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Section on Neonatal-Perinatal Medicine

## ARTICLES OF INTEREST – August 2024

Effect of early clinical management on metabolic acidemia in neonates with hypoxic-ischemic encephalopathy
Erastus Thuo, Elizabeth R Lyden and Eric S Peeples. J Perinatol.

This retrospective study included infants born at ≥35 weeks of gestation and receiving therapeutic hypothermia to determine the safety and effectiveness of sodium bicarbonate administration in the management of metabolic acidemia and short-term outcomes in neonates with hypoxic-ischemic encephalopathy (HIE). Of the 129 infants who met inclusion criteria, 39 infants received bicarbonate and 90 infants did not. The authors found that there was higher mortality ($p = 0.010$) and injury on MRI ($p = 0.008$)-primarily deep gray matter ($p < 0.001$) and cortical injury ($p = 0.003$)-in the bicarbonate group compared to controls in univariate analysis. The combined outcome of death or abnormal MRI was not significantly associated (OR 1.97, 95% CI 0.80-4.87, $p = 0.141$) with bicarbonate administration when adjusting for sex, 5-minute Apgar, and initial base deficit.

Long-term growth and neurodevelopmental outcomes of neonates infected with SARS-CoV-2 during the COVID-19 pandemic at 18–24 months corrected age: a prospective observational study
Medha Goyal, Dwayne Mascarenhas, Prashanth Rr, et al. Neonatology.

This prospective study included 20 neonates who acquired severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection during the first wave of the pandemic (April-July 2020). At 18-24 months corrected age, the authors found developmental delay in nearly half of the children with scores below one standard deviation in the Bayley Scales of Infant and Toddler Development (third edition). Mild delay in either motor, cognitive, or language domains was found in 9 (45%) children and moderate delay in 2 (10%). Expressive language, fine motor, and receptive language were predominantly affected. None of the children had hearing impairment, blindness, or significant growth faltering. The mean composite cognitive, language, and motor scores were significantly lower in those with neurodevelopmental delay (p value - 0.02, 0.000, and 0.03, respectively) without any differences in their disease characteristics.

Acetaminophen for patent ductus arteriosus and risk of mortality and pulmonary morbidity
Erik A Jensen, Sara B DeMauro, Matthew A Rysavy, et al. Pediatrics.

Emerging data indicate that acetaminophen may adversely affect lung health. The authors examined whether acetaminophen compared with cyclooxygenase (COX) inhibitor alone for patent ductus arteriosus (PDA) is associated with mortality or respiratory morbidity in extremely preterm infants. This retrospective cohort study used data from the National Institute of Child Health and Human Development Neonatal Research Network. Infants were born at 22 to 28 weeks' gestation or weighing 401 to 1000 g between 2016 and 2020 and received acetaminophen, ibuprofen, and/or indomethacin for PDA closure. The authors found that treatment with acetaminophen versus COX inhibitor alone for PDA was not associated with the composite outcome of death or BPD in extremely preterm infants. Their results support further evaluation of whether acetaminophen for PDA increases mortality.

Quality improvement interventions to prevent intraventricular hemorrhage: a systematic review
Erika M Edwards, Danielle E Y Ehret, Howard Cohen, Denise Zayack, et al. Pediatrics.

Quality improvement may reduce the incidence and severity of intraventricular hemorrhage in preterm infants. In this systematic review, the authors evaluated quality improvement interventions (QIIs) that sought to prevent or reduce the severity of intraventricular hemorrhage. PubMed, CINAHL, Embase, and citations of selected articles were searched. QIIs that had reducing incidence or severity of intraventricular hemorrhage in preterm infants as the primary outcome. Eighteen quality improvement interventions involving 5906 infants were included. The authors found that QIIs demonstrated reductions in the incidence and severity of intraventricular hemorrhage in preterm infants in some but not all settings. Which specific interventions and quality improvement methods were responsible for those reductions and why they were successful in some settings but not others are not clear.

Magnesium sulfate before preterm birth for neuroprotection: an updated Cochrane systematic review
Emily S Shepherd, Shona Goldsmith, Lex W Doyle, et al. Obstet Gynecol.

This is an updated meta-analysis studying magnesium sulfate as a fetal neuroprotective agent when given to individuals at risk of preterm birth. It includes six RCTs (5,917 pregnant participants and 6,759 fetuses at less than 34 weeks of gestation at randomization). They were conducted in high-income countries and commenced between 1995 and 2018. Magnesium sulfate compared with placebo reduced the risk of cerebral palsy (risk ratio [RR] 0.71, 95% CI, 0.57-0.89) and death or cerebral palsy (RR 0.87, 95% CI, 0.77-0.98). Magnesium sulfate had little or no effect on death up to 2 years of corrected age. In pregnant individuals it increased adverse effects severe enough to stop treatment (RR 3.21, 95% CI, 1.88-5.48). Secondary outcome: magnesium sulfate reduced the risk of severe neonatal intraventricular hemorrhage. This updated meta-analysis re-iterates the neuro-protective effects of antenatal Magnesium sulfate even after inclusion of a more contemporary cohort of patients in the era of universal antenatal steroids.

Impact of neonatal sepsis on neurocognitive outcomes: a systematic review and meta-analysis
Wei Jie Ong, Jun Jie Benjamin Seng, Beijun Yap, et al. BMC Pediatr.

This systemic review and meta-analysis evaluated neurocognitive outcomes in neonates less than 90 days old (regardless of gestational age) with sepsis (positive blood culture). The primary outcome of interest was impaired neurocognitive outcome defined by (1) Cognitive Delay, (2) visual impairment, (3) auditory impairment and (4) Cerebral palsy. Of 7,909 studies reviewed, 24 studies (n = 121,645) were included in the analysis. Sepsis was associated with increased risk of cognitive delay [aOR 1.14 (95% CI: 1.01—1.28)], visual impairment [aOR 2.57 (95%CI: 1.14- 5.82)], hearing impairment [aOR 1.70 (95% CI: 1.02–2.81)] and cerebral palsy [aOR 2.48 (95% CI: 1.03–5.99)]. However, the data is heterogenous and there is lack of data specific for term/post-term infants.

Maternal major depression during early pregnancy is associated with impaired child executive functioning at 4.5 years of age
Robert D Levitan, Leslie Atkinson, Julia A Knight, et al. Am J Obstet Gynecol.

Maternal depression affects up to 1 in 7 pregnancies and can have affect fetal outcomes. This study examined the timing and severity of maternal depression and/or anxiety during pregnancy affect child executive functioning at age 4.5 years. Maternal symptoms of depression and anxiety were assessed at 12 to 16 and 28 to 32 weeks of gestation. Child executive functioning was measured using the Flanker test (a measure of attention) and the Dimensional Change Card Sort (a measure of cognitive flexibility) 4.5 years of age. The results of the study showed that fetal exposure to maternal major depression, not milder forms, at 12 to 16 weeks of gestation is associated with impaired executive functioning in the preschool years. The study emphasizes the importance of recognizing and treating maternal depression, particularly in early pregnancy due to its negative effects on both the mother and the child.

Blocking IL-17a signaling decreases lung inflammation and improves alveolarization in experimental bronchopulmonary dysplasia
Meagan Goates, Amrit Shrestha, Shyam Thapa, et al. Am J Pathol.

This study tested the hypothesis that blocking IL-17a signaling decreases lipopolysaccharide (LPS)-mediated experimental BPD in neonatal mice. LPS-injected mice had higher pulmonary IL-17a protein levels and IL-17a(+) and IL-22(+) cells. Gamma delta T cells, followed by non-T lymphoid cells, were the primary producers of IL-17a. LPS-mediated alveolar simplification, apoptosis, and cell proliferation inhibition were significantly greater in mice treated with isotype Ab than in those treated with IL-17a Ab. Furthermore, STAT1 activation and IL-6 levels were significantly greater in LPS-exposed mice treated with isotype Ab than in those treated with IL-17a Ab. The study results indicate that blocking IL-17a signaling decreases LPS-mediated experimental BPD.

Risk factors and clinical outcomes of pulmonary hypertension associated with bronchopulmonary dysplasia in extremely premature infants: A systematic review and meta-analysis
Bo Li, Shuang-Shuang Qu, Ling-Xue Li, et al. Pediatr Pulmonol.

This systematic review and meta-analysis evaluated the risk factors for bronchopulmonary dysplasia associated pulmonary hypertension (BPD-PH) in extremely premature infants (gestational age < 32 weeks) and its impact on outcomes. Meta-analysis of 2137 extremely premature infants revealed that oligohydramnios (OR = 2.21, 95% CI 1.06-4.61), low gestational age (SMD = -0.36, 95% CI -0.47 to -0.24), low birth weight (SMD = -0.54, 95% CI -0.74 to -0.35), small for gestational age (OR = 1.61, 95% CI 1.06-2.44), neonatal respiratory distress syndrome (OR = 2.05, 95% CI 1.45-2.91), grade III bronchopulmonary dysplasia (OR = 4.67, 95% CI 1.34-16.30), and sepsis (OR = 2.25, 95% CI 1.69-4.66) were risk factors for BPD-PH, whereas antenatal steroids (OR = 0.66, 95% CI 0.49-0.88) were protective. BPD-PH led to the extension of oxygen therapy (SMD = 0.67, 95% CI 0.42-0.92) and hospital stay (SMD = 0.77, 95% CI 0.14-1.40), and elevated the risk of discharged on oxygen (OR = 2.77, 95% CI 1.35-5.70) and death (OR = 4.38, 95% CI 2.21-8.69).

Cerebral palsy and motor impairment after extreme prematurity: prediction of diagnoses at ages 2 and 10 years
Timothy Marinelli, Joe X Yi, T Michael O'Shea, et al. J Pediatr.

Participants of the Extremely Low Gestational Age Newborns Study (ELGANS) were classified as: no MI (Motor Impairment), MI only at 2 years, MI only at 10 years, and MI at both 2 and 10 years, based on a standardized neurological examination at 2 and the Gross Motor Function Classification System (GMFCS) at 10 years of age. Least Absolute Shrinkage and Selection Operator (LASSO) regression was used to develop the final predictive model. Of the 849 study participants, 64 (7.5%) had a diagnosis of MI at both 2 and 10 years and 63 (7.4%) had a diagnosis of MI at 1 visit but not the other. Of 22 total risk factors queried, 4 variables most reliably and accurately predicted MI: gestational age, weight z-score growth trajectory during neonatal intensive care unit (NICU) stay, ventriculomegaly, and cerebral echolucency on head ultrasound. By selecting probability thresholds of 3.5% and 7.0% at ages 2 and 10, respectively, likelihood of developing MI can be predicted with a sensitivity and specificity of 71.2%/72.1% at age 2 and 70.7%/70.7% at age 10.

Initial oxygen concentration for the resuscitation of infants born at less than 32 weeks' gestational systematic review and individual participant data network meta-analysis
James X Sotiropoulos, Ju Lee Oei, Georg M Schmölzer, et al. JAMA Pediatr.

To evaluate the relative effectiveness of initial FiO2 on reducing mortality, severe morbidities, and oxygen saturations (SpO2) in preterm infants born at less than 32 weeks' gestation using network meta-analysis (NMA) of individual participant data (IPD). Eligible studies were randomized clinical trials enrolling infants born at less than 32 weeks' gestation comparing at least 2 initial oxygen concentrations for delivery room resuscitation, defined as either low (≤0.3), intermediate (0.5-0.65), or high (≥0.90) FiO2. IPD were provided for 1055 infants from 12 of the 13 eligible studies (2005-2019). Resuscitation with high (≥0.90) initial FiO2 was associated with significantly reduced mortality compared to low (≤0.3) (odds ratio [OR], 0.45; 95% credible interval [CrI], 0.23-0.86; low

certainty) and intermediate (0.5-0.65) FiO2 (OR, 0.34; 95% CrI, 0.11-0.99; very low certainty). High initial FiO2 had a 97% probability of ranking first to reduce mortality. The effects on other morbidities were inconclusive.

**OTHER NOTEWORTHY PUBLICATIONS – August 2024**

Pediatrics

Acetaminophen for patent ductus arteriosus and risk of mortality and pulmonary morbidity
https://pubmed.ncbi.nlm.nih.gov/39011550/
Quality improvement interventions to prevent intraventricular hemorrhage: a systematic review
https://pubmed.ncbi.nlm.nih.gov/38982935/
Transcatheter and surgical ductus arteriosus closure in very low birth weight infants: 2018–2022
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Treatment outcomes for maple syrup urine disease detected by newborn screening
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The importance of timing when evaluating PDA treatment outcomes
https://pubmed.ncbi.nlm.nih.gov/39005113/
Identification and management of ankyloglossia and its effect on breastfeeding in infants: clinical report https://pubmed.ncbi.nlm.nih.gov/39069819/
Implementation of universal screening for G6PD deficiency in newborns
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Respiratory arrest in a late preterm infant presenting for a 2-week well-visit
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Apnea, intermittent hypoxemia, and bradycardia events predict late-onset sepsis in infants born extremely preterm
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Cerebral palsy and motor impairment after extreme prematurity: prediction of diagnoses at ages 2 and 10 years
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Association between early basal ganglia and thalami perfusion assessed by color doppler ultrasonography and brain injury in infants with hypoxic-ischemic encephalopathy: a prospective cohort study
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Congenital diaphragmatic hernia patients with left heart hypoplasia and left ventricular dysfunction have highest odds of mortality
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Initial oxygen concentration for the resuscitation of infants born at less than 32 weeks' gestational systematic review and individual participant data network meta-analysis
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Successful treatment of Enterococcus gallinarum infection in a neonate with vancomycin: a case report
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Early neonatal mortality and determinants in Ethiopia: multilevel analysis of Ethiopian demographic and
health survey, 2019
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Pediatric Critical Care Medicine
Changes in inhaled nitric oxide use across ICUs after implementation of a standard pathway

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Clinical course and outcomes of infants with streptococcus bovis/streptococcus gallolyticus subspecies pasteurianus infection: a systematic review and meta-analysis
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Maternal risk factors for respiratory syncytial virus lower respiratory tract infection in otherwise healthy preterm and term infants: a systematic review and meta-analysis
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Hepatitis C exposure diagnosis and testing in infants born to Hepatitis C virus-infected mothers
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Pediatric Cardiology
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https://pubmed.ncbi.nlm.nih.gov/36178495/
Prenatal detection of congenital heart disease: importance of fetal echocardiography following normal fetal cardiac screening
https://pubmed.ncbi.nlm.nih.gov/36329329/
Outcomes in infants with supraventricular tachycardia: risk factors for readmission, recurrence and ablation
https://pubmed.ncbi.nlm.nih.gov/36271968/

Pediatric Neurology
Adapting evidence-based practice guidelines for emergency management of seizures in children beyond the neonatal period
https://pubmed.ncbi.nlm.nih.gov/38838593/
Neuroimaging and neurological outcomes in perinatal arterial ischemic stroke: a systematic review and meta-analysis
https://pubmed.ncbi.nlm.nih.gov/38848613/
Infantile epileptic spasms syndrome complicated by leigh syndrome and leigh-like syndrome: a retrospective, nationwide, multicenter case series
https://pubmed.ncbi.nlm.nih.gov/38848614/

Obstetrics and Gynecology
Magnesium sulfate before preterm birth for neuroprotection: an updated Cochrane systematic review
https://www.ncbi.nlm.nih.gov/pubmed/38830233
Congenital syphilis in live births: adverse outcomes, hospital length of stay, and costs
https://www.ncbi.nlm.nih.gov/pubmed/38870533
Racial disparities in newborn drug testing after implementation of question-based screening for prenatal substance use
https://www.ncbi.nlm.nih.gov/pubmed/38843536

American Journal of Obstetrics & Gynecology
Maternal major depression during early pregnancy is associated with impaired child executive functioning at 4.5 years of age
https://pubmed.ncbi.nlm.nih.gov/38042244/

Hospital Pediatrics
No relevant articles

**BASIC SCIENCE SELECTIONS**
Eclipta prostrata improves alveolar development of bronchopulmonary dysplasia via suppressing the NLRP3 inflammasome in a DLD-dependent manner
https://www.ncbi.nlm.nih.gov/pubmed/39115441
Targeting miR-146b-5p to Regulate KDM6B Expression Aggravates Bronchopulmonary Dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/37584827
Development of a hybrid rhodamine-hydrazine NIR fluorescent probe for sensitive detection and imaging of peroxynitrite in necrotizing enterocolitis model
https://www.ncbi.nlm.nih.gov/pubmed/39178703
Vitamin E and GPX4 cooperatively protect treg cells from ferroptosis and alleviate intestinal inflammatory damage in necrotizing enterocolitis
https://www.ncbi.nlm.nih.gov/pubmed/39137584
Blocking IL-17a signaling decreases lung inflammation and improves alveolarization in experimental bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/39117111

Other relevant articles
Risk factors and clinical outcomes of pulmonary hypertension associated with bronchopulmonary dysplasia in extremely premature infants: A systematic review and meta-analysis
https://www.ncbi.nlm.nih.gov/pubmed/39177287
Association between Ureaplasma urealyticum colonization and bronchopulmonary dysplasia in preterm infants: a systematic review and meta-analysis
https://www.ncbi.nlm.nih.gov/pubmed/39175806
The association of different types of human milk with bronchopulmonary dysplasia in preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/39171103
Mother's own milk and bronchopulmonary dysplasia in appropriate for

gestational age preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/38816495
Blood pressure in preterm infants with bronchopulmonary dysplasia in the first three months of life
https://www.ncbi.nlm.nih.gov/pubmed/38536515
Estimating the effect of diuretics and inhaled corticosteroids for evolving bronchopulmonary dysplasia in preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/38192005
Methylxanthine use in infants with hypoxic-ischemic encephalopathy: a retrospective cohort study
https://www.ncbi.nlm.nih.gov/pubmed/39154109
Human milk microbiota, oligosaccharide profiles, and infant gut microbiome in preterm infants diagnosed with necrotizing enterocolitis
https://www.ncbi.nlm.nih.gov/pubmed/39216480
Umbilical arterial catheter duration as risk factor for Bell's Stage III necrotizing enterocolitis in preterm neonates
https://www.ncbi.nlm.nih.gov/pubmed/39149196
Intranasal dexmedetomidine reduces pain scores in preterm infants during retinopathy of prematurity screening
https://www.ncbi.nlm.nih.gov/pubmed/39156022
The association between serum 25-hydroxyvitamin D levels and retinopathy of prematurity in preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/39156015
Administering Intravitreal Bevacizumab for Retinopathy of Prematurity: 8-Year Cognitive Outcomes in a Prospective Cohort
https://www.ncbi.nlm.nih.gov/pubmed/39121508
Cord blood transfusions in extremely low gestational age neonates to reduce severe retinopathy of prematurity: results of a prespecified interim analysis of the randomized BORN trial
https://www.ncbi.nlm.nih.gov/pubmed/39113069
Lowering platelet-count threshold for transfusion in preterm neonates decreases the number of transfusions without increasing severe hemorrhage events
https://www.ncbi.nlm.nih.gov/pubmed/39120698
Long-term outcomes of congenital cytomegalovirus infection in children early identified by extended hearing-targeted screening
https://www.ncbi.nlm.nih.gov/pubmed/39191004