

## **WHAT'S NEW IN OBSTETRIC ANESTHESIA FROM 2008?**

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### **Policies, Procedures & Guidelines**

- CDC guidelines on wearing masks during neuraxial procedures
- Joint ASA-ACOG statement "Optimal Goals" revision
- ASA guidelines on respiratory depression after neuraxial opioids
- Other guidelines: CT/MRI scans during pregnancy, endocarditis prophylaxis, oral intake
- Pregnancy testing – help or hindrance?
- Liability issues
- Lay press: cesarean rates and home births

### **Labor Analgesia**

- Adverse effects of labor pain
- Physiology of pain and pain relief
- Neuraxial technique
- CLE / CSE / PCEA / CSA

### **Cesarean Anesthesia**

- Spinal anesthesia hemodynamics
- General anesthesia – airway and BIS
- Intraoperative and surgical issues
- Postoperative pain management and side effects
- Unusual cases and their management

### **Anesthetic Complications**

- Maternal mortality updates
- ASA Closed Claims update: 1990-2003
- Cardiac arrest on L&D
- Thrombophilia and anti-coagulants
- Management of post-dural puncture headache
- Local anesthetic toxicity
- Non-obstetric surgery during pregnancy
- Neurotoxicity of anesthetics in the developing brain

### **Obstetric Complications and Co-Morbidities**

- Preeclampsia: diagnosis, complications, future health issues
- Postpartum hemorrhage
- Obesity
- Management of diabetes, VBAC and external version for breech
- Maternal cardiac disease
- Early elective cesareans and late preterm births
- Other maternal co-morbidities

### **The Fetus & Newborn**

- Electronic fetal monitoring
- Breast feeding and HIV transmission
- Neonatal analgesia in the ICU
- Preventing prematurity and its complications
- Odds and ends

## POLICIES, PROCEDURES & GUIDELINES

- CDC guidelines: The CDC published a massive 219-page document entitled “Guidelines for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings 2007”. Of interest to anesthesia providers, the new guidelines specifically require that practitioners “wear a surgical mask when placing a catheter or injecting material into the spinal canal or epidural space (i.e., during spinal or epidural anesthesia).”<sup>1</sup> They note that “Face masks are effective in limiting the dispersal of oropharyngeal droplets and are recommended for the placement of central venous catheters....[we] reviewed the evidence and concluded that there is sufficient experience to warrant the additional protection of a face mask for the individual placing a catheter or injecting material into the spinal or epidural space.” Note: this would also include pain procedures. An article they quote describes 6 cases of meningitis after spinal anesthesia associated with a single anesthesiologist in whom the organism cultured was *Streptococcus salivarius*.<sup>2</sup> An accompanying letter to the editor notes that a British survey of obstetric anesthesiologists found that 50% did not wear masks during placement of spinal or epidural anesthetics!
- The ASA approved a revised version of “Optimal Goals for Anesthesia Care in Obstetrics” in October 2008.<sup>3</sup> For those who run an Anesthesiology service or are in charge of an L&D unit, this is a must-read with excellent supporting statements for optimizing maternal and newborn care – useful for discussion with other physicians and administrators since it is a joint statement supported by both ASA and ACOG.
- The ASA also approved revisions of the “Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration” in October 2008.<sup>4</sup> The changes mainly relate to monitoring after use of neuraxial opioids, specifically whether continuous pulse oximetry was useful or practical. It was certainly neither of these in the L&D setting! The new recommendations state that: “All patients receiving neuraxial opioids should be monitored for adequacy of ventilation (e.g., respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (e.g., pulse oximetry when appropriate), and level of consciousness.” In other words, your orders need to include monitoring, but the guidelines do not specify what type of monitoring you should use on your unit. Specific to neuraxial morphine, they state that “Monitoring should be performed for a minimum of 24 hours after administration. Monitoring should be performed at least once per hour for the first 12 hour after administration, followed by monitoring at least once every 2 hour for the next 12 hours...After 24 hours, frequency of monitoring should be dictated by the patient’s overall clinical condition and concurrent medications.” An excellent review summarizes the mechanism and incidence of respiratory depression, as well as prevention, detection, and management specific to the L&D and post-cesarean delivery setting.<sup>5</sup>
- ACOG’s new guidelines of interest to anesthesiologists include “Guidelines for Computed Tomography and Magnetic Resonance Imaging Use During Pregnancy and Lactation”<sup>6</sup> and “Antibiotic Prophylaxis for Infective Endocarditis”.<sup>7</sup> The

- imaging guidelines are evidence-based and emphasize use of ultrasound initially where feasible (e.g., appendicitis, renal stones, trauma) but also use of CT or MRI when needed (e.g., appendicitis when ultrasound is negative, suspected pulmonary embolus, trauma). They also state that although iodinated contrast is safe, IV gadolinium is contraindicated. The endocarditis guidelines state that prophylaxis is *no longer recommended* for vaginal or cesarean delivery in the absence of infection, regardless of the type of maternal cardiac lesion. If infection is present (e.g., chorioamnionitis) the underlying infection should be treated with a regimen effective for endocarditis prophylaxis. This is probably a different approach than most practices have been using.
- It is probably good for anesthesiologists to know that the American College of Nurse-Midwives has published a clinical bulletin entitled “Providing Oral Nutrition to Women in Labor”.<sup>8</sup> These are not endorsed by any other organization, but they do reference a number of anesthesiology publications and include risk factors for obstetric emergencies that might require cesarean delivery and also discuss risk factors for difficult intubation. The recommendations state that midwives should evaluate all women who are at increased risk for operative birth and notify anesthesia services of these women in a timely manner.
  - A policy of routine, mandatory pregnancy testing in a busy orthopedic ambulatory surgery practice led to some interesting results.<sup>9</sup> They had 8 positive urine pregnancy tests in 2588 women (0.3%). All had their elective surgery cancelled. Four were false positives and the patients had their surgery done after a negative serum hCG. Three were true positives, and 1 was an asymptomatic ectopic pregnancy. Besides the inconvenience of postponing surgery for the false positive results, the number needed to treat (NNT) was 647 and the cost of a true positive pregnancy test confirmed by hCG was \$3273 – in my opinion, a significant cost for an unknown benefit.
  - Two interesting publications on medical liability..... The Texas Supreme Court held that an on-call anesthesiologist was not entitled to the Good Samaritan defense in caring for a neonate in the delivery room.<sup>10</sup> The anesthesiologist was providing general anesthesia to the mother during an emergency cesarean when asked by the neonatology team to assist intubating the newborn. He complied, but during CPR the tube was found to be in the esophagus. The court stated that the defendant was part of the team administering to both mother and baby and therefore it was part of his job rather than a case of providing voluntary aid. This is a sobering decision for anesthesia providers who might be called on for help with a depressed newborn. Another publication surveyed obstetricians in Michigan and found that (surprise!) malpractice litigation risk strongly influenced providers' decisions about whether to provide obstetric care or limit their practices only to gynecology.<sup>11</sup> 20% of obstetricians (and 12% of midwives) said they planned to stop delivering babies in the next 5 years.
  - In the lay press, there were discussions about the lack of FDA approval and lack of information about use of medications during pregnancy (the woman featured had Crohn's disease)<sup>12</sup>, why the cesarean rate is so high including cesarean delivery by choice (rather than medical indication)<sup>13</sup>, and the perceived increase in home births (since these aren't tracked well there are no good statistics).<sup>14</sup>

## LABOR ANALGESIA

- In the never-ending discussions about the merits of analgesia versus unmedicated or “natural” childbirth, the adverse effects of labor pain are rarely noted. A British study examining the attitude of first-time fathers and their partners toward epidural analgesia found that on admission, 64% of fathers and 79% of mothers wanted to use epidural analgesia.<sup>15</sup> Later in labor it increased to 78% of fathers and 87% of mothers with 95% of mothers ultimately receiving epidural analgesia. The decision to use (or not) epidural analgesia was not affected by age, level of education, salary or attendance at childbirth classes. Another study administered surveys to first-time fathers after delivery; 60% of the mothers had received epidural analgesia and 40% had not.<sup>16</sup> Fathers whose partners did not receive epidural analgesia felt their presence was troublesome and unnecessary ( $p < 0.001$ ). When the mothers did receive epidural analgesia, fathers felt 3 times more helpful and more involved and they had less anxiety and stress (anxiety scores of 30 versus 75 when partners did or did not receive an epidural). Maternal analgesia greatly increased paternal satisfaction.
- Postnatal depression occurs in about 15% of mothers, and there are a number of risk factors. A prospective follow-up of 185 mothers evaluated whether adequate pain relief during labor has an effect on postnatal depression and mother-infant bonding.<sup>17</sup> They found the risk of depression one week after delivery was lower in the epidural group than the group receiving no analgesia (OR 0.25), although there was no difference at 4 months postpartum.
- A dynamic model of pain scores during labor that accounts for cervical dilation and oxytocin use (versus the more commonly used average pain score over all of labor) was developed for use in studying pain over the entire course of labor.<sup>18</sup> The authors found that knowledge of what to expect and effective pain relief have a strong positive effect on patients' satisfaction with labor.
- Only 27% of women who exercised during pregnancy requested pain medication during labor versus 71% of those who did not exercise, although there was no difference in length of labor or mode of delivery.<sup>19</sup> The exercise group did three 50-minute sessions of water aerobics per week. Exercise had no detrimental effects on the fetus/newborn.
- What are the physiologic effects of labor analgesia and its effects on maternal and uterine blood flow? Why do we so often see decelerations develop after effective analgesia, even in the absence of hypotension? An in vitro study on uterine microvessels found that concentrations of epinephrine found in the plasma of laboring women *vasodilate* uterine resistance vessels (through its  $\beta$ -agonist effects) and prevent norepinephrine-induced  $\alpha$ -agonist vasoconstriction.<sup>20</sup> When we provide analgesia, we decrease maternal epinephrine levels and may change uterine blood flow by allowing vasoconstriction.
- Another in vitro study examined the physiology of local anesthetic effects on myometrial contractility; could local anesthetics absorbed during epidural analgesia decrease amplitude and/or frequency of contractions in the

- myometrium?<sup>21</sup> They found the concentrations of bupivacaine and levobupivacaine needed to decrease contractility were 33-fold higher than the clinically relevant plasma concentrations of these drugs after epidural administration. So the answer is “no”.
- Technique is something we often take for granted when performing neuraxial techniques. An interesting study of videos taken of CA-2 anesthesia residents over 6 months found a strong correlation between increasing experience and manual skills.<sup>22</sup> However, there was almost no correlation between the aseptic technique checklist score and number of epidurals performed. Most of the time residents did not recognize breaches in sterile technique and therefore did not correct them. Clearly this is an area we could teach more effectively.
  - A troubling conflict in recommended technique for neuraxial anesthesia is the use of chlorhexidine prep. The ASRA guidelines state it is the antiseptic of choice for regional techniques<sup>23</sup>, but the package of the Chloraprep applicator states that the solution should not be used when working in proximity to meningeal structures. An article in the Anesthesia Patient Safety Foundation (APSF) newsletter notes that the FDA has no prospective evaluation of chlorhexidine in the setting of epidural and spinal anesthesia that would support a change their labeling.<sup>24</sup> The expense for the manufacturer to seek a label change is prohibitive. No resolution of that problem is in sight.
  - Other technical advances in placement of neuraxial techniques are being developed. The Episure™ syringe was used in another successful study in which 325 women underwent epidural analgesia for labor.<sup>25</sup> The failure rate to achieve successful analgesia was 5/157 in the glass syringe group and 0/168 in the spring-loaded syringe group (p=0.025). Another study compared palpation to ultrasound location of the lumbar interspace level used for epidural analgesia.<sup>26</sup> Anesthesiologists used palpation to determine the interspace for epidural placement. After delivery, ultrasound was used to identify the interspace that had been used and compared it to the interspace documented in the anesthesia record. Ultrasound estimation agreed with the documented level only 55% of the time; 32% of the time the anesthesiologist had gone at least one interspace higher than they thought.
  - Both continuous lumbar epidural (CLE) and combined spinal-epidural (CSE) techniques are highly effective for providing labor analgesia. A retrospective study of 6497 women who received regional analgesia for labor found no difference in labor outcome, wet tap or headache between the techniques.<sup>27</sup> Quality of analgesia was better with CSE, but pruritus, paresthesia and back pain were more frequent. A prospective, double-blind RCT questioned whether a dural puncture without intrathecal drug administration prior to epidural drug placement would improve labor analgesia compared to a traditional epidural technique without the prior dural puncture.<sup>28</sup> The women who received a prior dural puncture had better block of sacral dermatomes, lower pain scores (< 10 at 20 minutes) and fewer one-sided blocks.
  - There are many different regimens for patient-controlled epidural analgesia (PCEA) in labor. A prospective, randomized, double-blind study compared 3 PCEA regimens during labor: demand-only (5ml bolus with 15 minute lockout),

- mixed (5ml basal, 5ml bolus, 12-minute lockout) or infusion (10ml basal, 5ml bolus, 10-minute lockout) – all with a 20ml per hour maximum.<sup>29</sup> Demand-only resulted in the most breakthrough pain and the lowest maternal satisfaction scores, but had the lowest local anesthetic consumption. The two regimens with basal infusions were comparable, although the higher basal infusion was associated with a longer duration of the second stage of labor.
- A long-awaited RCT comparing a 28-gauge spinal catheter for continuous spinal analgesia (CSA) to conventional epidural analgesia for labor found a similar incidence of neurologic complications or headache (<1%), better initial pain relief with higher maternal satisfaction in the spinal catheter group, but more technical difficulties and catheter failures with the spinal catheters.<sup>30</sup> These devices are not easy to work with. An accompanying editorial notes that this will allow the FDA to approve the device, although with extensive postmarket surveillance.<sup>31</sup> Unfortunately no company has chosen to market the device, so we are not likely to see the microspinal catheters available in the near future. Fortunately, the acceptance of CSE has provided an alternative that has many of the same advantages of CSA.
  - NMDA antagonists like ketamine have been touted as providing excellent analgesia in neuraxial techniques. However an animal study examining the safety of NMDA antagonists in a chronic intrathecal catheter model found spinal pathology including local demyelination and necrotizing lesions.<sup>32</sup> This should serve as a reminder that no medication should be placed in the spinal or epidural space before adequate neurotoxicity studies have been performed to establish their safety.

## CESAREAN ANESTHESIA

- In another approach to studying ephedrine versus phenylephrine to treat hypotension after spinal anesthesia, investigators compared varying combinations of the two drugs given by infusion to keep blood pressure at baseline.<sup>33</sup> They found that as the proportion of phenylephrine increased, hemodynamic control was better for the mother and acid-base status was better in the fetus. There appeared to be no advantage to including ephedrine in the treatment of hypotension unless maternal heart rate is low and phenylephrine might precipitate serious bradycardia.
- Another study examined low and high dose bupivacaine spinal anesthesia (7 or 10mg) with or without phenylephrine (versus placebo).<sup>34</sup> Not surprisingly, low dose bupivacaine with phenylephrine provided the best hemodynamic stability. By using the LiDCO*plus* device to measure cardiac output non-invasively, they were also able to show a significant increase in cardiac output after spinal anesthesia accompanied by decreases in SVR. Phenylephrine attenuated these changes.
- Spinal anesthesia has been avoided in the past in parturients with severe preeclampsia because of concerns about significant hypotension. In another study

- using the LiDCOplus non-invasive cardiac output monitor, 15 consecutive women with severe preeclampsia received spinal anesthesia for cesarean and had hypotension treated with phenylephrine.<sup>35</sup> They found that cardiac output remained stable throughout, with the main hemodynamic effect being modest afterload reduction. Even during episodes of hypotension, cardiac output was stable or increased. The most significant change in hemodynamics occurred not after spinal anesthesia, but when oxytocin was given as a 2.5U bolus. At that time, BP and SVR fell and CO increased significantly. An accompanying editorial asks whether we should be focusing more on cardiac output and blood flow than blood pressure to assess hemodynamics and uterine perfusion.<sup>36</sup>
- General anesthesia for cesarean delivery requires careful evaluation of the airway. In one study, investigators used both Mallampati class (with photographs) at the beginning and end of labor plus acoustic reflectometry to measure airway volumes before and after labor.<sup>37</sup> They found that airway class increased by one grade in 33% of women and by two grades in 5%. This was accompanied by decreases in airway volume as well. These changes did not correlate with duration of labor or fluids administered. An editorial reminds us that the Mallampati classification is not static and should be assessed just before instrumentation, even if an evaluation was done a few hours before.<sup>38</sup> A study in non-obstetric patients evaluated the predictors of difficult intubation and found that obesity, thyromental distance, Mallampati score  $\geq 3$  and large neck circumference were most useful.<sup>39</sup> They suggest that neck circumference should be included in our preoperative assessment. A neck circumference  $> 43\text{cm}$  + a Mallampati score  $\geq 3$  had a positive predictive value of 44%. Tape measure in the preop holding area?!
  - General anesthesia during cesarean has also been associated with awareness, but interest in using the BIS has been limited because of the time needed to apply it during emergency cases. A study compared BIS values during Sevoflurane-N<sub>2</sub>O in women who had urgent cesareans following labor versus those who had elective cesareans without laboring.<sup>40</sup> They found that women who had labored had lower BIS values during surgery and lower postoperative analgesic consumption than women without prior labor. Plasma norepinephrine levels were also higher in the labor group, and the authors postulate that release of endorphins during painful labor might explain some of their findings.
  - Intraoperative issues other than the anesthetic can affect our management as well, including use of oxytocics. A study of 40 women undergoing elective cesarean under spinal anesthesia randomized them to receive an IV bolus of either 10 U oxytocin or 0.2 mg methylergonovine.<sup>41</sup> Surprisingly, the methylergonovine produced only mild hypertension (MAP 91→102) and no ECG changes. In contrast the oxytocin bolus produced hypotension, tachycardia, chest pain and signs of myocardial ischemia on 12-lead ECG. These signs were also present when non-pregnant women who were not undergoing surgery received an IV oxytocin bolus. Oxytocin is not safe to give as an IV bolus (see 3 bullets above also!).
  - Intraoperative surgical issues are also relevant to our practice. The uterus can be repaired at cesarean by exteriorization or leaving it in situ. An RCT of 637

women found no significant differences in any variables except a shorter surgical time with exteriorization and less pain at 6 hours with in situ repair.<sup>42</sup> A Pfannenstiel incision is most commonly used for cesarean deliveries. 690 women responded to a survey about chronic pain 1-3 years following their Pfannenstiel incision.<sup>43</sup> The investigators found that one third (223/690) reported chronic pain at the incision site, 7% reported moderate or severe pain, and 9% of respondents reported their pain impaired daily activities. On examination, over half of patients with moderate-to-severe pain had nerve entrapment (iliohypogastric or ilioinguinal nerves).

- A very large study in 13 tertiary care hospitals questioned whether adverse maternal or perinatal outcomes were affected by physician and/or nursing shift changes; in other words, do handoffs of multiple patients during shift change for their providers increase risk for the patients?<sup>44</sup> The answer was “no”. Physician change of shift was not associated with increases in maternal or neonatal morbidities. They speculate that formal physician sign out, when plans are discussed and critiqued, usually occur on teaching services and lead to increased scrutiny and communication. If possible, the anesthesiology providers should also participate in these sign-outs so they are aware of ongoing or upcoming patient care issues.
- Intraoperative nausea and vomiting is distressing to patient and providers and can be difficult to prevent and treat. A systematic review of randomized controlled trials that evaluated P6 stimulation during cesarean under neuraxial anesthesia included 6 studies with 649 patients.<sup>45</sup> It concluded that inconsistent design and results prevent any definitive conclusions on P6 stimulation's efficacy at preventing IONV and PONV.
- Intrathecal morphine and clonidine were studied for postoperative pain management after cesarean delivery under spinal anesthesia. A randomized double-blind study comparing varying doses of intrathecal morphine from 0mg to 0.4 mg found no additional analgesic benefit above 0.1mg.<sup>46</sup> Interestingly, there was no difference in the incidence of nausea and vomiting, even at high doses, but pruritus increased in direct proportion to the dose. Addition of intrathecal clonidine is known to potentiate intraoperative analgesia during spinal anesthesia, but can it prevent postoperative *hyperalgesia* that may be associated with development of chronic pain?<sup>47</sup> Parturients undergoing elective cesarean were randomized to 75µg, 150µg or no clonidine plus bupivacaine and sufentanil. Those receiving the higher dose of clonidine had a reduced area of hyperalgesia around their incision site, but postoperative morphine consumption and pain scores did not differ between the groups.
- Genetic variability affects patient response to intravenous morphine, especially variability at position 118 of the human  $\mu$ -opioid receptor gene. It is not known whether this variability affects response to neuraxial morphine used in cesarean deliveries. A study of 588 women administered 0.1mg intrathecal morphine as part of a spinal anesthetic for cesarean, and sampled their blood for genotyping of the A118G polymorphism.<sup>48</sup> The AA polymorphism group (46% of women) had the lowest pain scores and IV PCA morphine consumption, and the highest incidence of nausea and vomiting when compared to women with the AG (40% of

- women) and GG (14% of women) polymorphisms. Genomics begins to become practical in our day-to-day practices!
- In research unrelated to obstetric anesthesia, new work suggests that some cannabis (marijuana) like drugs – agonists that bind to only 1 of the 2 cannabinoid receptors that are activated by cannabis – can relieve pain while leaving the brain unaffected.<sup>49</sup> These CB2 receptors are present only in the peripheral nervous system. Wouldn't that be an ideal labor analgesic; pain free but alert.
  - A number of unusual cases or case series involving cesarean delivery were reported in the last year. These included: an emergency cesarean for umbilical cord prolapse with a spinal anesthetic placed in the knee-chest prone position because of a Mallampati class IV airway<sup>50</sup>, combined spinal-epidural anesthesia for cesarean in a parturient with twins, type 1 von Willebrand disease and scoliosis<sup>51</sup>, management of Guillain-Barre' syndrome during early pregnancy with a cesarean delivery at term<sup>52</sup>, general anesthesia for a parturient with Marfan's syndrome and a dilated aortic root<sup>53</sup>, a review of anesthetic management of parturients with sickle cell disease including postnatal sickling complications, and anesthetic management of cesarean delivery in a patient with Shone's Syndrome (a congenital cardiac condition with up to four obstructive left-sided cardiac lesions).<sup>54</sup>

## ANESTHETIC COMPLICATIONS

- The United Kingdom published their latest triennial report on maternal deaths that occurred between 2003 and 2005.<sup>55</sup> The leading overall causes of maternal death were cardiac pathology and thromboembolism. Over half the women who died were obese, leading one of the authors to say "Obesity represents one of the greatest and growing threats to the childbearing population." Anesthesia deaths were eighth in frequency, but all were associated with substandard care and deemed avoidable as judged by the reviewers. The six deaths included 2 obese women in early pregnancy, anesthetized by trainees, who suffered postoperative respiratory failure. Another obese woman with asthma had postoperative respiratory failure following cesarean under spinal. One woman had her bupivacaine epidural connected in error to her IV, and one died of complications of central venous access. The cause of death is unclear in the final case. Although practice differs to some degree between the U.S. and the U.K., their ability to review cases in detail is far superior to ours, and all anesthesiologists who provide obstetric care should read the discussions and recommendations in their report.<sup>56</sup>
- A very large retrospective review of maternal deaths in a large U.S. health care delivery system (HCA - the Hospital Corporation of America) found 95 maternal deaths in 1.5 million deliveries (6.5 deaths per 100,000 pregnancies) between 2000 and 2006.<sup>57</sup> Leading causes of death were preeclampsia, pulmonary thromboembolism, amniotic fluid embolism, hemorrhage and cardiac disease. Rate by mode of delivery was 0.2 per 100,000 for vaginal and 2.2 per 100,000 for

- cesarean deliveries. Anesthesia is not listed as a cause of death in their series. They conclude that most maternal deaths in the U.S. are not preventable and occur in low risk pregnancies. They also emphasize universal thromboembolism prophylaxis for cesarean deliveries, and because neuraxial anesthesia is most commonly used during cesarean, they recommend pneumatic compression devices rather than anti-coagulation for most women.
- The ASA Closed Claims Project recently published an update of their obstetric anesthesia claims providing a contrast between those claims occurring before 1990 and those claims occurring after 1990 (through 2003).<sup>58</sup> There *are* some significant contrasts. Although most claims are related to cesarean deliveries (58%), those relating to vaginal delivery are increasing. Compared to claims prior to 1990, maternal death and brain damage are decreasing, but nerve injury claims are increasing and are now the most common cause of a lawsuit. Claims with substandard care decreased to 22%, payment was made less frequently (42% versus 58% previously), and the median payment made also decreased from \$455K to \$222K – all good news! Other positive points are that there were no local anesthetic toxicity cases since 1990, and all cases of difficult intubation occurred before 1999. However the bad news is that cases related to undetected intrathecal catheters increased and providers were not always prepared to treat hypotension or airway emergencies when placing labor epidurals. Four cases describe patients having to be transferred to an O.R. for resuscitation because there was no resuscitation equipment in the labor room! Anesthesia delay was alleged in numerous cases of neonatal death or brain damage. The provider either attempted a neuraxial technique for too long before converting to general anesthesia or they were not in the hospital while taking call from home. Poor communication was also a big factor when obstetricians, nurses and anesthesiologists didn't work together to move urgently to delivery of a distressed fetus. And finally, illegible, inaccurate and incomplete anesthesia records and poor English skills also led to payouts in some cases. An accompanying editorial provides an excellent overview of the new findings.<sup>59</sup> These articles should be required reading for anyone practicing on L&D.
  - Several papers addressed cardiac arrest on L&D. One surveyed clinicians in the hospital at Stanford<sup>60</sup> and another in Israel.<sup>61</sup> Both concluded there was inadequate and limited knowledge among obstetric, anesthesia and emergency medicine personnel about basic concepts, including the need for left uterine displacement, the location of external chest compression and paddle placement, and the benefits of early cesarean delivery. Another review of a large registry from Thailand analyzed 40,271 spinal anesthetics and found 11 cardiac arrests (5 during cesarean and 6 during extremity surgery) for an incidence of 2.73 per 10,000 cases.<sup>62</sup> Mortality was very high at 91%! By multivariate analysis they found the greatest risk associated with cardiac arrest was during spinals administered by the surgeon (OR 23.5). In a sad and amazing case report, a mother committed suicide during labor by jumping from the fourth-floor window of L&D.<sup>63</sup> The fetus was delivered by cesarean *30 minutes* after she was declared dead. After a rocky course in the NICU (pH 6.79, BE -19.6), the baby showed

slow but continued neurologic improvement, with normal neurologic testing at the age of 9 months and continued improvement at 4 years!

- Embolism remains the #1 cause of maternal death in the U.S., so naturally it is a focus of research and publications. Anesthetic decisions must be made on the basis of maternal anti-coagulation. An excellent "Current Concepts" review was published on *Venous Thromboembolic Disease and Pregnancy*.<sup>64</sup> It discusses the inherited thrombophilias being diagnosed much more frequently, and the clinical diagnosis of DVT and pulmonary embolism. The advantages of LMWHs are discussed and weight-based dosing regimens are given, e.g. Enoxaparin 80mg BID or Dalteparin 8000U BID for a 70-kg patient. Women are at highest risk the week after a cesarean delivery, and ACOG recommendations are for early ambulation in low risk patients, LMWH or compression stockings in moderate risk, and LMWH and compression stockings in high risk patients.
- An excellent review on use of anti-coagulant drugs with neuraxial anesthetics includes guidelines for anti-platelet drugs, LMWH and unfractionated heparins, direct thrombin inhibitors (e.g. Hirudin and Argatroban), and synthetic AT III-dependent factor Xa inhibitors (e.g. Fondaparinux).<sup>65</sup> They parallel the ASRA consensus statements but also include recent literature and case reports. Anti-factor Xa plasma levels are used to monitor women receiving LMWHs. A troubling study found that 26% of pregnant women remained sub-prophylactic on their LMWH, unrelated to maternal age, weight, BMI or gestational age.<sup>66</sup> The authors recommend serial anti-factor Xa assessment for dose adjustment to be sure pregnant women are receiving adequate prophylaxis. A case report describes use of lepirudin during pregnancy in a woman with antiphospholipid syndrome and a dural venous thrombosis that developed despite use of enoxaparin and aspirin.<sup>67</sup>
- Post dural puncture headache (PDPH) is one of our more common and most frustrating anesthetic complications. Aside from the epidural blood patch, what pharmacologic methods do we have to treat this problem? Caffeine has long been a stand-by, but an article from Mayo Clinic entitled in part *Debunking the Myth*, finds no valid pharmacological rationale exists for caffeine as an antinociceptive agent for PDPH.<sup>68</sup> Clinical trials are few in number, small in sample size, methodologically flawed, and either demonstrate no effectiveness, contradictory and conflicting results, or invalid answers. They conclude that the wide endorsement for caffeine appears to be unwarranted. In contrast, a prospective randomized double-blind trial of 25 parturients used epidural morphine 3mg to prevent headache after wet tap.<sup>69</sup> They found that headache developed in 12% of the morphine group and 48% of the saline group. No patient in the morphine group required blood patch while 24% of the saline group did. An abstract presented at the ASRA meeting in 2008 described a small non-randomized trial using Tramadol 50-100mg q 6 hours for up to 48 hours in patients who would otherwise be candidates for blood patch.<sup>70</sup> They found that all 6 patients obtained relief without significant side effects except residual neck stiffness.
- There were also several case reports describing unusual headache diagnoses and reminding us that not all postpartum headaches are PDPH. In the first patient, headache and seizures developed 12 hours after a vaginal delivery using epidural

analgesia.<sup>71</sup> MRI and CT scans showed partial thrombosis of a venous sinus, and further investigation showed she had factor V Leiden mutation. Fortunately she recovered uneventfully with anticoagulation. Another parturient sustained a wet tap during an initial epidural placement, followed by an intrathecal catheter placement on a subsequent attempt.<sup>72</sup> She developed a headache the next day, failed conservative treatment for 24 hours, and then had a blood patch. For some reason they only used 10ml blood, but she had immediate though partial relief. Ten days after delivery and 3 days after discharge (only in the UK could you stay in the hospital for a week after your vaginal delivery because of a headache!) she presented with worsening headache and neurologic signs. Work-up revealed a thrombosis leading to a deep basal ganglion infarct, but with heparin therapy she recovered. Finally, a multiparous patient sustained a wet tap and PDPH for which she received a blood patch of 20ml.<sup>73</sup> She was discharged with relief of her headache, but within hours developed severe radicular back pain radiating to her right leg that worsened to a VAS of 8. Her PCP treated her for a year (!) with conservative therapy until she finally saw an orthopedic surgeon who obtained an MRI. It showed a calcified, organized epidural hematoma at the site of the blood patch. Following surgery for its removal she had complete recovery from her back pain and radiculopathy.

- Both animal studies and human case reports continue to show the utility of intralipid for treatment of local anesthetic toxicity. Using a rat model of bupivacaine overdose, investigators compared resuscitation with lipid emulsion infusion to epinephrine or saline control.<sup>74</sup> 30% lipid emulsion or epinephrine 30µg/kg was begun after asystole and during ventilation and chest compressions. Hemodynamics and metabolic measures improved during resuscitation with lipid infusion, while epinephrine performed no better than saline. A porcine model of intravenous bupivacaine-induced cardiac arrest compared lipid emulsion to a combination of epinephrine and vasopressin.<sup>75</sup> In contrast to the previous results, they found that all pigs in the vasopressor group survived and none in the intralipid group survived. They suggest that coronary perfusion pressure is the basis for improving outcome and the lipid group remained below the critical threshold of 20-30 mmHg. Perhaps a combination of lipid and vasopressors?
- More human case reports of local anesthetic toxicity treated with lipid infusion are appearing – at least 5 in 2008, although none involved obstetric patients. One involved a brachial plexus block using 30ml 1.5% mepivacaine and 10ml 0.5% bupivacaine.<sup>76</sup> Resuscitation was unsuccessful until lipid therapy (20% fat emulsion 250ml over 30 minutes) was initiated 10 minutes after arrest. Another brachial plexus block using 30ml 1% mepivacaine and 10ml 1% prilocaine was followed by agitation, dizziness, and then unresponsiveness with bigeminy on ECG.<sup>77</sup> 20% lipid emulsion 200ml was infused and symptoms resolved over 15 minutes. Interestingly the patient then underwent his surgical procedure using the block! A 13-year old received a lumbar plexus block under general anesthesia using 20ml of a lidocaine/ropivacaine mixture.<sup>78</sup> About 15 minutes after the injection, she developed sustained ventricular tachycardia at 150 bpm with normal blood pressure. 20% lipid emulsion 150ml was injected over 3 minutes with resolution of the arrhythmia, and surgery was begun. In another case report, a

femoral catheter was injected with 30ml 0.5% ropivacaine, followed by administration of 30ml of 0.5% bupivacaine for a sciatic block.<sup>79</sup> Seizures and ventricular tachycardia developed for which she received 150mg amiodarone and 100ml 20% Intralipid followed by synchronized countershock and an additional 400ml Intralipid. She recovered and demonstrated surgical anesthesia from her blocks. Finally, a bupivacaine –induced cardiac arrest following femoral and sciatic blocks was treated with 250ml 20% lipid emulsion during CPR.<sup>80</sup> The patient eventually recovered. The resident providers taking care of him had previously undergone simulation training in which one scenario involved a cardiac arrest due to local anesthetic cardiac toxicity. Treatment in the scenario included ACLS and 20% Intralipid. Both residents noted that when faced with a real-life case, their recognition of the diagnosis and subsequent therapy was strongly influenced by their simulation training.

- Several excellent reviews on surgery during pregnancy were published this year. Neurosurgical procedures on the pregnant patient with intracranial bleeding, tumors, trauma or spinal cord pathology or injury are discussed relevant to intraoperative management and timing of delivery.<sup>81</sup> Two reviews discuss trauma management in both early and advanced pregnancy.<sup>82,83</sup> A case report describes maternal pulmonary edema during combined spinal-epidural anesthesia for fetoscopic surgery for twin reverse arterial perfusion (TRAP) syndrome.<sup>84</sup> A large volume of irrigating fluid was used (8 liters) during a long procedure, and the authors speculate that absorption through myometrial venous channels may have been the source of fluid overload.
- The potential neurotoxicity of anesthetic agents on the developing brain of the fetus and newborn, when received during surgical procedures on the pregnant mother or newborn child, continues to create controversy and inspire ongoing discussion and research. This affects obstetric anesthesiologists who must counsel and consent women needing a surgical procedure while they are pregnant. How do you counsel her on the safety of her anesthetic choices; regional versus general, IV anesthetics versus volatile agents, etc.? In June 2008, an excellent editorial,<sup>85</sup> pro-con debate,<sup>86,87</sup> and several articles attempt to summarize the current state of the art on the main aspects of this topic. The “Pro” side of the debate is authored by eminent neuroscientists who relate the neuroapoptosis seen with anesthetic agents to the animal work they have done with alcohol toxicity. The “Con” side is defended by pediatric anesthesiologists who make the point that evidence obtained in developing animal models does not easily translate into direct applicability to current anesthetic practice. The editorial provides a 9-point action plan to move research forward, but emphasizes that there is no scientific basis at this time to recommend changes in clinical practice. An article in the same issue of the journal reviews neuroprotective strategies for the neonatal brain.<sup>88</sup> It discusses magnesium for preterm newborns and hypothermia in term newborns, but concludes that without a pathophysiologic mechanism for the injury to the perinatal brain, it is difficult to develop neuroprotective interventions. How do you block brain damage without affecting normal brain development that occurs at a rapid rate in the fetus and newborn? There has been success in reducing death and disability by inducing hypothermia in neonates

within 6 hours of a hypoxic or ischemic injury.<sup>89</sup> That success has encouraged scientists to test whether induced hypothermia may offer protection from anesthetic neurotoxicity in mice. Stay tuned – there is much left to be done in this area!

## OBSTETRIC COMPLICATIONS

- Preeclampsia / Eclampsia remain leading causes of maternal and fetal morbidity and mortality worldwide. There is an ongoing quest to find a marker that would tell us when a woman is at high risk or destined to develop preeclampsia so she can be monitored more closely and treated earlier. A giant step forward occurred in 2008 with the publication of a study showing that a preeclampsia-like syndrome developed in mice injected with autoantibodies that activate the angiotensin II type 1a (AT1 receptor), and that the syndrome was prevented when the mice were also injected with losartan, an AT1 receptor antagonist.<sup>90</sup> If confirmed in human studies, clinicians could monitor autoantibody levels and detect the disease weeks before symptoms of hypertension, proteinuria, glomerular endotheliosis, placental abnormalities and growth-restricted fetuses develop. Drugs could be developed to inhibit the activation of the AT1 receptor, since ACE inhibitors such as losartan are teratogenic in humans.<sup>91</sup> The hypertension and proteinuria manifested in preeclampsia are mediated in part by soluble fms-like tyrosine kinase-1 (sFlt 1 – much easier!) and soluble endoglin (sEng); factors produced by the placenta that block vascular endothelial growth factor and placental growth factor. The appearance of these factors (sFlt 1 and sEng) in the maternal blood indicates onset of clinical symptoms of preeclampsia will occur in about a month. AT1 autoantibodies may be one of the early events that activate this disease cascade of preeclampsia.
- Other authors reported that an increase in circulatory soluble endoglin (sEng) in second trimester pregnancies with abnormal uterine perfusion suggests an accurate way to predict preeclampsia.<sup>92</sup> They measured uterine perfusion by Doppler in women having scans between 19-24 weeks gestation. Those who had abnormal flow and later experienced pregnancy complications (IUGR, preeclampsia) also had significantly higher maternal sEng concentrations than women with a normal pregnancy outcome. Using the measures together – uterine perfusion, sFlt 1, and sEng – was highly accurate at predicting early-onset preeclampsia: sensitivity 100% and specificity of 93%! Another group measured maternal cardiac output by ECHO at 11-13 weeks gestation and found those who ultimately developed preeclampsia or pregnancy-induced hypertension had significantly *higher* cardiac outputs, while those who would deliver small for gestational age babies had significantly *lower* cardiac outputs in early gestation.<sup>93</sup>
- A sad but enlightening retrospective review from Ivory Coast looked at 313 eclamptic patients admitted to the ICU between 2001-2006.<sup>94</sup> Both maternal and perinatal mortality was 16%. Risk factors for mortality included transfer from outside the university hospital, delay in admission for over 12 hours, Glasgow

- coma score  $\leq 8$  on admission, and status eclampticus. Compliance with treatment was poor, with over 30% of patients not receiving appropriate therapy. An accompanying editorial notes that magnesium sulfate was not used in their protocols for a variety of reasons, and women received diazepam as an anti-convulsant instead.<sup>95</sup> In developed countries, eclampsia is an uncommon obstetric emergency. A randomized controlled trial of training for eclampsia either in local hospitals or a simulation center found that both methods of training provided marked and similar improvement, although teamwork theory had no effect at all over simply rehearsing the scenario.<sup>96</sup>
- Does development of preeclampsia provide a marker for maternal disease risks later in life?<sup>97</sup> A large registry of births in Norway was used to link preeclampsia in one or more pregnancies with subsequent development of end-stage renal disease.<sup>98</sup> They found that although the absolute risk of developing ESRD is low, the risk increased with each pregnancy that carried a diagnosis of preeclampsia with it: RR 4.7 with one diagnosis, RR 6.4 if preeclampsia occurred during two pregnancies, and RR 15.5 during more pregnancies. Other authors found women who had preeclampsia developed insulin resistance and arterial dysfunction when compared to women with normal pregnancy, and postulate that preeclampsia could be the first manifestation of the metabolic syndrome.<sup>99</sup> What about the fetus? Prenatal exposure to both preeclampsia and eclampsia is associated with an increased risk of epilepsy in children born of term gestations (ie, not associated with prematurity).<sup>100</sup> The implications of this disease do not end at delivery.
  - In this day of multiple cesareans, the risk of peripartum hysterectomy has gone up. Centers in Canada<sup>101</sup> and the United Kingdom<sup>102</sup> reviewed databases from their surveillance systems and found their incidences of peripartum hysterectomy were 0.8 per 1000 deliveries and 0.4 per 1000 deliveries respectively. Uterine atony and abnormal placentation (placenta accreta) were the most common indications, and prior cesarean deliveries were the most common risk factor.
  - Use of cell salvage during obstetric hemorrhage has been reported, but is generally considered a last resort because of fears of precipitating amniotic fluid embolism. An excellent review of cell salvage in obstetrics found that no single serious maternal complication leading to poor outcome has ever been associated with its use.<sup>103</sup> However, the fact remains there are no large prospective trials in obstetric patients. A case report of a Jehovah's Witness who had four previous cesareans and a complete previa describes use of acute normovolemic hemodilution, intraoperative cell salvage and PulseCO hemodynamic monitoring for her cesarean hysterectomy.<sup>104</sup> She had a general anesthetic and did well despite a 5500ml EBL. However, the authors responded to an "urgent request" from the obstetricians to give a 5U bolus of oxytocin and (surprise, surprise!) precipitated profound hypotension characterized by an SVR of  $\sim 300$  and a low cardiac output.
  - Numerous other case reports describe methods of dealing with peripartum hemorrhage. Two patients had conservative management of placenta percreta by leaving the placenta in situ during cesarean and administering methotrexate. These cases were complicated by infection, further hemorrhage, and ultimately hysterectomy in both.<sup>105</sup> In contrast, another two patients with bladder invasion

received conservative management including endovascular intervention, leaving the placenta in situ, methotrexate, and delayed hysterectomy and both had acceptable outcomes.<sup>106</sup> In another woman, super-selective embolization during uncontrolled bleeding from an abdominal pregnancy at 14 weeks was successful.<sup>107</sup> Finally, uterine necrosis was reported following use of uterine compression sutures to control uterine atony.<sup>108</sup> Persistent fevers not responsive to antibiotics brought her back to the O.R. on postoperative day 8 for total abdominal hysterectomy. Management of these cases requires creativity and adaptability!

- The national obesity epidemic is felt in obstetrics as elsewhere. Women aged 18-45 account for half of all bariatric surgeries, so not surprisingly data is accumulating on pregnancy and fertility following bariatric surgery. Pregnancy following bariatric surgery has become common enough that a systematic review of the literature could be done.<sup>109</sup> They found that rates of adverse maternal (diabetes and preeclampsia) and neonatal (prematurity, low birth weight and macrosomia) outcomes were *lower* in women who had become pregnant after bariatric surgery when compared to women who were obese; rates approached those of non-obese controls. A “Clinician’s Corner” article in JAMA discusses management of a 40-year old woman with diabetes and chronic hypertension who is status post gastric bypass and wants to become pregnant.<sup>110</sup> The discussants conclude her surgery is likely to ameliorate her diabetes, but that special attention must be paid to her nutrition during pregnancy.
- A number of articles discuss policy and epidemiologic issues associated with obesity and pregnancy in the U.S. Because obesity increases obstetrical health risks, investigators queried a large HMO database to determine the relationship between obesity and mean length of hospital stay for delivery – an indirect measure of use of health care services.<sup>111</sup> They found the mean length of hospital stay increased directly with BMI (especially BMI > 35), primarily related to increased cesarean delivery rate. Higher BMI was associated with more prenatal fetal tests, ultrasounds, medications, phone calls and prenatal visits. These visits were also more often with physicians than nurse practitioners or PA’s. Another article reviews the scope of the problems associated with obesity in pregnancy, pointing out that children of obese parents have a strong tendency toward obesity and all the associated complications such as diabetes, hypertension, etc.<sup>112</sup> Quite depressing! A longitudinal study of quality of life in obese pregnant women tied their BMI at the beginning of pregnancy, weight gain during pregnancy and quality of life.<sup>113</sup> They found both the mental and physical QOL component scores were lower in the obese group. Complications during pregnancy such as diabetes and hypertension were also more common in the obese group and adversely affected their quality of life scores.
- Two studies in non-obstetric obese populations should be applicable to pregnant women as well. The first found that even mild sleep apnea (no daytime somnolence) impaired endothelial function and increased arterial stiffness, an independent predictor of cardiovascular events.<sup>114</sup> The second randomized adults with BMI > 30 to a head-up position with either blankets under the back or by configuring the OR table into a back-up position for laryngoscopy, and found they

- were equivalent for achieving good laryngeal exposure and intubating conditions.<sup>115</sup>
- Two articles and an editorial address management of maternal glucose levels during pregnancy. In the first, 25,505 pregnant women received an oral glucose tolerance test at 24-32 weeks, but their caregivers were blinded to the results unless they were grossly abnormal.<sup>116</sup> The investigators hoped to clarify risks of adverse outcomes associated with degrees of maternal glucose intolerance that were less severe than overt diabetes. There was no obvious threshold for increasing complications; risks increased linearly with glucose levels including: birth weight > 90<sup>th</sup> percentile, cord blood serum C-peptide level above the 90<sup>th</sup> percentile, primary cesarean delivery and clinical neonatal hypoglycemia. We may see even mild maternal hyperglycemia being treated more aggressively. The second study compared metformin to insulin for treatment of gestational diabetes and found that metformin was not associated with increased perinatal complications and the women preferred metformin to insulin treatment.<sup>117</sup> The accompanying editorial notes that diagnosing gestational diabetes improves the mother's care but also predicts the possibility of future diabetes, so obstetricians need to share that information more freely with primary care physicians.<sup>118</sup>
  - Counseling women about a trial of labor after prior cesarean delivery (VBAC) is tricky. A study of 13,532 women compared outcomes of labor to the number of previous *successful* VBACs – in other words, these women had had one previous cesarean followed by one or more trials of labor.<sup>119</sup> VBAC success increased with increasing number of prior VBACs; from 63% for the first VBAC attempt to 92% for those with 4 or more prior VBACs. The rate of uterine rupture decreased after the first successful VBAC from 0.87% to 0.52% with 4 or more prior VBACs. The risk of other perinatal morbidities also declined – good news for women wishing to avoid a cesarean delivery. A systematic review and metaanalysis of maternal morbidity following trial of labor versus elective repeat cesarean delivery found that VBAC was successful 73% of the time, and maternal outcomes were more favorable for successful VBAC than cesarean.<sup>120</sup> However, the complications were highest when VBAC was not successful and cesarean followed the trial of labor. Unfortunately no study has been able to predict which women will be successful in their trial of labor. An amazing “Image in Clinical Medicine” shows a uterine rupture diagnosed on CT and the view of the fetal hand protruding from the uterus at cesarean!<sup>121</sup> The woman refused cesarean for 12 hours after the diagnosis of uterine rupture, but the infant was still vigorous at birth with a 5-minute Apgar of 9.
  - External cephalic version is performed to convert a breech to a vertex presentation and avoid cesarean delivery. A meta-analysis of risks associated with version found a 0.24% rate of serious complications and 0.35% rate for emergency cesarean delivery.<sup>122</sup> Complications were not related to whether the version was successful or not.
  - Cardiac disease in pregnancy is now a leading cause of maternal mortality in the U.S. and Great Britain. Even small case series are useful to show us methods of management, since none of us are likely to have a large number of these patients in our own practices. A single tertiary care center reviewed 74 deliveries in 69

women with congenital cardiac disease.<sup>123</sup> They found favorable maternal and neonatal outcomes in the majority of cases, although patients with shunt morphology (ASD, VSD, PDA, anomalous pulmonary venous return, aortopulmonary window) were more likely to experience adverse outcomes (including the 2 maternal deaths). Complications usually occurred in the postpartum period. Another series describes 3 parturients with congenitally corrected transposition of the great arteries, 2 of whom had cesarean deliveries and 1 who had induction and vaginal delivery.<sup>124</sup> A third review describes 6 cases of coronary heart disease including their anesthetic management during delivery.<sup>125</sup> A large review of 103 cases of MI during pregnancy found the risk of MI in parturients has increased from 1:73,400 to 1:24,000 in the last decade.<sup>126</sup> The mortality rate was 11% in cases since 1995. Almost all deaths occurred at the time of infarction, and death was more likely if the MI occurred around the time of delivery. Interestingly the cesarean delivery rate was only 10% in these 103 women!

- Two interesting case reports describe innovative management. A presumed amniotic fluid embolism was successfully resuscitated after placement of a right ventricular assist device.<sup>127</sup> The second describes a woman who had had a mitral valve replaced at age 4, and who had not received prenatal obstetric or cardiology care.<sup>128</sup> She suffered cardiac collapse during cesarean and maternal death despite emergency mitral valve replacement
- There has been a great deal of attention in the obstetric literature related to scheduling of elective cesarean deliveries. ACOG has very strict dating criteria to be used before elective cesarean or induction is performed to ensure delivery no earlier than 39 weeks gestation, thus hopefully avoiding iatrogenic prematurity in the newborn. Despite this, a large observational study of 13,258 women undergoing elective repeat cesarean found that 36% were delivered at less than 39 weeks gestation.<sup>129</sup> These early deliveries had increased rates of adverse respiratory outcomes, mechanical ventilation, newborn sepsis, hypoglycemia, ICU admission and hospitalization for 5 days or more. An accompanying editorial notes the conflict in avoiding “early” (< 39 week) deliveries while also avoiding the risk of late stillbirth after completion of 38 weeks – a rare but devastating complication.<sup>130</sup> It has been proposed that if all women who progress to term gestation were delivered at 39 weeks gestation (versus letting the pregnancy continue longer), it would prevent 6000 stillbirths in the U.S. alone! A conundrum indeed – not too early and not too late! Similar findings come from a large study of over 2 million pregnancies that compared outcome at 39 weeks with outcome at 37 and 38 weeks gestation.<sup>131</sup> Again, they found the risk of respiratory morbidity was higher at 37 (OR 3.1) and 38 (OR 1.3) weeks gestation than term. However, these babies were less likely to have meconium aspiration and neonatal injury than those born at 40 or 41 weeks.
- Using 34-36 weeks gestation to define late preterm births, researchers found these babies had outcomes similar to those delivered at 32-34 weeks gestation; both acute morbidities that affected length of NICU stay and also longer-term morbidities.<sup>132</sup> They stress that delivery of a 34-week infant should not be considered routine or without potentially significant risk. This is a big change to

- current obstetric practice, which deems 34 weeks a “watershed” of fetal maturity at which time tocolytics and steroids are not necessary and augmentation of labor may be indicated. Similarly, review of a Kaiser database covering 141,321 children born  $\geq 30$  weeks gestation found those born at 34-36 weeks were over 3 times as likely as full-term babies to be diagnosed with cerebral palsy and also at increased risk for developmental delay or mental retardation.<sup>133</sup> And finally, a single hospital review of their outcomes at 34-36 weeks compared to 39 weeks found significantly higher infant mortality and increases in ventilator-treated respiratory distress, transient tachypnea, intraventricular hemorrhage, sepsis work-ups and culture-proven sepsis, phototherapy for hyperbilirubinemia and intubation in the delivery room.<sup>134</sup> 80% of these late preterm births were attributed to idiopathic preterm labor or ruptured membranes and 20% to obstetric complications. An accompanying editorial to reference #131 notes that we have an acute need for longitudinal studies to better characterize risks of short-and long-term morbidity for infants delivered at less than 39 weeks.<sup>135</sup>
- Before mentioning just a few of the multitude of publications on maternal co-morbidities, I want to put in a plug for the obstetric medicine specialists. These are internists who specialize in management of medical disorders during pregnancy – if you have such a person available to you in your institution, they are a tremendous resource! Their organization is called the North American Society of Obstetric Medicine.<sup>136</sup> I will just mention a few of the reviews or case series published this year on maternal medical conditions. There is an ACOG Practice Bulletin on asthma in pregnancy<sup>137</sup>, reviews on pregnancy after solid organ transplantation<sup>138</sup> and vasculopathies (systemic sclerosis, pulmonary hypertension, and sickle cell disease)<sup>139</sup>, and case reports on catastrophic antiphospholipid antibody syndrome<sup>140</sup>, cancer and chemotherapy<sup>141,142</sup>, maternal hyperhomocysteinemia<sup>143</sup>, and maternal congenital myasthenia syndrome.<sup>144</sup>

## FETAL AND NEWBORN ISSUES

- Electronic fetal heart rate monitoring is used in about 85% of labors, or 3.4 million births each year. The National Institute of Child Health and Human Development (NICHD) published an update on definitions, interpretation and research guidelines for electronic fetal heart rate monitoring this year.<sup>145</sup> This is an excellent summary document and includes terminology for description of fetal heart tracings and uterine contractions. A 3-tier system for fetal heart rate tracing interpretation is described. Level III tracings are predictive of fetal acidosis and include absent baseline FHR variability with either recurrent late decelerations, recurrent variable decelerations or bradycardia and/or a sinusoidal pattern. But even with these definitions, is the interpretation reproducible and reliable? Four MFM specialists reviewed 100 FHR tracings and could not agree on which were reassuring, which fetuses had undergone cesarean for non-reassuring FHR, or which babies had been acidotic (pH < 7.0) at birth or had an Apgar score of  $\leq 3$  at 5 minutes.<sup>146</sup> They concluded the interobserver variability of FHR is excessive

- and that the ability to identify newborns with low Apgar scores or acidosis is poor.
- A systematic review was done to determine the proportion of cerebral palsy associated with intrapartum hypoxia-ischemia in term infants.<sup>147</sup> They conclude the overall incidence of hypoxic-ischemic encephalopathy is 0.25%, and the proportion of cerebral palsy associated with intrapartum events is 14.5%. The vast majority of cerebral palsy in term infants is not associated with intrapartum events. An editorial notes this is a huge area of medical liability for obstetricians and concludes that tort reform requiring causation would help, but initiatives focused on intrapartum communication, education and protocols are also important.<sup>148</sup> Basic science work in rabbits found that maternal intrauterine endotoxin administration near term leads to a phenotype of cerebral palsy with motor deficits.<sup>149</sup> A cohort study of 8299 laboring women found that fever and umbilical cord acidosis were risk factors for neonatal encephalopathy.<sup>150</sup> If both factors were present, the risk was 12.5%; when both were absent, the risk was 0.3%. Fever/infection and acidosis are clearly harmful to the developing brain.
  - Breastfeeding conveys significant benefit to an infant in terms of enhanced immunity, but is risky when the mother is HIV positive because the virus can be passed in breast milk. Two major studies on preventing mother-to-child transmission of HIV were published this year. The first showed that either nevirapine (Viramune) or nevirapine plus zidovudine (AZT) given to the child until 14 weeks of age reduced the rate of postnatal HIV infection at nine months of age by almost half – from 11% in controls to about 6%.<sup>151</sup> The second study found that abrupt weaning at 4 months did not improve the rate of HIV-free survival in babies of HIV-positive mothers.<sup>152</sup> In fact, if the babies were already HIV-positive, the weaning was actually harmful; a 74% mortality by 2 years of age versus 55% mortality if mothers continued to breastfeed. An accompanying editorial notes that although the studies give direction for future research, they do not help clarify direction for policy.<sup>153</sup> Mothers in low-resource settings will choose to breastfeed or not based on their own cultural, economic and psychological needs. How do we promote breast-feeding to improve child survival without exposing more infants to HIV transmission?
  - A sad but eye-opening study found that during neonatal intensive care at tertiary care centers in France, large numbers of painful and stressful procedures were performed without any type of analgesia.<sup>154</sup> Each neonate experienced a median of 115 procedures during the study period, or 16 procedures per day of hospitalization. Overall, only 21% of painful procedures were carried out with specific analgesia before the procedure. Surely we can do better! Coverage in the New York Times quotes 2 anesthesiologists, Mark Rosen at UCSF and Laura Myers at Boston Children's.<sup>155</sup> Rosen, active in fetal surgery research, has published an article in JAMA proposing that a fetus cannot feel pain until ~30 weeks gestation. Myers researched the Unborn Child Protection Act for the abortion-rights organization Physicians for Reproductive Choice and Health and concluded that abortion clinics do not have the equipment or expertise necessary to supply fetal anesthesia as the bill requires.

- Preterm labor and delivery remains baffling as to its cause and treatment, and the morbidity associated with prematurity can be severe. A multicenter, placebo-controlled, double-blind trial assigned women at imminent risk for delivery between 24 and 31 weeks gestation to receive magnesium (bolus and infusion) or placebo.<sup>156</sup> Although the risk of death by one year was no different (9.5 vs. 8.5%), the risk of moderate or severe cerebral palsy at or beyond 2 years was reduced to 1.9% with magnesium versus 3.5% without. An editorial recommends caution until we better understand which factors indicate which infants will benefit from treatment.<sup>157</sup> When women do not deliver with their first episode of preterm labor, is there advantage to repeating their corticosteroids at intervals until the fetus is closer to term? A randomized trial of antenatal corticosteroids every 14 days until 33 weeks gestation found no impact on overall morbidity and mortality.<sup>158</sup> Instead there were *adverse* effects associated with multiple doses of steroids including lower birth weight, length and head circumference. Other studies have found adverse neonatal effects of weekly steroids including higher risk for cerebral palsy and attention problems.
- A large cohort study of extreme prematurity compared neonatal mortality and morbidity by method of delivery in vertex fetuses weighing 500-1500 grams.<sup>159</sup> They found no benefit to cesarean delivery over vaginal delivery. Once delivered, it can be very hard to decide whether to initiate resuscitation and intensive care for extremely premature infants – those 22-25 weeks gestation. A prospective study of 4446 infants found that 49% died, 61% died or had severe impairment, and 73% died or had impairment.<sup>160</sup> Four factors increased the likelihood of a *favorable* outcome: female sex, exposure to antenatal steroids, single gestation, and higher birth weight. Coverage of this study in the New York Times<sup>161</sup> gives several examples of scenarios and neonatal outcomes, and introduces an on-line calculator developed to generate statistics on chances of the baby's survival and likelihood of disabilities.<sup>162</sup>
- One of the serious morbidities of prematurity is bronchopulmonary dysplasia associated with ventilation and oxygen treatment. A randomized trial of CPAP versus intubation and ventilation, initiated in the delivery room 5 minutes after birth for infants born at 25-28 weeks gestation, found similar rates of death or BPD. Half the CPAP infants were intubated in the first 5 days and their incidence of pneumothorax was 9% versus 3% in the intubated group. Infants in the CPAP group had fewer days of assisted ventilation overall.
- What is the long-term effect of preterm birth on survival, reproduction and next-generation preterm birth? A study using registry data from Norway followed births that occurred from 1967-1988 until 2002 to determine ongoing mortality through childhood and adolescence and reproductive outcomes in adulthood.<sup>163</sup> Those born preterm had higher mortality than their term peers throughout childhood (worse for boys), although survival improves to adulthood. Later reproduction was diminished and women born preterm (but not preterm men) had an increased risk of having preterm offspring. An editorial points out the many improvements in care of preterm infants since the 1970s and 1980s that may continue to improve outcomes.<sup>164</sup>

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- <sup>1</sup> [www.cdc.gov/ncidod/dhqp/gl\\_isolation.html](http://www.cdc.gov/ncidod/dhqp/gl_isolation.html) (see III.a.1.c)
  - <sup>2</sup> Infect Control Hosp Epidemiol 2007;28:1187
  - <sup>3</sup> [www.asahq.org](http://www.asahq.org) (see Clinical information, then Standards, Guidelines and Statements)
  - <sup>4</sup> [www.asahq.org](http://www.asahq.org) (see Clinical information, then Standards, Guidelines and Statements)
  - <sup>5</sup> Anesth Analg 2008;107:956
  - <sup>6</sup> Obstet Gynecol 2008;112:333
  - <sup>7</sup> Obstet Gynecol 2008;112:1193
  - <sup>8</sup> J Midwifery Women's Health 2008;53:276
  - <sup>9</sup> Anesth Analg 2008;106:1127
  - <sup>10</sup> ASA Newsletter, May 2008;72:39
  - <sup>11</sup> Am J Obstet Gynecol 2008;198:205
  - <sup>12</sup> USA Today 6/3/2008
  - <sup>13</sup> Time 4/28/08
  - <sup>14</sup> Time 8/18/08 and NY Times 11/13/2008
  - <sup>15</sup> Int J Obstet Anesth 2008;17:243
  - <sup>16</sup> Int J Obstet Anesth 2008;16:110
  - <sup>17</sup> Acta Obstet Gynecol Scand 2004;83:257
  - <sup>18</sup> Anesth Analg 2008;106:1509
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  - <sup>21</sup> Anesth Analg 2008;107:1303
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  - <sup>28</sup> Anesth Analg 2008;107:1646
  - <sup>29</sup> Anesth Analg 2008;107:1968
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  - <sup>31</sup> Anesthesiology 2008;108:184
  - <sup>32</sup> Anesthesiology 2008;108:938
  - <sup>33</sup> Anesth Analg 2008;107:1295
  - <sup>34</sup> Anesthesiology 2008;109:856
  - <sup>35</sup> Anesthesiology 2008;108:802
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