ARTICLES OF INTEREST – September, 2023

Early human milk fortification in infants born extremely preterm: a randomized trial

This was a masked, randomized trial. Starting on feeding day 2, extremely preterm infants 28 weeks or younger fed maternal or donor milk were randomized to receive either a diet fortified with a human-based product (intervention group) or a standard, unfortified diet (control group). This practice continued until the feeding day when a standard bovine-based fortifier was ordered. Caregivers were masked. The primary outcome was Fat Free Mass-for-age z score at 36 weeks of postmenstrual age (PMA). The primary outcome was assessed in 105 infants (70%). FFM-for-age z scores did not differ between groups. Length gain velocities from birth to 36 weeks PMA were higher in the intervention group. Declines in head circumference-for-age z score from birth to 36 weeks' PMA were less pronounced in the intervention group.

Percutaneous closure of the patent ductus arteriosus in infants ≤2 kg: IMPACT registry insights

This was a cohort study using the IMPACT Registry (Improving Pediatric and Adult Congenital Treatments) from the American College of Cardiology Foundation’s National Cardiovascular Data Registry. Percutaneous PDA closure appears to be safe and feasible procedures in infants ≤2 kg. The incidence of major adverse events has continued to decline over the years and seems to have a strong correlation with individual center case volumes and expertise. A total of 1587 attempted PDA closures were included, with a 3% incidence of technical failure and 5.5% incidence of the composite outcome. Major adverse events were observed in 3.8% of the patients; the most common events were device embolization requiring retrieval and unplanned cardiac or vascular surgery in 1.3% and 1.3% of cases, respectively. The incidence of the composite outcome was associated with the need for arterial access (P < .001) as well as annual hospital volume of percutaneous PDA closures in infants ≤2 kg (P = .001).

Timing of primary surgery for cleft palate

This study from 23 centers across Europe and South America randomly assigned 558 infants with nonsyndromic isolated cleft palate, in a 1:1 ratio, to undergo standardized primary surgery at 6 months of age (6-month group) or at 12 months of age (12-month group) for closure of the cleft. Insufficient velopharyngeal function at 5 years of age was observed in 21 of 235 infants (8.9%) in the 6-month group as compared with 34 of 226 (15.0%) in the 12-month group (risk ratio, 0.59; 95% confidence interval, 0.36 to 0.99; P = 0.04). The authors concluded that medically fit infants who underwent primary surgery for isolated cleft palate in adequately resourced settings at 6 months of age were less likely to have velopharyngeal insufficiency at the age of 5 years than those who had surgery at 12 months of age.
Two-year outcomes after minimally invasive surfactant therapy in preterm infants: follow-up of the OPTIMIST-a randomized clinical trial
Peter A Dargaville, C Omar F Kamlin, Francesca Orsini, et al. JAMA.

This follow-up study included infants randomly assigned to minimally invasive surfactant therapy [MIST, exogenous surfactant (200 mg/kg poractant alfa) via a thin catheter] (n=242) versus sham treatment (n=244). This trial included 486 infants from 33 tertiary-level neonatal intensive care units in 11 countries with a gestational age of 25 to 28 weeks supported with CPAP. Death or neurodevelopmental disability at two years occurred in 78 infants (36.3%) in the MIST group and 79 (36.1%) in the control group (risk difference, 0% [95% CI, -7.6% to 7.7%]; relative risk [RR], 1.0 [95% CI, 0.81-1.24]). Hospitalization with respiratory illness occurred in 49 infants (25.1%) in the MIST group vs 78 (38.2%) in the control group (RR, 0.66 [95% CI, 0.54-0.81]) and parent-reported wheezing or breathing difficulty in 73 (40.6%) vs 104 (53.6%), respectively (RR, 0.76 [95% CI, 0.63-0.90]). The authors concluded that MIST compared with sham treatment did not reduce the incidence of death or NDD by 2 years of age. However, infants who received MIST had lower rates of adverse respiratory outcomes during their first 2 years of life.

Short-course antibiotic therapy for pneumonia in the neonatal intensive care unit

The authors sought to determine the adherence and safety outcomes of a 5-day antibiotic course with a "time-out" for treatment of "blood culture-negative" pneumonia in the NICU. Safety outcomes were defined a priori by re-initiation of antibiotic therapy within 14 days after discontinuation and overall and sepsis-related mortality. 128 infants from 7 NICUs were diagnosed with 136 episodes of pneumonia; 88% (n = 119) were treated with 5 days of definitive antibiotic therapy. Antibiotics were restarted within 14 days in 22 (16%) of the 136 pneumonia episodes. However, only 3 (3%) of the 119 episodes of pneumonia treated for 5 days had antibiotics restarted for pneumonia. Mortality was 5% (7/128); 5 of the 7 deaths were assessed as sepsis-related. The authors conclude that adherence to the 5-day definitive antibiotic treatment for "culture-negative" pneumonia was high and the intervention seemed safe.

Early antibiotic exposure in very-low birth weight infants and infection risk at 3–7 days after birth

The authors sought to determine rates of late-onset infection (LOI) during postnatal days 3-7 among preterm infants based on antibiotic exposure during days 0-2. The cohort included 88,574 infants <1500 grams and ≤30 weeks gestation, of whom 85% were antibiotic-exposed. Fewer antibiotic-exposed compared to unexposed infants developed LOI (1.5% vs. 2.1%; adjusted hazard ratio, 0.28, 95% CI 0.24-0.33). Among antibiotic-exposed compared to unexposed infants, Gram-negative (38% vs. 28%, p = 0.002) and fungal (11% vs. 1%, p < 0.001) species were more commonly isolated, and gram-positive organisms (49% vs. 70%, p < 0.001) were less commonly isolated. The authors observed low overall rates of LOI at days 3-7 after birth, but antibiotic exposure from birth was associated with lower rates, and with differing microbiology, compared to no exposure.
Differences between early and late MRI in infants with neonatal encephalopathy following therapeutic hypothermia

This retrospective cohort study compared the MRI findings of infants who received therapeutic hypothermia (TH) for neonatal encephalopathy (NE). Only infants who had two MRIs: early (≤7 days) and late (>7 days) were included. 94 infants with NE were included. Twenty-four infants (26%) had a normal early scan of which 3/24 (13%) had injury noted on repeat MRI. Seventy infants (74%) had abnormal findings noted on early MRI, of which 4/70 (6%) had further evolution of injury while 11/70 (16%) had complete resolution of findings. In infants who received TH for, 19% had changes noted between their early and late MRIs. Relying solely on early MRI may overestimate injury in a proportion of infants and miss injury in others.

How well does neonatal neuroimaging correlate with neurodevelopmental outcomes in infants with hypoxic-ischemic encephalopathy?

Infants with HIE underwent neonatal MRI/MR spectroscopy (MRS) at 4–6 days of age. The severity of brain injury was measured with a validated scoring system. Using proportional odds regression, adjusted odds ratios (aOR) for the associations between MRI/MRS measures of injury and NDI at 2 years was assessed. 451 infants were included. Outcomes were normal in 51%; mild NDI in 12%, moderate NDI in 14%, severe NDI in 13%. MRI injury score (aOR 1.06, 95% CI 1.05, 1.07), severe brain injury (aOR 39.6, 95% CI 16.4, 95.6), and MRS lactate/n-acetylaspartate (NAA) ratio (aOR 1.6, 95% CI 1.4,1.8) were associated with worse NDI outcomes. Infants with mild/moderate MRI brain injury had similar BSID-III cognitive, language, and motor scores as infants with no injury. This data suggests that in the absence of severe injury, brain MRI/MRS does not accurately discriminate the degree of NDI.

Neurobehavioral and medical correlates of autism screening: 2-year outcomes for infants born very Preterm

This is a multi-center study involving infants enrolled in the Neonatal Neurobehavior and Outcomes in Very Preterm Infants (NOVI) study. The findings from the study showed that neonatal neurobehavior and medical morbidities were associated with positive M-CHAT-R/F screens at age 2 years in toddlers born very preterm. In addition, infants with positive M-CHAT-R/F screens had lower Bayley composite scores and greater CBCL problem scores than infants with negative M-CHAT-R/F screen results. These findings demonstrate the potential utility of the M-CHAT-R/F as a global developmental screener in infants born very preterm, regardless of whether there is a later autism diagnosis.

Smartphone-based video antenatal preterm birth education the preemie prep for parents randomized clinical trial

This is a randomized trial that evaluated maternal knowledge of preterm birth, preparation for decision-making, and anxiety between parental groups who received smartphone-based gestational age-specific short animated videos starting at 18 weeks’ gestation of pregnancy versus control group receiving links to patient education webpages on ACOG. Participants in the smartphone group had more knowledge of core competencies and were more prepared to make decisions without experiencing worse anxiety. Mobile antenatal preterm birth education may be beneficial for parents expecting preterm birth.
Recombinant CXCL17 treatment alleviates hyperoxia-induced lung apoptosis and inflammation in vivo and vitro by activating the AKT pathway: a possible therapeutic approach for bronchopulmonary dysplasia

Elevated serum CXCL17 levels were observed in human premature infants with hyperoxia-induced lung injury, suggesting that CXCL17 might be involved in BPD. These authors conducted studies in a hyperoxia-induced lung injury mouse model and primary murine alveolar epithelial cells Type II (T2AEC) cells exposed to hyperoxia. The results showed that hyperoxia exposure increased CXCL17 levels in newborn mice pups. Hyperoxia exposure increased lung wet-weight/dry-weight ratio, increased alveolar diameter and enlarged alveoli, and reduced surfactant protein C expression. However, recombinant CXCL17 (rCXCL17) treatment alleviated hyperoxia-induced lung injury. rCXCL17 treatment inhibited hyperoxia-induced inflammation, oxidative stress, and apoptosis in neonatal mice. Additionally, rCXCL17 treatment activated the AKT pathway, which is a protective pathway in BPD. Collectively, rCXCL17 alleviates hyperoxia-induced lung injury in neonatal mice by activating the AKT pathway, indicating that CXCL17 may be a promising target for BPD therapy.

Chondroitin sulfate supplementation improves clinical outcomes in a murine model of necrotizing enterocolitis

Chondroitin sulfate (CS) is a naturally occurring glycosaminoglycan (GAG) in human breast milk (HM) and has been shown to reduce inflammation. The authors hypothesized that supplementation with CS in an experimental NEC model would alter microbial diversity, favorably alter the cytokine profile, and (like other sulfur compounds) improve outcomes in experimental NEC via the eNOS pathway. Six groups were studied (n = 9-15/group): (1) WT breastfed and (2) Formula fed controls, (3) WT NEC, (4) WT NEC + CS, (5) eNOS KO (knockout) NEC, and (6) eNOS KO NEC + CS. CS supplementation in formula improved experimental NEC outcomes when compared to NEC alone. CS supplementation resulted in similar improvement in NEC in both the WT and eNOS KO mice. CS supplementation did not result in microbial changes when compared to NEC alone. Our data suggest that although CS supplementation improved outcomes in NEC, this protection is not conferred via the eNOS pathway or alteration of microbial diversity.

OTHER NOTEWORTHY PUBLICATIONS – September 2023

COVID-19
Neonatal outcomes of maternal SARS-CoV-2 infection in the UK: a prospective cohort study using active surveillance
Cesarean birth morbidity among women with SARS-COV-2
Early treatment of multisystem inflammatory syndrome in children

Pediatrics
Early human milk fortification in infants born extremely preterm: a randomized trial
Quality indicators to evaluate essential newborn care in low- and middle-income countries
Percutaneous closure of the patent ductus arteriosus in infants ≤2 kg: impact registry insights
Neonatal admission temperature in middle- and high-income countries
Strengthening reporting of neonatal trials
Heterogeneity and gaps in reporting primary outcomes from neonatal trials
Sooner is better: early human milk fortification for hospitalized preterm infants <29 weeks
Hearing assessment in infants, children, and adolescents: recommendations beyond neonatal screening
Reducing severe intraventricular hemorrhage in preterm infants with improved care bundle adherence
Congenital rubella syndrome following rubella vaccination during pregnancy
Rapid infant weight gain: critique of the Gilley et al paper and thoughts on how to move the field forward

Journal of Pediatrics
Latent class analysis of prenatal substance exposure and child behavioral outcomes
Improving early colostrum administration to very low birth weight infants in a level 3 neonatal intensive care unit: a quality improvement initiative
Racial and ethnic disparities in sudden unexpected infant death among us infants born preterm
Structural racism operationalized via adverse social events in a single-center neonatal intensive care unit
Securement of umbilical venous catheter using cyanoacrylate glue: a randomized controlled trial
Maternal prenatal risk phenotypes and neurobehavioral outcomes among infants born very preterm
Genetic testing guidelines impact care in newborns with congenital heart defects
Congenital heart disease with congenital diaphragmatic hernia: surgical decision making and outcomes
Characteristics, genetic testing, and diagnoses of infants with neonatal encephalopathy not due to hypoxic ischemic encephalopathy: a cohort study
Does growth velocity affect associations between birth weight and neurodevelopment for infants born very preterm?
Neurobehavioral and medical correlates of autism screening: 2-year outcomes for infants born very preterm

Pediatric Research
Protein and growth during the first year of life: a systematic review and meta-analysis
Hyperglycemia and prematurity: a narrative review
Postnatal cerebral hemodynamics in infants with severe congenital heart disease: a scoping review
Novel metrics to characterize temporal lobe of very preterm infants on term-equivalent brain MRI

Impaired myocardial deformation persists at 2 years in offspring of mothers with diabetes mellitus

Adverse short- and long-term outcomes among infants with mild neonatal encephalopathy

Differences between early and late MRI in infants with neonatal encephalopathy following therapeutic hypothermia

How well does neonatal neuroimaging correlate with neurodevelopmental outcomes in infants with hypoxic-ischemic encephalopathy?

Associations of intrapartum antibiotics and growth, atopy, gastrointestinal and sleep outcomes at one year of age

Organ dysfunction and mortality in preterm neonates with late-onset bloodstream infection

Standardized growth charts for children with osteogenesis imperfect
https://www.ncbi.nlm.nih.gov/pubmed/36922619

The impact of pandemic restrictive visiting policies on infant wellbeing in a NICU

The association of intrapartum deceleration and acceleration areas with MRI findings in neonatal encephalopathy

Postnatal catch-up growth in term newborns with altered fetal weight patterns. The GROWIN study

Circulating progranulin in human infants: relation to prenatal growth and early postnatal nutrition
https://www.ncbi.nlm.nih.gov/pubmed/37031297

Curriculum and assessment tool for less invasive surfactant administration: an international Delphi consensus study

Omega-3 polygenic score protects against altered eating behavior in intrauterine growth-restricted children

Archives of Disease in Childhood - Fetal & Neonatal Edition
No new content

Journal of Perinatology
Antenatal magnesium sulfate and adverse gastrointestinal outcomes in preterm infants—a systematic review and meta-analysis

Flat maternal glucose response curve and adverse pregnancy outcome

A decade of evidence: standardized feeding initiative targeting feeding milestones and predicting NICU stays in premature infants in an all-referral level IV NICU

A comparison of tertiary level NICU costs for infants born <1250 g supplemented with human versus bovine milk-based fortifiers

Can the triglyceride-glucose index predict insulin resistance in LGA newborns?
Remote monitoring for neonates requiring continued nasogastric tube feeding: implementation, patient characteristics, and early outcomes

Enteric tube position on preoperative radiographs predicts clinical outcomes in neonatal congenital diaphragmatic hernia with and without prenatal diagnosis

Prophylactic fluconazole protocol in very low birth weight infants: invasive candidiasis prevention in a Latin American neonatal intensive care unit

Short-course antibiotic therapy for pneumonia in the neonatal intensive care unit

Epidemiology, risk factors, and applicability of CDC definitions for healthcare-associated bloodstream infections at a level IV neonatal ICU

Early antibiotic exposure in very-low birth weight infants and infection risk at 3–7 days after birth

Association of delivery risk phenotype with early-onset sepsis in preterm infants

Fragmented red blood cell counts of neonates with new-onset gastrointestinal disturbances

Impact of early formula supplementation on breastfeeding duration, National Immunization Survey, 2019 births

Pilot study using an optical fiber light source to guide nasogastric/orogastric tube insertion in neonates

How much glucose is in Sweet Cheeks oral glucose gel?

Implementing food insecurity screening in a level IV neonatal intensive care unit

Dilemmas in the delivery of intravenous lipid emulsions and approach to hypertriglyceridemia in very preterm and low birth weight infants

Dilemmas in establishing preterm enteral feeding: where do we start and how fast do we go?

Dilemmas in parenteral glucose delivery and approach to glucose monitoring and interpretation in the neonate

Neonatology
No new content

American Journal of Perinatology
Impact of state prioritization of safe infant sleep programs on supine sleep positioning for non-hispanic white and non-hispanic black infants

Non-nutritive sweeteners in human amniotic fluid and cord blood: evidence of transplacental fetal exposure

The anesthetic modality but not the mode of delivery seem to modulate the methylation status of cyclooxygenase-2 promoter of the newborns

Correlation between perfusion index and left ventricular output in healthy late preterm infants
Clinical study on different delivery methods of twin pregnancy

Serum cotinine and adverse cardiovascular outcomes: a cross-sectional secondary analysis of the numom2b heart health study

The association between early gram-negative bacteria in tracheal aspirate cultures and severe bronchopulmonary dysplasia among extremely preterm infants requiring prolonged ventilation

Shallow placentation: a distinct category of placental lesions

Cardiac dysfunction in neonatal hie is associated with increased mortality and brain injury by MRI

Fluid intake in the first week of life and the duration of hemodynamically significant patent ductus arteriosus in extremely preterm infants

The effect of betamethasone dosing interval on perinatal outcomes: 12 hours or 24 hours apart

Trib3-regulated akt signal pathway affects trophoblast invasion in the development of preeclampsia

Journal of Neonatal-Perinatal Medicine
No new content

Maternal Health, Neonatology and Perinatology
No relevant articles

Neoreviews
Malaria in pregnancy: key points for the neonatologist

The role of the neonatologist in fetuses diagnosed with congenital heart disease

The placenta in congenital heart disease: form, function and outcomes

A neonate presenting with cholestasis and thrombocytopenia

Spastic paralysis in a full-term newborn

An unusual forearm skin lesion in a newborn infant

Maternal atrial fibrillation and neonatal complications

Persistent work of breathing in a term neonate

A fetus with tetralogy of fallot with absent pulmonary valve syndrome

JAMA Pediatrics
Effectiveness and costs of molecular screening and treatment for bacterial vaginosis to prevent preterm birth: the AuTop randomized clinical trial

Smartphone-based video antenatal preterm birth education the preemie prep for parents randomized clinical trial
Community health worker home visiting, birth outcomes, maternal care, and disparities among birthing individuals with medicaid insurance

BMC Pediatrics
No relevant articles

Pediatric Critical Care Medicine
No relevant articles

New England Journal of Medicine
Timing of primary surgery for cleft palate
Antibiotic prophylaxis in infants with grade III, IV, or V vesicoureteral reflux

Lancet
No relevant content

JAMA
CDC recommends RSV immunization for infants
Cannabis use and perinatal health research
Two-year outcomes after minimally invasive surfactant therapy in preterm infants: follow-up of the OPTIMIST-A randomized clinical trial

BMJ
No new content

Pediatric Infectious Disease Journal
High rates of ESBL-producing and gentamycin-resistant gram-negative bacteria during the first week of life: a multicenter cross-sectional study among infants younger than 2 months with urinary tract infection
Neonatal parotitis: a case report and review of the literature
Discrepancies in management of congenital cytomegalovirus in preterm infants: an international survey
Long duration of oral care using mother’s own milk influences oral microbiota and clinical outcomes in very-low-birthweight infants: randomized controlled trial
Evaluating the impact of the 2017 Dutch neonatal early-onset sepsis guideline
Planned out-of-hospital birth as a risk factor for nonreceipt of hepatitis B immunization

Pediatric Cardiology
Utility of screening fetal echocardiograms at a single institution following normal obstetric ultrasound in fetuses with down syndrome
Virtually delivered psychosocial intervention for prenatally diagnosed congenital heart disease: feasibility and acceptability of heartprep
Impact of prenatal diagnosis of critical congenital heart disease on preoperative and postoperative outcomes
Changes in cerebral regional oxygen saturation variability in neonates undergoing cardiac surgery: a prospective cohort study
Atrial septal defect: larger right ventricular dimensions and atrial volumes as early as in the first month after birth—a case–control study including 716 neonates

**Pediatric Neurology**
No relevant articles

**Obstetrics and Gynecology**
Risk factors for perinatal transmission of hepatitis C virus
Perinatal mortality despite prenatal diagnosis of vasa previa: a systematic review
Gestational glucose intolerance and birth weight–related complications
Duration and timing of in utero opioid exposure and incidence of neonatal withdrawal syndrome
Risk of miscarriage in relation to seasonal influenza vaccination before or during pregnancy
The limits of viability
Viral hepatitis in pregnancy: ACOG Clinical Practice Guideline No. 6

**American Journal of Obstetrics & Gynecology**
Whole genome sequencing vs chromosomal microarray analysis in prenatal diagnosis
Obstetrical, perinatal, and genetic outcomes associated with nonreportable prenatal cell-free DNA screening results

**Hospital Pediatrics**
Implementing higher phototherapy thresholds for jaundice in healthy infants 35 plus weeks

**BASIC SCIENCE SELECTIONS**
IL-17a-producing gammadeltaT cells and NKG2D signaling mediate bacterial endotoxin-induced neonatal lung injury: implications for bronchopulmonary dysplasia
Recombinant CXCL17 treatment alleviates hyperoxia-induced lung apoptosis and inflammation in vivo and vitro by activating the AKT pathway: a possible therapeutic approach for bronchopulmonary dysplasia
Conditional knockout of ITGB4 in bronchial epithelial cells directs bronchopulmonary dysplasia
Granulocyte colony-stimulating factor is a determinant of severe bronchopulmonary dysplasia and coincident retinopathy
CircABPD1 alleviates oxidative lung injury of bronchopulmonary dysplasia through regulating miR-330-3p/HIF1alpha axis
Tat-P combined with GAPR1 releases Beclin1 to promote autophagy and improve Bronchopulmonary dysplasia model
Type 2 innate lymphoid cell-derived amphiregulin regulates type II alveolar epithelial cell transdifferentiation in a mouse model of bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/37480752
High-mobility group box-1 peptide ameliorates bronchopulmonary dysplasia by suppressing inflammation and fibrosis in a mouse model
Novel pathogenic GATA6 variant associated with congenital heart disease, diabetes mellitus and necrotizing enterocolitis
Chondroitin sulfate supplementation improves clinical outcomes in a murine model of necrotizing enterocolitis
Suppressive role of vascular endothelial growth factor on intestinal apoptosis in induced necrotizing enterocolitis in rats
NAMPT inhibition relieves intestinal inflammation by regulating macrophage activation in experimental necrotizing enterocolitis

ADDITIONAL JOURNAL SELECTIONS

Effect of breast milk on the frequency of bronchopulmonary dysplasia in very low birth weight premature infants: a meta-analysis
Association between plasma lysophosphatidic acid levels and bronchopulmonary dysplasia in extremely preterm infants: A prospective study
Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are early predictors of bronchopulmonary dysplasia
Modified lung ultrasound score for bronchopulmonary dysplasia predicts late respiratory outcomes in preterm infants
Comparison among three lung ultrasound scores used to predict the need for surfactant replacement therapy: a retrospective diagnostic accuracy study in a cohort of preterm infants
Plasma anti-myosin autoantibodies in the diagnosis of necrotizing enterocolitis
Ex-utero third trimester developmental changes in functional brain network organization in infants born very and extremely preterm
Diameter of ductus arteriosus on postnatal Day 7 is associated with late pulmonary hypertension in extremely preterm infants

Neuroimaging in infants with congenital cytomegalovirus infection and its correlation with outcome: emphasis on white matter abnormalities

The role of distance from home to hospital on parental experience in the NICU: a qualitative study

Two-year outcomes following a randomised platelet transfusion trial in preterm infants

Gross and histologic placental abnormalities associated with neonatal hypoxic-ischemic encephalopathy

Outcomes for non-treatment-requiring infants evaluated for retinopathy of prematurity

A network meta-analysis of success rates following low dosage anti-VEGF for retinopathy of prematurity

Early hyperglycemia is associated with increased incidence of severe retinopathy of prematurity in extremely low birth weight infants

Erythrocyte transfusions are associated with retinopathy of prematurity in extremely low gestational age newborns