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Tracy A. Manuck, Rebecca C. Fry, and Barbara L. McFarlin

Billions of dollars are spent yearly in perinatal medicine on studies designed to improve outcomes for mothers and their neonates. However, implementing research findings is challenging and imperfect. Strategies for implementation must be multifaceted and comprehensive. These implementation challenges extend to, and are often greater in, translational and basic science research. This article discusses current challenges in the provision of quality perinatal and neonatal medical care, particularly those related to preterm birth, and provides examples of prematurity-related perinatal quality collaborative initiatives. Finally, the authors review considerations in implementing both clinical and translational/basic science prematurity research.

Improving Uptake of Key Perinatal Interventions Using Statewide Quality Collaboratives	165
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Vidya V. Pai, Henry C. Lee, and Jochen Profit

Regional and statewide quality improvement collaboratives have been instrumental in implementing evidence-based practices and facilitating quality improvement initiatives within neonatology. Statewide collaboratives emerged from larger collaborative organizations, such as the Vermont Oxford Network, and play an increasing role in collecting and interpreting data, setting priorities for improvement, disseminating evidence-based clinical practice guidelines, and creating regional networks for synergistic learning. In this article, the authors highlight examples of successful statewide collaborative initiatives, as well as challenges that exist in initiating and sustaining collaborative efforts.

Antenatal Corticosteroids: Who Should We Be Treating?	181
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Whitney A. Booker and Cynthia Gyamfi-Bannerman

Antenatal corticosteroids remain one of the crucial interventions in those at risk for imminent preterm birth. Therapeutic benefits include reducing major complications of prematurity, such as respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis, as well as an overall decrease in neonatal deaths. Optimal reductions in neonatal

morbidity and mortality require a thoughtful review of the timing of administration. In addition, a thorough understanding is required of which patients maximally benefit from this intervention in the management and counseling of those at risk for preterm birth.

Delivery at Term: When, How, and Why

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Kate F. Walker and Jim G. Thornton

There is growing evidence from randomized trials that induction of labor at or near term does not increase cesarean delivery; observational data show that the optimal gestation for spontaneous delivery for the baby is 39 weeks. Elective cesarean at these gestations is also sometimes considered, but evaluating the associated risks is complex. For the baby, although cesarean obviates the risks of labor, it carries a risk of respiratory problems, which may be severe. For the mother, cesarean is more dangerous than vaginal and emergency cesarean is more dangerous than elective. The authors consider the evidence base for near-term induction of labor and cesarean for a range of scenarios.

Perinatal Care of Infants with Congenital Birth Defects

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Elizabeth K. Sewell and Sarah Keene

Prenatal diagnosis has changed perinatal medicine dramatically, allowing for additional fetal monitoring, referral and counseling, delivery planning, the option of fetal intervention, and targeted postnatal management. Teams participating in the delivery room care of infants with known anomalies should be not only knowledgeable about specific needs and expectations but also ready for unexpected complications. A small number of neonates need rapid access to postnatal interventions, such as surgery, but most can be stabilized with appropriate neonatal care. These targeted perinatal interventions have been shown to improve outcome in selected diagnoses.

Prognosis as an Intervention

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Matthew A. Rysavy

This article elaborates on how neonatologists and perinatologists might conceive of prognosis as an intervention with outcomes relevant to patients, families, and society at large and highlights aspects of this important area of practice requiring further study.

Therapeutic Hypothermia: How Can We Optimize This Therapy to Further Improve Outcomes?

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Girija Natarajan, Abbot Laptook, and Seetha Shankaran

Neonatal hypoxic-ischemic encephalopathy remains associated with considerable death and disability. In multiple randomized controlled trials, therapeutic hypothermia for neonatal moderate or severe hypoxic-ischemic encephalopathy among term infants has been shown to be safe and effective in reducing death and disability in survivors. In this article, the current status of infant and childhood outcomes following this therapy is reviewed. The clinical approaches that may help to optimize this innovative neuroprotective therapy are presented.

Preventing Continuous Positive Airway Pressure Failure: Evidence-Based and Physiologically Sound Practices from Delivery Room to the Neonatal Intensive Care Unit 257

Clyde J. Wright, Laurie G. Sherlock, Rakesh Sahni, and Richard A. Polin

Routine use of continuous positive airway pressure (CPAP) to support pre-term infants with respiratory distress is an evidenced-based strategy to decrease the incidence of bronchopulmonary dysplasia. However, rates of CPAP failure remain unacceptably high in very premature neonates, who are at high risk for developing bronchopulmonary dysplasia. Using the GRADE framework to assess the quality of available evidence, this article reviews strategies aimed at decreasing CPAP failure, starting with delivery room interventions and followed through to system-based efforts in the neonatal intensive care unit. Despite best efforts, some very premature neonates fail CPAP. Also reviewed are predictors of CPAP failure in this vulnerable population.

Optimizing Caffeine Use and Risk of Bronchopulmonary Dysplasia in Preterm Infants: A Systematic Review, Meta-analysis, and Application of Grading of Recommendations Assessment, Development, and Evaluation Methodology 273

Mitali Atul Pakvasa, Vivek Saroha, and Ravi Mangal Patel

Caffeine reduces the risk of bronchopulmonary dysplasia (BPD). Optimizing caffeine use could increase therapeutic benefit. The authors performed a systematic review and random-effects meta-analysis of studies comparing different timing of initiation and dose of caffeine on the risk of BPD. Earlier initiation, compared with later, was associated with a decreased risk of BPD (5 observational studies; $n = 63,049$; adjusted OR, 0.69; 95% CI, 0.64–0.75; GRADE, low quality). High-dose caffeine, compared with standard dose, was associated with a decreased risk of BPD (3 randomized trials; $n = 432$; OR, 0.65; 95% CI, 0.43–0.97; GRADE, low quality). Higher-quality evidence is needed to guide optimal caffeine use.

Oxygen Therapy in the Delivery Room: What Is the Right Dose? 293

Vishal Kapadia and Myra H. Wyckoff

Oxygen is the most common medicine used during neonatal resuscitation in the delivery room. Oxygen therapy in the delivery room should be used judiciously to avoid oxygen toxicity while delivering sufficient oxygen to prevent hypoxia. Measurement of appropriate oxygenation relies on pulse oximetry, but adequate ventilation and perfusion are equally important for oxygen delivery. In this article, the authors review oxygenation while transitioning from fetal to neonatal life, the importance of appropriate oxygen therapy, its measurement in the delivery room, and current recommendations for oxygen therapy and its limitations.

Detection and Prevention of Perinatal Infection: Cytomegalovirus and Zika Virus 307

Amber M. Wood and Brenna L. Hughes

Congenital cytomegalovirus is the most common viral congenital infection and affects up to 2% of neonates. Significant sequelae may develop after congenital cytomegalovirus, including hearing loss, cognitive defects,

seizures, and death. Zika virus is an emerging virus with perinatal implications; a congenital Zika virus syndrome has been identified and includes findings such as microcephaly, fetal nervous system abnormalities, and neurologic sequelae after birth. Screening, diagnosis, prevention, and treatment of these perinatal infections are reviewed in this article.

Current Strategies to Prevent Maternal-to-Child Transmission of Human Immunodeficiency Virus

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Leilah Zahedi-Spung and Martina L. Badell

The World Health Organization's Millennium Development Goal 6 includes eliminating human immunodeficiency virus (HIV) in children as a top priority. Many states in the United States report maternal-to-child transmission rates less than 1% using the current recommendations for the management of HIV-infected pregnant women. This article summarizes the most current management guidelines in caring for HIV-infected women and their infants to prevent maternal-to-child transmission.

Relationships Between Perinatal Interventions, Maternal-Infant Microbiomes, and Neonatal Outcomes

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Gregory Valentine, Derrick M. Chu, Christopher J. Stewart, and Kjersti M. Aagaard

The human microbiome acquires its vastness and diversity over a relatively short time period during development. Much is unknown, however, about the precise prenatal versus postnatal timing or its sources and determinants. Given early evidence of a role for influences during pregnancy and early neonatal and infant life on the microbiome and subsequent metabolic health, research investigating the development and shaping of the microbiome in the fetus and neonate is an important arena for study. This article reviews the relevant available literature and future questions on what shapes the microbiome during early development and mechanisms for doing so.

Perinatal Brain Injury: Mechanisms, Prevention, and Outcomes

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Christopher M. Novak, Maide Ozen, and Irina Burd

Perinatal brain injury may lead to long-term morbidity and neurodevelopmental impairment. Improvements in perinatal care have resulted in the survival of more infants with perinatal brain injury. The effects of hypoxia-ischemia, inflammation, and infection during critical periods of development can lead to a common pathway of perinatal brain injury marked by neuronal excitotoxicity, cellular apoptosis, and microglial activation. Various interventions can prevent or improve the outcomes of different types of perinatal brain injury. This article reviews the mechanisms of perinatal brain injury, approaches to prevention, and outcomes among children with perinatal brain injury.