

# Gerard W. Ostheimer Lecture

## What's New in Obstetric Anesthesia - 2011?

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**Objectives:** The primary objective of this review is to highlight key papers published from January 2011 to December 2011 which have major scientific and clinical relevance to practicing obstetric anesthesiologists. Relevant topics in this review originate from published research in the fields of obstetric anesthesia, obstetrical medicine, perinatology, pediatrics, epidemiology, maternal health, health policy and affiliated clinical specialties (internal medicine, surgery, pathology).

**Methods:** 74 journals and newsletters published in the English language were hand-searched from January 2011 to December 2011 for the purposes of sourcing articles for this review. The journals were chosen based on a number of factors: scientific/clinical relevance to the fields of obstetric anesthesia, obstetrics and perinatology; prior Ostheimer journal lists; journal impact factor; and the quality of published work. In addition, other electronic and media sources were used to supplement the primary search including: Pubmed, SciVerse Scopus, Obstetric Anesthesia Digest, MDLinx, Obstetric and Gynecologic Survey, Journal of Women's Health, Journal Watch Women's Health Alerts (<http://womens-health.jwatch.org/>); electronic RSS feeds including: <http://tinyurl.com/ob-anes-feed>.

A systematic approach incorporating checklists was used as a method for assessing the scientific quality for four types of research: systematic reviews; randomized controlled trials, observational studies (including studies with nonexperimental/quasi-experimental designs with or without control or comparison groups), and investigations of diagnostic tests/monitoring devices. Each study was evaluated using criteria previously described by the Research Triangle Institute, University of North Carolina for the US Agency for Healthcare Research and Quality (AHRQ) [West S, King V, Carey TS, et al. Systems to Rate the Strength of Scientific Evidence. Evidence Report/Technology Assessment No. 47 (AHRQ Publication No. 02-E016. Rockville, MD: April 2002); URL: <http://www.thecre.com/pdf/ahrq-system-strength.pdf>]. Specific domains were used in the criteria for evaluating four types of system to grade the quality of individual studies (Table).

Level of evidence for each article was also estimated using the most recent guidelines from the Oxford Centre for Evidence-Based Medicine (Howick J et al; Centre for Evidence Based Medicine, Oxford, UK: URL: <http://www.cebm.net/index.aspx?o=5653>).

Each article selected for the final syllabus was categorized into a specific topic area (see Table of Contents). The categories for the Table of Contents for the 2012 Ostheimer lecture were based on key areas of clinical and scientific interest. Categories were also determined based on important topics of interest which offer new or advanced clinical and research perspectives, challenge current practice paradigms or describe novel / new techniques or scientific approaches for advancing clinical care.

The syllabus primarily aims to include systematic reviews, randomized controlled trials, observational studies, diagnostic/device studies, and a limited number of case series that are of genuine scientific interest. Relevant correspondence associated with each article, such as editorials, letters to the editor, commentary articles, were considered for the final syllabus. In addition, a select number of high caliber journal articles (such as review articles, commentary or opinion-based articles), and important peer and non-peer reviewed publications from established regional, national or international organizations related to maternal health (such as Centre for Maternal and Child Enquiries - United Kingdom) have also been included in the syllabus. Due to the limitations on the number of articles in the syllabus, the following articles were not included: case reports, unaccompanied letters of correspondence, articles from non-index linked journals, journals not published using English language.

The lecturer wishes to apologize to investigators whose articles were not selected in the final syllabus. As a disclaimer, the syllabus aims to provide a broad overview of key papers from scientific disciplines that are indirectly or directly relevant to obstetric anesthesiologists. Selecting papers for the final syllabus proved challenging due to the high number of quality articles published in 2011. This lecturer acknowledges that all clinicians and investigators should be congratulated for their efforts in publishing work which advances the knowledge and practice of obstetric anesthesiology.

*Table. Domains evaluated in each study type to assess scientific quality for the syllabus for the Ostheimer lecture.*

Systemic Reviews	Randomized Controlled trials	Observational studies	Diagnostic tests/ Device studies
Study question	Study question	Study question	Study population
Search strategy	Study population	Study population	Adequate description of test/device
Inclusion and exclusion criteria	Randomization	Compatibility of subjects	Appropriate reference standard
Interventions	Blinding	Exposure or intervention	Blinded comparison of test or standard
Outcomes	Interventions	Outcome measures	Avoidance of verification bias
Data extraction	Outcomes	Statistical analyses	
Study quality and validity	Statistical Analyses	Results	
Data synthesis and analysis	Results	Discussion	
Results	Discussion	Funding or sponsorship	
Discussion	Funding or sponsorship		
Funding or sponsorship			

Source = West SL et al. *Systems to Rate the Strength of Scientific Evidence*. AHRQ, 2002.

## LIST OF JOURNALS:

### Anesthesia, Intensive Care, Pain Journals:

Acta Anaesthesiologica Scandinavica  
Anaesthesia  
Anesthesiology  
Anesthesia & Analgesia  
Anesthesia and Intensive Care  
Anesthesiology Clinics of North America  
ASA Newsletter  
British Journal of Anaesthesia  
Canadian Journal of Anaesthesia  
Critical Care medicine  
European Journal of Anaesthesiology  
European Journal of Pain  
International Anesthesiology Clinics  
International Journal of Obstetric Anesthesia  
Journal of Clinical Anesthesia  
Journal of Critical Care  
Journal of Pain  
Pain  
Regional Anesthesia and Pain Medicine

### Perinatology and Pediatric Journals

American Journal of Perinatology  
BMC Pediatrics  
Early Human Development  
Journal of Paediatrics and Child Health  
Journal of Pediatrics  
Journal of Perinatology  
Pediatrics  
Obstetric Journals

Acta Obstetrica et Gynecologica Scandinavica  
American Journal of Maternal/Child Nursing  
American Journal of Obstetrics and Gynecology  
The Australian and New Zealand Journal of  
Obstetrics and Gynaecology  
Birth  
British Journal of Obstetrics and Gynecology  
(BJOG)  
Clinical Obstetrics and Gynecology  
Current Opinion in Obstetrics and Gynecology  
European Journal of Obstetrics & Gynecology &  
Reproductive biology  
Fertility and Sterility  
Gynecologic and Obstetric Investigation  
International Journal of Gynecology and Obstetrics  
Journal of Maternal-Fetal and Neonatal medicine  
Journal of Midwifery and Women's Health  
Journal of Women's Health  
Obstetrical and Gynecological Survey  
Obstetrics and Gynecology  
Obstetrics and Gynecology Clinics of North America  
Obstetrics, Gynaecology & Reproductive Medicine  
Obstetric Medicine: The Medicine of Pregnancy  
Placenta

### Health Services Research Journals

Health Affairs  
Quality and Safety in Health Care

### General Medicine Journals

American Journal of Epidemiology

Annals of Internal Medicine  
Blood  
British Medical Journal  
Chest  
Circulation  
European Heart Journal  
Heart  
Intensive Care Medicine  
Journal of American College of Cardiology  
Journal of Clinical Epidemiology  
Journal of the American Medical Association  
Journal of Thrombosis and Hemostasis  
Lancet  
Medical Care  
Morbidity and Mortality Weekly Report  
New England Journal of Medicine  
Nature - Medicine  
PNAS - Proceedings of National Academy of  
Sciences of USA  
Resuscitation  
Science  
Social Science and Medicine  
Thrombosis Research  
Thrombosis and Haemostasis  
Transfusion

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# What's New in Obstetrics (Articles published in 2011)

1. Mhyre JM: What's new in obstetric anesthesia? *Int J Obstet Anesth* 2011; 20: 149-59.
2. Toledo P: What's new in obstetric anesthesia? The 2011 Gerard W. Ostheimer Lecture. *Anesth Analg* 2011; 113: 1450-58.

## Co-existing/Acquired Disease and Maternal Health

### Cardiac Disease

3. Hidano G, Uezono S, Terui K: A retrospective survey of adverse maternal and neonatal outcomes for parturients with congenital heart disease. *Int J Obstet Anesth* 2011; 20: 229-35.

Retrospective review of maternal and neonatal outcomes in women with congenital cardiac disease (n=151) at a single obstetric center over a 7 yr period. Of note, a high proportion of parturients had favorable baseline functional status (NHYA class I/II=91%). No maternal deaths and low neonatal mortality (1 patient) were observed. Maternal cardiac events occurred in 1% of vaginal deliveries and 15% of Cesarean deliveries; however patients with greater co-morbidity underwent Cesarean delivery (CD).

4. Lui GK, Silversides CK, Khairy P, Fernandes SM, Valente AM, Nickolaus MJ, Earing MG, Aboulhosn JA, Rosenbaum MS, Cook S et al: Heart rate response during exercise and pregnancy outcome in women with congenital heart disease. *Circulation* 2011;123: 242-48.

In this retrospective analysis of obstetric patients with congenital heart disease, investigators used pre- or antenatal cardiopulmonary exercise testing parameters to predict adverse pregnancy outcomes (n=89 pregnancies). Increases in heart rate (HR) response reduced the risk of major maternal and neonatal cardiac events; a 10 bpm increase in maternal HR reduced the risk of a maternal and neonatal event (OR=0.71; 95% CI=0.53-0.94 and OR=0.75; 95% CI=0.58-0.98, respectively). However, the multivariate logistic regression models used in this study suffered from 'overfitting'.

5. Kuklina E, Callaghan W: Chronic heart disease and severe obstetric morbidity among hospitalisations for pregnancy in the USA: 1995-2006. *BJOG* 2011; 118: 345-52.

Massive, population-wide, retrospective study of chronic heart disease among obstetric-related hospitalizations using US administrative data between 1995 to 2006 (n=approx. 48 million). One of the main findings was a tripling in the rate of postpartum hospitalizations for chronic heart disease over the study period (4.8 to 14.4 per 10,000 deliveries; P<0.01). Rates of major co-morbid conditions (especially cardiac arrest/VF) associated with chronic heart disease among delivery hospitalizations also substantially increased from 1995-7 to 2004-6.

6. Karamlou T, Diggs BS, McCrindle BW, Welke KF: A growing problem: maternal death and peripartum complications are higher in women with grown-up congenital heart disease. *Ann Thorac Surg* 2011; 92: 2193-98; discussion 2198-99.

Using data from the Nationwide Inpatient Sample between 1998-2007 (total births=39.9 million), this observational study assessed the prevalence of adult congenital heart disease (CHD) among pregnant women. A 43% increase in deliveries to CHD patients occurred over the study period, and the rate of maternal mortality was 18-fold higher in CHD versus non-CHD women. As observed in other mortality reviews, obstetricians and anesthesiologists should adequately prepare for an increasing number of women with CHD at high risk of severe maternal and perinatal morbidity and mortality.

7. Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, Cifkova R, Ferreira R, Foidart JM, Gibbs JS, Gohlke-Baerwolf C, Gorenek B, Iung B et al: ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2011; 32: 3147-97.

This must-read document by an expert taskforce within the European Society of Cardiology encompasses guidelines for the screening, work-up, optimization and management of obstetric patients with acquired and congenital heart disease.

8. Arendt KW, Fernandes SM, Khairy P, Warnes CA, Rose CH, Landzberg MJ, Craig PA, Hebl JR: A case series of the anesthetic management of parturients with surgically repaired tetralogy of Fallot. *Anesth Analg* 2011; 113: 307-17.

Retrospective study analyzing anesthetic, obstetric and cardiac outcomes over a 14 yr period in pregnant patients with surgically corrected Tetralogy of Fallot (n=27 deliveries). All patients underwent neuraxial blockade for labor or delivery. Cardiac outcomes were generally favorable, with no episodes of new or sudden-onset peripartum congestive heart failure and only one episode of non-sustained ventricular tachycardia.

### Respiratory Disease

9. Higgins N, Leong E, Park CS, Facco FL, McCarthy RJ, Wong CA: The Berlin Questionnaire for assessment of sleep disordered breathing risk in parturients and non-pregnant women. *Int J Obstet Anesth* 2011; 20: 22-25.

Exploratory prospective study comparing the rate of self-reported sleep disordered breathing (using a Berlin questionnaire) in pregnant (n=4074) and non-pregnant women (n=490). A significantly higher proportion of pregnant women had a positive Berlin questionnaire (33% vs 20%; OR=2.0, 95% CI=1.6-2.5) However, more research is needed to validate this screening tool for correctly identifying sleep disordered breathing in the pregnant population.

### Infectious Disease

#### *Influenza and Pregnancy*

10. Influenza vaccination coverage among pregnant women, United States, 2010-11 influenza season. *MMWR Morb Mortal Wkly Rep* 2011; 60: 1078-82.

This Internet panel survey assessed influenza vaccination uptake during the 2010-11 influenza season (n=1457); 49% of respondents who were pregnant between Oct 2010 - Jan 2011 received vaccination, with increased uptake among those who had contact with a health-care provider. This report emphasizes that health-care providers are integral for promoting the safety and effectiveness of influenza vaccination for pregnant patients.

#### *H1N1: Obstetrical and Perinatal Outcomes*

11. Pierce M, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M: Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. *BMJ* 2011; 342: d3214.

High-quality, national cohort study (UK) reporting maternal and perinatal outcomes in women identified with H1N1 infection in 2009 (n=256). Infected women (in-patients) were at higher risk of preterm delivery (adj OR=4; 95% CI=2.7-5.9) and CD (adj OR=2.3; 95% CI=1.7-3.2) compared to historical non-infected controls. A high proportion of infected women who underwent preterm delivery required ICU admission versus women delivering at term (54% vs 12%; P<0.001), with a worryingly low rate of immunization (5%) among all women infected before 37 weeks. This data has important public health ramifications in advance of future viral pandemics.

Accompanying editorial: Joseph KS, Liston RM: H1N1 influenza in pregnant women. *BMJ* 2011; 342: d3237.

12. Varner MW, Rice MM, Anderson B, Tolosa JE, Sheffield J, Spong CY, Saade G, Peaceman AM, Louis JM, Wapner RJ et al: Influenza-like illness in hospitalized pregnant and postpartum women during the 2009-2010 H1N1 pandemic. *Obstet Gynecol* 2011; 118: 593-600.

In this study, maternal outcomes were assessed in 356 in-patients with influenza-like illness at 28 US hospitals in the MFMU network during the H1N1 pandemic. ICU admission occurred in 9.8% patients and CD was needed in 44% patients. Risk factors for ICU admission were cigarette smoking (OR=2.8; 95% CI=1.2-6.5) and chronic hypertension (OR=6.9; 95% CI=2.2-21.5). Patients receiving early antiviral treatment had a lower risk of ICU admission (OR=0.4; 95% CI=0.2-0.8).

13. Creanga AA, Kamimoto L, Newsome K, D'Mello T, Jamieson DJ, Zotti ME, Arnold KE, Baumbach J, Bennett NM, Farley MM et al: Seasonal and 2009 pandemic influenza A (H1N1) virus infection during pregnancy: a population-based study of hospitalized cases. *Am J Obstet Gynecol* 2011; 204: S38-45.

In response to the 2009 H1N1 pandemic, the CDC convened a meeting in August 2010 to provide recommendations, described in this consensus document, for the provision of care to pregnant women, newborns and health care providers in the event of an influenza pandemic. The importance of vaccinating pregnant women, a high-risk group for severe influenza, is emphasized. Early antiviral treatment is recommended for pregnant women or women <2 weeks postpartum with suspected influenza.

14. Mosby LG, Rasmussen SA, Jamieson DJ: 2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature. *Am J Obstet Gynecol* 2011; 205: 10-18.

Recent systematic review of 120 publications describing cases of 2009 H1N1 influenza during pregnancy. Maternal hypoxia or maternal decompensation were frequently described as indications for urgent or emergency CD, which highlight the adverse impact of H1N1 influenza on pregnant women and perinatal care.

15. Maternal and infant outcomes among severely ill pregnant and postpartum women with 2009 pandemic influenza A (H1N1)–United States, April 2009–August 2010. *MMWR Morb Mortal Wkly Rep* 2011; 60: 1193-96.

In this CDC report of H1N1 influenza between April 2009 and August 2010, 247 severely ill pregnant women were admitted to ICU and 75 maternal deaths occurred due to H1N1. Maternal survival was significantly improved with early treatment with antiviral therapy within 2 days of illness onset. High rates of preterm birth (64%) were also found for liveborn singleton infants born during the hospitalization.

### *H1N1: Maternal Critical Illness*

16. Nair P, Davies AR, Beca J, Bellomo R, Ellwood D, Forrest P, Jackson A, Pye R, Seppelt I, Sullivan E et al: Extracorporeal membrane oxygenation for severe ARDS in pregnant and postpartum women during the 2009 H1N1 pandemic. *Intensive Care Med* 2011; 37: 648-54.

In this case series, the use of ECMO is described for 12 pregnant/postpartum patients with severe ARDS due to H1N1 influenza. Circuit-related problems were rare; however 67% of patients had major bleeding requiring transfusion. The maternal and infant survival rates were 66% and 71% respectively; all surviving mothers were ambulant at discharge.

17. Maravi-Poma E, Martin-Loeches I, Regidor E, Laplaza C, Cambra K, Aldunate S, Guerrero JE, Loza-Vazquez A, Amau E, Almira J et al: Severe 2009 A/H1N1v influenza in pregnant women in Spain. *Crit Care Med* 2011; 39: 945-51.

In this population-wide, prospective study in 148 Spanish intensive care units, 234 women of reproductive age were admitted with A/H1N1 infection between April 2009 – Feb 2011; 50 cases (21.4%) were pregnant. In pregnant patients, 94% incurred primary viral pneumonia, 78% required mechanical ventilation and 14% died. Only a minority of patients (5/36) received antiviral treatment within 48 hr of symptom onset, adding further weight to the importance of early therapy for improving maternal outcomes.

Accompanying editorial: Joseph KS, Liston RM: H1N1 influenza in pregnant women. *BMJ* 2011; 342: d3237.

### **Obesity**

18. Blomberg M: Maternal and neonatal outcomes among obese women with weight gain below the new Institute of Medicine recommendations. *Obstet Gynecol* 2011; 117: 1065-70.

Retrospective cohort study in Sweden (n=46,595) investigating the adverse maternal and perinatal outcomes associated with gestational weight gain in class I – III obese women. Women in obesity class III who lost weight had a decreased risk of having a large-for-gestational-age baby (OR=0.64; 95% CI=0.46-0.9). In women with no weight gain or who lost weight in pregnancy, the rates of CD were significantly reduced in obesity classes II (34%) and III (23%) women. Nonetheless, rates of CD were highest for class III women (24%-31%) in all weight-gain categories.

### **Latex Sensitization**

19. Draisci G, Zanfini BA, Nucera E, Catarci S, Sangregorio R, Schiavino D, Mannocci A, Patriarca G: Latex sensitization: A special risk for the obstetric population? *Anesthesiology* 2011; 114: 565-69.

In this prospective study, the prevalence of latex sensitization was significantly higher among 294 patients undergoing CD compared to 294 non-pregnant patients undergoing gynecologic surgery (5.1% vs 1.7%; P<0.05). Higher specific immunoglobulin E serum concentration were also reported in the CD group. Improved perioperative vigilance is advised for pregnant patients with an atopic history or an itch response using rubber gloves.

Letters to the author: Weiniger CF, Pe'er L, Shalit M: Remove latex from the labor and delivery suite. *Anesthesiology* 2011; 115: 903; author reply 903-904.

Abouleish AE: Evidence does not show that pregnancy is a risk factor for latex allergy. *Anesthesiology* 2011; 115: 902-3; author reply 903-904.

### **Nutritional Deficiency**

20. Mei Z, Cogswell ME, Looker AC, Pfeiffer CM, Cusick SE, Lacher DA, Grummer-Strawn LM: Assessment of iron status in US pregnant women from the National Health and Nutrition Examination Survey (NHANES), 1999-2006. *Am J Clin Nutr* 2011; 93: 1312-20.

Using data from NHANES database, investigators in this epidemiologic study aimed to investigate changing trends and disparities in rates of iron-deficiency (ID) in pregnancy. The prevalence of ID was observed to increase with advancing gestation (6.9%, 14.3%, 29.5% for 1st, 2nd, 3rd trimester respectively). Non-hispanic white parturients had a lower prevalence of ID (13.9%) than Mexican Americans (23.6%) and non-Hispanic black parturients (29.6%). Unfortunately, adverse maternal/perinatal outcomes associated with ID were not described.

Accompanying editorial: Lynch S: Improving the assessment of iron status. *Am J Clin Nutr* 2011; 93: 1188-89.

# Obstetric Management – Antenatal Period

## Preterm Labor and Preterm Birth

21. Lee HC, Lyndon A, Blumenfeld YJ, Dudley RA, Gould JB: Antenatal steroid administration for premature neonates in California. *Obstet Gynecol* 2011; 117: 603-609.

Retrospective cohort study (n=15343) that reported that 23% of mothers of premature infants did not receive antenatal steroids; study data were sourced from Californian hospitals with neonatal intensive care facilities between 2005-2007. Inequalities in care are partly responsible, as evidenced by Hispanic mothers, mothers <20 yr of age and those with no prenatal care being less likely to receive antenatal steroids. Insufficient time to administer steroids may explain why patients undergoing vaginal delivery or diagnosed with fetal distress - adj OR=1.3 respectively - were at higher risk of not receiving steroids.

22. Esplin MS, Merrell K, Goldenberg R, Lai Y, Iams JD, Mercer B, Spong CY, Miodovnik M, Simhan HN, van Dorsten P et al: Proteomic identification of serum peptides predicting subsequent spontaneous preterm birth. *Am J Obstet Gynecol* 2011; 204: 391.e1-8.

Exploratory (nested case-control) study to identify serum and proteomic markers for preterm delivery at 24 weeks and 28 weeks (n=160). A prediction model, which included serum and proteomic markers, had 86% sensitivity and 80% specificity in identifying women at risk of preterm birth. Mechanistic studies are needed to explain these findings.

23. Conde-Agudelo A, Romero R, Kusanovic JP: Nifedipine in the management of preterm labor: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2011; 204: 134.e1-20.

Well-constructed systematic review and meta-analysis of 26 RCTs investigating the safety and efficacy of administering nifedipine for tocolysis for preterm labor (PTL). Compared to  $\beta_2$  agonists, nifedipine posed lower risk of delivery within 7 days of starting treatment (RR=0.82; 95% CI=0.7-0.9) and adverse maternal effects (RR=0.31; 95% CI=0.18-0.54). There were no differences between nifedipine and magnesium sulphate in tocolytic effect; however fewer maternal adverse effects occurred with nifedipine (RR=0.63; 95% CI=0.48-0.82). Nifedipine maintenance tocolysis was ineffective in reducing the incidence of preterm birth compared to placebo or no treatment.

Letter to the author: Caritis SN: Metaanalysis and labor inhibition therapy. *Am J Obstet Gynecol* 2011; 204: 95-96.

24. Crump C, Sundquist K, Sundquist J, Winkleby MA: Gestational age at birth and mortality in young adulthood. *JAMA* 2011; 306: 1233-40.

High-quality cohort study investigating the association between gestational age at birth and postnatal mortality until early adulthood (n=674,820). Significant inverse associations between gestational age at birth and mortality in childhood (age 6-12 yr: adj HR 0.92; 95% CI=0.89-0.94) and young adulthood (age 18-36 yr; adj HR 0.96; 95% CI=0.94-0.97) were observed. Late preterm (34-36 weeks) birth was associated with increased mortality in young adulthood (adj HR 1.31; 95% CI=1.13-1.5). Although this study did not account for all potential confounders that impact mortality, these findings highlight an underappreciated yet important association of preterm birth on long-term health sequelae.

Letter to the author: Strunk T, Simmer K, Burgner D: Prematurity and mortality in childhood and early adulthood. *JAMA* 2012; 307: 32; author reply 32-33.

25. Cheng Y, Kaimal A, Bruckner T, Hallaron D, Caughey A: Perinatal morbidity associated with late preterm deliveries compared with deliveries between 37 and 40 weeks of gestation. *BJOG* 2011; 118: 1446-54.

Retrospective cohort study detailing differences in the risk of postnatal complications in neonates born between 34-36 weeks gestation (n=3,167,615). Using multivariate analyses, investigators found neonates born between 34-36 weeks respectively were at increased risk of perinatal complications (including low APGAR scores, neonatal seizures, ICU admission, respiratory compromise) compared to infants born between 37-40 weeks. This study is important in highlighting the adverse outcomes associated with late preterm delivery.

## Preeclampsia

### *Predicting Preeclampsia*

26. North RA, McCowan LM, Dekker GA, Poston L, Chan EH, Stewart AW, Black MA, Taylor RS, Walker JJ, Baker PN et al: Clinical risk prediction for preeclampsia in nulliparous women: development of model in international prospective cohort. *BMJ* 2011; 342: d1875.

High quality, international, prospective cohort study using clinical data to investigate risk factors for preeclampsia among healthy nulliparous patients (n=3529). Risk-factors identified at 14-16 weeks gestation included: age, mean arterial blood pressure, BMI, family history (FH) of preeclampsia, FH of coronary artery disease, maternal birthweight and vaginal bleeding  $\geq$ 5days. The area under the ROC curve (after internal validation) was 0.71, and model performance did not improve after accounting for uterine artery Doppler indices. Using these variables, investigators found predicting preeclampsia in healthy nulliparous patients is suboptimal.

27. von Dadelszen P, Payne B, Li J, Ansermino JM, Broughton Pipkin F, Cote AM, Douglas MJ, Gruslin A, Hutcheon JA, Joseph KS et al: Prediction of adverse maternal outcomes in preeclampsia: development and validation of the fullPIERS model. *Lancet* 2011; 377: 219-27.

High-quality prospective multicenter study that developed and validated an adverse outcome-prediction model for preeclamptic women admitted to tertiary units (n=2023). Six predictors were included in the final model: gestational age, chest pain or dyspnea, oxygen saturations, platelet count, serum creatinine, and AST (sensitivity=0.76 and specificity=0.87). This model could be used to alter and improve approaches to patient care for preeclamptic patients.

Accompanying editorial: Teela KC, Ferguson RM, Donnay FA, Darmstadt GL: The PIERS trial: hope for averting deaths from pre-eclampsia. *Lancet* 2011; 377: 185-86.

Letter to the editor: Tajik P, Oude Rengerink K, Ganzevoort W, Zwinderman AH, Mol BW, Bossuyt PM: Prediction of preeclampsia complications. *Lancet* 2011; 377: 1313; author reply 1314.

### *Blood Pressure Trends*

28. Gaillard R, Bakker R, Willemsen SP, Hofman A, Steegers EA, Jaddoe VW: Blood pressure tracking during pregnancy and the risk of gestational hypertensive disorders: The Generation R Study. *Eur Heart J* 2011; 32: 3088-97.

Prospective cohort study (n=8482) that provides evidence that blood pressure changes track differently between hypertensive versus non-hypertensive pregnancies. Second to third trimester increases in systolic, diastolic and mean blood pressures were significantly associated with a later diagnosis of preeclampsia. Unfortunately, selection bias, measurement error (from an automated cuff) and residual confounding were major study limitations.

Accompanying editorial: Cifkova R: Can blood pressure in the first trimester predict the development of gestational hypertensive disorders? *Eur Heart J* 2011; 32: 3067-69.

## Prevention and Treatment Options

29. Rossi AC, Mullin PM: Prevention of preeclampsia with low-dose aspirin or vitamins C and E in women at high or low risk: a systematic review with metaanalysis. *Eur J Obstet Gynecol Reprod Biol* 2011; 158: 9-16.

In this meta-analysis of 15 studies published between 1988-2010, neither low-dose aspirin nor vitamin C and E were observed to significantly reduce the risk of preeclampsia in high-risk or low-risk women. Further work is needed to assess whether these regimens can reduce the severity of preeclampsia in low and high-risk groups.

30. Thadhani R, Kisner T, Hagmann H, Bossung V, Noack S, Schaarschmidt W, Jank A, Kribs A, Cornely OA, Kreyssig C et al: Pilot study of extracorporeal removal of soluble fms-like tyrosine kinase 1 in preeclampsia. *Circulation* 2011; 124: 940-50.

This interesting exploratory work shows that extracorporeal apheresis can lower circulating soluble fms-like tyrosine kinase 1 (sFlt-1) in vitro and in vivo (8 women with very preterm pre-eclampsia and elevated sFlt-1 levels). This intervention may play an important role in prolonging pregnancy and improving maternal and fetal outcomes for preterm pre-eclampsia.

## Maternal/Perinatal Outcomes

31. Thangaratnam S, Koopmans CM, Iyengar S, Zamora J, Ismail KM, Mol BW, Khan KS: Accuracy of liver function tests for predicting adverse maternal and fetal outcomes in women with preeclampsia: a systematic review. *Acta Obstet Gynecol Scand* 2011; 90: 574-85.

This systematic review pooled 13 studies and 3497 women to assess the accuracy of liver function tests (LFTs) in predicting maternal or fetal complications in women with preeclampsia. Across all studies, the sensitivity of LFTs to predict any maternal complication varied considerably (0.04-0.95). The specificity was slightly better for predicting any maternal complication (0.17-0.79). LFTs, in isolation, are unreliable in predicting complications in women with preeclampsia.

32. Liu S, Joseph KS, Liston RM, Bartholomew S, Walker M, Leon JA, Kirby RS, Sauve R, Kramer MS: Incidence, risk factors, and associated complications of eclampsia. *Obstet Gynecol* 2011; 118: 987-94.

Using a population-wide administrative dataset (n=1,910,729), investigators in this Canadian study reported that the rate of eclampsia has decreased in recent years (12.4/10,000 deliveries [in 2003] to 5.9/10,000 deliveries [in 2009]). However, eclampsia was associated with maternal/fetal death as well as major maternal morbidity (including assisted ventilation, renal failure, embolism, ARDS). Further research is needed to optimize prophylactic and therapeutic regimens to reduce the rate and severity of these adverse outcomes.

Accompanying editorial: Sibai BM: Disparity in the rate of eclampsia and adverse pregnancy outcome from eclampsia: a tale of two countries. *Obstet Gynecol* 2011; 118: 976-77.

Accompanying editorial with a salient reminder that, despite the adverse outcomes associated with eclampsia, the absolute risks for maternal death (0.34%) and severe obstetric morbidities (0.4-0.95%) are extremely low.

## Congenital Anomalies

33. Smith LK, Budd JL, Field DJ, Draper ES: Socioeconomic inequalities in outcome of pregnancy and neonatal mortality associated with congenital anomalies: population based study. *BMJ* 2011; 343: d4306.

Using a UK-based regional case registry for congenital anomalies (n=1579 fetuses), investigators observed socioeconomic differences in rates of termination after antenatal diagnosis of 9 major anomalies. Rates of termination were lower in the least deprived versus most deprived areas (63% vs 79%: rate ratio=0.8; 95% CI=0.65-0.97). After adjusting for maternal age, patients from the most deprived areas were 85% more likely to have a live births with an anomaly and 123% more likely to incur a neonatal death for congenital anomalies versus the least deprived areas. Differences in socioeconomic class among patients may influence the decision to terminate pregnancy after antenatal detection of these anomalies.

## Inherited Thrombophilias

34. Lockwood C, Wendel G: Practice bulletin no. 124: inherited thrombophilias in pregnancy. *Obstet Gynecol* 2011; 118: 730-40.

The latest Practice Bulletin from ACOG regarding screening and thromboprophylaxis for obstetric patients with inherited thrombophilias. Converting subcutaneous low-molecular weight heparin (LMWH) to unfractionated heparin (UF) for patients receiving thromboprophylaxis at 36 weeks gestation is recommended to allow for neuraxial anesthesia for labor and delivery. Discontinuing subcutaneous UF or LMWH 24-36 hr prior to scheduled induction of labor or elective CD is also advised.

## External Cephalic Version

35. Kabiri D, Elram T, Aboo-Dia M, Elami-Suzin M, Elchalal U, Ezra Y: Timing of delivery after external cephalic version and the risk for cesarean delivery. *Obstet Gynecol* 2011; 118: 209-13.

The risk of intrapartum CD after external cephalic version (ECV) has not been clearly elucidated. In this retrospective cohort study of ECV (n=502), 10% patients required intrapartum CD. The incidence of CD within 96 hr of performing ECV was 16.5%, with an increased risk for CD in primiparous and multiparous patients (OR=2.97 and 2.27 respectively). Unfortunately, the influence of analgesia for ECV on delivery outcomes was not studied.

36. Hutton EK, Hannah ME, Ross SJ, Delisle MF, Carson GD, Windrim R, Ohlsson A, Willan AR, Gafni A, Sylvestre G et al: The Early External Cephalic Version (ECV) 2 Trial: an international multicentre randomised controlled trial of timing of ECV for breech pregnancies. *BJOG* 2011; 118: 564-77.

High-quality multicenter RCT comparing delivery and perinatal outcomes in women undergoing ECV at 34/7 weeks versus  $\geq 37/7$  weeks. The rates of success (cephalic presentation) were higher for early ECV (41%) versus late ECV (49.1%); P=0.002. However, this did not translate into a lower rate of CD, and a non-significant increase in preterm birth occurred in the early ECV group. Patients should receive a full discussion of benefits versus risks according to the timing of ECV.

Letter to the editor: Hutton EK, Hannah ME, Ross SJ, Delisle MF, Carson GD, Windrim R, Ohlsson A, Willan AR, Gafni A, Sylvestre G et al: Early versus late external cephalic version Reply. *BJOG* 2011; 118: 1272-73.

37. Goetzinger KR, Harper LM, Tuuli MG, Macones GA, Colditz GA: Effect of regional anesthesia on the success rate of external cephalic version: a systematic review and meta-analysis. *Obstet Gynecol* 2011; 118: 1137-44.

In this meta-analysis pooling data from 6 RCTs, regional anesthesia was associated with increased ECV success compared to no regional anesthesia (57.6% vs 37.6%; RR=1.58; 95% CI=1.29-1.93). However, no statistically significant difference in the rate of CD was observed (48.4% vs 59.3%). Despite favorable improvements in ECV success with regional anesthesia, more work is needed to investigate why a concomitant reduction in CD rates did not occur.

## Fertility Care

38. de Graaff AA, Land JA, Kessels AG, Evers JL: Demographic age shift toward later conception results in an increased age in the subfertile population and an increased demand for medical care. *Fertil Steril* 2011; 95: 61-63.

In this interesting observational study from Holland (between 1995-2008), a demographic age shift towards later conception was accompanied by an increasing demand for fertility care at an institutional level. Specifically, for each year that the mean age at first delivery increased, the mean age of patients entering a fertility clinic increased by 1.1 yr.

## Small for Gestational Age

39. Mikolajczyk RT, Zhang J, Betran AP, Souza JP, Mori R, Gulmezoglu AM, Meriardi M: A global reference for fetal-weight and birthweight percentiles. *Lancet* 2011; 377: 1855-61.

This study comprises an innovative mathematical approach for calculating fetal weight and birthweight percentiles using current fetalweight references and adjusting for proportionality (using country-specific and obstetric co-variables). Using WHO Maternal and Perinatal data (290,610 births), investigators' classification of infants as small-for-gestational age (SGA) improved substantially after applying country or ethnic origin to the mathematical model for calculating fetal weight. Fetal growth and birthweight standards adjusted for the respective population's average birthweight can identify SGA babies who are more likely to have adverse outcomes than if no adjustment for average birthweight is made.

Accompanying editorial: Gardosi J: Fetal growth standards: individual and global perspectives. *Lancet* 2011; 377: 1812-14.

## Gestational Diabetes Mellitus

40. Durwald CP, Mele L, Spong CY, Ramin SM, Varner MW, Rouse DJ, Sciscione A, Catalano P, Saade G, Sorokin Y et al: Glycemic characteristics and neonatal outcomes of women treated for mild gestational diabetes. *Obstet Gynecol* 2011; 117: 819-27.

In this secondary analysis of a multicenter MFMU RCT of patients with gestational diabetes (GDM) (n=460), higher median fasting glucose levels in the last 2 weeks of pregnancy were observed to be significantly associated with a large-for-gestational age neonate, macrosomia and elevated C-peptide. Tight glycemic control during pregnancy is advised to optimize maternal and neonatal outcomes for patients with GDM.

41. Committee opinion no. 504: Screening and diagnosis of gestational diabetes mellitus. *Obstet Gynecol* 2011; 118: 751.

The latest Practice Bulletin from ACOG on diagnosing gestational diabetes. All pregnant patients should undergo screening, and a 100g, 3 hr oral glucose tolerance test is recommended for making a formal diagnosis.

42. Ryan EA: Diagnosing gestational diabetes. *Diabetologia* 2011; 54: 480-86.

In this excellent commentary article, the newly proposed criteria for diagnosing GDM (from the International Association of Diabetes in Pregnancy Study Groups) is questioned. The strength of association between GDM and large-for-gestational age infants, and optimal methods for population-wide screening are also reviewed.

Accompanying editorial: Long H: Diagnosing gestational diabetes: can expert opinions replace scientific evidence? *Diabetologia* 2011; 54: 2211-13.

Letter to the editor: Iafusco D, Galderisi A, Lombardo F, Scaramuzza A, Tartaglia E, Cocca A, Giugliano R, Giugliano B, Sena T, Napoli A et al: All classifications not built on pathogenesis become inadequate sooner or later. *Diabetologia* 2011; 54: 1583-84.

## Peripartum Obstetric Management and Modes of Delivery

### Cesarean Delivery

43. Tita AT, Lai Y, Landon MB, Spong CY, Leveno KJ, Varner MW, Caritis SN, Meis PJ, Wapner RJ, Sorokin Y et al: Timing of elective repeat cesarean delivery at term and maternal perioperative outcomes. *Obstet Gynecol* 2011; 117: 280-86.

Although neonatal outcomes are improved in women who undergo elective CD >39 weeks (compared to <39 weeks), the effect of timing of CD on maternal outcomes is unknown. This multicenter (NICHD-MFMU), retrospective cohort study (n=11,255) reported no reduction in composite adverse maternal outcomes in women undergoing elective CD before 39 weeks versus delivery at 39 weeks (adj OR=1.16; 95% CI=1.0-1.34). This study substantiates current practices of performing elective CD ≥39 weeks in the absence of obstetric and medical indications.

Letter to the editor: Salim R, Shalev E: Timing of elective repeat cesarean delivery at term and maternal perioperative outcomes. *Obstet Gynecol* 2011; 117: 1437; author reply 1437-38.

44. Fyfe EM, Anderson NH, North RA, Chan EH, Taylor RS, Dekker GA, McCowan LM: Risk of first-stage and second-stage cesarean delivery by maternal body mass index among nulliparous women in labor at term. *Obstet Gynecol* 2011; 117: 1315-22.

This secondary analysis using data from an established research consortium assesses the risk of CD in the 1st and 2nd stages of labor among nulliparous patients in different weight classes (n=2629). Surprisingly, only overweight and obese women were at increased risk for intrapartum CD during the 1st stage of labor (adj OR overweight=1.39, 95% CI=1.1-1.8; adj OR obese=2.9; 95% CI=2.2-3.8) but not during the 2nd stage of labor compared to women with normal BMI values. Unfortunately, neither weight gain in pregnancy nor epidural usage were accounted for in the analyses.

45. Barber EL, Lundsberg LS, Belanger K, Pettker CM, Funai EF, Illuzzi JL: Indications contributing to the increasing cesarean delivery rate. *Obstet Gynecol* 2011; 118: 29-38.

Single-center retrospective study assessing the changing indications for CD between 2003 and 2009 (n=32,443). The CD rate increased during the study period from 21% to 36%; 50% percent of this increase was attributable to primary CD. Non-reassuring fetal status was the main contributor (32%) to the total increase in the primary CD rate. Medical and non-medical factors are likely to be the main drivers for this change in practice.

46. Solheim KN, Esakoff TF, Little SE, Cheng YW, Sparks TN, Caughey AB: The effect of cesarean delivery rates on the future incidence of placenta previa, placenta accreta, and maternal mortality. *J Matern Fetal Neonatal Med* 2011; 24: 1341-46.

Investigators in this interesting study used published data and assumptions, as inputs for decision analytics, to estimate the future incidence of placenta previa, accreta and maternal death using current US birth data and assumptions on previa/accreta for multiple prior CDs. For the year 2020, the projected number of CDs is 2.2 million; the accompanying projections for obstetric-related morbidity/mortality are alarming: 730 maternal deaths, 8056 cesarean hysterectomies, and 8864 accretas.

47. ACOG Practice Bulletin No. 120: Use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol* 2011; 117: 1472-83.

Latest practice bulletin on prophylactic antibiotics from ACOG. Within 60 min before starting a CD, a single dose of a 'targeted antibiotic' (e.g. 1st generation cephalosporin) is recommended. A higher dose of prophylactic antibiotic is recommended for obese patients. Clindamycin and an aminoglycoside are suggested for patients with a history of 'significant' penicillin or cephalosporin allergy.

48. Pearson GA, Kelly B, Russell R, Dutton S, Kurinczuk JJ, MacKenzie IZ: Target decision to delivery intervals for emergency caesarean section based on neonatal outcomes and three year follow-up. *Eur J Obstet Gynecol Reprod Biol* 2011; 159: 276-81.

Retrospective study from a single-center in the UK evaluating decision-to-delivery intervals (DDI) and neonatal outcomes for 591 women undergoing emergency CD [categories 1 and 2: NICE classification]. Only three surviving babies had neurologic impairment at aged 3 yr related to perinatal ischemia (DDI were 18, 36, 61 min). Interestingly, general anesthesia was used for 58% of category 1 CD, with a shorter DDI compared to regional anesthesia (21 vs 29 min;  $P=0.02$ ). All category 2 CD were started under regional anesthesia, yet a surprisingly high proportion (8.4%) required conversion to general anesthesia.

49. Brennan DJ, Murphy M, Robson MS, O'Herlihy C: The singleton, cephalic, nulliparous woman after 36 weeks of gestation: contribution to overall cesarean delivery rates. *Obstet Gynecol* 2011; 117: 273-79.

Moderate quality, descriptive study of changing trends and indications for CD in a single obstetric center between 1974 and 2008. There were similar increases in the rates of overall CD and CD among term singleton nulliparous patients (3.8 and 3.4-fold increases respectively; correlation:  $r=0.93$ ). The increase in the induction rate among singleton nulliparous patients was presumed to be a major contributor to the overall rate of CD.

## Vaginal Delivery

### *Labor Induction*

50. Rouse DJ, Weiner SJ, Bloom SL, Varner MW, Spong CY, Ramin SM, Caritis SN, Grobman WA, Sorokin Y, Sciscione A et al: Failed labor induction: toward an objective diagnosis. *Obstet Gynecol* 2011; 117: 267-72.

Moderate quality secondary analysis of a multicenter MFMU study assessing labor induction in 1347 nulliparous women. In this study, 60% of women in the latent phase of labor who received 12 hr of oxytocin and membrane rupture required CD. Of note, rates of chorioamnionitis and uterine atony were positively associated with latent-phase duration (adj ORs for each hr of the latent phase=1.12 and 1.13 respectively;  $P<0.001$ ).

51. Kaimal AJ, Little SE, Odibo AO, Stamilio DM, Grobman WA, Long EF, Owens DK, Caughey AB: Cost-effectiveness of elective induction of labor at 41 weeks in nulliparous women. *Am J Obstet Gynecol* 2011; 204: 137.e1-9.

This study incorporated a decision analytic model with data sourced from the National Birth Cohort ( $n=200,000$ ); the incremental cost effectiveness ratio was \$10,945 for induction of labor per quality-adjusted life year gained. The results indicate that elective induction of labor at 41 weeks in nulliparous women is more cost-effective and has fewer perinatal adverse outcomes than expectant management.

52. Patterson JA, Roberts CL, Ford JB, Morris JM: Trends and outcomes of induction of labour among nullipara at term. *Aust N Z J Obstet Gynaecol* 2011; 51: 510-17.

In this retrospective, population-wide cohort study in New South Wales (Australia), the rate of term inductions in nulliparous women with singleton pregnancies increased from 6.8% to 12.5% from 2001 to 2007. More than 61% of all inductions occurred before 41 weeks' gestational age. More detailed examination of the decision-making processes and appropriateness of induction of labor before 41 weeks were highlighted in the discussion.

53. Jozwiak M, Rengerink KO, Benthem M, van Beek E, Dijksterhuis MGK, de Graaf IM, van Huizen ME, Oudijk MA, Papatsonis DNM, Perquin DAM et al: Foley catheter versus vaginal prostaglandin E2 gel for induction of labour at term (PROBAAT trial): an open-label, randomised controlled trial. *Lancet* 2011; 378: 2095-103.

High-quality multicenter RCT comparing modes of delivery and perinatal outcomes in laboring patients undergoing induction of labor (IOL) with a Foley catheter versus vaginal prostaglandin E2 gel ( $n=824$ ). The use of a Foley catheter did not reduce rates of CD compared to the use of PGE2 (23% vs 20%; risk ratio=1.13; 95% CI=0.87-1.47). Fewer patients undergoing IOL with a Foley catheter had adverse perinatal/maternal outcomes (operative deliveries; intrapartum pyrexia; uterine hyperstimulation; postpartum hemorrhage); however, these between-group differences were not statistically significant.

Accompanying editorial: Norman JE, Stock S: Intracervical Foley catheter for induction of labour. *Lancet* 2011; 378: 2054-55.

### *Bishop Scores*

54. Laughon SK, Zhang J, Troendle J, Sun L, Reddy UM: Using a simplified Bishop score to predict vaginal delivery. *Obstet Gynecol* 2011; 117: 805-11.

High-quality study to investigate the ability of a simplified Bishop score to predict vaginal delivery in uncomplicated, nulliparous pregnancies ( $n=5610$ ). On the basis of multivariate logistic regression, investigators constructed a simplified score using cervical dilatation, station and effacement. The simplified score compared favorably with the original Bishop score in predicting vaginal delivery in women undergoing either spontaneous labor or indicated inductions of labor.

Letter to the editor: Tajik P, Bossuyt PM, Willem Mol B: Using a simplified bishop score to predict vaginal delivery. *Obstet Gynecol* 2011; 118: 360; author reply 360.

### *Fetal Monitoring*

55. Chen HY, Chauhan SP, Ananth CV, Vintzileos AM, Abuhamad AZ: Electronic fetal heart rate monitoring and its relationship to neonatal and infant mortality in the United States. *Am J Obstet Gynecol* 2011; 204: 491.e1-10.

High quality retrospective cohort study that incorporated linked US birth and infant death data from 2004 ( $n=1,732,211$  singleton live births) to assess postnatal outcomes related to the use of electronic fetal monitoring (EFM) compared to no EFM. EFM was associated with reduced early neonatal mortality (RR=0.5; 95% CI=0.44-0.57) and decreased risk of Apgar scores <4 at 5 min (RR=0.54; 95% CI=0.49-0.59). The benefits of EFM appeared to be gestational age-dependent; the number needed was lowest (1:15) for gestations between 24-27 weeks. However, EFM was also associated with an increased risk of operative vaginal delivery (RR=1.39; 95% CI=1.34-1.42) and primary CD for fetal distress (RR=1.81; 95% CI=1.74-1.88).

Letter to the editor: Klebanoff MA, Branum AM, Schoendorf KC, Lynch CD: Electronic fetal heart rate monitoring and its relationship to neonatal and infant mortality in the United States. *Am J Obstet Gynecol* 2012; 206: e18-e19.

Reply by the author: Chauhan SP, Chen H-Y, Ananth CV, Vintzileos AM, Abuhamad AZ: Reply. *Am J Obstet Gynecol* 2012; 206: e19-e20.

56. Reitman E, Conell-Price J, Evansmith J, Olson L, Drosinos S, Jasper N, Randolph P, Smiley RM, Shafer S, Flood P: beta2-adrenergic receptor genotype and other variables that contribute to labor pain and progress. *Anesthesiology* 2011; 114: 927-39.

Investigators in this prospective observational study in 150 nulliparous patients used mixed-effects modeling to examine the association between genetic and demographic factors with labor pain and progress. Slower progress in labor was significantly associated with patients expressing CC allele at position 27 on the  $\beta_2$  adrenoceptor gene (ADRB2), increased weight, black patients and neuraxial analgesia. Asian ethnicity is likely to be a proxy for ADRB2 genotype. In a separate model designed to investigate predictors for labor pain, the authors noted that patients who required instrumental delivery had significantly higher pain scores in early labor compared to patients undergoing vaginal delivery, and that cold sensitivity is a significant predictor for labor pain. These mathematical models offer great potential in predicting labor progress and dynamic changes in labor pain for individual patients attempting vaginal delivery.

57. Miller RS, Smiley RM, Daniel D, Weng C, Emala CW, Blouin JL, Flood PD: Beta-2 adrenoceptor genotype and progress in term and late preterm active labor. *Am J Obstet Gynecol* 2011; 205: 137.e1-7.

Retrospective study assessing whether polymorphisms in the  $\beta_2$  adrenoceptor gene (ADRB2) influence progress of active labor in term and preterm parturients (n=401). Using linear regression, investigators reported that the rate of labor progress was slower in patients with the homozygous genotype encoding for Arg/Arg 16 compared to other genotypes (0.64 cm/hr vs 0.8 cm/hr respectively). As seen in the Reitman study (referenced above), this study opens the door to further exploratory work examining the genotypic factors that influence labor progress.

## Vaginal Birth After Cesarean Delivery

58. Ouzounian JG, Miller DA, Hiebert CJ, Battista LR, Lee RH: Vaginal birth after cesarean section: risk of uterine rupture with labor induction. *Am J Perinatol* 2011; 28: 593-96.

In this retrospective cohort study of patients undergoing trial of labor after cesarean delivery (TOLAC), investigators reported uterine rupture rates in women experiencing spontaneous onset of labor versus induced labor (1% vs 1.2% respectively;  $P=0.51$ ) (n=6832). No differences in rupture were observed between oxytocin or prostaglandin  $E_2$  induction (1.4% vs 1.0%;  $P=0.59$ ). Labor induction may not increase the risk of uterine rupture in women undergoing TOLAC.

59. Sharma PS, Eden KB, Guise JM, Jimison HB, Dolan JG: Subjective risk vs. objective risk can lead to different post-cesarean birth decisions based on multiattribute modeling. *J Clin Epidemiol* 2011; 64: 67-78.

In this thought-provoking study of how women with a prior CD determine risk related to childbirth, absolute (objective) risks of elective CD vs vaginal birth after cesarean were compared with patients' (subjective) interpretation of the same risks (n=96). Using decision analytic techniques, the results of risk modeling based on patient preference favored repeat CD (73% vs 18%;  $P<0.001$ ), as women prioritized any risk to the infant over risks to their own health. In contrast, TOLAC was associated with lower probabilities of risk to the mother with modeling using objective measures of risk. This study highlights the challenges that clinicians and patients with a prior CD face when discussing childbirth-related risks.

## Twin Delivery

60. Rossi AC, Mullin PM, Chmait RH: Neonatal outcomes of twins according to birth order, presentation and mode of delivery: a systematic review and meta-analysis. *BJOG* 2011; 118: 523-32.

In this meta-analysis (18 studies) of neonatal outcomes after twin delivery, investigators reported that the risk of neonatal morbidity and mortality was lower for twin A compared to twin B (OR=0.53 and 0.55 respectively). Favorable outcomes were generally noted for twins born by vaginal delivery compared to CD. A key observation was that the observed rate of neonatal morbidity was highest for twin B after a CD following a failed attempt at vaginal delivery compared to either vaginal or CD.

## Postpartum Period Management

### Uterotonics

61. Langesaeter E, Rosseland LA, Stubhaug A: Haemodynamic effects of oxytocin in women with severe preeclampsia. *Int J Obstet Anesth* 2011; 20: 26-29.

Observational study reporting important hemodynamic effects of 2.5 units oxytocin (using LiDCOplus) in 18 severe preeclampsia undergoing CD with spinal anesthesia. After oxytocin dosing, all patients exhibited tachycardia and an SVR decrease; however, the secondary effects on stroke volume and cardiac output were more unpredictable.

62. Yamaguchi ET, Cardoso MM, Torres ML, Nascimento RC, Ribeiro MC, Frerichs E, Payen D: Serum oxytocin concentrations in elective caesarean delivery: a randomized comparison of three infusion regimens. *Int J Obstet Anesth* 2011; 20: 224-28.

This RCT assessed the effect of three, different oxytocin infusions - Ox1=0.33 U infused over 30 min; Ox2=2.67 U infused over approx. 4 min; Ox3=2.67 U infused over 30 min - on serum oxytocin levels in patients undergoing elective CD. Serum oxytocin levels were higher at 5 and 30 mins in patients receiving Ox3 compared to Ox1 and Ox2. However formal longitudinal analysis was not performed to assess within/between group differences. Future studies are needed to determine if these increases in serum oxytocin concentration promote adequate uterine activity after delivery.

63. Sheehan SR, Montgomery AA, Carey M, McAuliffe FM, Eogan M, Gleeson R, Geary M, Murphy DJ: Oxytocin bolus versus oxytocin bolus and infusion for control of blood loss at elective caesarean section: double blind, placebo controlled, randomised trial. *BMJ* 2011; 343: d4661.

High quality multicenter double-blind RCT comparing oxytocin bolus (5 U) with and without an infusion (40 U in 500 mL Normal Saline over 4hr) in patients undergoing elective CD (n=2058). Similar proportions of patients in each group experienced major obstetric hemorrhage; however, women receiving oxytocin bolus plus infusion were less likely to receive an additional uterotonic agent than women in the bolus only group (12.2% vs 18.4%). These data suggest that the use of a post-bolus 'maintenance' oxytocin infusion is advantageous.

64. Moertl M, Friedrich S, Kraschl J, Wadsack C, Lang U, Schlembach D: Haemodynamic effects of carbetocin and oxytocin given as intravenous bolus on women undergoing caesarean delivery: a randomised trial. *BJOG* 2011; 118: 1349-56.

RCT comparing the hemodynamic effects of a bolus of 5U oxytocin versus 100 mcg carbetocin in women undergoing elective CD (n=56). Similar hemodynamic perturbation was observed in each study group (maximal increase in HR=18 bpm vs 14 bpm, and maximal decrease in systolic BP=27 vs 23 mmHg with

oxytocin vs carbetocin respectively). Peak effects were observed for both drugs at 30-40s after dosing. Further studies assessing the minimal effective dose of carbetocin based on hemodynamic and uterotonic effects are warranted.

## Thromboprophylaxis

65. Boyce H, Hume-Smith H, Ng J, Columb MO, Stocks GM: Use of thromboelastography to guide thromboprophylaxis after caesarean section. *Int J Obstet Anesth* 2011; 20: 213-18.

Prospective observational study to quantify the anticoagulant effect of unfractionated subcutaneous heparin (7500 u subcutaneous) using thromboelastography (TEG) and laboratory analyses in 19 women undergoing elective CD. In the first 4 hr post-CD, anti-Xa levels were predominantly undetectable in all patients, and there was limited TEG evidence of a heparin effect (based on r time using native/heparinase samples). Overall, a dose of 7500 u subcutaneous heparin produced, at best, a modest hypocoagulable effect post-CD.

66. Roeters van Lennep JE, Meijer E, Klumper FJ, Middeldorp JM, Bloemenkamp KW, Middeldorp S: Prophylaxis with low-dose low-molecular-weight heparin during pregnancy and postpartum: is it effective? *J Thromb Haemost* 2011; 9: 473-80.

Retrospective cohort study evaluating the incidence of venous thromboembolism (VTE) in patients at intermediate or high-risk for VTE, who received prophylaxis with low-dose low-molecular weight heparin (LMWH) in 126 pregnancies. All events occurred in women considered at high risk for VTE receiving LMWH, with the vast majority receiving nadroparin 2850 anti-Xa IU during the antepartum and postpartum periods. The incidence of VTE was surprisingly high: 5.5%; 95% CI=2.4-12.3%. The efficacy of thromboprophylactic dosing with nadroparin in at-risk patient subpopulations should be questioned.

Letter to the editor: Lindqvist PG, Hellgren M: Is obstetric thromboprophylaxis with low-molecular-weight heparin effective? Yes, if administered properly. *J Thromb Haemost* 2011; 9: 1669-70.

Patel JP, Patel RK, Davies JG, Arya R: Prophylaxis with low-dose low molecular weight heparin during pregnancy and the puerperium: is it effective? A rebuttal. *J Thromb Haemost* 2011; 9: 1269-71; author reply 1272-73.

Stratta P, Canavese C, Cena T, Quaglia M, Pergolini P, Bellomo G, Magnani C: Low-molecular-weight-heparin and pregnancy, when the dose does it: a nephrologist's opinion: a rebuttal. *J Thromb Haemost* 2011; 9: 2127-29; author reply 2129-30.

## Psychiatric Disease

67. Munk-Olsen T, Laursen TM, Pedersen CB, Lidegaard O, Mortensen PB: Induced first-trimester abortion and risk of mental disorder. *N Engl J Med* 2011; 364: 332-39.

High quality population-based cohort study (n=84620) to assess if first trimester abortion was associated with an increased risk of subsequent psychiatric referral. The observed incidence rate of psychiatric contact within 12 months after induced first-trimester abortion (14.6 per 1000 person-years; 95% CI=13.7-15.6) was similar to the rate during the 9 month period prior to abortion (13.7; 95% CI=14.4-16.1), which did not support the primary study hypothesis.

## Maternal Mortality

68. Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM: Anesthesia-related maternal mortality in the United States: 1979-2002. *Obstet Gynecol* 2011; 117: 69-74.

Based on data from the CDC, a dramatic reduction (59%) in anesthetic-related maternal deaths in the USA from 1979-1990 compared to 1991-2002 (2.9 deaths vs 1.2 deaths per million live births respectively) has occurred. Improvements in

anesthetic monitoring and difficult airway/failed intubation management are likely to have been instrumental in: (i) reducing the case fatality rates due to general anesthesia (GA); and (ii) promoting the reduction in the rate ratio for maternal death due to GA versus regional anesthesia. Unfortunately, familiar causes of death associated with GA remain prevalent - intubation failure/complications due to induction (23%). High spinal and epidural blocks were reported as the leading causes of death (26%) due to regional anesthesia.

69. Paxton A, Wardlaw T: Are we making progress in maternal mortality? *N Engl J Med* 2011; 364: 1990-93.

Commentary article on recent changes in international rates of maternal mortality. Improvements in access of health resources and obstetrical care have contributed to a 2.3% decline in the global maternal mortality ratio between 1990 and 2008 (UN interagency estimates).

70. The California Pregnancy-Associated Mortality Review. Report from the 2002 and 2003 Maternal Death Reviews. Sacramento. California Department of Public Health, Maternal Child and Adolescent Health Division. 2011. <http://cdph.ca.gov/data/statistics/Documents/MO-CA-PAMR-MaternalDeathReview-2002-03.pdf>.

This is must-read document comprises detailed information of maternal deaths reported in California from 2002 and 2003 (from the California Pregnancy-Associated Mortality Review); 386 women died during childbirth or within one year of a live birth or fetal death, 98 of whom died of causes directly related to pregnancy or pregnancy management. Reported disparities in outcome were based on race, income and education. On the basis of case reviews, cardiovascular disease was a leading cause (20%) of pregnancy-related death.

71. Centre for Maternal and Child Enquiries (CMACE): Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG* 2011; 118 Suppl 1: 1-203.

Key report of 261 maternal deaths in the UK that occurred between 2006-2008. The maternal mortality rate for this triennium was 11.39/100,000 maternities. Rates of death from maternal causes decreased due to presumed improvements in the prevention and treatment of thromboembolism and hemorrhage. Cardiac disease remained the leading indirect cause of maternal death (2.31/100,000 maternities). The overall rate of death from sepsis also increased (1.13 deaths/100,000 maternities). Key recommendations for reducing the number of maternal deaths, especially for high-risk parturients, center on improving the quality of interdisciplinary and subspecialist maternal care and ease of patient access to experienced maternal care providers.

Editorials affiliated with the CMACE report:

Reidy J, Russell R: Cmac 2006-2008. *Int J Obstet Anesth* 2011; 20: 208-12.

Wong CA: Saving mothers' lives: the 2006-8 anaesthesia perspective. *Br J Anaesth* 2011; 107: 119-22.

Nelson-Piercy C, Mackillop L, Williams DJ, Williamson C, Swiet M, Redman C: Maternal mortality in the UK and the need for obstetric physicians. *BMJ* 2011; 343: d4993.

Editorial stressing importance of obstetric physicians' early recognition of comorbid states that may be exacerbated by pregnancy and potentially lead to major maternal morbidity or mortality.

Review article related to CMACE report:

McClure JH, Cooper GM, Clutton-Brock TH: Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006-8: a review. *Br J Anaesth* 2011; 107: 127-32.

A summary review of CMACE findings relevant to anesthesiologists and intensive care physicians caring for obstetric patients. Deaths directly or indirectly related to anesthetic interventions are reviewed and discussed.

72. MacKay AP, Berg CJ, Liu X, Duran C, Hoyert DL: Changes in pregnancy mortality ascertainment: United States, 1999-2005. *Obstet Gynecol* 2011; 118: 104-10.

In this study investigators assessed the effects of the 1999 transition from ICD-9 to ICD-10 coding, and check boxes related to pregnancy status on US death certificates (since 2003) on pregnancy-related deaths were assessed. Using data from the National Vital Statistics System and Pregnancy Mortality Surveillance System, investigators found the maternal mortality ratio had increased significantly from 1995-7 to 1999-2002 to 2003-2005 (11.6; 13.1, and 15.3 respectively). Unfortunately, the ICD coding changes and 2003 death certificate revisions ('check boxes') have almost certainly influenced data reporting for maternal deaths in the US, and thus negatively impacted on the interpretation of pregnancy related and maternal mortality ratios.

73. Lozano R, Wang H, Foreman KJ, Rajaratnam JK, Naghavi M, Marcus JR, Dwyer-Lindgren L, Lofgren KT, Phillips D, Atkinson C et al: Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis. *Lancet* 2011; 378: 1139-65.

Based on expanded access to international data sources, this paper is a highly impressive analysis of maternal and child mortality for the world's poorest countries. Alternative population-wide modeling for maternal mortality was performed to generate estimates for maternal death in 2011. Only 13 countries, representing 19% of livebirths in developing countries, were likely to achieve MDG 5 targets by 2015. Although improvements in maternal mortality have occurred (409,100 deaths in 1990; 273,500 deaths in 2011), the pace of change has been sluggish. More international effort and action has been called for to achieve the MDG 4 and 5 targets.

Accompanying editorial: Byass P, Graham WJ: Grappling with uncertainties along the MDG trail. *Lancet* 2011; 378: 1119-20.

74. Bonnet M-P, Deneux-Tharoux C, Bouvier-Colle M-H: Critical care and transfusion management in maternal deaths from postpartum haemorrhage. *Eur J Obstet Gynecol Reprod Biol* 2011; 158: 183-88.

Retrospective study of suspected root causes for 38 maternal deaths due to postpartum hemorrhage in France. Suboptimal practices identified as having a major contributory role included: inadequate hemodynamic monitoring, lack of laboratory assessment, and delays in transfusion. Of note, 5 patients developed cardiac arrest after induction of general anesthesia, and five patients were extubated, despite active hemorrhage.

## Cardiac Arrest and Resuscitation

75. Jeejeebhoy FM, Zelop CM, Windrim R, Carvalho JC, Dorian P, Morrison LJ: Management of cardiac arrest in pregnancy: a systematic review. *Resuscitation* 2011; 82: 801-09.

Systematic review of studies related to resuscitation of pregnant patients experiencing cardiac arrest. Unsurprisingly, there are only five studies assessing maternal outcomes and optimal modes of resuscitation. Key findings were that perimortem CD is rarely performed within five minutes of onset of maternal arrest (see reference 202), and the quality of chest compressions is lessened due to left lateral tilt. This review highlights the lack of scientific evidence on optimal resuscitative strategies for the parturient during cardiac arrest.

Accompanying editorial: King SE, Gabbott DA: Maternal cardiac arrest—Rarely occurs, rarely researched. *Resuscitation* 2011; 82: 795-96.

# Maternal Morbidity

## Venous Thromboembolism

76. Duran-Mendicuti A, Sodickson A: Imaging evaluation of the pregnant patient with suspected pulmonary embolism. *Int J Obstet Anesth* 2011; 20: 51-59.

Detailed review article which provides useful information on different radiologic diagnostic modalities for confirming the diagnosis of venous thromboembolic disease, including a diagnostic imaging algorithm for patients with suspected pulmonary embolism.

77. Ferres MA, Olivarez SA, Trinh V, Davidson C, Sangi-Haghpeykar H, Aagaard-Tillery KM: Rate of wound complications with enoxaparin use among women at high risk for postpartum thrombosis. *Obstet Gynecol* 2011; 117: 119-24.

Retrospective cohort study to identify wound complications (wound separation, hematoma) in 'at-risk' post-cesarean patients (n=1677) receiving enoxaparin thromboprophylaxis versus 'at-risk' controls (no enoxaparin; n=1024). Inconsistent effects were observed, including a higher rate of wound separation (6.8% vs 3.6%; P=0.003) in the enoxaparin group versus control group respectively, with no between-group difference in the rate of wound hematoma. The study was underpowered for assessing between-group differences in rates of VTE.

78. Practice Bulletin No. 123: Thromboembolism in Pregnancy. *Obstet Gynecol* 2011; 118: 718-29.

The latest practice bulletin from ACOG provides guidelines for using prophylactic and therapeutic anticoagulation regimens in the antepartum and postpartum periods. Consideration for converting LMWH to unfractionated heparin (UH) from 36 weeks gestation is advised, and ACOG recommend ASRA guidelines for timing neuraxial blockade in patients anticoagulated with LMWH and UH. Restarting UH or LMWH is advised >4-6 hr after vaginal delivery, and >6-12 hr post-CD.

79. Jackson E, Curtis KM, Gaffield ME: Risk of venous thromboembolism during the postpartum period: a systematic review. *Obstet Gynecol* 2011; 117: 691-703.

Excellent systematic review of risk of VTE for postpartum patients. Key findings are that incidence rates for VTE during the first six weeks postpartum are 2.5-21.5 times greater than in nonpregnant women. Of note, the incidence of VTE was highest immediately after delivery. Unfortunately no studies in this review stratified VTE rates according to known risk factors.

80. Blondon M: Thromboprophylaxis after cesarean section: decision analysis. *Thromb Res* 2011; 127 Suppl 3: S9-S12.

Interesting review describing a decision-analysis for justifying 7 day thromboprophylaxis with LMWH versus no prophylaxis after CD. A modest net gain of 1.5 days in quality-adjusted life expectancy per treated patient was calculated with LMWH prophylaxis, assuming a VTE incidence=0.22% in low-risk women. Using different case scenarios, LMWH had a greater impact in reducing thrombotic events than inducing major hemorrhage events in women with known risk factors for VTE: smoking, obesity, emergency CD.

81. Virkus RA, Lokkegaard EC, Bergholt T, Mogensen U, Langhoff-Roos J, Lidegaard O: Venous thromboembolism in pregnant and puerperal women in Denmark 1995-2005. A national cohort study. *Thromb Haemost* 2011; 106: 304-09.

Data from all Danish women of childbearing age was used in this retrospective cohort study to assess incidence rates of VTE in pregnancy and the puerperium over a 10 yr period (n=817,751). The risk of VTE increased exponentially during

pregnancy, reaching peak levels in the early postpartum period (unadj risk=60 per 10,000 pregnant years). Interestingly, risk was not affected by maternal age; however, the incidence of postpartum thromboprophylaxis was not reported.

## Postpartum Hemorrhage

### *Associative Factors/Risk Factors for Postpartum Hemorrhage*

82. Driessen M, Bouvier-Colle MH, Dupont C, Khoshnood B, Rudigoz RC, Deneux-Tharaux C: Postpartum hemorrhage resulting from uterine atony after vaginal delivery: factors associated with severity. *Obstet Gynecol* 2011; 117: 21-31.

High-quality retrospective cohort study assessing risk factors associated with severe postpartum hemorrhage (PPH) due to uterine atony after vaginal delivery (n=4550). Interestingly, delays in the provision of care, including: oxytocin administration, alerting an obstetrician and anesthesiologist, manual examination of the uterus and delivery in a public, non-university hospital were independently associated with severe PPH. One of the most interesting findings was that the use of epidural anesthesia was found to be a protective risk factor for severe PPH.

Accompanying editorial: Zelop CM: Postpartum hemorrhage: becoming more evidence-based. *Obstet Gynecol* 2011; 117: 3-5.

83. Sosa CG, Althabe F, Belizan JM, Buekens P: Use of oxytocin during early stages of labor and its effect on active management of third stage of labor. *Am J Obstet Gynecol* 2011; 204: 238.e1-5.

Secondary analysis of a multicenter RCT study of vaginal deliveries in South America (n=11,323). The effect of oxytocin for induction or augmentation of labor on the incidence of PPH was assessed in women receiving active management of the third stage of labor (AMTSL). Surprisingly, there were no significant associations between induced/augmented labor and moderate PPH, severe PPH and blood transfusion among patients undergoing AMTSL. Unfortunately the temporal and dose-related effects of oxytocin in labor on the primary outcomes were not assessed.

84. Blomberg M: Maternal obesity and risk of postpartum hemorrhage. *Obstet Gynecol* 2011; 118: 561-68.

In this population-wide study investigators studied whether differences in prevalence of PPH exist among patients according to body mass index (BMI) class (n=1,114,071). The main finding was that the risk of atonic hemorrhage increased with increasing BMI class – adj OR for patients with BMI $\geq$ 40 versus normal BMI group=2.14. The effects of anesthesia, oxytocin and other uterotonics were not accounted for in the analyses.

85. Gayat E, Resche-Rigon M, Morel O, Rossignol M, Mantz J, Nicolas-Robin A, Nathan-Denizot N, Lefrant JY, Mercier FJ, Samain E et al: Predictive factors of advanced interventional procedures in a multicentre severe postpartum haemorrhage study. *Intensive Care Med* 2011; 37: 1816-25.

Retrospective study investigating prediction factors for severe PPH requiring specialized treatment (uterine artery embolization or surgical intervention) following initial resuscitation. Five independent predictors for severe PPH were abnormal placental implantation, INR  $>$ 1.64, fibrinogen  $<$ 2g/dl, a detectable troponin I level, and maternal heart rate  $>$ 115 bpm. Prediction models for severe PPH had moderate accuracy (AUROC =approx. 0.8 [2 cohorts: n=257 and 239]). Unfortunately, predictive factors were not assessed in non or poorly-resuscitated patients during the early stages of severe PPH. Variations in clinical practice, such as specialized treatment versus medical management for severe PPH. limit the clinical applicability of this model.

86. Grotegut CA, Paglia MJ, Johnson LN, Thames B, James AH: Oxytocin exposure during labor among women with postpartum hemorrhage secondary to uterine atony. *Am J Obstet Gynecol* 2011; 204: 56.e1-6.

Case-control study investigating the influence of oxytocin during labor on severe PPH secondary to uterine atony (n=108). Oxytocin exposure, calculated as area under the curve, was significantly higher in women with severe PPH versus control (adj. OR=1.58; 95% CI=1.05-2.57). These data add support to prior findings that oxytocin receptor desensitization and reduced contractile responsiveness occur with exogenous oxytocin administration.

87. Chang CC, Wang IT, Chen YH, Lin HC: Anesthetic management as a risk factor for postpartum hemorrhage after cesarean deliveries. *Am J Obstet Gynecol* 2011; 205: 462.e1-7.

Using nationwide Taiwanese datasets, investigators assessed the association between anesthetic modality for CD (general versus regional) and PPH (n=67,328). The adjusted OR for PPH with general anesthesia was 8.15 higher (95% CI=6.43-10.33) than for epidural/spinal anesthesia. Severity of PPH is likely to have confounded results in the multivariate analyses.

### *Placenta Accreta*

88. Eller AG, Bennett MA, Sharshiner M, Masheter C, Soisson AP, Dodson M, Silver RM: Maternal morbidity in cases of placenta accreta managed by a multidisciplinary care team compared with standard obstetric care. *Obstet Gynecol* 2011; 117: 331-37.

Retrospective cohort study comparing maternal outcomes in patients with placenta accreta delivering in tertiary-care obstetric centers with multidisciplinary care (n=79) versus standard care obstetric centers (n=62) in Utah. Delivery at a tertiary-care center reduced composite early maternal morbidity (OR=0.46; 95% CI=0.22-0.95). Interestingly, a higher proportion of cases initially managed with regional anesthesia were converted to general anesthesia at a standard versus tertiary-care center (36% vs 8%; P $<$ 0.01).

89. Wright JD, Pri-Paz S, Herzog TJ, Shah M, Bonanno C, Lewin SN, Simpson LL, Gaddipati S, Sun X, D'Alton ME et al: Predictors of massive blood loss in women with placenta accreta. *Am J Obstet Gynecol* 2011; 205: 38.e1-6.

Single-center descriptive study of transfusion outcomes in a cohort (n=77) with placenta accreta. Median blood loss was 5000 mL, and median red cell transfusion was five units. Predictors for major hemorrhage/massive transfusion could not be clearly elucidated due to the limited size of the study cohort.

90. Sadashivaiah J, Wilson R, Thein A, McLure H, Hammond CJ, Lyons G: Role of prophylactic uterine artery balloon catheters in the management of women with suspected placenta accreta. *Int J Obstet Anesth* 2011; 20: 282-87.

For caption – see reference 91.

91. Lilker SJ, Meyer RA, Downey KN, Macarthur AJ: Anesthetic considerations for placenta accreta. *Int J Obstet Anesth* 2011; 20: 288-92.

Two interesting case series detailing the anesthetic management for placenta accreta using varying neuraxial anesthetic techniques (epidural de-novo; 'two-space' combined spinal and epidural technique). Lilker et al. studied 17 patients who received neuraxial anesthesia for CD, five of whom required intraoperative conversion to general anesthesia for excessive bleeding. Sadashivaiah et al. reported two cases of fetal bradycardia following uterine artery balloon catheterization prior to CD.

### *Pharmacologic and Non-Pharmacologic Therapeutic Regimens*

92. Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M: Specific second-line therapies for postpartum haemorrhage: a national cohort study. *BJOG* 2011; 118: 856-64.

Interesting UK study describing outcomes following 2nd line therapy for PPH (n=471). Despite obvious heterogeneity amongst cases, success rates due to uterine compression sutures (75%) and interventional radiologic techniques (89%) were higher than recombinant factor VIIa (31%) and vessel ligation (36%).

93. Thon S, McLintic A, Wagner Y: Prophylactic endovascular placement of internal iliac occlusion balloon catheters in parturients with placenta accreta: a retrospective case series. *Int J Obstet Anesth* 2011; 20: 64-70.

Case series (n=14) highlighting important complications and unpredictable efficacy of internal iliac balloon catheterization (IIBC) performed for patients with abnormal placentation. Procedure-related vascular complications highlight the uncertain clinical value of IIBC in this setting.

Letter to the editor: Palacios-Jaraquemada JM: Proximal vascular control in cases of abnormal placentation. *Int J Obstet Anesth* 2011; 20: 266.

94. Logan AC, Yank V, Stafford RS: Off-label use of recombinant factor VIIa in U.S. hospitals: analysis of hospital records. *Ann Intern Med* 2011; 154: 516-22.

Interesting retrospective study detailing the estimated national usage of recombinant factor VIIa (rVIIa) based on data sourced from 615 US academic and non-academic hospitals. From 2000-2008, the off-label use of rVIIa increased 140-fold; 672 cases (0.9% of total) were obstetric hemorrhage who received rVIIa (15% died, 78% discharged home, 8% required further care). Despite the lack of robust evidence to justify the therapeutic efficacy of rVIIa, these data highlight the increasing off-label use of rVIIa for presumed obstetric and nonobstetric hemorrhage.

Accompanying editorial: Avorn J, Kesselheim A: A hemorrhage of off-label use. *Ann Intern Med* 2011; 154: 566-67.

Letters to the editor: Hayanga AJ: Off-label use of recombinant factor VIIa. *Ann Intern Med* 2011; 155: 337-38; author reply 338-39.

Phillips A: Off-label use of recombinant factor VIIa. *Ann Intern Med* 2011; 155: 337; author reply 338-39.

95. Lester F, Stenson A, Meyer C, Morris J, Vargas J, Miller S: Impact of the Non-pneumatic Antishock Garment on pelvic blood flow in healthy postpartum women. *Am J Obstet Gynecol* 2011; 204: 409.e1-5.

In this interesting prospective observational study, the impact of a non-pneumatic antishock garment (NASG) on the resistive index (RI) in the internal iliac artery, as a marker for approximating pelvic blood flow, was investigated in 10 postpartum patients. With full application of the NASG (leg, pelvic and abdominal segments), the RI values (1.05) were significantly higher than baseline values with no NASG applied (RI=0.83). These data provides a physiologic basis for using NASG as a therapeutic intervention for PPH.

### Cell Salvage

96. Ralph CJ, Sullivan I, Faulds J: Intraoperative cell salvaged blood as part of a blood conservation strategy in Caesarean section: is fetal red cell contamination important? *Br J Anaesth* 2011; 107: 404-408.

In this single-center descriptive study, cell salvage was used for 70 women undergoing CD. Volumes of salvaged blood infused were moderate (median [range]=324 mL [119-1690 mL]). No adverse maternal outcomes were reported. Fetal red blood cell volumes (FRCV) in the re-infused blood were small (median [range]=0.8 mL [0.2-12.9 mL]). The relevance of FRCV in the development of maternal alloimmunization is uncertain.

### Laboratory Tests and Postpartum Hemorrhage

97. de Lloyd L, Bovington R, Kaye A, Collis RE, Rayment R, Sanders J, Rees A, Collins PW: Standard haemostatic tests following major obstetric haemorrhage. *Int J Obstet Anesth* 2011; 20: 135-41.

Single-center retrospective study investigating hematologic indices and transfusion data in 456 patients with severe PPH ( $\geq 1500$  mL blood loss) over

a 3 yr period. The most interesting finding was that fibrinogen levels had the strongest association with blood loss ( $r=0.4$ ;  $P<0.01$ ) unlike other parameters (PT, aPTT). These results add to prior work indicating that fibrinogen levels appear to be sensitive to early and severe changes in blood loss in severe PPH.

### Protocols for Obstetric Hemorrhage Management

98. Shields LE, Smalarz K, Reffigee L, Mugg S, Burdumy TJ, Propst M: Comprehensive maternal hemorrhage protocols improve patient safety and reduce utilization of blood products. *Am J Obstet Gynecol* 2011; 205: 368.e1-8.

This article describes a structured protocol, designed on the basis of degree of blood loss and subjective response to intervention, for treating maternal hemorrhage. After protocol implementation at a medium sized obstetric center (<3000 deliveries/year), crude data analyses suggested a reduction in hemorrhage-related morbidity: earlier resolution of bleeding, the use of fewer blood products and reduced coagulopathy. Rates of severe bleeding (blood loss >1500 mL) were similar pre versus post protocol, suggesting that more strategic intervention may be necessary to improve outcomes in patients experiencing major hemorrhage.

### Genital Tract Trauma

99. Landy HJ, Laughon SK, Bailit JL, Kominiarek MA, Gonzalez-Quintero VH, Ramirez M, Haberman S, Hibbard J, Wilkins I, Branch DW et al: Characteristics associated with severe perineal and cervical lacerations during vaginal delivery. *Obstet Gynecol* 2011; 117: 627-35.

Multicenter, observational study exploring risk factors for 3rd/4th degree vaginal lacerations and cervical lacerations in patients undergoing vaginal delivery (n=87,267). The strongest risk factors for 3rd/4th degree lacerations were nulliparity (7.2-fold risk), being an Asian or Pacific-Islander, increasing birth weight, episiotomy, long second stage and operative vaginal delivery. Risk factors for cervical laceration were heterogeneous among nulliparous and multiparous patient groups; however, cerclage stood out as a strong risk factor in both groups (nulliparous: OR=3.7; multiparous: 12.7). Of note, epidural analgesia was significantly associated with a reduced risk of 3rd/4th degree lacerations in nulliparous and multiparous patients (OR=0.7 and 0.5 respectively).

### Stroke

100. Kuklina EV, Tong X, Bansil P, George MG, Callaghan WM: Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: reasons for concern? *Stroke* 2011; 42: 2564-70.

Using hospitalization data from the Nationwide Inpatient Sample, investigators in this observational study reported trends and risk factors for in-hospital pregnancy-related stroke. The rate of all-cause stroke increased between 1994-1995 and 2006-2007 for antenatal hospitalizations (0.15 to 0.22 per 1000 deliveries) and postpartum hospitalizations (0.12 to 0.22 per 1000 deliveries). Hypertensive disease and heart disease were highlighted as important risk factors associated with stroke, particularly among postpartum hospitalizations.

### Cardiomyopathy

101. Gunderson EP, Croen LA, Chiang V, Yoshida CK, Walton D, Go AS: Epidemiology of peripartum cardiomyopathy: incidence, predictors, and outcomes. *Obstet Gynecol* 2011; 118: 583-91.

Retrospective study using data from Kaiser Northern California and state databases (between 1995-2004) to investigate the incidence and risk factors for peripartum cardiomyopathy (n=227,224). The incidence was 4.84 per 10,000 live births (95% CI=3.98-5.83), and was highest among women aged  $\geq 40$  yr. A progressive increase in the risk of cardiomyopathy with severity of hypertensive disorders was observed (independent of other risk factors). The 3 yr postdelivery mortality rate was 1.8%.

## Surgical Site Infections

102. Tsai PS, Hsu CS, Fan YC, Huang CJ: General anaesthesia is associated with increased risk of surgical site infection after Caesarean delivery compared with neuraxial anaesthesia: a population-based study. *Br J Anaesth* 2011; 107: 757-61.

Retrospective cohort study assessing differences in surgical site infection (SSI) among Taiwanese patients undergoing neuraxial anesthesia (NA) versus general anesthesia (GA) for CD (n=303,834). Using a national dataset, investigators found the risk of SSI upto 30 days post-CD was higher among patients undergoing GA compared to NA (adjusted OR=3.73; 95% CI=3.07-4.53). Of note, prophylactic antibiotics (dosing and timing of delivery), BMI, and information validating methods of anesthesia were not accounted for in this study.

## Amniotic Fluid Embolus

103. Leighton BL, Wall MH, Lockhart EM, Phillips LE, Zatta AJ: Use of recombinant factor VIIa in patients with amniotic fluid embolism: a systematic review of case reports. *Anesthesiology* 2011; 115: 1201-208.

In this review of case reports of amniotic fluid embolism from 2003-2009, a higher proportion (14 of 16 of patients who received recombinant factor VIIa (rVIIa) had negative outcomes - permanent disability or death - compared to 11 of 28 patients not receiving rVIIa (risk ratio=2.2 (95% CI=1.4-3.7)). Ascertaining true between-group differences in patient outcomes was limited for several reasons: the retrospective study design; probable reporting biases; a wide dosing range in the cohort receiving rVIIa; and missing data on the blood loss, clinical indications and timing of rVIIa therapy during resuscitation.

## Anesthesia-related Maternal Morbidity

104. Paech MJ, Doherty DA, Christmas T, Wong CA: The volume of blood for epidural blood patch in obstetrics: a randomized, blinded clinical trial. *Anesth Analg* 2011; 113: 126-33.

Multicenter prospective, single-blinded randomized trial (n=121) to compare the therapeutic effects of different volumes of autologous blood (15mL, 20mL, 30mL) as an epidural blood patch for treating postdural puncture headache (PDPH). No differences between groups in the incidence of partial-complete and complete relief of PDPH were observed, however patients who received 15 mL blood experienced the highest postprocedural back pain scores. Based on this study, the optimal volume for blood injection is 20mL.

105. Paranjothy S, Griffiths JD, Broughton HK, Gyte GM, Brown HC, Thomas J: Interventions at caesarean section for reducing the risk of aspiration pneumonitis. *Int J Obstet Anesth* 2011; 20: 142-48.

Meta-analysis of 22 studies (n=2658) demonstrating that antacids, H2 antagonists and proton-pump inhibitors reduce the risk of intragastric pH <2.5 compared to placebo or no treatment. Combined use of antacids and H2 antagonists also reduces the risk of intragastric pH <2.5 compared to placebo or antacids alone (RR 0.02; 95% CI 0-0.2). The quality of the pooled studies was weak, and the use of surrogate markers of aspiration pneumonitis (gastric pH; gastric volume) requires formal validation.

## Predicting Severe Maternal Morbidity/Mortality Among Obstetric Patients

106. Mhyre JM, Bateman BT, Leffert LR: Influence of patient comorbidities on the risk of near-miss maternal morbidity or mortality. *Anesthesiology* 2011; 115: 963-72.

Using a population-wide, administrative dataset, study investigators aimed to identify predictive factors associated with near-miss morbidity or mortality. Using ICD-9 codes, near miss morbidity was defined as a major medical/obstetric complication and a prolonged hospital stay or discharge to a second medical

facility. Patients with pulmonary hypertension (98/1000 deliveries), malignancy (23/1000 deliveries), and systemic lupus erythematosus (21/1000 deliveries) had the highest rates of near-miss morbidity/mortality. Future clinical studies are needed to investigate the true nature of near-miss morbidity, validate relevant predictive factors and improve preventative strategies to reduce rates of near-miss morbidity and maternal death.

107. Lapinsky SE, Hallett D, Collop N, Drover J, Lavercombe P, Leeman M, Moola S, Paruk F, Bernstein M, Moodley J: Evaluation of standard and modified severity of illness scores in the obstetric patient. *J Crit Care* 2011; 26: 535.e1-7.

In this retrospective study, investigators tested two well-described severity of illness scoring systems, APACHE-II and SAPS-II risk prediction scores for discrimination and calibration using a multicenter, obstetric cohort (n=332). Reasonable discrimination was observed: AUROC=0.82 for APACHE-II and 0.78 for SAPS-II. Interestingly, no improvement was observed after each score was modified to account for altered physiologic changes in pregnancy.

108. Farquhar C, Sadler L, Masson V, Bohm G, Haslam A: Beyond the numbers: classifying contributory factors and potentially avoidable maternal deaths in New Zealand, 2006-2009. *Am J Obstet Gynecol* 2011; 205: 331.e1-8.

In this retrospective root-cause review of 49 maternal deaths in New Zealand between 2006-2009, the authors describe a new classification system for reporting contributory factors linked to these deaths. A panel of reviewers identified potential avoidability in 35% of maternal deaths. This innovative approach to 'root cause' analysis may lead to important policy changes for improving maternal quality of care at a national level.

## Pregnancy Basic Science and Physiology

### Implantation

109. Li Q, Kannan A, DeMayo FJ, Lydon JP, Cooke PS, Yamagishi H, Srivastava D, Bagchi MK, Bagchi IC: The antiproliferative action of progesterone in uterine epithelium is mediated by Hand2. *Science* 2011; 331: 912-16.

In this high-quality murine study, the intrinsic cellular mechanisms by which progesterone influences implantation are detailed. Progesterone regulates Hand2, a key transcription factor, which ultimately suppresses estrogen-mediated cell proliferation by inhibiting fibroblast growth factor expression.

Accompanying journal perspective: Hewitt SC, Korach KS: Cell biology. A hand to support the implantation window. *Science* 2011; 331: 863-64.

### Metabolic Pathways at the Placental Level

110. Bonnin A, Goeden N, Chen K, Wilson ML, King J, Shih JC, Blakely RD, Deneris ES, Levitt P: A transient placental source of serotonin for the fetal forebrain. *Nature* 2011; 472: 347-50.

This high-quality murine study identified the placenta as a site of serotonin (5-HT) production. Using an innovative ex-vivo model to deliver exogenous maternal tryptophan precursor, investigators observed that metabolism of these precursors by the placenta led to subsequent 5-HT production. As 5-HT is known to be an important neurotransmitter for fetal development, impaired placental production of 5-HT may have important clinical relevance for adult psychiatric disorders associated with defective 5-HT transmission.

Accompanying journal article: McKay R: Developmental biology: Remarkable role for the placenta. *Nature* 2011; 472: 298-99.

## Chorioamnionitis and Neurodevelopment

111. Burd I, Brown A, Gonzalez JM, Chai J, Elovitz MA: A mouse model of term chorioamnionitis: unraveling causes of adverse neurological outcomes. *Reprod Sci* 2011; 18: 900-907.

In this study using term mice, intrauterine inflammation was induced with lipopolysaccharide (LPS) or saline. Neuronal cell injury was observed in LPS mice, which was characterized by abnormal cytoskeletal formation and decreased neuronal arborization (with immunocytochemistry) with evidence of fetal brain inflammation. These results provide supporting mechanistic evidence to indicate how long-term fetal brain injury may develop after exposure to chorioamnionitis at term.

112. Elovitz MA, Brown AG, Breen K, Anton L, Maubert M, Burd I: Intrauterine inflammation, insufficient to induce parturition, still evokes fetal and neonatal brain injury. *Int J Dev Neurosci* 2011; 29: 663-71.

Accompanying murine study to Burd study (reference 111) suggesting that intrauterine inflammation (IUI) without accompanying maternal inflammation can cause neuronal injury in the fetus during the term and preterm period. Also, differences in gene expression in the fetal brain at the time of IUI may lead to heterogeneity in postnatal neurobehavioural outcomes. Worryingly, the authors speculate that IUI that does not cause preterm labor but may still evoke injury to the developing fetal brain.

## Intra-Uterine Growth Retardation and Adult-onset Diabetes

113. Pinney SE, Jaeckle Santos LJ, Han Y, Stoffers DA, Simmons RA: Exendin-4 increases histone acetylase activity and reverses epigenetic modifications that silence Pdx1 in the intrauterine growth retarded rat. *Diabetologia* 2011; 54: 2606-14.

In this novel study, postnatal administration of exendin-4, a drug used for adults with type II diabetes, was found to have epigenetic-modifying effects on Pdx1 expression, a gene necessary for normal beta cell function, in rats induced with IUGR. This therapy may ultimately be used in the post-natal period in 'at-risk' infants to prevent adult-onset diabetes.

## Anesthesia and Analgesia

### Anesthesia Guidelines

114. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology* 2011; 114: 495-511.

These updated ASA guidelines serve as a useful reference for obstetric anesthesiologists wishing to update institutional policies for preoperative fasting in obstetric patients. The ASA state that its guidelines may be used or modified for pregnant patients but they are 'not intended for women in labor'. Of note, the minimum fasting period for clear fluids=2 hr and a 'light meal'=6 hr.

115. Practice advisory for the prevention of perioperative peripheral neuropathies: an updated report by the American Society of Anesthesiologists Task Force on prevention of perioperative peripheral neuropathies. *Anesthesiology* 2011; 114: 741-54.

This practice advisory updates guidelines for preventing perioperative peripheral neuropathies; an updated literature search was performed between 1996-2010. The recommendations include avoiding >90 degrees abduction of the upper limb, avoiding pressure on the postcondylar groove of the humerus, and a

neutral or supinated arm position +/- arm padding on upper limb boards. An adequately positioned noninvasive BP cuff does not influence any risk of upper limb neuropathy.

## Anesthesia for Cesarean Delivery

### Neuraxial Anesthesia: Local Anesthetics

116. Carvalho B, Collins J, Drover DR, Atkinson Ralls L, Riley ET: ED(50) and ED(95) of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. *Anesthesiology* 2011; 114: 529-35.

The results of this dose-finding study are important in refuting claims that the effective dose of intrathecal (IT) bupivacaine is less in morbidly obese patients undergoing elective CD (compared to non-obese patients). Using a CSE technique, investigators reported that the derived ED50 and ED95 of IT bupivacaine for achieving successful surgical anesthesia were 9.8 mg and 15 mg respectively; these values are similar to those previously reported values in non-obese patients. IT bupivacaine <10 mg is not recommended for morbidly obese patients undergoing elective CD for single-shot spinal anesthesia. Neuraxial catheter-based techniques are prudent as greater variability in dose response in morbidly obese patients may occur compared to nonobese patients.

Accompanying editorial: Palmer CM: Let's just call it "evidence-based practice". *Anesthesiology* 2011; 114: 481-82.

Equivalent dosing of IT bupivacaine in morbidly obese patients (compared to nonobese patients) undergoing CD is advocated in this editorial. The editorial also questions the derived ED95 value for successful surgical anesthesia in this patient subpopulation, as wide variability in response was observed with IT bupivacaine >10 mg in this study.

Letter to the editor: Pace NL: Intrathecal dosing for cesarean delivery in obese and nonobese patients. *Anesthesiology* 2011; 115: 899-900; author reply 900.

117. Bouvet L, Da Col X, Chassard D, Dalry F, Ruynat L, Allaouchiche B, Dantony E, Boselli E: ED and ED95 of intrathecal levobupivacaine with opioids for Caesarean delivery. *Br J Anaesth* 2011; 106: 215-20.

Using a dose-finding approach, this prospective study (n=85) determined the ED50 and ED95 of IT levobupivacaine (in combination with sufentanil 2.5 mcg+morphine 100 mcg) for elective CD to be 6.2 mg (95% CI=2.6-7.6 mg) and 12.9 mg (95% CI=11.1-17.9 mg) respectively. The CIs for the ED50/ED95 suggest wide variability in dose-response among patients. A CSE technique is suggested for intrathecal doses lower than the ED95 for levobupivacaine reported in this study.

Letter to the editor: Birts W, Combeer A: Consent of subjects for general anaesthetic in Caesarean section. *Br J Anaesth* 2011; 107: 639-40; author reply 640.

118. Camorcia M, Capogna G, Columb MO: Effect of sex and pregnancy on the potency of intrathecal bupivacaine: determination of ED for motor block with the up-down sequential allocation method. *Eur J Anaesthesiol* 2011; 28: 240-44.

After assessing the degrees of motor block, investigators in this observational study (n=90) suggested that sex and pregnancy differentially influence the potency of IT bupivacaine. The ED50 for motor (NOT anesthetic) block were 6.9 mg for men, 5.2 mg for women and 3.4 mg for pregnant women.

Accompanying editorial: Benhamou D: Sex-based differences in local anaesthetic-induced motor block. *Eur J Anaesthesiol* 2011; 28: 235-36.

119. Zhan Q, Huang S, Geng G, Xie Y: Comparison of relative potency of intrathecal bupivacaine for motor block in pregnant versus non-pregnant women. *Int J Obstet Anesth* 2011; 20: 219-23.

A similar pharmacologic study to reference 119 assessing potency differences of IT bupivacaine between pregnant women (undergoing CD) and nonpregnant women (undergoing gynecologic surgery). Using an up-down sequential allocation technique, investigators calculated the relative potency ratio for motor block for pregnant (n=35) versus non-pregnant (n=35) women to be 1.14 (95% CI=1.05-1.24).

120. Arzola C, Wiczorek PM: Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. *Br J Anaesth* 2011; 107: 308-18.

Meta-analysis of RCTs comparing 'low dose' IT bupivacaine ( $\leq 8$  mg) to standard dose IT bupivacaine ( $> 8$  mg) for elective CD; 12 studies (n=693) were included in the final analyses. The need for analgesic supplementation was higher (RR=3.8 [95% CI=2.4-5.9] with low dose IT bupivacaine; number needed to harm=4), with no heterogeneity between studies. This analysis was limited by the arbitrary 'cutpoint' for differentiating low dose versus standard dose, and by the use of analgesic supplementation (as opposed to block assessment) for determining anesthetic efficacy.

### *Neuraxial Anesthesia: Opioids*

121. Atkinson Ralls L, Drover DR, Clavijo CF, Carvalho B: Prior epidural lidocaine alters the pharmacokinetics and drug effects of extended-release epidural morphine (DepoDur(R)) after cesarean delivery. *Anesth Analg* 2011; 113: 251-58.

In this RCT (n=30), the pharmacokinetic and pharmacodynamic effects of extended-release epidural morphine 8 mg (EREM) were compared in patients undergoing CD with epidural anesthesia (using lidocaine) versus a CSE technique with no prior epidural local anesthetic; EREM was given 1 hr after CSE or  $\geq 1$  hr post-epidural lidocaine. The maximum concentration of morphine was higher in the epidural lidocaine group versus CSE group (11.1 vs 8.3 ng/mL; P=0.04). Also, more patients experienced side-effects (nausea, vomiting, hypotension, oxygen use) in the epidural lidocaine group. These results suggest that epidural lidocaine may interfere with EREM pharmacokinetics. Close monitoring is advised in patients receiving EREM  $\geq 1$  hr after epidural lidocaine for CD.

### *Maternal Hypotension/Fetal Acidosis*

122. Landau R, Liu SK, Blouin JL, Smiley RM, Ngan Kee WD: The effect of maternal and fetal beta2-adrenoceptor and nitric oxide synthase genotype on vasopressor requirement and fetal acid-base status during spinal anesthesia for cesarean delivery. *Anesth Analg* 2011; 112: 1432-37.

Interesting RCT in 104 Chinese women undergoing CD assessing the influence of maternal and neonatal  $\beta_2$  adrenoceptor (ADRB2) genotype on post-spinal hypotension and fetal acidemia. For the treatment of maternal hypotension, neither ephedrine nor phenylephrine requirements were influenced by maternal ADRB2 genotype. Although neonatal ADRB2 p.Arg16 homozygosity attenuated the degree of ephedrine induced fetal acidemia, neonatal acid-base balance did not differ according to maternal or neonatal genotype in response to phenylephrine. Variations in genotype expression and differences in ephedrine delivery (bolus versus infusion) may explain why ephedrine requirements vary among different cesarean study populations.

123. McDonald S, Fernando R, Ashpole K, Columb M: Maternal cardiac output changes after crystalloid or colloid coload following spinal anesthesia for elective cesarean delivery: a randomized controlled trial. *Anesth Analg* 2011; 113: 803-10.

This RCT (n=60) is among the first to directly compare the effects on maternal cardiac indices (measured by suprasternal Doppler) of coload with 1 L crystalloid versus 1 L colloid (6% hydroxyethylstarch) during spinal anesthesia for CD. All patients received a phenylephrine infusion. No significant differences between groups were observed in cardiac output, stroke volume, hypotension, and phenylephrine requirements. In the presence of a phenylephrine infusion,

colloid coload offers no hemodynamic advantages over a crystalloid coload in this setting.

Accompanying editorial: Mercier FJ: Fluid loading for cesarean delivery under spinal anesthesia: have we studied all the options? *Anesth Analg* 2011; 113: 677-80.

124. Ghabach MB, El-Khatib MF, Zreik TG, Matta MS, Mouawad JJ, Karam CJ, Ayoub CM: Effect of weight gain during pregnancy on heart rate variability and hypotension during caesarean section under spinal anaesthesia. *Anaesthesia* 2011; 66: 1106-11.

RCT that explores the influence of antenatal weight gain on pre- and peri-operative cardiovascular indices for 66 patients undergoing elective CD under spinal anesthesia. Patients with  $< 11$  kg weight gain had significantly higher baseline heart rate variability (entropy) and a greater incidence of postspinal hypotension than patients with either 11-16 kg or  $> 16$  kg weight gain. Further work is needed to examine the degree of influence of antenatal weight gain on peri- and post-cesarean maternal outcomes.

125. El-Hakeem E, Kaki A, Almazrooa A, Al-Mansouri N, Alhashemi J: Effects of sitting up for five minutes versus immediately lying down after spinal anesthesia for Cesarean delivery on fluid and ephedrine requirement; a randomized trial. *Can J Anaesth* 2011; 58: 1083-89.

RCT investigating the postspinal effects of prolonged sitting up (5 mins) or immediately lying down during elective CD (n=120). 'Sitting up' patients had significantly lower intraoperative sensory block heights (T4 vs T2), received less iv fluid (709 vs 789 mL) and had more prolonged motor block recovery (101 vs 88 min) compared with 'lying down' patients, and fewer patients required ephedrine (8% vs 47% respectively) (P<0.001). At best, modest perioperative benefits are proffered by sitting up for 5 min postspinal.

### *General Anesthesia*

126. Park BY, Jeong CW, Jang EA, Kim SJ, Jeong ST, Shin MH, Lee J, Yoo KY: Dose-related attenuation of cardiovascular responses to tracheal intubation by intravenous remifentanyl bolus in severe pre-eclamptic patients undergoing Caesarean delivery. *Br J Anaesth* 2011; 106: 82-87.

RCT comparing the hemodynamic effects of remifentanyl 0.5 mcg/kg and 1.0 mcg/kg postinduction in patients with preeclampsia undergoing general anesthesia for CD (n=48). After tracheal intubation, maternal systolic blood pressure values did not increase above baseline values in each study group. In addition, similar neonatal outcomes (APGAR/blood gases) were observed between groups. After intubation, these doses of remifentanyl may be effective in controlling maternal blood pressure in preeclampsia.

Letter to the editor: Birts W, Combeer A: Consent of subjects for general anaesthetic in Caesarean section. *Br J Anaesth* 2011; 107: 639-40; author reply 640.

127. Cook TM, Woodall N, Frerk C: Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: anaesthesia. *Br J Anaesth* 2011; 106: 617-31.

Important national audit project describing major airway complications related to anesthesia (including obstetrics) over a 1 yr period in the UK. Four out of a total of 184 events (2.2%) occurred in pregnant women. All obstetric cases involved airway problems during intubation for emergency CD, of whom two patients had BMI  $> 35$ . These data adds to our knowledge of problems due to airway mismanagement for non-scheduled or emergency CD, especially in obese parturients.

128. McKeen DM, George RB, O'Connell CM, Allen VM, Yazer M, Wilson M, Phu TC: Difficult and failed intubation: Incident rates and maternal, obstetrical, and anesthetic predictors. *Can J Anaesth* 2011; 58: 514-24.

Retrospective, single-center cohort study to assess the incidence of difficult and failed tracheal intubation in 1,052 obstetric general anesthetics from 1984 to 2003 (4.7% and 0.08% respectively). Despite the expected rise in rates of regional anesthesia over this time-frame, there was, reassuringly, no increasing rate of difficult/failed intubation that one may have expected.

Letter to the editor: Boutonnet M, Pasquier P, Ausset S, Tourtier JP: The difficult airway in obstetrical anesthesia: advocacy to improve the quality of assessment. *Can J Anaesth* 2011; 58: 1053-54.

129. Erden V, Erkalp K, Yangin Z, Delatioglu H, Kiroglu S, Ortakuz S, Ozdemir B: The effect of labor on sevoflurane requirements during cesarean delivery. *Int J Obstet Anesth* 2011; 20: 17-21.

Prospective observational study (n=50) comparing sevoflurane requirements in patients undergoing prelabor (elective) cesarean delivery (CD) versus intrapartum CD (during labor) with general anesthesia. Using targeted Bispectral index values, sevoflurane requirements were significantly higher in patients during intrapartum CD, which were not explained by between-group differences in prolactin, progesterone or cortisol levels.

## Neuraxial Labor Analgesia

### *PCEA Regimens*

130. Wong CA, McCarthy RJ, Hewlett B: The effect of manipulation of the programmed intermittent bolus time interval and injection volume on total drug use for labor epidural analgesia: a randomized controlled trial. *Anesth Analg* 2011; 112: 904-11.

High-quality RCT (n=190) in nulliparous patients receiving CSE labor analgesia. Women were randomized to receive three different programmed intermittent bolus dose regimens for the maintenance of labor analgesia. Bupivacaine consumption was decreased in women receiving the 'high volume- long bolus interval' regimen [10mL/60 min] versus consumption in women whose regimens involved smaller boluses [2.5 -5mL] and shorter bolus intervals [15-30 min] respectively. Measures of analgesic quality e.g. number of PCEA requests, number of manual bolus doses, cumulative fentanyl doses were not significantly different between groups. Future studies are still needed to determine optimal programmed intermittent bolus regimens.

131. Capogna G, Camorcia M, Stirparo S, Farcomeni A: Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: the effects on maternal motor function and labor outcome. A randomized double-blind study in nulliparous women. *Anesth Analg* 2011; 113: 826-31.

Moderate quality RCT (n=145) assessing maternal motor block in patients receiving continuous epidural analgesia [CEA] at 10 mL/hr versus programmed intermittent epidural analgesia [PIEB] at 10 mL bolus/hr. Both regimens used 0.0625% levobupivacaine + sufentanil 0.5 mcg/mL with a PCEA function. Motor block and instrumental delivery were less common with PIEB compared to CEA (37% vs 2.7%; 20% vs 7% respectively). Unfortunately, data were not provided on important obstetric and intrapartum confounders that may have influenced the risk of instrumental delivery; therefore, it is uncertain if and to what degree PIEB reduces rates of instrumental delivery.

132. Bazin M, Bonnin M, Storme B, Bolandard F, Vernis L, Lavergne B, Pereira B, Bazin JE, Duale C: Addition of clonidine to a continuous patient-controlled epidural infusion of low-concentration levobupivacaine plus sufentanil in primiparous women during labour. *Anaesthesia* 2011; 66: 769-79.

Double-blind RCT (n=115) to assess the analgesic effects in labor of adding clonidine (1.36 mcg/mL) to a standard PCEA regimen (0.0625% levobupivacaine + sufentanil 0.45 mcg/mL). Patients in the clonidine group required significantly

fewer epidural bolus doses during labor (6 vs 10 boluses;  $P < 0.001$ ), and lower pain scores compared to the control group (group vs time interaction;  $P < 0.001$ ). However, maternal blood pressure readings were lower and the rate of instrumental delivery was surprisingly higher in the clonidine group.

### *Effects on Uteroplacental Blood Flow*

133. Fratelli N, Prefumo F, Andrico S, Lorandi A, Recupero D, Tomasoni G, Frusca T: Effects of epidural analgesia on uterine artery Doppler in labour. *Br J Anaesth* 2011; 106: 221-24.

RCT in 52 women comparing the effects of epidural labor analgesia versus control on maternal uteroplacental blood flow (using a uterine pulsatility flow index). Uterine flow was significantly decreased at 30 min after epidural analgesia was initiated compared to the control group. However no adverse fetal or neonatal outcomes were observed; thus, the clinical relevance of these findings remain uncertain.

### *Epidural-associated Maternal Fever*

134. Riley LE, Celi AC, Onderdonk AB, Roberts DJ, Johnson LC, Tsen LC, Leffert L, Pian-Smith MC, Heffner LJ, Haas ST et al: Association of epidural-related fever and noninfectious inflammation in term labor. *Obstet Gynecol* 2011; 117: 588-95.

Interesting observational study investigating inflammatory markers and placental cultures during labor and their potential associations with labor analgesia. Although more women receiving epidurals had fever compared to those receiving no epidural (23% vs 6%;  $P = 0.009$ ), most fevers were not associated with infection (rates of placental infection with epidural=5.4% vs no epidural=4.3%;  $P = NS$ ). On the basis of high rates of elevated IL-6 levels at hospital admission in the epidural group (36%) versus no epidural group (16%), investigators postulated an inflammatory association with epidural analgesia. Important obstetric confounders (methods of induction or augmentation of labor) and other co-variables (labor pain; time of epidural placement in relation to labor) were not assessed.

135. Wang LZ, Hu XX, Liu X, Qian P, Ge JM, Tang BL: Influence of epidural dexamethasone on maternal temperature and serum cytokine concentration after labor epidural analgesia. *Int J Gynaecol Obstet* 2011; 113: 40-43.

RCT investigating the effect of epidural dexamethasone (DEX) 0.2 mg versus control on maternal temperature in women receiving epidural analgesia (PCEA) in labor (n=60). Increases in maternal temperature and serum IL-6 levels were reported in the epidural DEX group compared to control. However, the lack of difference in the reported incidence of maternal fever between groups (10% DEX group vs 3.3% control;  $P = 0.6$ ) may be due to a type II error related to a small sample size.

136. de Orange FA, Passini R, Jr., Amorim MM, Almeida T, Barros A: Combined spinal and epidural anaesthesia and maternal intrapartum temperature during vaginal delivery: a randomized clinical trial. *Br J Anaesth* 2011; 107: 762-68.

RCT assessing maternal temperature in patients undergoing combined spinal-epidural analgesia versus non-pharmacologic labor analgesia (n=70). There was a trend towards higher maternal temperatures in the CSE group up to 6 hours after randomization. More patients in the CSE group developed maternal pyrexia ( $>38^{\circ}C$ ) compared to the non-CSE group (14% vs 0% respectively;  $P = 0.03$ ). Similar to epidural analgesia, CSE analgesia appears to be associated with intrapartum fever.

### *Epidural Analgesia and Neonatal Pyrexia*

137. Agakidis C, Agakidou E, Philip Thomas S, Murthy P, John Lloyd D: Labor epidural analgesia is independent risk factor for neonatal pyrexia. *J Matern Fetal Neonatal Med* 2011; 24: 1128-32.

Single-center, retrospective observational study examining the association between epidural analgesia and neonatal pyrexia (n=960). Using multivariate logistic regression, investigators observed maternal epidural analgesia to be an independent predictor for neonatal pyrexia (OR=3.44; 95% CI=1.9-6.3; P<0.001). Selection bias was not adequately accounted for in the study methodology.

### *Treatment of Side Effects*

138. Sinha A, Paech MJ, Thew ME, Rhodes M, Luscombe K, Nathan E: A randomised, double-blinded, placebo-controlled study of acupressure wristbands for the prevention of nausea and vomiting during labour and delivery. *Int J Obstet Anesth* 2011; 20: 110-17.

Well-designed, double-blind RCT assessing P6 acupressure (Pressure Right™ wrist band) versus sham for preventing nausea and vomiting in labor (n=340). Similar rates of nausea and vomiting were found in both study groups, which suggested a lack of effect by P6 acupressure in nausea/vomiting prophylaxis.

### *BMI and Labor Epidurals*

139. Sharma V, Swinson AK, Hughes C, Mokashi S, Russell R: Effect of ethnicity and body mass index on the distance from skin to lumbar epidural space in parturients. *Anaesthesia* 2011; 66: 907-12.

This UK observational study confirms that body mass index and ethnicity are independently associated with distance from skin to epidural space in parturients receiving labor epidural analgesia (n=1406). Of note, African and white patients had significantly greater spinal-epidural space distances than Asian and Chinese patients.

### *Mode of Delivery and Labor Epidurals*

140. Wassen MM, Zuijlen J, Roumen FJ, Smits LJ, Marcus MA, Nijhuis JG: Early versus late epidural analgesia and risk of instrumental delivery in nulliparous women: a systematic review. *BJOG* 2011; 118: 655-61.

In this systematic review, nulliparous patients receiving epidural analgesia with a cervical dilatation of  $\leq 3$  cm were not at increased risk of instrumental vaginal delivery or CD compared with patients receiving 'later' epidural placement [6 studies; n=15,399]. However, marked differences in methodology were noted for the pooled studies in this analysis.

Letter to the editor: Klein MC: Early versus late epidural analgesia and the risk of instrumental delivery in nulliparous women. *BJOG* 2011; 118: 1540-41; author reply 1541-42.

### *Epidemiology: Neuraxial Labor Analgesia*

141. Osterman MJ, Martin JA: Epidural and spinal anesthesia use during labor: 27-state reporting area, 2008. *Natl Vital Stat Rep* 2011; 59: 1-13, 16.

CDC report which contains a treasure trove of epidemiologic data related to epidural and spinal anesthesia usage among singleton women undergoing vaginal delivery in 27 states in 2008. Overall, 61% of women received epidural/spinal anesthesia; there were racial/ethnic disparities and age-related differences in the use of neuraxial anesthesia. Patients undergoing forceps or vacuum assisted deliveries had higher rates of neuraxial anesthesia than for those undergoing spontaneous vaginal delivery (84%; 77%; 60% respectively); this is most likely associative not causal.

### *Patients' Attitudes to Labor Epidural Analgesia*

142. Chang KY, Tsou MY, Chan KH, Chen HH: Application of the Rasch model to develop a simplified version of a multiattribute utility measurement on attitude toward labor epidural analgesia. *Anesth Analg* 2011; 113: 1444-49.

Multi-attribute utility (MAU) based questionnaires have been used to understand patients' attitudes towards labor analgesia (ATLA), but they may be overly complicated for practical use. In this study, investigators simplified MAU questionnaire by using a psychometric method - Rasch technique - to create a unidimensional measure. Reliability and validity were similar for the simplified and full scores of ATLA, which suggest a simplified questionnaire may prove valuable in optimizing assessments of patient attitudes to labor analgesia.

### *Intravenous Labor Analgesia*

143. Volmanen PV, Akural EI, Raudaskoski T, Ranta P, Tekay A, Ohtonen P, Alahuhta S: Timing of intravenous patient-controlled remifentanyl bolus during early labour. *Acta Anaesthesiol Scand* 2011; 55: 486-94.

Cross-over, placebo-controlled study (n=41) assessing analgesic differences using two, different, i.v. remifentanyl PCA regimens: bolus delivery after immediate trigger versus delayed delivery (140 secs after trigger). Mean pain and pain relief scores and maternal side-effects (SpO<sub>2</sub>, maternal hemodynamics, supplementary oxygen usage) were similar in the two dosing regimens. Pain and pain relief were analyzed separately for each study period due to a 'carryover effect' which almost certainly limited statistical power and the study findings.

144. Leong WL, Sng BL, Sia AT: A comparison between remifentanyl and meperidine for labor analgesia: a systematic review. *Anesth Analg* 2011; 113: 818-25.

Meta-analysis of three, labor analgesia studies comparing meperidine to remifentanyl PCA. More favorable analgesic profiles were seen with remifentanyl versus meperidine (reduced mean VAS score of 25 mm at 1 hr; P<0.001). Although no differences in maternal desaturation rates were found between remifentanyl and meperidine, limited conclusions can be drawn due to marked study heterogeneity and insufficient data on adverse outcomes.

### *Anesthesia for Other Pregnancy-related Procedures*

#### *In Vitro Fertilization*

145. Circeo L, Grow D, Kashikar A, Gibson C: Prospective, observational study of the depth of anesthesia during oocyte retrieval using a total intravenous anesthetic technique and the Bispectral index monitor. *Fertil Steril* 2011; 96: 635-37.

Prospective study (n=50) investigating depth of anesthesia, using BIS and sedation scoring, for achieving optimal surgical conditions for women undergoing oocyte retrieval with total intravenous anesthesia (fentanyl and propofol infusion). Moderate sedation was observed during the first 5-10 min of oocyte retrieval, with deep sedation/general anesthesia deemed necessary (mean BIS=47-53) for preventing painful stimulation.

#### *Abortion*

146. Dean G, Jacobs AR, Goldstein RC, Gevirtz CM, Paul ME: The safety of deep sedation without intubation for abortion in the outpatient setting. *J Clin Anesth* 2011; 23: 437-42.

In this retrospective, single-center descriptive study, no cases of pulmonary aspiration were reported in 62,125 surgical abortions during 'deep sedation' with propofol without planned intubation. Although these data indicate that the risk of aspiration of pregnant patients undergoing 'deep sedation' may be overplayed, no cases >24 weeks gestational age were included in this study.

## Post-Cesarean Analgesia

### Systemic Analgesia

147. Moore A, Costello J, Wieczorek P, Shah V, Taddio A, Carvalho JC: Gabapentin improves post delivery pain management: a randomized, placebo-controlled trial. *Anesth Analg* 2011; 112: 167-73.

RCT (n=46) in which healthy term parturients undergoing CD were randomized to preoperatively receive either 600 mg gabapentin or placebo. Pain scores with movement were significantly lower in the gabapentin group up to 48 hr post-CD, although the incidence of severe sedation was significantly higher in the gabapentin group up to 24 hr post-CD.

### Transversus Abdominis Plane (TAP) Blocks

148. McMorro RC, Ni Mhuirheartaigh RJ, Ahmed KA, Aslani A, Ng SC, Conrick-Martin I, Dowling JJ, Gaffney A, Loughrey JP, McCaul CL: Comparison of transversus abdominis plane block vs spinal morphine for pain relief after Caesarean section. *Br J Anaesth* 2011; 106: 706-12.

RCT (n=80) to assess the analgesic effects of bilateral transversus abdominis plane (TAP) blocks, using bupivacaine 2 mg/kg, ± IT morphine (100 mcg) in women after elective CD. No clear analgesic benefit was observed between study groups. Therefore the use of TAP blocks may be unnecessary post-CD in women who receive IT morphine. Of note, ultrasound was not used for TAP block placement in this study.

## Spinal Anesthesia Failure

149. Fuzier R, Bataille B, Fuzier V, Richez AS, Magues JP, Choquet O, Montastruc JL, Lapeyre-Mestre M: Spinal anesthesia failure after local anesthetic injection into cerebrospinal fluid: a multicenter prospective analysis of its incidence and related risk factors in 1214 patients. *Reg Anesth Pain Med* 2011; 36: 322-26.

Prospective, multicenter, cohort study to assess the incidence and risk factors related to spinal failure in an obstetric and non-obstetric surgical population (n=1214). The overall incidence was 3.2%, and spinal failure occurred in 12/270 (4%) of obstetric patients within the cohort.

## Experimental Pain Research

### Pain Assessment

150. Abrishami A, Chan J, Chung F, Wong J: Preoperative pain sensitivity and its correlation with postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 2011; 114: 445-57.

This article provides an interesting systematic review of prior studies investigating the relationships between measures of preoperative pain sensitization and postsurgical pain (acute and chronic). Although a formal meta-analysis was not performed, the intensity of suprathreshold pain (pain above the patient's pain threshold) was observed to be significantly correlated with the intensity of postoperative pain in four studies. Unfortunately marked heterogeneity between studies and the lack of multivariate analyses limit the clinical applicability of these findings.

151. Moore RA, Straube S, Paine J, Derry S, McQuay HJ: Minimum efficacy criteria for comparisons between treatments using individual patient meta-analysis of acute pain trials: examples of etoricoxib, paracetamol, ibuprofen, and ibuprofen/paracetamol combinations after third molar extraction. *Pain* 2011; 152: 982-89.

Very interesting study which examines individual patient responses as preferred outcome measures for determining analgesic efficacy for acute pain (as opposed to analyses of visual analog pain scores). Using individual data from

six RCTs investigating patients' responses to analgesics for pain after third molar extractions, minimum efficacy criteria from 0% to 70% pain relief and numbers needed to treat were calculated to assess time-dependent changes in total pain relief and summed pain intensity differences. These concepts are more likely to be commonly employed for RCTs assessing the comparative effects of analgesics for treating nociceptive pain and for rescue analgesia.

Accompanying editorial: Segerdahl M: Pain outcome variables--a never ending story? *Pain* 2011; 152: 961-62.

Accompanying editorial endorsing the development of number needed to treat and minimum efficacy criteria for better understanding the efficacy of analgesic response for postsurgical and chronic pain patients.

152. Ruysen-Witrand A, Tubach F, Ravaut P: Systematic review reveals heterogeneity in definition of a clinically relevant difference in pain. *J Clin Epidemiol* 2011; 64: 463-70.

Systematic review which highlights the lack of a standardized definition for a 'clinically relevant difference in pain' in RCTs of analgesics. Novel concepts for assessing subject-level analgesic responses are described.

153. Srikandarajah S, Gilron I: Systematic review of movement-evoked pain versus pain at rest in postsurgical clinical trials and meta-analyses: A fundamental distinction requiring standardized measurement. *Pain* 2011; 152: 1734-39.

Systematic review which exposes the lack of data about movement-evoked pain (MER) in postsurgical studies, as well as inadequate descriptors for defining MER. More consistent terminology is recommended to more clearly differentiate pain at rest and procedure-specific MER.

## Opioids and Chronic Pain

154. Gaveriaux-Ruff C, Nozaki C, Nadal X, Hever XC, Weibel R, Matifas A, Reiss D, Filliol D, Nassar MA, Wood JN et al: Genetic ablation of delta opioid receptors in nociceptive sensory neurons increases chronic pain and abolishes opioid analgesia. *Pain* 2011; 152: 1238-48.

High quality animal study in which investigators used conditional knock-out mice to study the influence of delta opioid receptors in pain control. Delta receptors were deleted in specific primary nociceptive neurons (Nav1.8). After investigators artificially induced inflammatory pain and neuropathic pain, mutant animals displayed increased allodynia compared to 'control mice'. The effects of central and peripheral administered delta agonist (SNC80) did not reduce thermal hyperalgesia or mechanical allodynia in mutant mice. These results suggest that delta receptors may play an important role in mediating analgesia in chronic pain.

Accompanying editorial: Cahill CM, Taylor A: A piece of the puzzle is revealed for delta opioid receptor-mediated analgesia. *Pain* 2011; 152: 1217-18.

## Radiologic and Ultrasound Studies: Neuraxial Anesthesia

### MRI

155. Higuchi H, Takagi S, Onuki E, Fujita N, Ozaki M: Distribution of epidural saline upon injection and the epidural volume effect in pregnant women. *Anesthesiology* 2011; 114: 1155-61.

Observational study assessing the anatomic changes induced by the introduction of epidural saline (10 mL) with MRI (at levels T12-L5) in term, pregnant patients (n=8) and in nonpregnant female volunteers (n=8). The reduction in CSF volume was significantly greater in pregnant patients, and epidural saline did not leak from intervertebral foraminae in pregnant patients. These anatomic effects may explain the longitudinal spread of epidural solutions and the epidural volume extension of spinal anesthesia (with a CSE technique) in pregnant patients.

## Ultrasound: New Techniques

156. Chiang HK, Zhou Q, Mandell MS, Tsou MY, Lin SP, Shung KK, Ting CK: Eyes in the needle: novel epidural needle with embedded high-frequency ultrasound transducer-epidural access in porcine model. *Anesthesiology* 2011; 114: 1320-24.

This novel study provides preliminary data on the use of an ultrasound transducer placed within a standard 18G Tuohy needle for locating the thoracic and lumbar epidural space. Using a paramedian insertion technique in anesthetized pigs, the ligamentum flavum was identified in 83% of insertions, with a strong ultrasonic signal identifying the dura mater. The use of an intra-needle ultrasound guided technique offers great opportunity to improve anatomic location during epidural procedures. The next obvious step is a study in human volunteers.

Accompanying editorial: Tsen LC: The all-seeing eye? Ultrasound technologies for neuraxial techniques. *Anesthesiology* 2011; 114: 1274-76.

## Ultrasound versus Clinical Assessment

157. Margarido CB, Mikhael R, Arzola C, Balki M, Carvalho JC: The intercrystal line determined by palpation is not a reliable anatomical landmark for neuraxial anesthesia. *Can J Anaesth* 2011; 58: 262-66.

Observational study in term parturients (n=45) indicating that the intersection of the intercrystal line (determined by manual palpation) was above the L4-5 vertebral interspace in all patients. Lumbar interspaces were assessed using spinal ultrasound in the sitting up position. Worryingly, the intersection was up to three interspaces higher than the L2-3 interspace in 36% of women in this study.

158. Lee AJ, Ranasinghe JS, Chehade JM, Arheart K, Saltzman BS, Penning DH, Birnbach DJ: Ultrasound assessment of the vertebral level of the intercrystal line in pregnancy. *Anesth Analg* 2011; 113: 559-64.

Observational study, which described poor agreement of clinical assessment of the intercrystal line (ICL) with ultrasonographic assessment (in 14/101 comparisons) in 51 term parturients. Clinical assessment of the ICL was  $\geq 1$  vertebral level higher than the anatomic position in 40% of assessments. Two experienced anesthesiologists performed the assessments, so the variation among non-experienced anesthesiologists is unclear.

## Electron Microscopic Studies

159. Reina MA, Collier CB, Prats-Galino A, Puigdemivol-Sanchez A, Maches F, De Andres JA: Unintentional subdural placement of epidural catheters during attempted epidural anesthesia: an anatomic study of spinal subdural compartment. *Reg Anesth Pain Med* 2011; 36: 537-41.

Interesting study in which investigators used samples of arachnoid lamina to assess the anatomy of the spinal subdural compartment with electron microscopy. Of note, 20-gauge catheters, with external diameters = 0.85mm, were inserted in vitro into the subdural space, thereby providing anatomic evidence that traction forces during catheter placement may separate the dura mater and arachnoid layer.

## Perioperative and Postoperative Patient Monitoring

### Hemodynamic Monitoring

160. Dyer RA, Piercy JL, Reed AR, Strathie GW, Lombard CJ, Anthony JA, James MF: Comparison between pulse waveform analysis and thermodilution cardiac output determination in patients with severe pre-eclampsia. *Br J Anaesth* 2011; 106: 77-81.

Observational study in postpartum patients with severe preeclampsia (n=18) to compare the accuracy and precision of cardiac output measurements derived from pulse waveform analysis (LiDCOplus) versus thermodilution (TD) using pulmonary artery catheters. Central venous calibration with lithium was associated with positive bias for TD (0.58 L/min [95% CI=0.77;0.39]). No significant bias was reported for peripheral calibration (0.16 L/min [95% CI=-0.37;-0.06]). For an average cardiac output of 7 L/min, the limits of agreement were within a 30% range, indicating that LiDCOplus is a viable option for cardiac output monitoring in this patient subpopulation.

See also - Review: Armstrong S, Fernando R, Columb M: Minimally- and non-invasive assessment of maternal cardiac output: go with the flow! *Int J Obstet Anesth* 2011; 20: 330-40.

Thorough review of published studies investigating minimally and noninvasive techniques for maternal cardiac output monitoring. It is certain that future technologic advances will ultimately lead to more sophisticated methods of measuring maternal cardiac output changes for low and high risk parturients during the peripartum period.

## Coagulation Monitoring

161. Butwick A, Ting V, Ralls LA, Harter S, Riley E: The association between thromboelastographic parameters and total estimated blood loss in patients undergoing elective cesarean delivery. *Anesth Analg* 2011; 112: 1041-47.

Prospective, observational study assessing the potential association between the maternal coagulation profile (assessed by kaolin-activated thromboelastography (TEG)) and total estimated blood loss (EBL) in women undergoing elective CD (n=52). Weak associations were observed between individual TEG parameters (maximum amplitude and maximum rate of thrombin generation) with EBL (r=0.3 respectively). The results of this study suggest that other physiologic/anatomic factors are more likely to be responsible for the degree of blood loss in women undergoing elective CD.

## Noninvasive Hemoglobin Monitoring

162. Butwick AJ, Hilton G, Riley ET, Carvalho B: Non-invasive measurement of hemoglobin during cesarean hysterectomy: a case series. *Int J Obstet Anesth* 2011; 20: 240-45.

In this case series, noninvasive hemoglobin monitoring (SpHb) was used for five patients with abnormal placentation undergoing CD. Their SpHb values were higher than laboratory Hb values in 16/17 (94%) blood samples (median difference between SpHb and laboratory Hb was 2 g/dl [range=0-3.8 g/d]). Further work is needed to assess the accuracy and precision of SpHb assessment in an obstetric setting.

## Effects of Anesthesia on Fetal/Neonatal Neurodevelopment

### Neuraxial Labor Analgesia

163. Flick RP, Lee K, Hofer RE, Beinborn CW, Hambel EM, Klein MK, Gunn PW, Wilder RT, Katusic SK, Schroeder DR et al: Neuraxial labor analgesia for vaginal delivery and its effects on childhood learning disabilities. *Anesth Analg* 2011; 112: 1424-31.

Previous epidemiologic research has suggested that the incidence of learning disabilities (LDs) is reduced in children born by CD in mothers receiving neuraxial anesthesia compared with vaginal delivery. In this large, retrospective cohort study in women undergoing vaginal delivery from 1976-1982 (n=4684), investigators further explored putative associations between the development of childhood learning disabilities and neuraxial analgesia. Using data from IQ and achievement tests for reading, written language and math, the authors observed that neuraxial labor analgesia was not associated with LDs before age 19 yr

(adj HR=1.05; 95% CI=0.85-1.31). This epidemiologic data suggest that the use of neuraxial labor analgesia does not appear to significantly influence the development of childhood LDs.

Accompanying editorials: Radcliffe J, Bellinger DC: Learning disability in children as an outcome in anesthesia and analgesia research. *Anesth Analg* 2011; 112: 1262-64.

Sun LS: Labor analgesia and the developing human brain. *Anesth Analg* 2011; 112: 1265-67.

## General Anesthesia

164. Rappaport B, Mellon RD, Simone A, Woodcock J: Defining safe use of anesthesia in children. *N Engl J Med* 2011; 364: 1387-90.

Commentary article which highlights growing concern about the neurotoxic effects of anesthetic exposure in neonates and children and the current steps being taken to better investigate these effects in human models.

Letter to the editor: Glass NL, Malviya S: Anesthesia in children-limitations of the data on neurotoxicity. *N Engl J Med* 2011; 364: 1466-67.

Review: Stratmann G: Review article: Neurotoxicity of anesthetic drugs in the developing brain. *Anesth Analg* 2011; 113: 1170-79.

Excellent review of the literature (up to early 2011) summarizing relevant data from studies examining the potential for anesthetic agents to cause neurotoxicity in the developing brain.

## *In Utero Exposure to General Anesthetic Agents*

165. Palanisamy A, Baxter MG, Keel PK, Xie Z, Crosby G, Culley DJ: Rats exposed to isoflurane in utero during early gestation are behaviorally abnormal as adults. *Anesthesiology* 2011; 114: 521-28.

Interesting experimental study in pregnant rats to assess the effects of 4 hr exposure of 1.4% isoflurane (equivalent to 1 MAC) at gestation day 14 - which equates to the 2nd trimester in humans - on behavioral impairment in rat pups compared to control (unexposed) rats. Exposed rats showed signs of impaired acquisition of spatial memory and reduced anxiety behaviour compared to unexposed rats. No differences in locomotor activity, exploratory behavior or object recognition between rat populations were observed. Despite the implication that general anesthesia may negatively impact fetal neurodevelopment, there remains a lack of substantive data to corroborate whether the adverse effects observed in animal studies apply in utero to human subjects.

Accompanying editorial: Flood P: Fetal anesthesia and brain development. *Anesthesiology* 2011; 114: 479-80.

Letter to the editor: Shear TD: Is a weekend too long? *Anesthesiology* 2011; 115: 904.

Reply by the authors: Palanisamy A, Crosby G, Culley DJ: In Reply. *Anesthesiology* 2011; 115: 904-905.

166. Kong F, Xu L, He D, Zhang X, Lu H: Effects of gestational isoflurane exposure on postnatal memory and learning in rats. *Eur J Pharmacol* 2011; 670: 168-74.

In this exploratory animal study, pregnant rats at gestational day 14 were exposed to 1.3% isoflurane or oxygen for 4 hr. Compared to controls, the isoflurane-exposed offspring rats displayed impaired spatial memory and learning. In the isoflurane group, cellular/molecular changes in synaptic architecture within the hippocampus, and higher levels of mediators (C/EBP homologous transcription factor protein and caspase-12) affiliated with neuronal cell death in the hippocampus were reported. This paper provides more

concerning findings, using a rat model, that exposure to isoflurane in utero has deleterious effects on postnatal memory and learning.

167. Culley DJ, Boyd JD, Palanisamy A, Xie Z, Kojima K, Vacanti CA, Tanzi RE, Crosby G: Isoflurane decreases self-renewal capacity of rat cultured neural stem cells. *Anesthesiology* 2011; 115: 754-63.

With anesthetic neurotoxicity of paramount scientific importance, this in vitro study aimed to investigate the effect of clinically relevant concentrations of isoflurane on rat embryo neural stem cells. Isoflurane concentrations up to 2.8% did not induce neural stem cell death; however, 1.4% and 2.8% isoflurane did significantly reduce stem cell proliferation. These results add to the growing body of evidence that suggest that inhalational agents, at clinically relevant concentrations, have time-dependent deleterious effects on fetal brain development.

## *Postnatal Effects of Anesthesia on Neurodevelopment*

168. Paule MG, Li M, Allen RR, Liu F, Zou X, Hotchkiss C, Hanig JP, Patterson TA, Slikker W, Jr., Wang C: Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys. *Neurotoxicol Teratol* 2011; 33: 220-30.

High-quality study indicating that 24 hr of ketamine exposure in postnatal rhesus monkeys (postnatal day 5-6) produces functional deficits in cognitive function after 7 months of age. Using standardized tests to assess learning, motivation, color discrimination and short-term memory, these investigators observed that ketamine-exposed animals had poorer performance in task performance compared to control (unexposed) animals (from week 24-63 of training). After week 36, ketamine exposed rates also displayed poorer performance in learning and color/position discrimination. Although this study provides further evidence that general anesthesia negatively impacts on critical phases of neurodevelopment, the applicability of these observations on human neurodevelopment (including precise thresholds for dose and duration of exposure and duration of effect) remain uncertain.

169. Zou X, Liu F, Zhang X, Patterson TA, Callicott R, Liu S, Hanig JP, Paule MG, Slikker W, Jr., Wang C: Inhalation anesthetic-induced neuronal damage in the developing rhesus monkey. *Neurotoxicol Teratol* 2011; 33: 592-97.

This study builds on prior work examining the neurotoxic effects of general anesthetic agents on GABA and NMDA receptors. Under physiologically controlled conditions, Rhesus monkeys underwent 8 hr exposure to N<sub>2</sub>O (70%) and/or isoflurane (1%), in isolation or in combination, and anesthetic-induced pathologic changes on neuronal architecture were examined. Interestingly, no notable effects were reported after isoflurane or N<sub>2</sub>O in isolation, but neuronal damage (apoptosis) was associated with combined N<sub>2</sub>O/isoflurane exposure.

See also comparative study: Istaphanous GK, Howard J, Nan X, Hughes EA, McCann JC, McAuliffe JJ, Danzer SC, Loepke AW: Comparison of the neuroapoptotic properties of equipotent anesthetic concentrations of desflurane, isoflurane, or sevoflurane in neonatal mice. *Anesthesiology* 2011; 114: 578-87.

This in vivo study examined the neuronal effects of 6hr exposure to equipotent concentrations of sevoflurane, isoflurane and desflurane (0.55-0.6 MAC) on postnatal day 7-8 mice. The three inhaled anesthetics all increased neocortical neuronal apoptotic cell death in neonatal mice to a similar degree. These results suggest that there may not be quantitative or qualitative differences in cytotoxic effect in neonatal mice among these anesthetic agents.

170. Zhao YL, Xiang Q, Shi QY, Li SY, Tan L, Wang JT, Jin XG, Luo AL: GABAergic excitotoxicity injury of the immature hippocampal pyramidal neurons' exposure to isoflurane. *Anesth Analg* 2011; 113: 1152-60.

Recent studies have shown that isoflurane exposure can induce neuronal excitotoxicity and apoptosis in the developing brain; however, detailed

mechanistic data has been lacking. This high quality in vitro study, using rat pup hippocampal tissue, investigated how isoflurane modulates GABA receptor evoked synaptic voltage dependent calcium channel overactivation and Ca<sup>2+</sup> ion influx, and how isoflurane modulates Ca<sup>2+</sup>-induced Ca<sup>2+</sup> release from intracellular stores. The overall increase in intracellular Ca<sup>2+</sup> concentration is postulated to be a critical component of excitotoxic cell damage and apoptosis induced by isoflurane.

Accompanying editorial: Wei H: The role of calcium dysregulation in anesthetic-mediated neurotoxicity. *Anesth Analg* 2011; 113: 972-74.

171. Sinner B, Friedrich O, Zink W, Zausig Y, Graf BM: The toxic effects of s(+)-ketamine on differentiating neurons in vitro as a consequence of suppressed neuronal Ca<sup>2+</sup> oscillations. *Anesth Analg* 2011; 113: 1161-69.

Exploratory study using hippocampal tissue from infant rat pups exposed to NMDA receptor antagonists, including ketamine, for 24 hr. The results of this study indicated that ketamine-induced neuronal apoptosis and disrupted synaptic integrity may be linked with suppression of neuronal Ca<sup>2+</sup> oscillations and reduced expression of target calcium regulatory proteins (CaMKII and synapsin) associated with neuronal development.

### *Epidemiologic Studies*

172. Hansen TG, Pedersen JK, Henneberg SW, Pedersen DA, Murray JC, Morton NS, Christensen K: Academic performance in adolescence after inguinal hernia repair in infancy: a nationwide cohort study. *Anesthesiology* 2011; 114: 1076-85.

Retrospective, population-wide, observational study in Denmark which compared the academic performance of all children undergoing inguinal hernia repair under general anesthesia ≤1 yr (n=2689) versus a randomly selected, aged matched control sample (n=14575). After adjustment (using logistic regression), no statistical differences in average test scores were found between groups for subjects' 9th grade test scores (-0.04; 95% CI=-0.09-0.01). Similar results were found using propensity scores, which supports a lack of neurotoxic effect of general anesthesia in infants aged up to 1 yr. However, a higher test score non-attainment rate in exposed subjects was observed; it is unclear if exposure to general anesthesia influenced this outcome.

Letter to the editor: Flick RP, Warner DO: Hernia repair, anesthetic exposure, and academic performance in children. *Anesthesiology* 2011; 115: 1387; author reply 1387-88.

173. Flick RP, Katusic SK, Colligan RC, Wilder RT, Voigt RG, Olson MD, Sprung J, Weaver AL, Schroeder DR, Warner DO: Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics* 2011; 128: e1053-61.

In this matched cohort study (n=1050) in Rochester, Minnesota, investigators aimed to provide further insight into the relationship between anesthesia delivered to children under 2 yrs of age and disorders of learning or cognition. Notable findings included a significantly increased risk of learning disabilities (adj HR=2.12; 95% CI=1.26-3.54) and speech-language disorders (adj HR=4.16; 95% CI=1.96-8.87) with ≥2 anesthesia episodes. However, no associations were observed between exposure and the need for educational plans for behavioral/emotional disorders.

Commentary: Williams RK: The pediatrician and anesthesia neurotoxicity. *Pediatrics* 2011; 128: e1268-70.

This article highlights study design flaws, including multiple confounders, age at exposure, comorbid disorders and the use of historical anesthetic agents (halothane) and monitoring. These flaws limit the analyses of the independent effects of general anesthesia on the neuropsychologic/cognitive outcomes.

## Prenatal Surgery

174. Adzick NS, Thom EA, Spong CY, Brock JW, 3rd, Burrows PK, Johnson MP, Howell LJ, Farrell JA, Dabrowiak ME, Sutton LN et al: A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011; 364: 993-1004.

The impact of a novel surgical strategy for reducing adverse outcomes in neonates with myelomeningocele are explored in this high-quality multicenter RCT. (n=183) A composite measure for adverse outcomes - the need for a CSF shunt or perinatal mortality - was used. Up to 12 months of age, adverse outcomes occurred in a lower proportion of patients undergoing prenatal repair (via hysterotomy and general anesthesia) versus traditional postnatal surgical repair (68% vs 98%, RR=0.7; 97.7% CI=0.58-0.84). Scores of pediatric mental development and motor function at 30 months were improved in the prenatal group. Interestingly, high rates of maternal and perinatal morbidity (e.g. oligohydramnios, preterm birth, chorioamniotic separation) were observed in the prenatal group. The long-term neurologic effects of prenatal repair also remain uncertain.

Accompanying editorial: Simpson JL, Greene MF: Fetal surgery for myelomeningocele? *N Engl J Med* 2011; 364: 1076-77.

This editorial advises caution in over-interpreting study findings based on the uncertain risk-benefit of prenatal repair due to mild-moderate improvement in neonatal outcomes versus the high rate of perinatal/maternal complications resulting from corrective surgery in-utero.

Letter to the editor: Prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011; 364: 2554-56.

175. Maternal-fetal intervention and fetal care centers. *Pediatrics* 2011; 128: e473-78.

Joint recommendations from the American Academy of Pediatrics and American College of Obstetricians and Gynecologists for women undergoing fetal interventions. The recommendations are aimed at optimizing fetal/neonatal outcomes. Issues pertaining to maternal consent, multidisciplinary care, patient advocacy, and resource allocation within fetal care centers are discussed.

See also - updated guidelines from the American College of Obstetricians and Gynecologists for non-obstetric surgery for obstetric patients. ACOG Committee Opinion No. 474: Nonobstetric surgery during pregnancy. *Obstet Gynecol* 2011; 117:420-1.

## Neonatology/Pediatrics

### Breastfeeding

176. Al-Tamimi Y, Ilett KF, Paech MJ, O'Halloran SJ, Hartmann PE: Estimation of infant dose and exposure to pethidine and norpethidine via breast milk following patient-controlled epidural pethidine for analgesia post caesarean delivery. *Int J Obstet Anesth* 2011; 20: 128-34.

Observational study assessing drug transfer and 'safety' in the infants of 20 breastfeeding women who received PCEA with pethidine (20 mg bolus; lockout 20 min) after CD. Absolute and relative infant doses for pethidine and norpethidine were subtherapeutic; infant exposure (ratio of drug in infant to maternal plasma) was 1.4% for pethidine and 0.4% for norpethidine. Overall, these drug levels appear to be safe for the breastfeeding neonate.

177. Sauberan JB, Anderson PO, Lane JR, Rafie S, Nguyen N, Rossi SS, Stellwagen LM: Breast milk hydrocodone and hydromorphone levels in mothers using hydrocodone for postpartum pain. *Obstet Gynecol* 2011; 117: 611-17.

This study provides important data on the pharmacokinetics of hydrocodone in breast milk of 30 postpartum, lactating mothers. Overall, the total neonatal opiate dosage (combined hydrocodone and hydromorphone [metabolite])=0.1-9.9%, which were within a 'safe' or subtherapeutic range. However, daily doses of hydrocodone >40 mg were not recommended for nursing mothers.

Letter to the editor: Koren G: Breast milk hydrocodone and hydromorphone levels in mothers using hydrocodone for postpartum pain. *Obstet Gynecol* 2011; 117: 1439; author reply 1439.

178. Vital signs: hospital practices to support breastfeeding --- United States, 2007 and 2009. *MMWR Morb Mortal Wkly Rep* 2011; 60: 1020-25.

A survey of US hospital and birth centers in 2009 indicated that best practices for breastfeeding are instituted comprehensively in only 3.4% of facilities. Local and national initiatives are needed to improve breastfeeding education and support for mothers prior to hospital discharge.

179. IPA, ICM, and FIGO joint statement on breastfeeding, including breastfeeding by HIV-infected mothers. *Int J Gynaecol Obstet* 2011; 114: 89-90.

Updated guidelines on breastfeeding by FIGO Committee for Safe Motherhood and Newborn health – in line with WHO guidelines – recommend exclusive breastfeeding for the first 6 months of life and continued breastfeeding for up to 2 yr.

180. Oddy WH, Li J, Whitehouse AJ, Zubrick SR, Malacova E: Breastfeeding duration and academic achievement at 10 years. *Pediatrics* 2011; 127: e137-45.

In this cohort study, academic achievement of children at 10 yr of age varied according to duration of breastfeeding (n=2868). Importantly, adjustments were made for family/parental socioeconomic status and early childhood stimulation. Breastfeeding for ≥6 months was associated with improved academic scores in mathematics, reading and spelling. In particular, boys appeared to have improved academic performance, if breastfed. This study adds weight to the promotion of breastfeeding for ≥6 months.

## Neonatal Outcomes for Preterm Infants

181. Carlo WA, McDonald SA, Fanaroff AA, Vohr BR, Stoll BJ, Ehrenkranz RA, Andrews WW, Wallace D, Das A, Bell EF et al: Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. *JAMA* 2011; 306: 2348-58.

In this high-quality multicenter cohort study, the use of antenatal steroids for mothers with preterm labor was linked with favorable outcomes for peri-viable infants born at 22-25 weeks' gestation with birth weights between 401g and 1000g (n=10,541). At 18-22 months follow-up, death or neurodevelopment impairment was significantly reduced in infants receiving antenatal steroids versus no steroids (adj OR=0.60; 95% CI=0.53-0.69).

## Improving Newborn Care and Assessment for Preterm Infants

182. Rüdiger M, Braun N, Gurth H, Bergert R, Dinger J: Preterm resuscitation I: Clinical approaches to improve management in delivery room. *Early Human Development* 2011; 87: 749-53.

For anesthesiologists with a specific interest in resuscitation of preterm infant, this commentary article is highly recommended. This paper describes new concepts for improving delivery room care and newborn assessment of preterm infants: individualized 'support of transition' as opposed to resuscitation, video-recordings to improve the quality of early post-delivery care and redefinition of the APGAR score, specifically for premature infants and infants receiving treatment.

## IVF Pregnancy and Neonatal Outcomes

183. Janvier A, Spelke B, Barrington KJ: The epidemic of multiple gestations and neonatal intensive care unit use: the cost of irresponsibility. *J Pediatr* 2011; 159: 409-13.

Interesting institutional analyses of neonatal complications related to IVF pregnancies. Infants born to mothers with multiple gestation due to artificial reproductive technologies accounted for 17% of neonatal ICU admissions. Significant reductions in neonatal complications were projected by using a single embryo transfer for infertile couples (such as assisted ventilation; number of NICU days).

## Neonatal Mortality

184. Reddy UM, Bettgowda VR, Dias T, Yamada-Kushnir T, Ko CW, Willinger M: Term pregnancy: a period of heterogeneous risk for infant mortality. *Obstet Gynecol* 2011; 117: 1279-87.

Large, population-wide study using National Center for Health Statistics data (n=46,329,018 singleton live births). Investigators assessed racial and ethnic differences in neonatal mortality rates between 37<sup>0/7</sup> and 41<sup>6/7</sup> weeks' gestation. Ethnic disparities were evidenced by small declines in infant mortality rate in blacks (7%) compared to Hispanics (35%) and whites (22%) from 1995 to 2006. The risk for neonatal mortality was higher at 37 weeks compared to 40 weeks for all ethnic groups.

Letter to the editor: Chabra S: Concept of gestational age in "completed weeks": lost in translation. *Obstet Gynecol* 2012; 119: 183-84; author reply 184-85.

## Hypoxic-Ischemic Encephalopathy

185. Higgins RD, Raju T, Edwards AD, Azzopardi DV, Bose CL, Clark RH, Ferriero DM, Guillet R, Gunn AJ, Hagberg H et al: Hypothermia and other treatment options for neonatal encephalopathy: an executive summary of the Eunice Kennedy Shriver NICHD workshop. *J Pediatr* 2011; 159: 851-858.e1.

Important document from an expert panel convened by the NICHD highlighting data and knowledge gaps for treatment options for hypoxic-ischemic encephalopathy (HIE). Although induced hypothermia is a promising therapy, there is a great need to (i) develop biomarkers for detecting disease and assessing therapeutic response, (ii) optimize management strategies, including hypothermia, and (iii) improve resources for effectively treating HIE.

## Neurodevelopment and Perinatal Factors

### *Cognitive Dysfunction and Perinatal Ischemic Injury*

186. Yang T, Zhuang L, Terrando N, Wu X, Johnson MR, Maze M, Ma D: A clinically relevant model of perinatal global ischemic brain damage in rats. *Brain Res* 2011; 1383: 317-23.

Compelling animal study, using term rat pups, demonstrating that perinatal ischemic injury leads to neuronal death in the hippocampus and long-lasting cognitive dysfunction. Of note, apoptotic changes and neurocognitive dysfunction were increased with longer periods of in utero hypoxia. This model of perinatal hypoxia/asphyxia should encourage future work to investigate targeted neuroprotective approaches.

## Cerebral Palsy

187. O'Callaghan ME, MacLennan AH, Gibson CS, McMichael GL, Haan EA, Broadbent JL, Goldwater PN, Dekker GA: Epidemiologic associations with cerebral palsy. *Obstet Gynecol* 2011; 118: 576-82.

Australian case-control study which aimed to identify risk factors for cerebral palsy using data from linked perinatal databases, cerebral palsy registers and maternal questionnaires (n=587 [cases], 1154 [controls]). Using univariate analyses, investigators found that preterm birth (<32 weeks gestation), intrauterine growth retardation, maternal infection during pregnancy, and multiple birth were strong risk factors for cerebral palsy. Unfortunately, recall bias, the use of unadjusted ORs and failure to account for interaction among independent variables affected the quality of the data analyses.

188. Carlo WA, McDonald SA, Tyson JE, Stoll BJ, Ehrenkranz RA, Shankaran S, Goldberg RN, Das A, Schendel D, Thorsen P et al: Cytokines and neurodevelopmental outcomes in extremely low birth weight infants. *J Pediatr* 2011; 159: 919-25.e3.

Based on the assumption that perinatal inflammation is associated with an increased risk of cerebral palsy (CP), this high quality multicenter cohort study sought to identify pro- and anti-inflammatory cytokines associated with CP in extremely low birth weight (ELBW) infants (n=755). After co-variate adjustment, interleukin 8 levels were significantly increased on days 0-4 and up to day 21 among the ELBW infants who developed CP. Future work is recommended to investigate the influence of altered cytokine-specific gene expression in CP infants.

## Autism and Perinatal/Obstetric and Neonatal Risk Factors

189. Gardener H, Spiegelman D, Buka SL: Perinatal and neonatal risk factors for Autism: a comprehensive meta-analysis. *Pediatrics* 2011; 128: 344-55.

Impressive meta-analysis of 40 studies assessing perinatal and neonatal risk factors for autism. Metaregression was used to identify methodologic differences between studies. In total, nine obstetric/perinatal (including maternal hemorrhage) and seven neonatal factors (including low 5 min APGAR) were associated with autism risk. Importantly, anesthesia was not associated with autism risk. However, our understanding of risk profiles is significantly limited by the heterogeneity of methodologies employed among studies.

## Psychological Impairment and Mode of Delivery

190. Li HT, Ye R, Achenbach TM, Ren A, Pei L, Zheng X, Liu JM: Caesarean delivery on maternal request and childhood psychopathology: a retrospective cohort study in China. *BJOG* 2011; 118: 42-48.

Retrospective cohort study which aimed to investigate whether mode of delivery influenced the development of childhood psychopathology (CPP) (n=4190). Using behavioral scoring assessments, investigators found that children born by CD and assisted vaginal delivery had the lowest and highest problem scores respectively. Mechanisms to explain variations in these problem scores according to mode of delivery remain uncertain.

## Academic Achievement and Gestational Age at Delivery

191. Aamoudse-Moens CS, Oosterlaan J, Duivenvoorden HJ, van Goudoever JB, Weisglas-Kuperus N: Development of preschool and academic skills in children born very preterm. *J Pediatr* 2011; 158: 51-56.

Retrospective study comparing cognitive and academic abilities of pre-school and primary school children, who were born very preterm (gestational age <30 weeks) versus term-born (n=200). Very preterm infants had significantly poorer numerical reasoning skills and mathematical abilities than term infants,

differences that persisted over time. Although these findings are interesting, future work needs to account for all factors (e.g., perinatal) that influence infants' academic achievement.

## Excessive Postnatal Weight Loss

192. Chantry CJ, Nommsen-Rivers LA, Peerson JM, Cohen RJ, Dewey KG: Excess weight loss in first-born breastfed newborns relates to maternal intrapartum fluid balance. *Pediatrics* 2011; 127: e171-79.

In this high-quality, prospective cohort study (n=316) of exclusively breastfed, first-born, term infants, the prevalence of excess weight loss, defined as  $\geq 10\%$  of birth weight at postnatal day 3, was surprisingly high (19%). Interestingly, a high rate of maternal intrapartum fluid balance was independently associated with excess weight loss (adj RR=3.18; 95% CI=1.4-13.3).

## Congenital Heart Disease at Birth

193. van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, Roos-Hesselink JW: Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol* 2011; 58: 2241-47.

This impressive systematic review, comprising 114 papers, summarizes changing patterns of birth prevalence of congenital heart disease (CHD). Total birth prevalence has increased over time; a current estimate is 9.1 per 1000 live births (95% CI=9.0-9.2), an estimate which forebodes a major global health burden. Steady increases in ventricular and atrial septal defects and patent ductus arteriosus have occurred since the 1970s.

## Health Care Reform and Health Policy

### United States

194. Institute of Medicine. Clinical preventive services for women: closing the gaps. 2011. <http://www.hrsa.gov/womensguidelines/>.

This important announcement from HRSA, based on a comprehensive IOM review, will ensure that the planned Affordable Care Act will provide women's preventative health care (including prenatal care, screening for GDM and breastfeeding education) with no cost sharing between new health plans. This forthcoming public health reform will have sweeping implications for improving women's health.

195. von Gruenigen VE, Deveny TC: Health care reform: will quality remodeling affect obstetrician-gynecologists in addition to patients? *Obstet Gynecol* 2011; 117: 1167-69.

Worthwhile commentary article summarizing the implications for practicing OB-GYN physicians of impending health care reform related to the Patient Protection and Affordable Care Act. The authors speculate that the 'knock-on effects' of implementing quality performance standards and more rigorous oversight of physician practice, using quality metrics, will reduce the number of elective inductions, antenatal fetal testing and ultrasounds.

196. Saleeby E, Brindis CD: Women, reproductive health, and health reform. *JAMA* 2011; 306: 1256-57.

This commentary article gives a good overview of how implementation of the Affordable Care Act will transform the current model of care for the health of women in the US.

See also: Johnson KA: Women's health and health reform: implications of the Patient Protection and Affordable Care Act. *Curr Opin Obstet Gynecol* 2010; 22: 492-97.

## Global Health

197. WHO. Priority medicines for mothers and children 2011. World Health Organization. 2011. <http://www.who.int/medicines/publications/A4prioritymedicines.pdf>.

This joint announcement by the WHO, UNICEF and UNFPA lists 30 essential drugs deemed essential for preventing or treating major diseases and complications impacting the mother and child. Relevant drugs include oxytocin; magnesium sulphate, calcium gluconate; betamethasone, nifedipine (for preterm birth); ampicillin, gentamicin, metronidazole and misoprostol (for maternal sepsis after unsafe abortion).

198. Mills M, Rindfuss RR, McDonald P, te Velde E: Why do people postpone parenthood? Reasons and social policy incentives. *Hum Reprod Update* 2011; 17: 848-60.

Fascinating review of evidence to confirm our suspicions that birth postponement of the first child has occurred in most Western societies. The mean age of mothers at first delivery has increased by 1 yr each decade across OECD countries since the 1970s. Progressive and/or societal changes in health policy, contraceptive use, the employment market, women's education, gender roles, economic uncertainty, personal/family/relationship dynamics are postulated to be important drivers of this change.

## The Practice of Research

199. Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC: The ClinicalTrials.gov results database--update and key issues. *N Engl J Med* 2011; 364: 852-60.

Interesting article highlighting concerns about the quality of data entry, such as the number of primary outcome measures and lack of specificity in describing study designs, in trial records registered at ClinicalTrials.gov. A total of 79,413 registry entries and 2178 trial records were analyzed between Sept 2009 – Sept 2010.

200. Riley RD, Gates S, Neilson J, Alfirevic Z: Statistical methods can be improved within Cochrane pregnancy and childbirth reviews. *J Clin Epidemiol* 2011; 64: 608-18.

Have you ever been skeptical about the accuracy of the systematic reviews of the Cochrane Pregnancy and Childbirth Group (CPCG)? This review paints a sobering picture of the statistical flaws that are likely to have weakened the methodologic rigor of existing CPCG reviews. In 75 reviews, areas of weakness included failure to adequately address publication bias, insufficient/incorrect interpretation of random-effects analyses, and inadequate assessment of between-study heterogeneity.

## Patient Safety

### Operating Room Drug Errors

201. Merry AF, Webster CS, Hannam J, Mitchell SJ, Henderson R, Reid P, Edwards KE, Jardim A, Pak N, Cooper J et al: Multimodal system designed to reduce errors in recording and administration of drugs in anaesthesia: prospective randomised clinical evaluation. *BMJ* 2011; 343: d5543.

In this prospective study, investigators compared the rates of anaesthesia-related drug errors between two delivery systems - a patented multimodal drug delivery system (DDS) versus conventional practice in drug administration - among 89 anaesthesiologists. The DDS includes customized drug trolleys, pre-filled labeled syringes, barcode readers, and a computerized system with audio-visual verification software for overseeing drug inventory. There were fewer drug errors per 100 administrations using the DDS compared to conventional practice (9.1 vs 11.6;  $P=0.045$ ). These systems may ultimately reduce iatrogenic patient harm, reduce documentation errors and allow more time for patient care in the operating room.

Accompanying editorial: Haller G, Clergue F: Drug administration errors in anaesthesia and beyond. *BMJ* 2011; 343: d5823.

### Simulation Research

202. Lipman S, Daniels K, Cohen SE, Carvalho B: Labor room setting compared with the operating room for simulated perimortem cesarean delivery: a randomized controlled trial. *Obstet Gynecol* 2011; 118: 1090-94.

Randomized study to compare practices for managing perimortem cardiac arrest in a labor room (primary site) using a manikin. Using 15 teams, the median time to perform incision was longer if the manikin was transferred from the labor room to the operating room compared to commencing incision in the labor room (7.5 min vs 4.3 min;  $P<0.004$ ). These findings suggest that perimortem CD should be performed in the labor room.

### Patient Safety Initiatives/Programs

203. Grunebaum A, Chervenak F, Skupski D: Effect of a comprehensive obstetric patient safety program on compensation payments and sentinel events. *Am J Obstet Gynecol* 2011; 204: 97-105.

This article describes details of a multidimensional, comprehensive patient-safety program for improving obstetric care and reducing severe perinatal adverse outcomes at a tertiary obstetric center. Within a 6 yr period, a substantial decrease in sentinel events and compensation payments was observed.