high in my opinion and based on a 1998 study.3 On the other hand, perinatal survival following often transient membrane rupture is, in my opinion, plausibly stated to be greater than 90%. The long-accepted conclusion that 10- to 13-week amniocentesis is not recommended was confirmed. Loss rates in multiple gestations are said to be 2%, perhaps high in experienced hands.

Laboratory tests and diagnostic accuracy

The most transformative guideline in Practice Bulletin 162 is its recommendation for DNA-based microarrays to determine status of all 24 chromosomes. A karyotype is no longer recommended.

This conclusion is based first on the 2012 National Institutes of Child Health and Human Development (NICHD) trial of Wapner and colleagues including this author4 followed by replication.5 The NICHD trial report compared accuracy and additional yield of microarray versus karyotype. Given a normal fetal ultrasound and a normal fetal karyotype, chromosomal microarrays identified clinically significant (chromosomal) abnormalities in 1.7% additional cases over that detected by karyotype alone. The additional abnormalities involved genomic material smaller than the 5 to 7 million base pair resolution possible with a high-resolution karyotype. If ultrasound had revealed a fetal anomaly, the yield catapulted an additional 6%. The take-home message is that an invasive prenatal procedure performed for any reason warrants a chromosomal microarray, and not simply a karyotype.

Chromosomal mosaicism is stated to occur in 0.25% of amniocenteses and in 1% of CVS samples. In amniotic cells and in chorionic villi analysis, providers have long applied algorithms to clarify the clinical significance of abnormal, non-modal cells. If a non-modal cell line in chorionic villi is believed confined to trophoblasts (placenta), the embryo itself should theoretically be normal: confined placental mosaicism (CPM). Extant recommendations for determining clinical significance remain.

Practice Bulletin 162 was prepared, however, prior to generation of new information derived from next generation sequencing (NGS). With NGS, mosaicism is unavoidably encountered, given its greater sensitivity, more often than with chromosomal microarrays. If NGS has been recently introduced into a lab to which prenatal samples are being sent, the provider should inquire if altered criteria for prenatal diagnosis of CVS or amniotic fluid cell mosaicism is being applied. NGS is now widely used in preimplantation genetic diagnosis (PGD), for which Practice Bulletin 162 was presumably not intended.

Testing in fetal death or stillbirth

Chromosomal microarrays have also replaced karyotypes as the recommended diagnostic test in evaluating tissue from a fetal demise. In addition to greater sensitivity, chromosomal microarrays do not require cultured cells. This has long been a major prob-
Mycoplasma genitalium: A Review of Current Issues and Challenges

Case Report: Persistent Discharge and Pelvic Pain in a 19 YO Female

A 19-year-old female patient with PID presented with persistent discharge and pelvic pain despite multiple rounds of treatment with azithromycin, the treatment of choice per the most recent CDC STD treatment guidelines. Her partner was subsequently seen for persistent penile discharge and diagnosed with non-gonococcal urethritis (NGU) but tested negative for Chlamydia trachomatis and Neisseria gonorrhoeae after treatment of an initial C. trachomatis infection. The couple reported to have continued intercourse due to the negative C. trachomatis/N. gonorrhoeae test results. The female patient was tested for Mycoplasma genitalium using a nucleic acid amplification test (NAAT) through a university research laboratory at her last visit. Further testing demonstrated the presence of a 23S rRNA gene mutation for macrolide resistance in the M. genitalium strain which explained the observed resistance to previous azithromycin treatment. Given these results, the couple was treated with moxifloxacin, a fourth-generation synthetic fluoroquinolone antibacterial agent, which eventually led to the resolution of reported symptoms.

While this case reports successful identification and treatment of M. genitalium, it reflects the current state of affairs in the management of sexually transmitted infections (STIs). In stark contrast to this case, an asymptomatic patient in a similar scenario or a symptomatic patient without access to advanced STI diagnostics would continue to harbor the azithromycin-resistant strain of M. genitalium, thereby remaining at risk for adverse reproductive outcomes and potentially transmitting the pathogen to other partners. M. genitalium has emerged as an important STI and warrants an accurate diagnosis and effective management strategies.

Mycoplasma genitalium: An Emerging STI that Demands Clinician Attention

Many clinicians haven’t heard of M. genitalium, even though it is now included in the CDC STD treatment guidelines. Although clearly sexually transmitted, with increasing evidence linking it to adverse reproductive outcomes for women, M. genitalium is still considered an emerging pathogen. Given potentially increasing prevalence and evidence of expanding antibiotic resistance, it is imperative to raise clinician awareness about this organism. Mycoplasma genitalium infects the male and female genital
tracts and is associated with NGU among males as well as cervicitis, endometritis, pelvic inflammatory disease (PID), infertility and adverse birth outcomes among women. It has also been associated with an increase in risk for human immunodeficiency virus (HIV) infection. Detection of *M. genitalium* in clinical practice is challenging given the absence of an FDA-approved diagnostic assay; therefore, most infections are managed symptomatically. Furthermore, treatment of *M. genitalium* infection poses increasing challenges due to rising antibiotic resistance. This case report and literature review discussed herein underscore the need for improved awareness of *M. genitalium*.

**Key Facts You Need to Know about Mycoplasma genitalium**

*M. genitalium* is more common than many other sexually transmitted pathogens.

Data from several population-based studies of low-risk individuals estimate that the prevalence of *M. genitalium* among women ranges from 0.8%-4.1% and among men ranges from 1.1%-1.2%. However, higher prevalence has been reported among patients attending STD clinics. For instance, among women attending an STD clinic in Seattle, WA, the prevalence of *M. genitalium* was 7.7%, but as high as 19% in both Baltimore, MD, and Durham, NC. Among men attending US STD clinics, prevalence ranged from 12%-15% in a similar time period. More recently, a multicenter clinical study from the US reported *M. genitalium* prevalence of 16.1% among women aged 14-70 years and 17.2% among men age 18-78 years, with the highest prevalence identified in adolescent and young adult men and women (>24%) as well as among black men and women (27.9% and 23.2%), consistent with risk factors identified in population-based studies. Similarly, a Midwestern commercial laboratory reported prevalence of 11.4% for females and 6.8% for males. In all but a few cases, *M. genitalium* prevalence was higher than all other bacterial STI in these more recent studies.

*M. genitalium* is sexually transmitted.

Several studies provide evidence that *M. genitalium* is sexually transmitted. *M. genitalium* is more common among sexually experienced than sexually-naive adolescents and occurs more frequently in individuals with more sexual partners. Similar to other STIs, sexual partners of *M. genitalium*-positive individuals are more likely to have *M. genitalium* than partners of *M. genitalium*-negative individuals. In addition, strain typing has demonstrated that most concordantly infected sex partners harbor genomically identical *M. genitalium* strains.

*M. genitalium* can travel with other sexually transmitted organisms.

The extent to which individuals with *M. genitalium* are co-infected with other STIs varies by geographic setting and gender. In the Pacific Northwest co-infections are rare; however, co-infection has been observed more frequently in other areas. In Baltimore STD clinic attendees, 37% of women but only 5.9% of men with *M. genitalium* were co-infected with another STI. Co-infection with chlamydia and *M. genitalium* in US women ranged from 3.1% in a recent multi-site study to 37.5% among adolescent females in the Midwest, whereas among men it ranged from 9.7% in 7 US clinics to 35% of men in New Orleans. Few instances of co-infection with *Trichomonas vaginalis* have been reported, with only 6.3% among women but none among men in 7 clinics. In contrast, bacterial vaginosis (BV) has been associated with *M. genitalium* in some studies, and a recent study among Kenyan women reported that BV may increase susceptibility to *M. genitalium*.

HIV is approximately twice as common in *M. genitalium*-infected as in *M. genitalium*-negative individuals and two studies have demonstrated that *M. genitalium* infection was associated with an increased risk for subsequent HIV acquisition. *M. genitalium* may also increase the risk of HIV transmission to sex partners, given the elevated HIV viral shedding observed in dually infected individuals.

Consider that *M. genitalium* may be a cause for symptoms.

Although most *M. genitalium* infections are asymptomatic, the organism has also been strongly associated with male and female reproductive tract syndromes. However, there are no distinguishing clinical features of an *M. genitalium* infection, making it infeasible to determine the presence or absence of *M. genitalium* based on clinical signs and symptoms alone. Symptoms, when present, are similar to those in individuals with C. trachomatis-associated urethritis, cervicitis and PID. *M. genitalium* is an acknowledged cause of male urethritis, and meta-analyses have demonstrated that men infected with *M. genitalium* are 5 and a half times more likely to have urethritis than men without *M. genitalium*. Balanitis and posthitis have been reported among *M. genitalium*-positive men in one study, and rectal infections have been detected in 2%-12%, particularly among men who have sex with men. Given the rising practice of anal intercourse among women, rectal infections are increasingly likely and have been reported in 2.7%-8.1% of women. In meta-analyses of female reproductive tract disease syndromes, *M. genitalium* was associated with an approximately 2-fold increase in the risk of cervicitis, PID, preterm delivery, spontaneous abortion, and infertility. This increased risk was statistically significant for all syndromes but infertility and was stronger in studies that controlled for other STIs. Although the meta-analysis strongly implicates *M. genitalium* in the etiology of female reproductive tract disease syndromes, additional definitive data are still lacking. Most studies of *M. genitalium* infection in women have been cross-sectional in nature and few have followed women over time to determine what proportion of infected women go on to experience severe sequelae. While an earlier randomized trial convincingly demonstrated the utility of screening and treating C. trachomatis infections in preventing PID, similar studies have not yet been carried out for *M. genitalium*.

Although few studies of ectopic pregnancy have been conducted, in vitro infection of tubal tissue with *M. genitalium* has been shown to result in deformation

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**Note:** The above content is a summary and does not include all details and references mentioned in the original text. Further research and consultation with medical professionals are recommended for comprehensive understanding and application.
and destruction of cilia, similar to events after C. trachomatis infection.\textsuperscript{44} This potential mechanism for ectopic pregnancy is consistent with a recent Saudi Arabian study, which tested tubal specimens by polymerase chain reaction (PCR). Women in whom M. genitalium was detected were 2-fold more likely to have an ectopic pregnancy suggesting that M. genitalium may be involved in the etiology of this syndrome as well.\textsuperscript{55}

**NAATs are the diagnostic method of choice for M. genitalium.**

M. genitalium is a slow-growing organism that lacks a cell wall and therefore cannot be detected by Gram staining. It is very fastidious and culture is not a feasible option for diagnostic testing. When achieved, culture requires up to 6 months.\textsuperscript{46,47} Current serological tests are insufficiently sensitive and specific and cannot differentiate between current and previous infection. Nucleic acid amplification tests (NAATs) are therefore the primary method of detection. Two types of NAATs have been developed and used to detect M. genitalium. PCR tests were initially developed by research laboratories for early research studies\textsuperscript{48,49} and variations of these PCR tests have now been implemented by several large commercial laboratories. There is no FDA-approved diagnostic NAAT assay available in the US.\textsuperscript{50}

All of the NAAT assays can be used with a variety of specimen types, including male and female urine, vaginal swabs (clinician- and self-collected), endocervical swabs; and male urethral, penile-mental and rectal swabs. M. genitalium is rarely detected in the oropharynx, so oropharyngeal swabs are less often utilized.\textsuperscript{34} Although most specimen types have good sensitivity and specificity, self-collected vaginal swabs have higher sensitivity than other female specimen types and self-collected penile-mental swabs have recently been found to have slightly higher sensitivity than other male specimen types.\textsuperscript{51-53}

**M. genitalium is increasingly resistant to recommended antibiotic regimens.**

Although the 2015 CDC STD treatment guidelines classify M. genitalium as an emerging sexually transmitted pathogen, in the absence of validated diagnostic tests, the treatment of most M. genitalium cases must rely on syndromic management.\textsuperscript{1} The recommended first-line therapy for urethritis or cervicitis is either 100 mg doxycycline twice daily for 7 days or a single 1 g dose of azithromycin. Moxifloxacin (400 mg daily x 7, 10 or 14 days) is recommended in cases of persistent/recurrent urethritis or persistent/recurrent cervicitis where M. genitalium is suspected. For cases of PID in which M. genitalium is suspected or detected, a 14-day regimen of moxifloxacin 400 mg daily is recommended. However, the CDC guidelines do not currently suggest routine tests-of-cure or re-screening among asymptomatic patients after treatment for any of these syndromes.\textsuperscript{1}

The 2016 European guidelines on M. genitalium make similar recommendations for treatment of urethritis, cervicitis and PID, but recommend a longer course of azithromycin instead of the 1g single dose (an initial 500-mg dose followed by 250 mg daily for 4 days).\textsuperscript{34} Nevertheless, more recent data suggest that there is limited additional benefit to the extended duration regimen.\textsuperscript{55} The European guidelines also suggest NAAT for initial detection of M. genitalium, followed by an assay to determine macrolide resistance to guide therapeutic decisions and tests-of-cure 3 weeks after the start of treatment.

The recommendation to employ a second assay to determine macrolide resistance is rooted in the rapid spread of macrolide resistance in M. genitalium. In most settings, azithromycin has been the treatment of choice for urethritis and cervicitis, in part due to its single-dose nature.\textsuperscript{56} However, although azithromycin was initially highly effective against M. genitalium, cure rates after the 1 g dose have diminished to 69% in studies after 2009.\textsuperscript{57} The emergence of resistance to azithromycin has been attributed to mutations in the 23S rRNA gene in M. genitalium that typically confer nearly complete resistance to macrolides.\textsuperscript{58} These mutations can be detected by either PCR amplification and sequencing of the 23S rRNA gene in M. genitalium or by multiplex qPCR utilizing coupled PlexZyme primers.\textsuperscript{39,60} In areas of the Asia-Pacific, where antibiotic resistance typically emerges first, these macrolide mediating resistance mutations (MRMM) have recently been detected in 63% of M. genitalium-positive patients in Melbourne, Australia, and 74% of Auckland, New Zealand patients.\textsuperscript{38,61} Although macrolide resistance has been slower to emerge in the US, a recent study demonstrated that MRMM were found in 50.8% of female patients and 42% of male patients with M. genitalium, with a higher prevalence among younger than older individuals and among those of African American descent relative to other race/ethnicities.\textsuperscript{15}

Moxifloxacin, the currently recommended second-line treatment, was initially highly successful in cases of azithromycin treatment failure, with cure rates of 100%.\textsuperscript{62} However, the first reports of treatment failure after moxifloxacin began appearing in 2012,\textsuperscript{63} and treatment failure in recent reports ranges from 12%-30%.\textsuperscript{64,65} This emerging resistance is most strongly associated with mutations in the parC region of the quinolone resistance determining region (QRDR) in M. genitalium. Although little data exist on the prevalence of parC mutations in the US, frequencies of 5%-6% in Eastern Europe, and up to 14% in Australia, have been recently reported.\textsuperscript{66,67} Of greater concern are increasing reports of markers of dual resistance to macrolides and quinolones and treatment failures after therapy with both antimicrobials.\textsuperscript{54,66-69,70} In these cases, pristinamycin, a streptogramin and spectinomycin, an aminoglycoside, have been effective.\textsuperscript{64,70} But in many locations, including the US, these antibiotics are not available.

**M. genitalium is a serious problem.**

M. genitalium infection is clearly and strongly associated with urethritis in men and can be sexually transmitted to female partners. In an increasing number of settings, prevalence is as high as or higher than other bacterial STI pathogens, and accumulating evidence suggests that infection in women is associated with adverse reproductive outcomes such as PID, preterm delivery, and potentially infertility. This is coupled with the substantial and increasing treatment challenges for this pathogen. Standard antibiotics used in syndromic
therapy for reproductive tract infections are waning in terms of efficacy, macrolide resistance may already be widespread, quinolone resistance is emerging, and cases of dual resistance are occurring. In addition, management of *M. genitalium* infections is challenged by the current lack of an FDA-approved diagnostic test. Although laboratory-developed tests validated for clinical use by large commercial laboratories or analytic specific reagents (ASRs) developed for existing platforms are becoming increasingly available, the US lacks guidelines for the use of these tests. In the absence of this, most patients with *M. genitalium* will not be diagnosed nor will they receive a test-of-cure after therapy which has a high likelihood of being ineffective. To mitigate these threats to female reproductive health, future directions should include making an FDA-approved assay widely available, instituting widespread resistance testing and surveillance, and developing novel therapeutic regimens. Until this has been accomplished, clinicians will need to be aware of *M. genitalium* and consider it when engaged in syndromic management of reproductive tract infections. (General guidelines to consider are summarized in Figure 1).

**Call to Action: Bringing Research into the Clinic**

Given potentially rising prevalence of *M. genitalium* among young adults and its associated adverse effects on the female genital and reproductive tract, *M. genitalium* represents a serious problem. Improved access to testing among high-risk populations and research to aid the development of evidence-based screening guidelines for the general population will be essential to adequately manage infections with this pathogen and prevent disease complications at the population level.

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• Global prevalence estimates vary. 
• Associated with genital and reproductive tract disease.
• More common than Neisseria gonorrhoeae.

Most infections are asymptomatic, but symptoms may occur. 

Clinical manifestations (if present)

Women
- Mucopurulent cervical discharge, cervical friability and increased number of polymorphonuclear leukocytes
- Silent or asymptomatic pelvic inflammatory disease (PID)

Men
- Dysuria
- Urethral pruritus
- Urethral discharge

Possible complications of untreated infections

- PID
- Preterm birth
- Spontaneous abortion
- Infertility

Types of samples used for women
- Vaginal swab*
- First-void urine
- Endocervical swab
- Rectal swab

Types of samples used for men
- First-void urine
- Penile meatal swab
- Urethral swab
- Rectal swab

*Clinician- or patient-collected; highest relative sensitivity for NAAT.

The CDC recommends nucleic acid amplification testing (NAAT); there is no FDA-approved diagnostic test for M. genitalium.

M. genitalium testing in men and women can be performed using many sample types.

Polymerase chain reaction (PCR)-mediated amplification of genomic regions

Transcription-mediated amplification (TMA) of 16S rRNA

Moxifloxacin
400 mg/day x 7–14 days

Azithromycin
1-g single dose

Macrolide resistance or persistent symptoms

M. genitalium testing in men and women can be performed using many sample types.

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The microbiome in prematurity: key messages from emerging science

Studies of the placental microbiome are a window into the complex interplay between microbiota and host in spontaneous PTB.

by KJERSTI MARIE AAGAARD, MD, AND DERRICK MICHAEL CHU, BSC

Although preterm birth (PTB) (<37 weeks at delivery) is a leading cause of perinatal morbidity and mortality worldwide, reliable tools to clinically predict both its occurrence and severity or the co-occurrence of infant morbidity are lacking. This clinical dilemma is further exacerbated by the absence of highly efficacious primary and secondary prevention measures, as well as reliable interventions.\(^1,2\)

Perhaps the greatest obstacle to their discovery is the likely multifactorial and varied etiology of PTB, which is undoubtedly a reflection of the “lumping” of what is actually a syndrome with varied etiologies into a single disorder. Indeed, PTB can be readily separated into spontaneous and indicated PTB, and, thus, treatment or prevention for one might be counterproductive for the other.

Take for example any day on a labor and delivery ward around the United States: 2 women deliver at 32 and 2/7 weeks’ gestation. The first was induced for 2 days secondary to her diagnosis of severe preeclampsia with concern for worsening symptoms. The second woman presented 3 hours ago in active labor with advanced cervical dilation to 7 cm and just ruptured her membranes. Working to identify the etiology of early severe preeclampsia in the first patient could be of benefit in future pregnancies (eg, treating instances of spontaneous preterm birth are thought to be associated with the presence of intrauterine infection and inflammation, with certain environmental factors also increasing the risk.

Attempts to treat existing infections with antibiotics do not appear to have a mitigating effect on the rate of spontaneous preterm birth and, in some instances increased the rate.

Instances of spontaneous preterm birth are thought to be associated with the presence of intrauterine infection and inflammation, with certain environmental factors also increasing the risk.

Attempts to treat existing infections with antibiotics do not appear to have a mitigating effect on the rate of spontaneous preterm birth and, in some instances increased the rate.
underlying systemic lupus erythematosus, providing low-dose aspirin). Conversely, in our second patient, attempts at preventing recurrent spontaneous PTB will be of benefit (eg, via administration of 17-alpha hydroxyprogesterone caproate). However, both outcomes would be classified as PTB even though their etiologies are likely quite distinct. Given the heterogeneous nature of PTB, we will focus this review on the spontaneous PTB syndrome and the potential of underlying inflammatory and infectious causes of its occurrence.

Etiologies of spontaneous preterm birth
Observational studies have identified a number of environmental and host factors that carry a greater risk of spontaneous PTB, including a prior history, maternal smoking, and maternal race/ethnicity. Intrauterine infection and associated inflammation has also been hypothesized as a potential contributor to spontaneous PTB, but a specific infectious etiology has yet to be identified. Moreover, empirical administration of antimicrobials for presumptive infectious processes have been uniformly shown to be non-efficacious in preventing spontaneous PTB, and may instead increase risk. In addition, bacterial vaginosis (BV) increases risk of PTB, but while antibiotic treatment of symptomatic BV is efficacious, PTB rates are unaffected. Even more concerning, several studies have found that empiric antibiotic administration to asymptomatic women increased the rate of PTB. These outcomes highlight the notion that PTB may be a result of aberrant shifts in maternal microbiota rather than by a single infectious microorganism per se. However, despite several decades documenting the co-association of altered vaginal microbiota and inflammation with spontaneous PTB, neither a clear pathologic agent nor targeted therapy has shown unmitigated success in combatting presumptive infectious or inflammatory PTB.

Lack of clear pathogenic microbes driving spontaneous PTB has spurred interest in the potential role of commensal microbes. Research on the trillions of commensal microorganisms that reside on and within our bodies, collectively known as the human microbiota, has begun to reorient how we think microorganisms may influence pregnancy outcomes. Recent advances in sequencing technologies have enabled in-depth interrogation of these microbial communities and their function without the limitations of culture-based methods. The normal vaginal microbiota of healthy non-pregnant and pregnant women has since been comprehensively characterized, providing a reference for the typical microbiota associated with obstetrical health. Furthermore, the low biomass microbial community of placenta, their membranes, and amniotic fluid in healthy pregnancies has been similarly identified and characterized by several investigators, which has contributed to the emerging body of evidence that is challenging the notion of a sterile intrauterine environment. These and other studies have subsequently begun to characterize the placental microbiota in cases of PTB, chorioamnionitis and other adverse pregnancy outcomes. In this review, we will briefly review the current literature exploring associations between the vaginal and placental microbiota and PTB, highlight the remaining gaps in our knowledge, and speculate on how this information may impact future clinical practice.

Vaginal microbiota and preterm birth
Given its proximity to the intrauterine environment, vaginal microbiota are hypothesized to play a role in maintaining a healthy pregnancy. Recently, the typical microbiota associated with healthy women before and during pregnancy have been catalogued using deep sequencing methods in an attempt to provide a “normal” reference before ascribing specific microbiota to disease risk or prevention trials. It has long been known that the vaginal microbiome of healthy non-pregnant and pregnant women tends to be dominated by Lactobacillus species, which produce lactic acid and other bacteriocidins that likely provide protection against pathogenic microorganisms. However, deep sequencing of the vaginal microbiota of reproductive-aged women has un-
OVA1 Reliably Detects Ovarian Cancer Better than CA-125

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<th>Sensitivity Across Histological Subtypes&lt;sup&gt;1&lt;/sup&gt;</th>
<th>CA-125</th>
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Longoria, et al. studied risk assessment of early stage cancers comparing CA-125, Clinical Impression, and the modified ACOG guidelines to OVA1 (MIA). Adding OVA1 to Clinical Impression reduced early-stage cancers missed from 31% to just 5% (85% reduction).

89 percent of pre-menopausal early-stage ovarian cancers were detected by OVA1 with clinical assessment compared to 66% with CA-125. Early-stage detection enables appropriate referral and surgery to avoid potential for upstaging.

The 2013 Bristow, et al. study included the effectiveness of using OVA1 (MIA) to detect ovarian cancer subtypes. OVA1 detected epithelial ovarian cancer (EOC) at a 99% rate compared to CA-125 at 89%. Additionally, OVA1 detected non-EOC at a 92% compared to CA-125 at 76%.

OVA1 plus clinical assessment has a sensitivity of 96% and an NPV of 98% (Bristow, 2013) allowing the provider to properly manage adnexal masses that may be cancer different than those that are truly benign.
covered further complexities within and between microbial communities not previously described. A seminal study of approximately 400 non-pregnant reproductive-aged women of various ethnicities and ages found that the dominant species of Lactobacillus found within their vaginal microbiota (e.g., L. crispatus, L. jensenii or lack thereof), which grouped them into 1 of 5 “community state types” (CSTs). While the CST representation was found to vary significantly among different ethnicities, indicating that host genetics, diet, or environment may influence the type and abundance of bacteria present within the vagina, caution must be used when using this terminology in clinical practice because CST identification may vary with analytical methods and may underestimate the true variation of vaginal microbiota that likely exists within the population. Moreover, the vaginal microbiome can be highly variable over time, thus it would be difficult to assign these women to a single CST at any given point. Nevertheless, these studies have provided an initial frame-work with which to interrogate the impact of microbiota in pregnancy.

Comparative studies of pregnant and non-pregnant women have found that the vaginal microbiome undergoes specific rearrangements that accompany pregnancy. In pregnancy, the vaginal microbiome tends to exhibit increased stability over time, harbors fewer unique bacteria, and experiences fewer shifts in community composition. These observations are likely a reflection of the increased abundance of Lactobacilli in the vagina, which tends to eventually dominate the vaginal flora as the pregnancy progresses. The role that Lactobacilli play in maintaining a healthy pregnancy remains poorly understood, but they may synergistically metabolize increased glycogen stores within the vaginal epithelium to acidify the vaginal environment to foster its own growth while inhibiting growth of other species. Despite these important observations, our understanding of the vaginal microbiome in healthy pregnancies remains incomplete. Individuals of different racial or ethnic backgrounds have varied risk profiles for adverse pregnancy outcomes and in a similar manner, the vaginal microbiota appear to vary substantially according to race and ethnicity. Individuals of different racial or ethnic backgrounds have varied risk profiles for adverse pregnancy outcomes and in a similar manner, the vaginal microbiota appear to vary substantially according to race and ethnicity. Hyman et al. similarly did not identify any microbiota associated with PTB. In the latter study, the overall diversity of the vaginal microbiome was significantly reduced in Caucasian women who delivered preterm, but the impact of such a reduction is unknown. In contrast, a subsequent study by DiGiulio et al. reported that women with reduced Lactobacilli and increased Gardnerella or Ureaplasma were at increased risk of PTB, but frequent sampling to detect these subtle variations was necessary. Differences in the ethnic demographics between these study cohorts may account for the disparate conclusions reached by each, with 90% of subjects in the Romero et al., study identifying as African American, while a majority of subjects in the DiGiulio et al. study identified as Caucasian. Thus, the discrepancies between the overall conclusions of these studies may re-
flect the difference in impact on host genetics and other factors on vaginal microbiome composition in the context of PTB, although it is clear that with such little evidence to date, additional studies are sorely needed to evaluate vaginal microbiota in cases of PTB.

**Placental microbiota and preterm birth**

The prevailing paradigm indicates that the intrauterine environment and its associated tissues are sterile, and that bacterial infection of the placenta results in adverse outcomes, including preterm labor. However, bacteria within the placenta are not restricted to subjects with PTB, as a number of studies have documented DNA and culture evidence of bacteria within the amniotic fluid, cord blood and placenta of healthy, term pregnancies. More recently, we used deep sequencing methods to describe the microbial community within the placenta of healthy, term pregnancies. Across 320 pregnancies, we identified a large diversity of microbiota present in the placental parenchyma with a notable predominance of *Escherichia coli*. Numerous groups have subsequently repeated this work and have further shown that the placental microbiota share similarity to those within the amniotic fluid and neonatal meconium. Interestingly, because the placental microbiome bore the greatest similarities to that of the oral cavity, we’ve speculated that many of the microorganisms found within the placenta originate from the oral gingiva. This could potentially explain the known association of periodontitis with PTB, although studies in well-controlled models are required to delineate this potential link further.

But what is the normal impact and function of these microbiota and how is this changed in disease? In our initial characterization of the normal placental microbiome, we found that the placental microbiome was significantly different in cases of PTB, in mothers with a remote history of antenatal infection, and more recently, in relation to histological chorioamnionitis. *Burkholderia* was increased in the placentae of PTB subjects, while *Streptococcus* and *Acinetobacter* were enriched in the placentae of subjects with a remote history of antenatal infection. We’ve further demonstrated that the “preterm” placental microbiome can be further distinguished in mothers with excess gestational weight gain, independent of maternal obesity. Interestingly, bacterial gene pathways related to butanoate metabolism were also decreased in mothers with excess gestational weight gain, which may have substantial implications on placental biology as butanoate has been shown to modulate inflammation in the gastrointestinal tract. Although additional studies are needed to ensure the robustness of these findings, these initial observations have nevertheless provided tangible hypotheses to drive future interrogations of the complex interplay between host and microbiota in the etiology of PTB.

**Microbiota of other body sites**

Studying microbiota in other areas of the body, including the maternal gut and oral cavity, may further inform our understanding of PTB. Periodontal disease is an associated risk factor for PTB, and a number of common oral pathogens, including *Fusobacterium nucleatum*, are frequently found in diagnostic cultures from patients with preterm labor, premature rupture of membranes and, stillbirth. In agreement with these clinical observations, the placental microbiome has been similarly shown to harbor many oral commensal bacteria, including *Streptococcus* species. But how do microbiota typical of the oral cavity come to inhabit the intrauterine space? One hypothesis indicates a potential hematogenous route. Translocation of gingival-associated microbes into the blood stream can occur as a result of periodontal disease or after dental procedures. In mouse models, it has been demonstrated that oral commensals can hematogenously spread to the placenta, potentially facilitated by specific bacterial cell surface proteins that can compromise endothelial adhesion junctions. Thus the possibility of oral to
placental transmission exists, though further studies are necessary to investigate this proposed mechanism in greater detail. If such a link does exist, then the gastrointestinal tract, which by far harbors the greatest biomass of bacteria, becomes another important organ system that may impact the placental microbiome. Certain disease states, including obesity, can compromise the intestinal barrier and increase permeability to microbiota. If and how such a state may impact the placental microbiome and pregnancy outcomes remains unknown, but together these observations indicate that the gut and oral microbiomes may be an important component of the complex pathophysiology that underlies PTB.

Summary
Advancements in sequencing technologies have provided more sophisticated tools to interrogate the role of maternal microbiota in obstetrical health and disease. This has greatly expanded our understanding of the microbiota present in the vagina and uncovered new areas of research into the low-biomass microbiome of the intrauterine space. Although studies of the vaginal microbiome have yet to consistently discriminate a microbial signature associated with PTB, studies of the placental microbiome are beginning to provide insight into the complex interplay between microbiota and host in the context of spontaneous PTB. Further investigation of this unique microbiome (including culturing of live microbes) and those of other tissues not typically associated with PTB (e.g., gut or oral cavity), may be necessary to fully understand how microbiota influence pregnancy outcomes. Microbiome science is emerging as a powerful approach to unraveling the complexities underlying PTB, but more questions have arisen than investigators have been able to answer. Adequately powered, large cohort studies inclusive of a diverse demographic population are required to fill the remaining gaps in our knowledge, but nevertheless, studies on our microbial counterparts, which have been aptly termed our second genome, offers tremendous promise to understand and eliminate PTB.

DISCLOSURES
The authors do not report any conflicts of interest with respect to this article.

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Do midpelvic vaginal operative deliveries lead to greater trauma?

Midpelvic forceps and midpelvic vacuum deliveries may be associated with a higher rate of maternal and infant trauma than other types of deliveries, according to a new study published in CMAJ.

Researchers in Quebec looked at all singleton deliveries in Canada that occurred between 2003 and 2013, by either attempted midpelvic operative vaginal or cesarean delivery with labor, with and without a prolonged second stage. Primary outcomes examined were composite severe maternal morbidity and mortality and composite severe perinatal morbidity and mortality.

In women with prolonged second stage labor and dystocia, midpelvic operative delivery was associated with higher rates of severe perinatal morbidity and mortality when compared to cesarean. Severe maternal morbidity and mortality rates were not significantly different following an operative vaginal delivery, but obstetric trauma rates were higher. In women with fetal distress, similar associations were seen for severe birth and obstetric trauma, but the vacuum was linked with lower rates of severe maternal morbidity and mortality.

The researchers concluded that while overall rates of perinatal and maternal morbidity and mortality vary by operative instrument and indication, midoperative delivery is linked with higher rates of severe birth and obstetric trauma.

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Study suggests lithium risk may be lower than believed

A new study in NEJM indicates that there may be less risk associated with using lithium in the first trimester than previously thought.

Researchers examined 1,325,563 pregnancies among women who were enrolled in Medicaid and delivered a live-born infant between 2000 and 2010. They compared risk of cardiac malformation among babies who were exposed to lithium during the first trimester versus in those with no exposure to the drug. A secondary analysis compared infants who had been exposed to lamotrigine.

Cardiac malformations were found in 11.15% of the infants who were unexposed; 1.39% of the infants who were exposed to lamotrigine; and 2.41% of the infants exposed to lithium. When compared with unexposed infants, those who had been exposed to lithium had an adjusted risk ratio (ARR) for cardiac malformations of 1.65.

Prevalence of right ventricular outflow tract obstruction defects was 0.60% among infants with lithium exposure and 0.18% among infants with no exposure. Similar results were seen when infants exposed to lamotrigine were used as the reference group.

Researchers concluded that while use of lithium during pregnancy is tied to increased risk of cardiac malformations, the magnitude of the issue is not as great as previously believed.

REFERENCES
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Ventriculomegaly is also part of the Arnold-Chiari Type II malformation, which is present in most cases of spina bifida. The spinal defect with herniated tissue, or meningomyelocele, has a negative pressure effect on the brain, with herniation of the hindbrain into the spinal canal. This causes the cerebellum to be elongated and distorted into a “banana” shape (Figure 14), the frontal bones of the calvarium to collapse, causing a “lemon shaped” skull (Figure 15), and obstruction of CSF flow leading to ventriculomegaly. Evaluation of the spine in sagittal and transverse views is necessary to confirm the presence and level of the spinal defect.

Ventriculomegaly, whether isolated or with associated structural abnormalities, is associated with genetic abnormalities. Mild ventriculomegaly is associated with Down syndrome. Hydrocephalus in a male fetus with no associated finding could reflect a mutation in the L1CAM gene associated with X-lined hydrocephalus. Dandy-Walker Malformation is associated with chromosomal abnormalities, as well as single gene disorders. While open neural tube defects are usually multifactorial in origin, they may be a feature of Trisomy 18. Genetic counseling is indicated when ventriculomegaly is identified.

Another diagnosis that can be suspected based on second-trimester ultrasound is agenesis of the corpus callosum (Figure 16), a condition in which the large midline bundle of white matter connecting neurons in the 2 hemispheres is absent. Agenesis of the corpus callosum should be suspected when the cavum septum pellucidum is not visible, the third ventricle appears prominent, and the lateral ventricles have a teardrop-shaped configuration, with dilation of the posterior horns.

**Face**

A profile view in the first and second trimester can identify a small mandible, or micrognathia (Figure 17). Median or bilateral cleft lip (Figures 18, 19) can also be suspected based on profile views. The lips and palate are best evaluated with coronal imaging and transverse views at the level of the palate. The most common clefts are unilateral, and generally will not be identified until the second trimester.

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Cleft-palate in the presence of a cleft-lip involves the bony palate, and it can generally be suspected. Isolated cleft palate typically affects the soft palate, and it is rarely detected. Real-time imaging of the entire face can identify masses, including teratomas and lymphangiomas.

**Neck**
The nuchal skin fold is visible in the same plane as the posterior fossa. A thickened nuchal skin fold is associated with chromosomal and cardiovascular abnormalities. The neck can also be evaluated and neck masses identified in the profile view. Persistent hyperextension of the neck can also indicate presence of an anterior neck mass.

**Chest**
In the second trimester, the heart should be visible in the middle of the chest with its axis pointed toward the fetal left, with lung surrounding the heart on both sides, left smaller than right. When the heart is not in the midline position, a mediastinal shift can indicate a unilateral lung mass or diaphragmatic hernia. Congenital pulmonary airway malformations are more echogenic or bright than normal lung tissue, and can appear solid or contain cysts. Diaphragmatic hernia should be
suspected if abdominal contents are visible in the chest in the presence of a mediastinal shift (Figures 20, 21). In the absence of significant mediastinal shift, smaller right-sided lesions are less likely to be detected. The echotexture of herniated liver in the right thorax may appear similar to that of lung, while the stomach bubble or small intestine in the chest with left-sided lesions is usually obvious. When transverse imaging of the chest is suggestive of diaphragmatic hernia, sagittal and coronal images can directly identify the defect in the affected hemi-diaphragm in most cases.

Heart and cardiac outflow tracts
A 4-chamber view can identify defects of the ventricular septum (or VSDs) (Figure 22), and abnormalities of chamber size such as hypoplastic right or left ventricles. Small VSDs are commonly missed, however, and atrial septal defects (ASDs) are generally not diagnosed in utero due to the presence of the foramen ovale, a physiologic connection between the atria. Obstruction of the aorta, such as with coarctation or stenosis, will typically cause enlargement of the right ventricle, which supplies most of the aortic blood flow through the ductus arteriosus. Because of the fetal circulation, however, milder degrees of aortic coarctation may be missed.

While the 4-chamber view of the heart is very useful, it alone will not detect several major abnormalities. Evaluation of the outflow tracts, or the aorta and pulmonary artery as they exit the left and right ventricles, is recommended if possible. Major conditions such as Tetralogy of Fallot (Figure 23), Transposition of the great vessels (Figure 24), and Truncus arteriosus will have a normal 4-chamber view of the heart in most cases, but will usually be apparent if the outflow tracts are included.

Abdominal structures
Structures that should be imaged include the stomach bubble, in the left upper quadrant, ventral wall, umbilical cord insertion, bowel, and gall bladder. Gastrointestinal obstruction, including intestinal atresia, is often not apparent before the third trimester. Esophageal atresia should be suspected if the stomach bubble is persistently small or absent. A cystic mass medial to the gall bladder connecting to the cystic duct is likely to represent a choledochal cyst. Anomalies that should not be
missed in the first trimester should not be missed in the second trimester, such as omphalocele (Figure 25) and gastroschisis (Figure 26).

**Genitourinary structures**
The kidneys should be visible in the renal fossae. Unilateral renal agenesis or ectopic kidney (Figure 27) may be missed, as the adrenal gland or adjacent bowel can be mistaken for a kidney in the renal fossa. To avoid that, the renal cortex and pelvis should be identified before concluding that the kidney is present in the renal fossa. Disorders affecting both kidneys, such as renal agenesis, dysplastic kidneys (Figure 28), or autosomal-recessive polycystic kidney disease are associated with oligohydramnios (Figure 29), and are seldom missed.

The urinary bladder is visible inferior to the umbilical cord insertion, and the umbilical arteries can be seen laterally using color Doppler. Normal amniotic fluid with a persistently non-visualized bladder is suggestive of bladder extrophy, a rare disorder.

The fetal genitalia can be evaluated starting early in the second trimester. Abnormalities in genitalia can include hypospadias and ambiguous genitalia. If the fetal genotype, based on karyotype or cell-free fetal
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DNA, is known, the appearance of the genitalia can be correlated with this information.

**Spine**

The cervical, thoracic, lumbar, and sacral spine should be imaged in sagittal and transverse planes. Real-time ultrasound can follow the spinal column from the base of the skull to the sacrum, evaluating each level. While spina bifida can be suspected based on sagittal imaging (Figure 30), smaller lesions may be apparent only with transverse imaging (Figure 31). Most cases will be associated with the Arnold-Chiari II malformation, with obvious abnormalities in the brain. Sagittal imaging can identify hemivertebra (Figure 32). The soft tissue superficial to the spine should be evaluated, and rare lesions such as sacrococcygeal teratoma can be identified.

**Extremities**

Measurement of the femur and humerus are done to confirm adequate growth of long bones. Assessment should also include documenting presence of other long bones in all extremities, including radius and ulna in the forearms and tibia and fibula in the legs. Abnormalities of skeletal structures can be quantitative or qualitative. Quantitative abnormalities involve abnormal growth of the long bones of the arms and legs, such as limb reduction defects (Figure 33). Qualitative abnormalities of bones include conditions leading to abnormal appearance, such as bowing, fractures, or hypomineralization (Figure 34). While severe skeletal dysplasias are usually apparent in the second trimester, mild skeletal dysplasias, such as achondoroplasia, are often not diagnosed until later in pregnancy.

Assessment of hands should include attempts to rule out polydactyly and syndactyly (Figure 35), and to document presence of the thumb. Assessment of the feet should include their position relative to the tibia and fibula to rule out signs of clubfoot deformity (Figure 36). Real-time ultrasound assessment is important to document normal movement and tone in all extremities, including opening and closing of the hands. Abnormal tone, such as fixed extension of the legs or clenching of the fingers...
Figure 37), can indicate a neurologic, neuromuscular, or musculoskeletal abnormality.

Skeletal dysplasias can involve abnormalities of structures other than the arms and legs, including the skull, spine, and ribcage (Figure 38). Evaluation of these structures is important when skeletal dysplasia is suspected based on abnormalities of the extremities.

**Conclusion**
Fetal anomalies can be diagnosed by ultrasound in early pregnancy, though second-trimester ultrasound can identify or exclude more conditions. There are some anomalies that are difficult to diagnose or that do not lend themselves to ultrasound diagnosis and will be missed.

**DISCLOSURES** The authors do not have any conflicts of interest to report with relation to this article.

**REFERENCES**


the pregnancy if abnormalities were found. He stated that the difficulty in visualizing the fetus in the second trimester was not uncommon and that he would have routinely ordered a follow-up ultrasound. He also argued that he was not responsible for discussing all prenatal testing with the parents since that discussion should happen in the first trimester when she was seeing her original physician; so he assumed that discussion had already taken place. Further, the defense argued that a prenatal screening pamphlet, which the patient signed at 10 weeks gestation, discussed amniocentesis as a diagnostic test. The jury returned a defense verdict after 4 1/2 hours of deliberations.

Claim that episiotomy led to fistula

A 31-year-old woman delivered her child at a New York hospital. During delivery of the head the obstetrician noticed the umbilical cord was wrapped around the neck. He performed an episiotomy and the infant was delivered safely. The next day the patient alleged she told the obstetrician that she noticed an odor from her vagina, and he told her it was a natural occurrence following delivery and would resolve. The woman soon became pregnant again and was examined by a midwife. The patient said she told the midwife about the odor, but there was no mention of it in the midwife’s notes. When she saw the same obstetrician from the previous delivery he determined she could deliver vaginally. After the delivery, the obstetrician then diagnosed a recto-vaginal fistula, which required 13 operations to repair.

The woman sued the physician and hospital and alleged that the fistula was caused by the episiotomy from the first delivery. She claimed the episiotomy should not have been done and that the obstetrician should have diagnosed and treated the fistula earlier, which would have prevented the many procedures needed to repair it. She also alleged that the second delivery should have been a cesarean and that the obstetrician’s decision to allow a vaginal delivery exacerbated the fistula. She claimed the caregivers should have investigated her complaint of the odorous discharge earlier which would have allowed an easier repair prior to the second delivery.

The defense argued the patient’s medical records showed no indication of the complaint of odor until after the delivery of her second child so he could not have provided earlier treatment. He also contended that the patient’s fistula was due to a malformation, not the episiotomy. A $50 million verdict was returned including $10 million personal injury, past pain and suffering, and $40 million personal injury future pain and suffering.

Alleged failure to timely diagnose breast cancer

A 44-year-old Arizona woman sued her gynecologist and claimed the doctor failed to diagnose breast cancer for 2 years, so that she required a mastectomy rather than a lumpectomy as treatment. The patient’s expert opined that the delay resulted in a 70% survival rate as opposed to a 90% rate had there been a timely diagnosis.

The gynecologist denied that the patient’s chance of survival had been reduced. The jury returned a defense verdict after deliberating a little over 5 hours following an 8-day trial.

Ovarian cyst removal results in sigmoid colon injury

A New York woman in her forties underwent surgical removal of a cyst on her ovary, performed by her gynecologist. Over the next few days the patient experienced severe abdominal pain. Tests showed varying amounts of white blood cells in her blood and she underwent exploratory surgery which revealed a tear in her sigmoid colon. She had a colostomy and a follow-up operation after that.

The patient sued the gynecologist and hospital and alleged they failed to properly perform the initial surgery even though the tear was a known risk of the operation – and that he failed to diagnose and treat the injury in a timely manner. She claimed she
had 10 days of symptoms that should have prompted more immediate action from the gynecologist, thereby avoiding the need for the colostomy. The defense maintained that the operation was not the cause of the injury to the colon, that the surgery did not take place near the sigmoid colon, but that injury to the bowel is an accepted risk to that procedure and days can pass before injuries can be identified. After deliberating for 4 1/2 hours at the conclusion of a 7-day trial, the jury returned a verdict in the amount of $1,520,000, including $20,000 past lost earnings capability; $700,000 past pain and suffering; and $800,000 future pain and suffering.

**Claim of delay in diagnosis of breast cancer**

A New York woman in her fifties learned she had breast cancer and underwent a bilateral mastectomy, chemotherapy and radiation. The cancer was found in the same spots as microcalcifications that were seen on a mammogram 1 year earlier but, at that time the radiologist did not think the microcalcifications necessitated further testing.

The patient sued the radiologist and alleged he failed to timely diagnose her cancer, that his supervisors failed to properly oversee him, and that her mammogram suggested possible cancer and further testing should have been done at that time. She claimed if the cancer had been detected a year earlier she could have undergone a less-invasive treatment. She also claimed she had a family history of cancer which presented another reason for her mammogram to have been taken more seriously.

The radiologist argued that the patient had dense breasts that contained microcalcifications under control and that any injury occurred prior to her arrival at the hospital when she noted decreased fetal movement. After deliberating 9 hours at the conclusion of a 3-week trial, a $30,545,655 verdict was returned, including $27,045,655 to the child for future medical costs and $3,500,000 to the mother for past and future pain and suffering.

**Delay in fetal monitoring with decreased fetal movement**

A 34-year-old Georgia woman was at 35 weeks gestation of her second pregnancy when she presented to her obstetrician for routine prenatal care. She had gestational diabetes and her visit was unremarkable. Two days later, the patient presented back to the office with complaints of decreased fetal movement. She was admitted to the hospital for continuous fetal monitoring, consultation with a perinatologist, and possible delivery. She was not placed on the fetal monitor until 2 hours after arrival, and 1 hour later, the perinatologist was consulted by phone and ordered a biophysical profile (BPP). Six hours after her arrival the BPP was performed and an emergency cesarean was done. The infant was diagnosed with spastic quadriplegic cerebral palsy, profound developmental delays, cortical blindness, and seizures. The infant requires around-the-clock care. She is at home with her mother and will never walk or talk, or care for herself.

The parents sued those involved and claimed the infant’s injuries were due to mismanagement of the mother’s labor and the delivery. They alleged that immediate BPP should have been performed which was the standard of care with decreased fetal movement but was not ordered until almost 4 hours after the patient was admitted to the hospital. They asserted that 3 ultrasound technicians were on duty at the time the patient was at the hospital and any one of them could have performed the essential test immediately, as hospital protocol requires.

One ultrasound tech was allegedly on break; another was performing other tests; and the third was not notified of the BPP order because of a problem with the hospital’s ordering system.

The defense claimed that the infant’s issues were a result of her mother’s failure to keep her gestational diabetes under control and that any injury occurred prior to her arrival at the hospital when she noted decreased fetal movement. After deliberating 9 hours at the conclusion of a 3-week trial, a $30,545,655 verdict was returned, including $27,045,655 to the child for future medical costs and $3,500,000 to the mother for past and future pain and suffering.

Even though the patient testified that she had not heard of amniocentesis until too late, there was contradicting testimony.
a large amount of fibroglandular tissue which reduced the sensitivity and reliability of mammograms. He claimed he properly interpreted the mammogram and that it had not changed from an earlier mammogram that had revealed 1 or 2 benign calcifications which did not require further screening. The jury returned a defense verdict after deliberating 3 hours at the conclusion of a 10-day trial.

**Claim of unnecessary hysterectomy**

A 41-year-old Pennsylvania woman who had been diagnosed with endometrial cancer underwent a robot-assisted hysterectomy and lymph node dissection performed by her gynecologist. Shortly after her diagnosis, at the consultation with her gynecologist, she had signed a "consent to surgery/anesthesia" form, in which she agreed to the operation or other procedures. After the surgery was performed the patient learned that the pathology department determined that the endometrial samples were "pre-cancerous" and that the gynecologist did not inform her of this fact and went ahead with the operation. The pathology report from the specimens taken during the operation showed that there was no evidence of cancer.

The woman sued the gynecologist alleging he was negligent for failing to inform the patient of her pathology results and for performing unnecessary surgery which caused long-term consequences. She claimed the standard of care was violated because the physician failed to rely on the pathology results of 'pre-cancerous' cells and thus recommended she undergo a hysterectomy, which was not required.

The gynecologist asserted that he was aware of the pathology results and so was the patient. They had discussed the results and the surgery was offered to the patient as an option. She had consented to it, which was reasonable in that she previously had a report of "pre-cancerous" cells which could evolve into cancer any time. The jury returned a defense verdict at the conclusion of a 4-day trial.

**Complications after anterior/posterior repair with mesh**

A Nevada woman underwent a laparoscopic vaginal hysterectomy with removal of both ovaries and fallopian tubes in 2010. The gynecologist then performed anterior and posterior repairs using mesh. The patient complained of vaginal discharge along with pain and bleeding shortly after surgery. She was treated with at least 2 courses of antibiotics and underwent an abdominal-pelvic CT scan for pelvic pain. She was diagnosed with vaginal cuff granulations as a cause of her vaginal discharge and pain. Her pain continued, and 10 months after her original surgery she underwent a vaginal tissue biopsy. The testing noted fecal material present and a small bowel-vaginal fistula was diagnosed. She then underwent a laparoscopic enterectomy, urethral lysis, anomen-tal pedicle flap, and a cystoscopy. On laparoscopic examination, there was a clear perforation of what appeared to be Gore-Tex mesh or graft material through the loop of the small bowel. One year after the initial operation the patient then experienced increased spinal pain, and a lumbar MRI revealed new fluid/abscess in the disk extending through the tract anterior into the soft tissues of the pelvis. She underwent intensive antibiotic therapy in the hospital and at home for a prolonged period.

The woman sued the gynecologist and alleged he fell below the standard of care in his treatment of her conditions.

The gynecologist denied all allegations and the jury returned a defense verdict.
that the risk of newborn infection is ing this 1%, Practice Bulletin 162 states women were infected.8 Notwithstanding fetuses (~1% of ART-treated HIV) recommendation was based, 30 of study on which Practice Bulletin 162 when affected women receive com-
mission in HIV is now greatly decreased high rate of maternal to fetal transmis-
ion can be mitigated. The once prohibitively
risk of maternal to fetal transmission of chronic
propriates counsels that Practice Bulletin 162 ap-
maternal infection to the fetus is increased if an invasive prenatal procedure

ACOG recommends that if only a karyotype were possible, cell culture
should be initiated from amniotic fluid obtained by amniocentesis. This should maximize the rate of successful
cell culture required for a karyotype.

Prenatal diagnosis procedures in maternal infection
Practice Bulletin 162 appropriately counsels that transmission of chronic maternal infection to the fetus is increased if an invasive prenatal procedure is performed in a mother who has hepatitis B, hepatitis C, or human immunodeficiency virus (HIV). However, risks can be mitigated. The once prohibitively high rate of maternal to fetal transmission in HIV is now greatly decreased when affected women receive combination antiretroviral therapy. In the study on which Practice Bulletin 162 recommendation was based, 30 of 2528 fetuses (~1% of ART-treated HIV) women were infected.9 Notwithstanding this 1%, Practice Bulletin 162 states that the risk of “newborn infection is not increased after amniocenteses, maternal viral load is low or undetectable.” A recommendation is made, however, to perform the necessary invasive procedure once viral loads are undetectable.

Conclusion
Practice Bulletin 162 states that loss rates following an invasive prenatal diagnostic procedure should now be communicated to be 1 in 769 for amniocentesis and 1 in 455 for CVS. For most practitioners, these new numbers will be more in sync with their clinical impressions. Also transformative in Practice Bulletin 162 is that chromosomal microarrays and not a karyotype should be ordered whenever an invasive prenatal procedure (CVS, amniocenteses) is performed. This holds whether evaluation is for a miscarriage or stillbirth.

REFERENCES
ACOG releases new study on ob/gyn workforce

Trends similar to those seen in previous studies expected to continue.

by Judith M. Orvos, ELS

Work-life integration, lower job satisfaction, increasing subspecialization, and concerns about income and professional liability are among the issues shaping the ob/gyn workforce and how they practice, according to a new report from the American Congress of Obstetricians and Gynecologists (ACOG). Available online, The Obstetrician-Gynecologist Workforce in the United States: Facts, Figures, and Implications, 2017 looks at how the landscape of the specialty has changed over the last 6 years.

ACOG last published a workforce analysis in April 2011, little more than a year after the Patient Protection and Affordable Care Act (PPACA) was signed into law. The trends identified in that report are strikingly similar, in some ways, to the findings in the new report. Representation of women in the specialty continues to increase; the ob/gyn workforce in the United States suffers from geographic maldistribution; and lack of growth in adjusted income remains a problem for clinicians (Table).

Ob/gyn demographics

Looking at how ob/gyns are distributed in the United States, ACOG found that in 2017, there are 35,586 ACOG Fellows in practice (31,163 Fellows and 4235 Junior Fellows), up slightly from 32,737 in 2011. Nearly half of all ob/gyn residents and 58.7% of practicing ob/gyns are women, a much higher proportion than any other group of active surgeons. In the next 10 years, according to ACOG, 66% of ob/gyns are expected to be female. While women are arguably overrepresented in the specialty, minorities—particularly African Americans (11.1%) and Hispanics (6.7%)—are underrepresented.

Of the 3143 counties in the United States, 49% have not 1 ob/gyn, which
ACOG says is largely because they lack a hospital with maternity services. More than 10 million US women live in the counties lacking in ob/gyn care, which are mainly rural and in the Central and Mountain West regions. Ob/gyns practicing in rural areas are more likely to be American Indians, Alaska Natives, or Pacific Islanders. Young, male, African-American or international graduates are the ob/gyns most likely to relocate and 6% of all physicians in the specialty did so from 2006 to 2015.

In the 2017 report, ACOG foresees a 6% increase in demand for women's healthcare in the United States over the next 10 years because of the ongoing increase in the female population (Figure 1). However, the organization also sounds a warning about geographic imbalances in availability of ob/gyns and the cost of training more clinicians to serve states such as Nevada, where the demand is expected to rise by 27%. Also compounding the supply-and-demand issue is the fact that one-third of ob/gyns are aged 55 years or older and so, potentially approaching retirement. "Without increases in the number of obstetric-gynecologic trainees," says ACOG, "the nation will rely heavily on services by nonphysician healthcare professionals. Furthermore, other physicians trained to address many of the general healthcare needs of women include obstetric-gynecologic subspecialists and primary care physicians in family medicine or ambulatory general internal medicine." According to the report, more than half of all ob/gyn offices already employ "physician extenders" such as nurse practitioners, certified nurse-midwives, and physician assistants.

**Financial concerns**

A piece of good news in the report is the finding that median compensation for clinicians in the specialty increased between 2010 and 2015 (from $281,190 to $330,696). However, ob/gyns are among the surgeons with the lowest annual compensation. Physicians who practice only gynecology earn approximately $100,000 less per year than their counterparts who practice both obstetrics and gynecology, whereas annual income goes up approximately $100,000 for those who subspecialize. It's not surprising, then, that more ob/gyn residency graduates are seeking American Board of Obstetrics and Gynecology-accredited fellowships—up from 7% in 2000 to 19.5% in 2012. As they enter practice, the ACOG report notes, these new clinicians will enter a practice environment with an increasing trend toward "value-based care models with payments dependent on reporting patient safety and quality of healthcare measures, achieving desired outcomes, and especially cost savings." For all ob/gyns, premiums for professional liability insurance continue to loom large as an issue in 2017, as they did in

**TABLE Selected trends impacting the ob/gyn workforce**

- Fewer residency graduates to serve a growing population
- More ob/gyn graduates seeking subspecialization
- Young ob/gyns searching for work/life balance and nontraditional schedules
- Declining satisfaction with the profession and stagnant income

2011, although both insurance premiums and the frequency and severity of lawsuits in obstetrics have decreased in recent years.

**Work-life balance and practice setting**

As was also underscored by the findings from *Contemporary OB/GYN’s* Second Annual Labor Force Survey (Figure 2), the new ACOG report shows that balancing work and home life and avoiding professional burnout are key challenges for ob/gyns. Some 40% to 70% of physicians in the specialty will experience some form of burnout, according to ACOG, and female surgeons are more likely to reduce their clinical work hours or to leave their current practices because of issues with balancing their work and family responsibilities. Data from the Association’s past professional liability surveys indicate that the proportion of ACOG Fellows in solo practice declined from 32% in 1992 to 19% in 2012 whereas the proportion in hospital physicians (15%) and on academic faculty (12%) increased. The report postulates that in the future, ob/gyn practice “will be increasingly office-based, efficient, and oriented toward standardizing practices and improving the patient experience.”

**A look into the future**

Among the predictions made by ACOG for the coming years in the 2017 report are that:
- Competition for residency positions will continue to increase;
- By 2020, at least one-third of ob/gyn residency graduates will subspecialize;
- By 2022, two-thirds of ob/gyns will be women;
- Ob/gyns’ role as coordinators of women’s healthcare will increase; and
- Competition for inpatient gynecologic surgery will increase.

The Association also calls for ongoing research about the ob/gyn research to address critical questions such as how payment models such as modifications to the PPACA will affect the specialty; whether new recommendations on the well-woman exam and routine pelvic examination will result in a decrease in office visits; and whether the demand for ob/gyns will be altered by the use of new technology, such as telemedicine.

**FIGURE 2**

**Q. WHAT HAVE THE TOP 5 CHALLENGES BEEN IN 2016 TO YOUR EFFECTIVE PRACTICE AS AN OB/GYN?**

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintaining work-life balance</td>
<td>47%</td>
</tr>
<tr>
<td>Dealing with insurance companies</td>
<td>46%</td>
</tr>
<tr>
<td>Professional liability concerns</td>
<td>33%</td>
</tr>
<tr>
<td>Compensation</td>
<td>29%</td>
</tr>
<tr>
<td>Adjusting to ICD-10 coding</td>
<td>12%</td>
</tr>
</tbody>
</table>

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**Second Annual Labor Force Survey**

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*Too Much Paperwork, Not Enough Sleep, Too Many Surgical Procedures to Learn, Not Enough Time with Family, Too Many Lawsuits, Too Many VTEs*

*Clinical Center Screening and Prevention*

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Physicians need to consider many factors when shopping for malpractice insurance, and while price is often the primary consideration, it is important to look deeper into the differences in coverage.

Diane Robben, JD, an attorney with Sandberg Phoenix’s medical malpractice group who advises independent physicians and their practices on buying insurance, argues that doctors are making a mistake if they focus only on price.

“There are many other differentiating factors that insurance companies compete on besides price,” she says. “Many insurance companies are offering value-add services such as risk analysis, policy review, online training, and other services to compete and stand apart. Don’t be afraid to shop around.”

Bill Fleming, chief operating officer of The Doctors Company, a medical malpractice insurance company headquartered in Napa, California, says it’s important for physicians to review a company’s history to learn how aggressive the carrier is in fighting claims.

The Physician Insurers Association of America (PIAA) and actuarial firms publish aggregated claims information that can be used to benchmark insurer results to some extent. Many insurers also publish their own claims data, including trial results, dismissals, and claims settled.

No matter which company physicians choose, experts advise 4 key steps before signing a contract.

QUICK TAKE

- Consult with colleagues to get recommendations for well-rated insurance providers that include special features with their coverage.
- Read the entire contract before finalizing a policy.
- Evaluate your coverage every year.

FOUR CONSIDERATIONS BEFORE BUYING

1 Talk to colleagues

Daniel Cavanaugh, assistant vice president of membership development for malpractice insurer Cooperative of American Physicians Inc., says young physicians going into private practice generally search the internet for information and coverage options or ask a colleague for a carrier or broker recommendation. Both of these, he notes, are a good start.
No one wants to get sued, but it is likely to happen at some point in a physician’s career. If it does, The Doctors Co. advises physicians to:

1. **Contact the malpractice insurer as soon as notification of a claim occurs.** There are often time limits surrounding notification; delay could result in a judgement against the doctor, regardless of merit.

2. **Discuss the claim only with the insurance specialist or defense attorney to avoid unwittingly involving other people as potential witnesses and jeopardizing any defense.**

3. **Comply with an authorized request to release patient medical records except in special circumstances, such as records that pertain to a patient’s mental illness.**

4. **Review any communication or information requests with your defense attorney prior to responding.** Responses are admissible in court so a calm approach and clear thinking must prevail.

5. **It is essential while the lawsuit is pending to communicate regularly with your defense attorney.**

Meanwhile, mid-career and older physicians are often more familiar with the insurance market and will gravitate toward carriers that have been in the marketplace for many years.

Older physicians are also more likely to seek coverage through an intermediary such as an insurance broker or financial adviser.

Robben advises physicians to pay attention to the laws for whatever jurisdiction they practice in. Talking to colleagues can help with this as well.

**2. Check the insurer’s rating.**

Fleming says independent physicians should choose a carrier with an A.M. Best rating in the “A” range and be aware of the class size from I to XV, as the smaller the number, the smaller the company. Even with a rating in the “A” range, if the carrier is very small, a few large losses can have a devastating effect on its financial security.

“**You’ll want a carrier with history and experience in your state and specialty,**” he says. “**Medical professional liability insurance has an industry reputation of producing more volatile results, so you’ll want an insurer that has weathered the cyclical conditions of this market.**”

**3. Remember, if it’s too good to be true …** Fleming also advises physicians to be wary of policies that offer numerous one-year discounts, because prices will almost always increase substantially and physicians will often be stuck paying more than what they were first led to believe.

Also, if a practice is multi-state or might become multi-state in the future, it’s important to choose a company that is licensed in the states where a physician might practice, including telemedicine visits.

Before finalizing a policy, a physician should read the entire document, including all addendums and exclusions and be proactive if there is something that is excluded that they thought was covered before it becomes an issue.

“**Know the scope of what is not included in the coverage such as HIPAA liability or cyber insurance coverage,**” Robben says. “**Also pay attention to whether the policy provides coverage for defense of licensure board complaints, or governmental investigations. Having a trusted and experienced lawyer to guide you through those scary and complex proceedings can help ease your fears and anxiety, and knowing there is coverage for the expenses is important.**”

A physician who does it the right way compares policies, including commercial carriers and risk retention groups, which are liability insurance companies owned by the people it insures. This will help physicians determine which offer the best protections and provide the ability to consent and/or select counsel of his/her choosing, Kutner says.

**4. Be upfront early.** When buying malpractice insurance, Fleming says, be candid with the underwriter. The more accurate and comprehensive the application is, the better.

“It is best to deal with issues like prior claims, changes in practice locations, negative news, or social media, at the beginning,” he says. “That way you have established that you are open and candid in your relationship with the carrier.”

**When to re-evaluate.**

Even if physicians are happy with their malpractice insurance, they shouldn’t...
ignore it. It should be evaluated yearly and kept up to date.

“Whenever you change in size, add or drop practitioners, or have a significant change in the scope of practice, you should evaluate your medical malpractice insurance needs,” Robben says. “At a minimum, I would recommend reviewing to review your malpractice insurance on an annual basis. You want to be sure there are no gaps in coverage and that you have coverage from term to term.”

Kutner adds that claims history should be reviewed each year and checked against the requirements for remaining on a managed care plan or affiliated with a healthcare facility such as a hospital.

“If there is no change in premium, reputation, or financial wherewithal of your current carrier, it is better to build a relationship with a carrier than to shop your coverage each year,” Fleming says. “If you have a claim, you might want to anticipate the reaction of the incumbent company and be ready to respond if you’re concerned about being non-renewed or surcharged significantly.”

However, he says, if physicians in primary care alter services or reduce practice from full- to part-time, they should check with their carrier about possible coverage changes and if not satisfied with the answer, shop around.

In addition, insurance experts warn, new developments can affect the industry, such as telemedicine or cyber risk. Many insurers provide baseline coverage in their policies with the ability to increase limits in specific areas, but physicians should talk to their agents to ensure they have enough protection.

And don’t wait until the last minute to make a change. It’s important to leave enough time before the expiration of one term to be able to evaluate other options and test the market by meeting with other insurance agents to see if a different policy would better fit a practice. ■
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A California woman was 35-years-old when she delivered an infant in 2014, and the father was 51-years-old. She was 10 weeks pregnant when she went to a clinic for care. She elected to participate in the state prenatal screening program, and the results of the screening tests were reported as within normal limits and the risk of birth defects was 1:230. Two weeks later she had her first appointment with an obstetrician and he informed her that the negative prenatal screening indicated that the infant most likely would be born without defects. He ordered an ultrasound to assess fetal structures. The radiologist reported that the ultrasound did not visualize the fetal anatomy well; however, the obstetrician allegedly told the patient at her next visit when she was 23 weeks that the ultrasound was normal. A month later the patient returned to her original physician who noticed that the ultrasound report indicated that the fetal survey was not complete. He ordered another ultrasound with a perinatologist. A significant cardiac defect in the fetal heart was found, and further testing confirmed the fetus had Down’s syndrome. The patient was scheduled for a late term abortion but she did not keep that appointment, fearing that it was illegal. The infant was born and has severe Down’s syndrome.

The parents sued all those involved with the prenatal care and alleged that both physicians were told the parents wanted all available testing because of a family history of birth defects, and that they would terminate the pregnancy if fetal abnormalities were found. They contended that the obstetrician was obligated to discuss diagnostic testing such as amniocentesis with the patient despite the negative screening tests and, because he did not, the diagnosis was made too late to terminate the pregnancy. The patient testified she never heard of amniocentesis until she was seen by the perinatologist.

The obstetrician denied having any discussions with the parents of their desire to have all tests possible or their wanting to terminate.

Ms Collins is an attorney specializing in medical malpractice in Long Beach, California. She can be reached at dawncfree@gmail.com.

ANALYSIS

In medical malpractice cases that involve delivery of an infant with an abnormality that can be detected by a specific laboratory test, like Down’s syndrome, the parents must show that the physician was below the standard of care in not offering the test, and they also must show they would have terminated the pregnancy had they known of the abnormality. In this case, even though the patient testified that she had not heard of amniocentesis until too late, there was contradicting testimony. The infant’s grandmother testified that she had a conversation about amniocentesis with the parents early in their pregnancy.

In addition, a former employee of the obstetrician’s office testified that after the Down’s syndrome diagnosis was made she asked the patient why she had not chosen amniocentesis earlier in the pregnancy, and the patient said she decided against it because her prenatal screening test was normal. So not only had she heard of amniocentesis, according to the employee’s recollection she had made the choice not to have it much earlier in the pregnancy.
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