MATERNAL MORTALITY

Hypertensive disorders

Charlene H. Collier, MD, MPH, MHS, FACOG and James N. Martin Jr., MD, FACOG, FRCOG, FAHA

Return of nitrous oxide in childbirth

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Risks and benefits of hormonal contraception

Despite hormonal contraception benefits, use of nonhormonal methods may be wise in women after 35—and even younger in those at increased risk of breast cancer.

Since hormonal contraception was introduced in the 1960s, the risks and benefits of the drugs have been the subject of considerable, and at times acrimonious, debate. Some risks have been well-established. For example, risk of thromboembolism is increased in users of combined oral contraceptives (OCPs) compared to non-users (relative risk [RR] of 3.5; 95%CI: 2.9-4.3) with estrogen exerting the major influence, though third-generation progestins also exert modest provocative effects.1 Far more controversial has been the putative link between hormonal contraception and breast cancer. A number of recent publications drawn from a large Danish national database add clarity to this debate and indicate that while on balance hormonal contraceptives used in the 1980s were linked to a modest increased risk of breast cancer diagnoses among current OCP users (RR 1.24; 95%CI: 1.15-1.33) and among users within the past 10 years but that this risk dissipated 10 years after use. Of note, cancers diagnosed among OCP users tended to be early-stage, lower-risk lesions.2 The authors did note that women who began OCPs prior to age 20 years had higher relative risks but that the absolute risk of such cancers was low. Similar findings were noted in the Nurses’ Health Study where current OCP use was associated with a higher risk of breast cancer (RR 1.33; 95%CI: 1.03-1.73) though the association with past use did not reach statistical significance (RR 1.12; 95% CI: 0.95-1.33).3 This study also reported that current use of triphasic levonorgestrel formulations was associated with a particularly elevated risk (RR 3.05; 95% CI: 2.00-4.66). In contrast, other large observational and case-control studies have shown no association between current and past use of OCPs and breast cancer.4,5 These older studies have been criticized for including patients who used higher-dose formulations. Complicating matters further, data from the Women’s Health Initiative (WHI), al-

Maternal Mortality: Hypertensive disorders of pregnancy
More than half of these deaths are preventable, and better strategies are needed to identify women at risk. Read more on page 14.

Zika news, cautions and precautions for 2018 Media attention to Zika may have dwindled but ob/gyns must continue to counsel patients. Read more on page 12.

Breast cancer risks
In 1996 the Collaborative Group on Hormonal Factors and Breast Cancer analyzed 54 studies and reported that hormonal contraceptives used in the 1980s were linked to a modest increased risk of breast cancer diagnoses among current OCP users (RR 1.24; 95%CI: 1.15-1.33) and among users within the past 10 years but that this risk dissipated 10 years after use. Of note, cancers diagnosed among OCP users tended to be early-stage, lower-risk lesions. The authors did note that women who began OCPs prior to age 20 years had higher relative risks but that the absolute risk of such cancers was low. Similar findings were noted in the Nurses’ Health Study where current OCP use was associated with a higher risk of breast cancer (RR 1.33; 95%CI: 1.03-1.73) though the association with past use did not reach statistical significance (RR 1.12; 95% CI: 0.95-1.33). This study also reported that current use of triphasic levonorgestrel formulations was associated with a particularly elevated risk (RR 3.05; 95% CI: 2.00-4.66). In contrast, other large observational and case-control studies have shown no association between current and past use of OCPs and breast cancer. These older studies have been criticized for including patients who used higher-dose formulations. Complicating matters further, data from the Women’s Health Initiative (WHI), al-

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beit in an older population, have implicated the progestin component of postmenopausal hormone therapy as the primary culprit in the higher rates of breast cancer seen in this population, with estradiol therapy alone being protective.6 Thus, there are at least theoretical reasons why OCPs and progestin-only forms of contraception may be linked to breast cancer.

**Contemporary data**

For all these reasons, results of the recent large prospective study by Mørch and colleagues are an important advance in our understanding the relative and absolute risks of breast cancer conferred by hormonal contraception.7 In Denmark, nearly 40% of women between ages 15 and 49 use hormonal contraception. Moreover, a fortuitous alignment and integration of national health-related registries and databases afforded the investigators the opportunity to examine the association between specific hormonal contraceptives, their precise duration of use and interval from discontinuation with the subsequent diagnosis of breast cancer.

The authors were thus able to study the link between breast cancer and OCPs with low estrogen doses and a wide variety of progestins, as well as with progestin-only formulations. The ascertainment of women’s contraceptive use in the population and the accuracy of cancer diagnoses were very high and investigators were even able to adjust for a number of cofounders.

Mørch et al. were able to follow 1.8 million women between ages 15 and 49 from 1995 through 2012 for an average of 11 years of follow-up. Of these individuals, 11,517 ultimately received breast cancer diagnoses. Compared with “never users,” women receiving “any” hormonal contraceptive had an adjusted (adj) RR of breast cancer of 1.2 (95%CI: 1.14-1.26). Adding biological plausibility to this finding, the investigators noted that risk difference among various OCP formulations and risk with levonorgestrel-releasing intrauterine devices (IUDs) was essentially the same as for oral agents (1.21; 95%CI: 1.11-1.33).

As in the Collaborative Group study, there was a suggestion that women who initiated hormonal contraception before age 20, and continued for prolonged durations, had enhanced risks. But only 2 additional breast cancers per 100,000 women under 35 could be ascribed to hormonal contraception. Adjusting risks for body mass index, smoking and age at first birth did not materially change the results. However, the authors could not adjust for other breast cancer risk-modifying factors including age at menarche, breastfeeding, alcohol use, and exercise. Finally, while RRs were increased across the entire population, absolute risks remained low – there was 1 additional breast cancer diagnosis per every 7690 women using hormonal contraception for a year!

**Benefits of hormonal contraception**

Counter-balancing the low absolute risk of breast cancer attendant hormonal contraception are a host of health benefits, first among them lower overall rates of cancer! Hannaford and associates interrogated a UK data base con-

Compared with never users, OCP ever users had lower rates of colon, endometrial, and ovarian cancer.
HORMONAL CONTRACEPTION

Dr. Lockwood’s Take

Hormonal contraception containing 339,000 woman-years for never users of OCPs compared with 744,000 woman-years for ever users of OCPs. Compared with never users, OCP ever users had statistically significant lower rates of colon, endometrial and ovarian cancers as well as lower overall rates of malignancies. In contrast, there was a modest increase in cervical cancer rates that likely reflected reduced condom use. The reduction in serous epithelial ovarian cancer risk associated with OCP use is particularly striking. One systematic review of 45 epidemiological studies found that 10 years of OCP use reduced ovarian cancer rates prior to age 75 from 1.2 to 0.8 per 100 users. Additional benefits of OCPs include treatment of dysmenorrhea, and polycystic ovarian disease-associated hirsutism, acne and anovulatory bleeding. Progestin-containing IUDs are particularly effective at reducing menorrhagia.

Take-home message

Use of progestin-containing contraceptives appears to be modestly linked to an increased incidence of breast cancers among current and past users. This risk increases with duration of use, but also attenuates > 5 to 10 years off treatment. Since most breast cancers occur in women after 40, it seems prudent to switch from hormonal contraceptives to non-hormonal methods such as copper IUDs, tubal ligation and barrier methods after age 35. This will also help mitigate risks of venous thromboembolism, stroke and myocardial infarction in this older age group. Women with a strong family history of breast cancer might consider such non-hormonal approaches even earlier. As in so many clinical settings, accurate, concise and clear counseling of patients about the risks, and many benefits, of hormonal contraception is the cornerstone of good practice.

Charles J. Lockwood

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REFERENCES


ACOG 2018: THANKS FOR THE MEMORIES

Our editors are back from Austin, invigorated by our conversations with Editorial Board members, authors, and readers. To everyone who came to the Contemporary OB/GYN booth, thanks for taking the time to talk with us.

If you didn’t have a chance to stop by and have an idea you’d like to share, write to COGEditorial@ubm.com. We love to hear from readers anytime about what they want to see in the pages of our magazine and on our website.
Nitrous oxide’s revival in childbirth

Widely used before the advent of epidural analgesia in the 1970s, patient-controlled nitrous oxide is re-emerging for analgesia in labor.

by JESSICA L. ILLUZZI, MD, MS, MICHELLE L. TELFER, CNM, DNP, MPH, AND PHIL RUBIN, MD

Across the United States, nitrous oxide (N₂O) is attracting attention as a desired option for analgesia during childbirth. Worldwide it remains one of the most common labor analgesics, utilized widely in many countries in Europe (up to 75% of women in the UK), the Middle East, Asia, and Australia. In the United States, nitrous oxide was commonly used during labor from the 1930s to the 1950s, often given with other potent agents, such as scopolamine, ketamine, or narcotics. It remains in frequent use today for outpatient pediatric dentistry.

In the 1970s, nitrous oxide use in childbirth declined with the increasing availability of epidural analgesia. Many hospitals in the United States no longer installed nitrous oxide gas lines in labor and delivery rooms, and the next generation of American obstetricians, anesthesiologists, and parturients became unfamiliar with its use in labor. Not until consumers and the midwifery community began seeking its use did nitrous oxide begin to re-emerge. The US Food and Drug Administration’s (FDA) approval of a portable nitrous oxide delivery system in 2012 further facilitated its re-emergence in this country. New protocols have developed via coordinated team efforts among obstetricians, midwives, nurses, and anesthetists. Today, dozens of hospitals and birth centers in the United States are offering nitrous oxide once again for pain management during labor. Interest in its use is accelerating for those parturients desiring low-intervention births. Centers are increasingly offering such services, as they aim to meet consumer needs and increase patient satisfaction.

Nitrous oxide increases dopamine, norepinephrine, and endogenous opioid release, decreasing pain perception and producing a sense of euphoria and sometimes psychedelic effects.

Nitrous oxide has no effect on cord blood gases, Apgar scores, or neonatal behavior but there are no extensive long-term studies on infants and children exposed to the gas during labor.

QUICK TAKE
Physiology and pharmacology
Nitrous oxide is a colorless, non-flammable, sweet-smelling gas with both anesthetic and analgesic properties when inhaled. Its analgesic and anxiolytic mechanisms of action include inhibition of N-methyl-D-aspartate (NMDA) antagonism, modulation of \( \gamma \)-aminobutyric acid (GABA) nerve pathways and glycine potentiation. Along with these effects, increases in dopamine, norepinephrine, and endogenous opioid release decrease pain perception, producing a sense of euphoria and sometimes psychedelic effects.

For labor-related analgesia, women inhale nitrous oxide just prior to the start of and throughout each contraction. Due to low solubility of the gas, there is rapid uptake within 3 to 4 breaths with maximum analgesic effect in 40 to 60 seconds. Following a contraction, there is rapid maternal clearance with cessation of nitrous oxide inhalation. Women remain alert, maintaining motor and sensory function, including a strong laryngeal reflex that helps to prevent aspiration. Intake is self-administered and self-regulated; if the patient becomes too drowsy, she will not be able to hold her mask in place, and the gas will rapidly clear within a few breaths.

Importantly, the FDA-approved portable nitrous oxide delivery systems for childbirth have safety features that limit gas concentration to a 50/50 mixture with oxygen. Demand valves permit nitrous oxide flow only when the patient establishes a good seal with the mask and engages in purposeful inspiration. In addition, these units are connected to scavenging systems to remove exhaled gas.

Maternal and fetal effects
A Cochrane review of 26 studies with randomization of a total of 2959 women to nitrous oxide found a decreased perception of pain intensity (RR 0.06, 95% CI 0.01-0.34), compared to placebo, decreased maternal anxiety, and increased satisfaction and sense of control. A more recent systematic review evaluated a total of 58 studies. The authors rated only 2 of these studies as good quality, 11 as fair quality, and 46 as poor quality, and concluded that, “further research is needed across all of the areas examined: effectiveness, satisfaction, and adverse effects.” One study of 2482 women found that 38% to 42% rated nitrous oxide as very effective pain management compared to 72% to 84% of those who received an epidural. In another study, only 35% of women receiving nitrous oxide and meperidine were satisfied with their pain management compared to 69% of women receiving an epidural. These findings underscore that nitrous oxide is not as effective as the US “gold standard” epidural analgesia. While not effective for some, patients may find the gas a useful alternative to other modalities or a strategy that represents minimal intervention.

Side effects of nitrous oxide during labor documented in 1000 women in Australia included nausea (13%) as the most common, followed by dizziness (5%) and drowsiness (4%). Eighteen percent of the patients reported reduced awareness, which may contribute to nitrous oxide’s effect on mediating pain.

Other studies have examined the effects of nitrous oxide on the fetus and neonate. Nitrous oxide crosses the placenta, achieving approximately 0.8 of the maternal level during peak use. It is also quickly eliminated by diffusion across the placenta and neonatal respiration at birth. In contrast to in utero fetal exposure to narcotics, there is no evidence of central nervous system or respiratory depression, or increased admission to intensive care among neonates exposed to nitrous oxide in utero. There is no effect on cord blood gases, Apgar scores, or neonatal behavior. In addition, there are no documented effects on fetal heart rate (FHR) patterns, labor progress, or incidence of meconium-stained amniotic fluid.

These findings are mitigated by the lack of extensive long-term studies on infants and children exposed to nitrous oxide during labor. However, long-term data are also lacking for other intrapartum medication exposures (e.g., narcotics, antibiotics, anesthetics, and uterotonic). While it is reassuring that widespread and historic use of nitrous oxide during labor has not been linked to specific long-term problems, the lack of data remains an important caveat to use of nitrous oxide. For example, in a 1991 case-control study of childhood leukemia,
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a trend toward higher odds of having been exposed in utero to nitrous oxide was observed among boys (OR = 1.4; 95% CI = 1.0, 1.9) but not girls (OR = 1.1; 95% CI = 0.8, 1.6), and this effect was noted in the cohorts born in 1973 and 1974 but not in later birth cohorts (1975-1984). The same study identified exposure to oxygen supplementation and hyperbilirubinemia as possible risk factors for childhood leukemia. Thus it is important that providers inform their patients interested in nitrous oxide during labor about its theoretical, but likely low risks to the newborn.

Contraindications
Though most parturients can opt for nitrous oxide, there are various contraindications to its use in labor. Because it must be self-administered, parturients who cannot hold their own masks, have impaired consciousness, or are intoxicated are not eligible for the gas. Similarly, patients receiving magnesium sulfate, intravenous narcotics, or other agents that may cause respiratory suppression may not be candidates. Relative contraindications include sleep apnea with or without constant positive airway pressure use or conditions that impair oxygenation. Less common contraindications include recent intraocular or middle ear surgery, bowel obstruction, known increased intracranial pressure, and pulmonary hypertension. Patients with a Category III FHR tracing or those with a Category II FHR tracing requiring resuscitative measures are also not considered good candidates for nitrous oxide.

In addition, in the presence of vitamin B12 deficiency nitrous oxide inhibits methionine synthase, an enzyme involved in the synthesis of DNA, RNA, myelin, and catecholamines. Therefore, vitamin B12 deficiency may also be a contraindication to use of the gas. This may involve patients who have had gastric bypass surgery or bowel resection, those with Crohn’s disease, hereditary B12 deficiency, or pernicious anemia, or who have chronic malnutrition or on vegan diets. Vitamin B12 levels in such patients can be evaluated during pregnancy and often replenished to normal levels that are considered safe for nitrous oxide use in labor.

Typical protocols
When considering introduction of nitrous oxide to a labor unit, it is vital to develop policies and protocols for its use, as well as programs to educate providers and staff. A standard protocol would include screening for contraindications, informing patients of risks and benefits, and educating on effective use of the gas. Providers must stress that the gas needs to be self-administered and used only by the parturient. Once the delivery system is set up and nitrous oxide is initiated, vital signs are monitored in standard intervals, and some hospitals also monitor oxygen saturation for a brief period of time upon initiating. The patient is monitored for safety and effectiveness of treatment, and the fetus is monitored in a standard fashion by intermittent auscultation or continuous FHR monitoring as appropriate. Patients who do not experience the desired effects or who develop intolerable effects can discontinue use at any time, which should result in prompt resolution of the symptoms due to rapid elimination of the gas.

Nitrous oxide can be used during all stages of labor. It has also been found to be helpful during laceration repair, vigorous fundal massage, manual extraction of the placenta, challenging intravenous access, epidural placement, and difficult vaginal exams. In partnership with the anesthesia team, it may also serve as a useful adjunct to epidural analgesia when there is a sensory window or significant maternal anxiety. Some institutions have also begun offering it during external cephalic version.

When offering nitrous oxide, it is necessary to have a functioning scavenging system in place to suction exhaled gas, adequate room ventilation, and equipment that can alarm for nitrous oxide leaks.
ppm in well-ventilated rooms. Levels above 500 to 1000 ppm have been associated with cell toxicity in animal studies and decreased fecundity in women working in dental offices without scavenging or adequate ventilation. Some hospitals perform regular monitoring in rooms where nitrous oxide is used, and others require staff to wear personal dosimetry badges.

**Our experience**

At the Vidone Birthing Center of Yale-New Haven Hospital (YNHH), we have been offering nitrous oxide for 3 years. During that time, 52% of women have opted for nitrous oxide during labor. The epidural rate has declined only slightly from 60% to 54% in our midwifery-based center, demonstrating that many women still commonly elect to receive an epidural for more effective and reliable analgesia. These numbers may also be confounded by the fact that nitrous oxide cannot be used as the sole anesthetic for cesarean delivery. We have observed, though, that epidurals are typically requested later in the course of labor, there is decreased utilization of narcotics, and that women remain more active during the early phase of labor, taking advantage of alternative therapies including hydrotherapy and water immersion.

In an era in which many women are seeking less intervention and more personal control over their birth experience, nitrous oxide is re-emerging as a useful pain management modality. Laboring patients who use nitrous oxide do not require intravenous fluid, continuous FHR monitoring, or bladder catheterization. While ambulation is not recommended during use of the gas, patients can sit in a chair, on a birthing ball or in various positions in bed. If they want to stand up, walk, or use the bathroom, they can simply stop using nitrous oxide and wait a few minutes before ambulating. In addition, they can easily move from the gas to other alternatives, including water immersion, hydrotherapy, narcotics or epidural analgesia. At YNHH, the increased mobility and active participation of par- turients with nitrous oxide use was an unanticipated outcome. Women who had received early narcotics or an epidural, on the other hand, often became bed-bound, remaining there until delivery. More women have remained mobile throughout their labors and often switch from one modality to another, often going back to nitrous oxide at a later point in their labors. Nitrous oxide also has been particularly helpful for sensory windows, maternal anxiety, and during difficult vaginal exams and repairs.

Use of nitrous oxide in hospitals and birthing centers in the United States is expanding, which requires collaboration with anesthesiologists in writing protocols and educating providers and staff. In some centers, the anesthesia service screens for eligibility and orders nitrous oxide for laboring patients, while in others, obstetric or midwifery providers independently manage this therapy. In most settings, nurses set up and monitor use of nitrous oxide during labor. As of this writing, there are currently no specific billing codes (DRG or CPT) for obstetric nitrous oxide use in labor, so many hospitals are providing this service inclusive in the global reimbursement. A working group has been working to address the deficiency in billing codes to allow for reimbursement for these particular services. Nitrous oxide itself is inexpensive, so the largest initial investment is for the portable equipment.

**Conclusion**

Nitrous oxide remains a popular modality for pain management for women around the globe. It can be used exclusively, or as an adjunct to other methods. Contraindications, side effects, and complication rates are low. Nitrous oxide may increase patient satisfaction by giving women a greater sense of control during labor in an era when more women are seeking this type of birthing experience.

**DISCLOSURES** The authors report no potential conflicts of interest with regard to this article.

**FOR REFERENCES VISIT** contemporaryobgyn.net/N2Orevival
In 2015, news began to surface about an epidemic of neonatal microcephaly in Brazil, eventually traced to infection with Zika Virus (ZIKV), an arthropod-borne flavivirus similar to Dengue and Chikungunya. Zika was identified back in 1947, but the 2015 outbreak was the first to gain international attention. Cases were soon reported throughout much of Central and South America, and eventually a link was made to a 2013 outbreak in French Polynesia, in which thousands of people were infected. Eventually, researchers assembled sufficient data to characterize the Congenital Zika Syndrome, a constellation of neurologic and physical findings attributed to congenital infection with ZIKV (Table 1).

Unlike other flaviviruses, Zika was noted to cause only mild illness in infected adults, with most adults (80%) showing no symptoms at all, and the remaining 20% describing a mild syndrome consisting of fever, conjunctivitis, rash, and mild arthralgias. Zika has also been associated with development of Guillain-Barré syndrome in adults, which can be life-threatening. Zika is primarily transmitted between adults through an arthropod vector, the Aedes aegypti mosquito, although other Aedes species have tested positive for virus particles. The virus can also be transmitted sexually; it can survive in vaginal secretions for up to 14 days and in semen for up to 188 days after onset of illness. It has also been detected in other body fluids including urine, saliva, and tears along with blood. Transplacental passage is the primary mode of perinatal transmission.

### Current epidemiology

A recent publication provided information with regard to incidence of infection and timing during pregnancy. Hoen et al followed 555 fetuses and infants born to women with symptomatic, polymerase chain reaction-confirmed ZIKV infection. They found a rate of microcephaly of 5.8%, and an overall birth defect rate of 7.0%. Neurologic and ocular defects were more common in cases in which ZIKV infection took place in the first trimester (12.7%) compared to second- or third-trimester infections (3.6% and 5.3%, respectively).

Although media attention on Zika virus has dwindled over the past year, the majority of countries in South and Cen-
Central America continue to report active transmission of virus, along with Southeast Asia, India and Pakistan, much of Africa, and the Pacific Islands. Therefore, it is important for obstetric care providers to query their patients at each visit about travel history or sexual partners’ travel and symptoms in those exposed or potentially exposed, and discuss options for screening in relevant populations. This is particularly important with summer approaching, and increased travel to areas with possible exposure. As with any disease process, prevention is key; patients who are not pregnant but are planning to become pregnant should be advised to avoid these areas with active transmission and avoid unprotected intercourse with anyone who has traveled to an area of active transmission within the last 6 months. If travel is unavoidable, using permethrin, DEET, and other mosquito-repellent behaviors such as remaining indoors with windows shut, wearing long sleeves, and removing sources of standing water are good advice.

How and when to screen
Screening algorithms for ZIKV are complex; providers should refer to the Centers for Disease Control and Prevention’s website for detailed information. Briefly, at this time, recommendations for testing are exclusively related to pregnant patients—there is no guidance for screening of non-pregnant women or their partners. The

Choice of screening test and interpretation are difficult in part because of cross-reactivity of the existing tests with other flaviviruses (particularly Dengue and Chikungunya). This is further complicated by the fact that these viruses are also endemic in the areas where Zika is found, and carried by the same arthropod vector. Initial symptoms of those infections can easily be confused with Zika, and coinfection is frequently reported. Dengue and Chikungunya have the benefit of not being associated with neurologic injury to the fetus, and it is unclear why such a discrepancy exists when these viruses are otherwise so similar.

Conclusion
In summary, providers should be discussing Zika with their patients and educating them about preventive strategies as well as offering screening and testing to relevant populations of pregnant women.

DISCLOSURE
The author reports no potential conflicts of interest with regard to this article.

FOR REFERENCES VISIT
contemporaryobgyn.net/Zika2018

Zika, HIV coinfection in pregnancy
A NICHD study hopes to determine if the presence of both Zika and HIV exacerbate the effects of either. 

Study: Clinical trials indicate positive results for Zika vaccine
Three Phase 1 human clinical trials evaluating the efficacy of an Army-developed Zika purified inactivated virus have shown it to be safe and well tolerated. 
http://bit.ly/ZikaVaccineResults

New ‘dipstick’ test for Zika, dengue
A fast and cost-effective dipstick test for Zika can distinguish between it and dengue viruses without cross-reactivity. 

The virus can survive in vaginal secretions for up to 14 days and in semen for up to 188 days after onset of illness.
Hypertensive disorders of pregnancy

As many as 60% of related deaths may be preventable; targeted strategies are needed to better identify and treat women at risk.

by CHARLENE H. COLLIER, MD, MPH, MHS, FACOG AND JAMES N. MARTIN JR., MD, FACOG, FRCOG, FAHA

Introduction
Hypertensive disorders of pregnancy are among the leading contributors to maternal mortality worldwide. Approximately 30,000 deaths annually are attributed to hypertensive disorders including preeclampsia, eclampsia, and HELLP syndrome. In the United States, hypertension-related disorders account for approximately 7.4% of the almost 800 pregnancy-related deaths that occur each year.3 Women with preeclampsia/eclampsia are at 3 to 25 times the risk of severe pregnancy complications including placental abruption, disseminated intravascular coagulation (DIC), renal failure, pulmonary edema and aspiration pneumonia.4,5 Recent reviews suggest that up to 60% of hypertension-related maternal deaths are potentially preventable—there continue to be missed opportunities for appropriate, recommended care of severe maternal hypertension.6

This review describes hypertension-related maternal mortality in the United States and key strategies to improve outcomes.

Recent trends in hypertension-related maternal mortality
Between 1990 and 2015, maternal mortality increased in the United States by an estimated 27% while other developed nations have experienced persistent declines.7 During that time, however, the proportion of maternal deaths attributed to hypertensive disorders declined in the United States to 7.4%, falling behind cardiovascular diseases and other medical conditions (Figure 1).7,8-10 Based upon a recent report from the Centers for Disease Control and Prevention, hypertensive disorders accounted for 6.6% of deaths during pregnancy, 9.3% of deaths within 42 days of pregnancy, and 5.4% of deaths happening between 42 days and 1 year.

- Women with preeclampsia/eclampsia are at 3 to 25 times the risk of severe pregnancy complications including placental abruption, disseminated intravascular coagulation, renal failure, pulmonary edema and aspiration pneumonia.
- Hypertensive disorders account for 6.6% of deaths during pregnancy, 9.3% of deaths within 42 days of pregnancy, and 5.4% of deaths happening between 42 days and 1 year.
9.3% of deaths within 42 days of pregnancy, and 5.4% of deaths happening between 42 days and 1 year.\(^1\)

Despite the declines in hypertension-related mortality, growing numbers of women are experiencing hypertensive disorders of pregnancy due to factors including the rising obesity epidemic, delayed childbearing and the use of assisted reproductive technologies. Between 1998 and 2006, the number of obstetric hospitalizations for hypertensive disorders significantly increased from 67.2 per 1,000 deliveries to 81.4 per 1,000 deliveries, mostly related to chronic hypertension (50% increase).\(^1\) Preeclampsia/eclampsia increased from 9.4 to 12.4 per 1,000 deliveries. Severe forms of preeclampsia were associated with 38% of acute renal failure hospitalizations and 19% to 24% of hospitalizations with complications involving DIC, acute respiratory distress syndrome (ARDS), cerebrovascular accidents, and pulmonary dysfunction/edema; 14% of the hospitalizations ended in death.

State-based reviews provide greater insight into hypertension-related maternal deaths.\(^1\) In California between 2002 and 2005, women dying from preeclampsia/eclampsia were more likely to be over 30 years old (67%), delivered preterm (61%), delivered by cesarean (83%) and/or primiparous (44% vs 21% for other mortality causes). The median timing of death was within 72 hours postpartum.\(^6\)

The Florida Pregnancy-Associated Mortality Review summary of preeclampsia-related deaths (1999-2012) found an elevated risk of death among women over 35, non-Hispanic black women, those with limited prenatal care (5.7 vs 1.7 pregnancy-related deaths per 100,000 live births), obese women (8.1 vs 1.1 per 100,000 live births) and those delivering preterm (47 per 100,000 if < 28 weeks, 10.2 per 100,000 if 29-36 weeks’ gestation at birth). Forty-three percent of women with hypertension-related deaths experienced cerebrovascular hemorrhage and 17% had HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome.\(^1\)

**Postpartum risk**

Several years ago, von Dadelszen and Magee astutely noted that delivery does not “cure” preeclampsia but initiates the process of recovery. Before complete recovery occurs, often there is evidence of a transient deterioration in key clinical parameters such as hypertension, thrombocytopenia and renal dysfunction. Thus, nearly 75% of maternal deaths associated with hypertensive disorders occur after birth with 41% occurring > 48 hours postpartum.\(^1\)

For postpartum stroke, the period of highest risk occurs during the first 10- days after hospital discharge—58% of stroke cases occurred during this time.\(^1\) This included 53% of strokes among women with a known hypertensive disorder of pregnancy and 66% of strokes among patients with chronic hypertension without superimposed preeclampsia—the median times to presentation were 8.9 and 7.8 days, respectively. These data underscore the importance of close monitoring of patients with hypertensive disorders for the first 72 hours postpartum, reevaluating them within 7 to 10 days postpartum as recommended by the American College of Obstetricians and Gynecologists.\(^1\) Practices are encouraged to coordinate early postpartum care with blood pressure assessment in concert with patient education, the assurance of patient access to prescribed medication(s), and appropriate long-term care.\(^1\)

**Racial disparities in hypertension-related mortality**

In comparison to US-born white women, nearly all other racial, ethnic and nativity groups face a greater risk of pregnancy-related mortality in the United States.\(^1\) Black women in the United States, in particular, are at significant risk of hypertension-related morbidity and mortality. Compared to white women, black women have nearly twice the incidence of preeclampsia (6.04 vs 3.75%), are more likely to suffer complications...

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**FIGURE 1** Percentage of Pregnancy-Related Deaths due to Hypertensive Disorders, US, 1987-2013

<table>
<thead>
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<td>17.6%</td>
<td>15.9%</td>
<td>12.3%</td>
<td>9.4%</td>
<td>7.4%</td>
<td></td>
</tr>
</tbody>
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Source: Centers for Disease Control and Prevention, Pregnancy-Related Mortality Surveillance System\(^2\)\(^-\)\(^7\)
such as cardiac arrest, ARDS and heart failure and are over 3 times more likely to die.20,21 While variations in disease severity explain some of these disparities, differences in care delivery and variations in hospital quality can significantly impact risk of maternal death for black women.22

Focus on severe persistent hypertension
Emergent treatment of severe acute-onset persistent hypertension (systolic BP > 160 mmHg or diastolic BP > 110 mmHg sustained > 15 minutes) constitutes an important component of high-quality obstetric care. Even in the absence of proteinuria, sudden development of sustained severe hypertension causes significant risk of hemorrhagic stroke and death. An estimated 25% to 45% of maternal strokes occur among patients with preeclampsia, eclampsia or HELLP syndrome.23 Severe systolic blood pressure is a consistent feature present before the onset of stroke in over 90% of women with hypertensive disorders.24

When reviewing factors contributing to preventable preeclampsia-related deaths, multiple state mortality reviews have identified instances of delayed medical staff response to both worrisome maternal symptoms and vital signs and inadequate staff knowledge and treatment of severe hypertension.6,25 There has been a national call to action for clinical practices to implement standardized systems to identify and treat severe maternal hypertension and associated disorders.26,27 A progressive algorithm for treatment within 60 minutes of confirmed measurement is recommended such as illustrated in the most recent ACOG Committee Opinion and otherwise summarized in Table 1. Staff should be educated on the algorithm including contraindications (i.e. labetalol contraindicated with asthma, heart disease or congestive heart failure) and patients informed about the goals of therapy, side effects and safety of these medications for breastfeeding mothers.

The recently released consensus bundle for severe hypertension includes guidance not only for standardization of antihypertensive therapy, but also for other important components of care such as discharge criteria, readmission criteria and guidance for postpartum outpatient surveillance all of which should be tailored to the unique maternity care setting.27 Use of such standardized treatment practices or safety bundles for maternal hypertensive disorders can significantly improve pregnancy outcomes.6,28 Shields demonstrated that compliance with blood pressure treatment recommendations increased from 50% to over 90% with a structured quality improvement initiative across 23 facilities. Importantly, this resulted in a 43% reduction in eclampsia and a 17% reduction in severe maternal morbidity.29

Reviews have identified instances of delayed medical staff response ... and inadequate staff knowledge and treatment of severe hypertension.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Treatment of Severe Persistent Hypertension &gt; 160 mmHg Systolic or &gt; 110 mmHg Diastolic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>20 mg IV, increase to 40 mg then 80 mg IV at 10-minute intervals if BP remains severe. If severe HTN is persistent, transition to hydralazine.</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5-10 mg IV, then 10 mg then 20 mg at 20-minute intervals if BP remains severe. If severe HTN is persistent, transition to labetalol.</td>
</tr>
<tr>
<td>Oral Nifedipine</td>
<td>Initial 10-mg PO dose increased to 20 mg for up to 2 more doses at 20-minute intervals if BP remains severe.</td>
</tr>
</tbody>
</table>

*Abbreviated. See resource for complete details.26,27 BP, blood pressure; HTN, hypertension; IV, intravenous

Magnesium sulfate to reduce risk of eclampsia-related mortality
Eclampsia complicates approximately 1 in 1,000 deliveries, affecting 0.5% to 3.0% of patients with preeclampsia.30 Women in developed nations who have regular prenatal care and delivery at tertiary care centers have mortality rates ranging between 0% to 1.8%, with the leading cause being intracranial hemorrhage. Magnesi-
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sium sulfate can reduce the incidence of eclampsia by 42.6% and reduce severe maternal morbidity from 16.7% to approximately 2%. Because nearly half of eclamptic convulsions in the US occur before a mother can be hospitalized and treated with magnesium sulfate, providing enhanced prenatal and postpartum care to patients at risk for eclampsia is important.

Acute pulmonary edema in preeclampsia
Acute pulmonary edema is a leading cause of maternal death that complicates approximately 3% of preeclampsia cases, with up to 70% occurring in the postpartum period. Pulmonary edema is more common among hypertensive women who are postoperative, receiving excess intravenous fluids and magnesium sulfate infusion. Restrictive fluid management is generally recommended for patients with preeclampsia/eclampsia so that euvolemia is not exceeded. Women reporting dyspnea or demonstrating decreased oxygen saturation should be suspected of developing acute pulmonary edema and urgently evaluated, initially with bedside exam and chest radiography. Physical exam alone and the absence of audible rales is insufficient to rule out pulmonary edema. EKG, transthoracic echocardiography and CT scan may be needed to clarify diagnosis and guide therapy. Intravenous diuretic therapy such as furosemide 20 – 40 mg should be administered along with oxygen support and ongoing hemodynamic monitoring.

HELLP syndrome
When pregnancy is complicated by HELLP syndrome, there is increased risk of maternal death particularly from hemorrhagic stroke. The mortality rate associated with HELLP syndrome ranges from less than 1% to up to 30%, depending upon site of treatment and associated patient comorbidities. Isler found among 54 deaths from HELLP syndrome that the majority of women (71%) presented with symptoms of nausea, vomiting and epigastric pain and 42% had or developed eclampsia. The primary causes of maternal death included intracranial hemorrhage (26.4%), cardiopulmonary arrest (15.1%), respiratory failure (13.2%), hepatic hemorrhage (7.5%), hypoxic ischemic encephalopathy (7.5%), and DIC (5.7%). Several analyses have demonstrated that clinical symptoms are more predictive of poor outcomes than lab values alone.

Preeclampsia prevention
To further reduce hypertension-related mortality, efforts must be undertaken to reduce the incidence of preeclampsia. Daily low-dose aspirin (81-150 mg) initiated between 12 and 24 weeks’ gestation has been shown in several score studies to reduce development of preeclampsia by 10% to 29%. In women with both moderate- and high-risk factors for preeclampsia, initiation of an aspirin regimen should be routine.

Patient education and empowerment
It is critical for pregnant women to know the warning signs of preeclampsia, when to seek medical attention and to encounter a medical system that listens and responds to their needs. In the ProPublica and National Public Radio series on 134 maternal deaths in the United States in 2016, Lost Mothers, many families reported instances of dismissed or discounted patient complaints prior to the death of a loved one. Physicians are encouraged to provide specific education to women with and/or at risk of a severe gestational hypertensive disorder and include patient and family interviews as part of debriefs and state morbidity and mortality reviews.

DISCLOSURES The authors report no potential conflicts of interest with regard to this article.

KEY STRATEGIES FOR PREVENTION OF HYPERTENSION-RELATED MATERNAL DEATH

1. Prevent preeclampsia with low-dose aspirin
2. Fully implement patient safety bundles for severe maternal hypertension
3. Urgently treat severe persistent hypertension (>160 systolic or >110 diastolic)
4. Utilize magnesium sulfate for seizure prophylaxis
5. Limit iatrogenic fluid overload and utilize appropriate hemodynamic monitoring/imaging to manage fluid balance
6. Provide enhanced/early postpartum care for women with a diagnosis of hypertensive disease as well as those at risk for its development
7. Educate women about the warning signs of preeclampsia and establish a culture of safety that empowers patient-family escalation of care

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6 ways to reduce physician frustration with EHRs

Time spent on EHRs is frustrating for many ob/gyns but taking certain measures can help ease the burden.

by TODD SHRYOCK

Time spent entering data into an electronic health record (EHR) instead of interacting with patients is a common complaint from doctors. Studies show that physicians spend as much time on entering information in their EHR as spending face-to-face time with patients, and it can have a direct effect on job satisfaction and contribute to burnout.

Results of Contemporary OB/GYN’s 2018 Labor Force Survey show that complicated or inadequate technology—especially EHRs—has taken the joy out of practice for many ob/gyns. One-third of respondents mentioned EHRs and most of them disliked the software. As one ob/gyn put it: “Electronic health record time requirements are eroding patient care.”

Martin Pricco, MD, MBA, an internist and president of Gould Medical Group in Modesto, Calif., did an evaluation with Paul DeChant, MD, MBA, deputy chief health officer of Simpler/IBM Watson Health, examining how Gould’s 360 physicians (including ob/gyns) and allied health practitioners were spending their time in the EHR. The goal was to help the physicians become more efficient and reduce their frustration with the system. He shared his experience at the 2018 Health Information and Management Systems Society (HIMSS) conference held in Las Vegas.

Here are 6 changes that can be implemented to reduce physician frustration with an EHR.

1. **Improve the password process.**
Physicians should not spend any time typing passwords into workstations in the practice. Instead, provide a proximity password device or other technology solution that does not require physicians to enter a password on a keyboard each time they enter a new room.

2. **Provide individual training.**
"There is a correlation between using personalization settings and physician satisfaction," said Pricco. EHR systems often have features for rapid access to data or customization options that physicians don’t know about, so investing time in training can pay off in long-term time savings and frustration reduction.

Pricco says Gould physicians needed a minimum of 6 hours of onboarding training, 4 hours in the classroom and a week of having a trainer spending one-on-one time with them. When complete, physicians can create filters, preference lists, and know how to find the data they need to deliver quality care.

"One of the most common doctor complaints is that they can’t find what they are looking for," Pricco said.

3. **Identify wasted time**
Most EHRs have charts that show exactly where physician time is being spent in the software. If there are multiple passwords, cumbersome or confusing configurations, printers or other needed items in remote locations - and take steps to correct those issues and streamline processes.

*Continued on page 31*
In the United States, 1% to 2.5% of pregnant women are infected with hepatitis C virus (HCV), which carries an approximately 5% risk of transmission from mother to infant. HCV can be transmitted to an infant in utero or during the peripartum period. Two primary concerns arise from HCV in pregnancy: 1) maternal well-being, i.e., the effect of pregnancy on the course of chronic HCV infection; and 2) fetal well-being, namely mother-to-infant transmission of HCV and the impact of maternal infection on pregnancy outcomes.

What is the natural course of HCV infection?
In addition to vertical transmission, HCV is transmitted through percutaneous exposure to blood through use of contaminated needles for injection of illicit drugs or during occupational exposure. Sexual intercourse is an inefficient means of transmission. The first 6 months after exposure to HCV is referred to as acute HCV infection, which is asymptomatic in 75% of cases. When symptoms occur, they include abdominal pain, nausea, anorexia, jaundice, or malaise. Without treatment, approximately 15% of infected individuals spontaneously clear HCV within 6 months of infection, although some estimate this number to be as high as 45%. Those who do not clear the virus harbor it for the rest of their lives and develop chronic HCV infection, which accounts for most HCV-associated morbidity and mortality, mainly due to cirrhosis and hepatocellular carcinoma.

What is the impact of pregnancy on HCV?
Researchers speculate that down-regulation of the maternal immune response that occurs during pregnancy may reduce the amount of immune-mediated hepatocellular damage caused by HCV. This mechanism would also account for the decrease in alanine transaminase (ALT) levels seen in pregnant women with HCV and the increase in serum levels of HCV RNA during the second and third trimesters of pregnancy. Some histological evidence also suggests that pregnancy may be associated with a decrease in HCV-mediated hepatic injury, but data are conflicting.

What is the impact of HCV on pregnancy outcomes?
HCV infection is associated with adverse pregnancy outcomes. Two population-based, retrospective cohort studies and a recent meta-analysis found that infants born to women infected with HCV were more likely to have poor birth outcomes, including fetal growth restriction, low birth weight (LBW), and congenital anomalies, and to be delivered preterm. It is difficult to know with certainty whether the increased risk of adverse outcomes such as fetal growth restriction and LBW is due to the viral effect of HCV or to potential confounders in the population being studied.
Best Practices in the Management of Complications following Early Pregnancy Loss

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In addition, several studies have reported higher rates of gestational diabetes in HCV-infected women compared with noninfected women, although in one of these studies, this association was limited to women with excessive weight gain during pregnancy. Another population-based, retrospective cohort study found that infants born to HCV-infected women were more likely to have feeding difficulties and other adverse neonatal outcomes, including cephalohematoma, brachial plexus injury, fetal distress, intraventricular hemorrhage, or neonatal seizures.

Intrahepatic cholestasis of pregnancy (ICP) has also been associated with HCV infection. The overall incidence of ICP in the general obstetric population is 0.2% to 2.5%, while the odds of developing ICP are 20-fold higher in HCV-infected pregnant women. Given the increased risk of fetal death associated with ICP, diagnosis of this disease in pregnant women is important.

Currently, a multicenter, prospective observational cohort study is underway to evaluate pregnancy outcomes in women with HCV. Outcomes being studied include preterm delivery, gestational diabetes, preeclampsia, cholestasis, and infant birth weight (Clinicaltrials.gov: NCT01959321).

What is the rate of vertical transmission of HCV?
Vertical transmission of HCV is the leading cause of HCV infection in children. While one-third to one-half of mother-to-child transmission of HCV appears to occur in utero prior to the last month of pregnancy, the remainder is thought to occur either in the last month of pregnancy or during delivery. In women who are coinfected with HIV and HCV, risk of vertical transmission is almost double that in women infected only with HCV.

In general, vertical transmission of HCV is thought to be a risk only for women with detectable HCV RNA during pregnancy. Whether the level of HCV viremia correlates with risk of transmission has yet to be determined. Several studies have shown that higher viral loads correlate with an increased risk of transmission, whereas other studies have failed to find such an association.

Who should be screened for HCV during pregnancy and what is the ideal screening test for HCV?
Current guidelines from the American College of Obstetricians and Gynecologists (ACOG) and the Centers for Disease Control and Prevention (CDC) recommend risk-based screening for HCV in pregnant women. We recommend that obstetric care providers screen women who are at increased risk for HCV by testing for anti-HCV antibodies at their prenatal visit. If initial results are negative, HCV screening should be repeated later in pregnancy in women with persistent or new risk factors for HCV infection after their initial screening (e.g., new or ongoing use of injected or intranasal illicit drugs).

The standard screening test for HCV is an anti-HCV antibody test. Anti-HCV antibodies usually develop 2 to 6 months after exposure—during the acute phase of infection—and persist throughout life. A positive test result indicates one of the following: the patient has active HCV infection (acute or chronic), the patient had a past infection that has resolved, or the result is a false positive.

A positive anti-HCV antibody result should be followed by a quantitative nucleic acid test for HCV RNA. Diagnosis of HCV infection depends on detection of anti-HCV antibodies and HCV ribonucleic acid (RNA). HCV viremia, i.e., the presence of HCV RNA in the blood, indicates active infection and can first be detected 1 to 3 weeks after exposure.

What other additional evaluation should occur?
For pregnant women with confirmed active HCV infection, a quantitative HCV RNA test should be done to determine baseline viral load. Basic laboratory testing to evaluate the extent of liver disease should include the following laboratory tests: bilirubin, ALT and aspartate aminotransferase (AST), albumin, platelet count, and prothrombin time. To help plan future treatment, testing for HCV genotype should also be performed (if not done previously).
In light of common risk factors, we recommend that obstetric care providers screen HCV-positive pregnant women for other sexually transmitted diseases, including HIV, syphilis, gonorrhea, chlamydia, and hepatitis B (HBV). Patients with HBV infection and a high viral load can be offered antenatal treatment; infants should receive the hepatitis B vaccine as well as hepatitis immune globulin. Hepatitis A virus (HAV) infection can also worsen hepatic damage if present with HCV infection. The Advisory Committee on Immunization Practices (ACIP) recommends that women with HCV infection who are found to be at risk of HBV and/or HAV be vaccinated, and it is safe to do so during pregnancy.

Q Should HCV be treated pharmacologically during pregnancy?

Until 2011, the standard-of-care treatment for chronic HCV was pegylated interferon (PegIFN)-α and ribavirin. In 2011, direct-acting antiviral medications (DAAs) were released, revolutionizing treatment of HCV. These drugs directly inhibit proteins involved in HCV replication, have fewer side effects than interferon-based regimens, and have led to sustained virological response (SVR) rates as high as 60% to 100%. Treatment regimens usually involve multiple DAAs to prevent viral resistance.

Because there are no adequate human data regarding any of the effects of second-generation DAAs in pregnancy, we recommend that DAA regimens only be used in the setting of a clinical trial or antiviral treatment should be deferred to the postpartum period as DAA regimens are not currently approved for use in pregnancy.

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Q What are the principles of medical management of HCV during pregnancy?

Any woman who is diagnosed with HCV infection during pregnancy should be referred to a hepatologist or infectious disease specialist experienced in management of hepatitis in order to establish long-term care.

Use of even modest amounts of alcohol has been associated with progression of liver disease, and we suggest that patients with HCV, including pregnant women, be counseled to abstain from alcohol.

Serial laboratory surveillance of liver function or serial viral load assessment during pregnancy in HCV-positive women is generally not recommended. As discussed previously, serum levels of ALT tend to decrease during the second and third trimesters of pregnancy, i.e., liver function is expected to improve, not worsen, during pregnancy.

Q Is invasive prenatal diagnostic testing safe in pregnant women with HCV?

Amniocentesis does not appear to increase risk of vertical transmission, although this conclusion is based on limited data. No studies have been published on risk of vertical transmission of HCV with other invasive prenatal testing modalities, including chorionic villus sampling (CVS). We suggest that if invasive prenatal diagnostic testing is requested, women be counseled that data on the risk of vertical transmission are reassuring but limited; amniocentesis is recommended over CVS given lack of data on the latter.

Q Does mode of delivery affect risk of vertical transmission?

Mode of delivery—vaginal versus cesarean—has not been shown to be a risk factor for vertical transmission of HCV. However, because all published studies on mode of delivery and risk of vertical transmission of HCV are observational and most did not assess viral load at the time of delivery, these results should be interpreted cautiously. We recommend against cesarean delivery solely for the indication of HCV.

Q Does labor management affect risk of vertical transmission?

Several factors in labor management may be associated with increased risk of vertical transmission of HCV, namely prolonged rupture of membranes, internal fetal monitoring, and episiotomy. Based on the available evidence, we recommend that obstetric care providers avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labor in HCV-positive women, unless it is unavoidable in the course of management. We also recommend that obstetric care providers avoid early amniotomy and episiotomy in managing labor in HCV-positive women.

Q Is breastfeeding safe for HCV-positive mothers?

Breastfeeding does not appear to affect the risk of vertical transmission of HCV. We recommend against discouraging breastfeeding based on a positive HCV infection status. If women have cracked and bleeding nipples, milk should be expressed and discarded.

Q How should infants born to HCV-positive women be screened for HCV infection?

Because anti-HCV antibodies can be transmitted across the placenta from a pregnant woman to the fetus, the presence of anti-HCV antibodies in a neonate’s serum soon after delivery is not diagnostic of neonatal infection. The American Academy of Pediatrics and CDC recommend screening of infants born to HCV-positive women for anti-HCV antibodies after age 18 months or for HCV RNA on two occasions in infants older than age 1 month.

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Dr Page is a resident physician, Department of OB/GYN at Duke University, Durham, NC

Dr Kuller is Professor, Division of Maternal-Fetal Medicine at Duke University, Durham, NC

Read more about labor management in Nitrous Oxide’s Revival in Childbirth on PAGE 7
to use no more than gentle traction in the face of a shoulder dystocia, only when the obstetrician believes that a maneuver has released the shoulder. If any resistance during use of gentle traction is encountered, this would indicate that the shoulder dystocia still exists, so traction must immediately cease and new maneuvers be employed to free the shoulder. It was his opinion that the obstetrician deviated from the standard of care by applying more than gentle traction to the fetal head when the shoulder was still impacted and asserting the severe permanent injury to the right brachial plexus nerve is just an unproven hypothesis.

**Question of bowel perforation during hysterectomy**

In 2013, a day after a Missouri woman underwent a hysterectomy, she felt ill and presented to the emergency room. She was diagnosed with a pulmonary embolism and treated with anticoagulants. Her problems persisted and over the next 17 days some computed tomography (CT) scans showed fluid in her abdomen and she developed a vaginal fistula. An exploratory laparotomy eventually was required, which revealed a bowel perforation.

The patient sued the surgeon who had performed the hysterectomy alleging that he had perforated her bowel during the procedure. She also sued the hospital where the procedure had taken place. She contended that CT scans showing fluid buildup and her early symptoms after surgery were consistent with a bowel perforation which ultimately caused leakage into the peritoneal cavity and eventually a fistula in the vagina. Her expert pathologist testified that the findings under the microscope could only exist if a bowel perforation had been there a significant period of time before the fistula developed. While she agreed that continuous leakage from the bowel for 17 days would have likely resulted in her death, she presented experts who argued that her injury was not a “free perforation” but had been contained by her body, preventing the spread of the infection.
The case against the hospital was resolved before trial. The matter proceeded against the surgeon only. He maintained that the perforation didn’t happen during the hysterectomy but developed in the days just before the perforation was discovered. The defense argued that a collection of infected fluid at the vaginal cuff over time eroded into the bowel, creating an entryway for stool to pass into the vagina. The defense experts testified that it would have been impossible for the patient to survive if she had an untreated bowel perforation for 17 days. The jury found in favor of the gynecologist.

**THE VERDICT** The jury found in favor of the gynecologist.

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**Hypoxic brain damage after failure to monitor FHR alleged**

A Texas woman delivered a baby in 2012. During the oxytocin-augmented labor, the fetal heart rate (FHR) tracing was not recording well on the monitor strip. At delivery the infant had a tight nuchal cord and at birth there were no signs of life. The child was successfully resuscitated but was found to have sustained severe brain damage as a result of profound fetal hypoxia and will require 24-hour nursing and supportive care for life.

The patient sued those involved with her delivery and alleged that losing the FHR tracing was below the standard of care and resulted in the caregivers being unaware of the increasing condition of fetal intolerance to labor, leading to the brain damage. They claimed the nuchal cord was cutting off the oxygen supply to the fetal brain, which would have been seen on the FHR monitor strip and earlier intervention would have prevented the injury.

The defense argued that the nurses continuously monitored by listening to sounds coming out of the bedside monitor even though no recording of the FHR was occurring on the central monitors or FHR monitor strip. They contended that the nuchal cord was an unforeseeable medical emergency and that nothing different could have been done to change the outcome.

**THE VERDICT** After a week of trial, the parties reached a settlement for an undisclosed amount.

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**Reduce physician frustration**

CONTINUED FROM PAGE 21

Multiple physicians in a practice, compare these results and see if someone is more (or less) efficient than everyone else. Share best practices to improve everyone’s efficiency. These charts are also a good way to measure the effect of training or other changes.

4 **Customize the EHR to workflow and specialty.**

The out-of-the-box desktop view from an EHR vendor may not have information organized that helps physicians find what they want and there are often tabs or other unnecessary information. Take the time to customize the view for each physician in a way that works best.

At Gould, there was a high correlation between customization of the EHR and physician satisfaction.

5 **Adapt time-saving methods for each physician**

At Gould, physicians create notes in the EHR through a variety of methods: 27% use voice recognition, 10% dictation, 7% scribes, 33% use templates, 4% use remote scribes, and 21% use some combination of the above. Pricco says the important point is that every physician works differently and it’s important to find the way that each physician is most comfortable with and make it available.

6 **Install a printer in each exam room.**

If physicians are spending time walking back and forth printing out information from the EHR, consider installing a printer in each exam room.

Finally, software systems are under constant review so it’s important to stay current, both with software upgrades and the training required to take advantage of new features. New functionality may be the answer to the frustrations and challenges physicians might struggle with now.

**TODD SHRYOCK** is a contributing author to Medical Economics.
Shoulder dystocia and brachial plexus injury

In 2012, a Virginia woman began receiving prenatal care for her seventh pregnancy, during which she was diagnosed with Type II diabetes and obesity. Given her history of large infants she was admitted to the hospital at 37 weeks' gestation for induction of labor. During the delivery, shoulder dystocia was encountered. The baby weighed 9 lb 10 oz at birth and her right arm was noted to be limp. She was diagnosed with a brachial plexus injury which involved C5, C6, C7, and C8 nerve roots and muscles. The injuries were evident from magnetic resonance imaging, which showed at least 2 nerve root avulsions, and by direct visualization by the surgeon who performed an extensive nerve graft to try to restore some function to the baby's right arm. Although the baby’s right arm function and range of motion has improved, she has not recovered normal function of the injured nerves nor the muscles they innervate.

The woman sued those involved with the delivery, claiming that during the course of her care, the history, physical examinations, and tests showed she had an increased risk for encountering shoulder dystocia during a vaginal delivery. The patient’s experts opined that the obstetrician was required under the standard of care to obtain informed consent from the patient prior to proceeding with a vaginal delivery, which he did not do. It was also the experts’ opinion that as a part of obtaining informed consent, a discussion was required regarding the risk of shoulder dystocia, the risk of injury to the baby’s brachial plexus nerves if shoulder dystocia were encountered, and the option of a cesarean section. The patient’s expert testified that the standard of care required a physician delivering a baby upon delivery of the head with the shoulder stuck behind the symphysis, even with no traction on the head, it is not always successful in defending the case. It is imperative that the person delivering the infant stop any traction once the shoulder dystocia is encountered and not apply anymore traction until one or more appropriate maneuvers are performed. This also needs to be documented in the chart in the delivery note at the time of delivery, and many institutions use a check list-based approach to assure that no critical information is left out. This should be done anytime there is an extra maneuver performed to deliver the shoulder, even if injury is not apparent at the time.

In malpractice cases that involve a brachial plexus injury from a shoulder dystocia encountered during delivery, the claim is always made that the person delivering the infant used excessive traction, as this connects a person to the injury. While the defense often offers the explanation that the brachial plexus became injured upon delivery of the head with the shoulder stuck behind the symphysis, even with no traction on the head, it is not always successful in defending the case. It is imperative that the person delivering the infant stop any traction once the shoulder dystocia is encountered and not apply anymore traction until one or more appropriate maneuvers are performed. This also needs to be documented in the chart in the delivery note at the time of delivery, and many institutions use a check list-based approach to assure that no critical information is left out. This should be done anytime there is an extra maneuver performed to deliver the shoulder, even if injury is not apparent at the time.

Ms Collins is an attorney specializing in medical malpractice in Long Beach, California. She can be reached at dawncf@msn.com.
SUPRAX® (cefixime)

BRIEF SUMMARY: This summary does not include all the information needed to use SUPRAX safely and effectively. Consult Full Prescribing Information for complete product information.

SUPRAX should only be used to treat infections that are proven or strongly suspected to be caused by bacteria.

INDICATIONS AND USAGE
SUPRAX (cefixime) is a cephalosporin antibacterial drug indicated in the treatment of adults and pediatric patients six months of age or older with the following infections when caused by susceptible isolates of the designated bacteria:

Uncomplicated Urinary Tract Infections caused by Escherichia coli and Proteus mirabilis.

Otitis Media caused by Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes. (Note: For patients with otitis media caused by Streptococcus pneumoniae, overall response was approximately 10% lower for cefixime than the comparator. Efficacy for Streptococcus pyogenes in this organ system was studied in fewer than 10 infections.)

Pharyngitis and Tonsillitis caused by Streptococcus pyogenes. (Note: Penicillin is the usual drug of choice in the treatment of Streptococcus pyogenes infections. SUPRAX is generally effective in the eradication of Streptococcus pyogenes from the nasopharynx; however, data establishing the efficacy of SUPRAX in the subsequent prevention of rheumatic fever is not available.)

Acute Exacerbations of Chronic Bronchitis caused by Streptococcus pneumoniae and Haemophilus influenzae.

Uncomplicated Gonorrhea (cervical/urethral) caused by Neisseria gonorrhoeae (penicillinase-and non-penicillinase-producing isolates).

CONTRAINDICATIONS
SUPRAX (cefixime) is contraindicated in patients with known allergy to cefixime or other cephalosporins.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have also been reported. Before therapy with SUPRAX is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. Discontinue SUPRAX if an allergic reaction occurs.

Clostridium difficile-Associated Diarrhea: Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including SUPRAX.

Dose Adjustment in Renal Impairment: The dose of SUPRAX should be adjusted in patients with renal impairment.

Coagulation Effects: Cephalosporins, including SUPRAX, may be associated with a fall in prothrombin activity. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Phenyketonurics: SUPRAX (cefixime) Chewable Tablets contain aspartame, a source of phenylalanine. 100 mg, 150 mg and 200 mg strength contains 3.3 mg, 5 mg and 6.7 mg of phenylalanine, respectively.

ADVERSE REACTIONS
The most commonly seen adverse reactions were gastrointestinal events, which were reported in 30% of adult patients on either the twice daily or the once daily regimen. Five percent (5%) of patients in the U.S. clinical trials discontinued therapy because of drug-related adverse reactions.

Individual adverse reactions included diarrhea 16%, loose or frequent stools 6%, abdominal pain 3%, nausea 7%, dyspepsia 3%, and flatulence 4%. The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in pediatric patients receiving the suspension was comparable to the incidence seen in adult patients receiving tablets.

DRUG INTERACTIONS
Carbamazepine: Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants: Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly.

Drug/Laboratory Test Interactions: A false-positive direct Coombs test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coombs test may be due to the drug.

USE IN SPECIFIC POPULATIONS
Pregnancy: Pregnancy Category B. Reproduction studies in mice have revealed no evidence of harm to the fetus due to cefixime. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery: Cefixime has not been studied for use during labor and delivery and should only be given if clearly needed.

Nursing Mothers: It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

Pediatric Use: Safety and effectiveness of cefixime in children aged less than six months old have not been established.

Geriatric Use: Clinical studies did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters, but they were small and do not indicate a need for dose adjustment.

Renal Impairment: Dose adjustment is advised in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully.

DOSEAGE AND ADMINISTRATION
Adults: The recommended dose of cefixime is 400 mg daily. This may be given as a 400 mg tablet or capsule daily or the 400 mg tablet may be split and given as one half tablet every 12 hours. The capsule and tablet may be administered without regard to food.

Pediatric Patients (6 months or older): The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours. Children weighing more than 45 kg or older than 12 years should be treated with the recommended adult dose. SUPRAX (cefixime) Chewable Tablets must be chewed or crushed before swallowing.

Dose Adjustment in Renal Impairment: Dose adjustment is advised in patients with renal impairment.

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.

Please note that this information is not comprehensive. Please visit www.supraxrx.com for Full Prescribing Information.
Consider Once-Daily Suprax® (cefixime) for Uncomplicated UTI

Suprax goes to work for patients with one dose per day:

• 99% of adults with UTI cured or improved after 3-7 days of treatment
• Simple dosing may improve patient adherence to regimen
• Delivers activity against E. coli and P. mirabilis with a low MIC90 (µg/mL)
• No boxed warning
• Pregnancy Category B

$35 co-pay card program available for eligible patients

For more information, visit www.supraxrx.com

INDICATIONS
• SUPRAX® (cefixime) is a cephalosporin antibacterial drug indicated in the treatment of adults and pediatric patients six months of age and older with the following infections when caused by susceptible isolates of the designated bacteria: Uncomplicated Urinary Tract Infections; Otis Media; Pharyngitis and Tonsillitis; Acute Exacerbations of Chronic Bronchitis; Uncomplicated Gonorrhea (cervical/urethral).

IMPORTANT SAFETY INFORMATION
SUPRAX should only be used to treat infections that are proven or strongly suspected to be caused by bacteria.

CONTRAINDICATIONS
• SUPRAX (cefixime) is contraindicated in patients with known allergy to cefixime or other cephalosporins.

WARNINGS & PRECAUTIONS
• Hypersensitivity reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. Before therapy with SUPRAX is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. Discontinue use if a reaction occurs.
• Clostridium difficile associated diarrhea: Evaluate if diarrhea occurs.
• Dose Adjustment in Renal Impairment: The dose of SUPRAX should be adjusted in patients with renal impairment and those undergoing continuous ambulatory peritoneal dialysis and hemodialysis.
• Coagulation Effects: Cephalosporins, including SUPRAX, may be associated with a fall in prothrombin activity. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.
• Phenylketonurics: SUPRAX Chewable Tablets contain aspartame, a source of phenylalanine.

ADVERSE REACTIONS
• Most common adverse reactions are gastrointestinal such as diarrhea (16%), loose or frequent stools (6%), abdominal pain (3%), nausea (7%), dyspepsia (3%), and flatulence (4%).
• Adverse reactions during postmarketing experience occurred at rates less than 2%. Some serious adverse reactions included: pseudomembranous colitis, hypersensitivity reactions including Stevens-Johnson syndrome and serum sickness, acute renal failure, seizures, agranulocytosis, and toxic epidermal necrolysis.

DRUG INTERACTIONS
• Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly.
• Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly with warfarin and anticoagulants.
• A false positive reaction for ketones and glucose in urine may occur with certain test kits. A false positive direct Coombs test has also been reported.

USE IN SPECIAL POPULATIONS
• Efficacy and safety in infants aged less than six months have not been established.
• Cefixime should be used during pregnancy only if clearly needed.
• Consideration should be given to discontinuing nursing temporarily during treatment with cefixime.

Please note this information is not comprehensive. Please see Brief Summary of Prescribing Information on the following page.

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.


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