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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – January 2023

A randomised trial comparing weaning from CPAP alone with weaning using heated humidified high flow nasal cannula in very preterm infants: the CHiPS study
Joanne Clements, Pernille M Christensen and Michael Meyer. *Arch Dis Child Fetal Neonatal Ed.*

This single-center, non-inferiority, randomized controlled study of preterm infants (< 30wk) investigating weaning from nCPAP using high flow nasal cannula (nHF) compared to weaning using nCPAP. Infants (n=120) were randomized to nHF 6 L/min (n=59) or bubble CPAP 6 cm (n=61). The primary outcome was time on respiratory support from randomization to 72 hours off respiratory support or 36 weeks' PMA; non-inferiority threshold set at 15%. No differences in baseline demographics between the groups. The mean duration of respiratory support following randomization for the nCPAP group was 401 hours and 375 hours in the nHF group. The study concluded that for infants ready to wean from nCPAP, nHF weaning was non-inferior to nCPAP weaning. In addition, stress scores were reduced in the nHF group. However, in a subgroup analysis for infants <27 weeks' GA, it was nonconclusive that nHF weaning is non-inferior to nCPAP weaning.

Double-blinded randomized controlled trial of optimizing nutrition in preterm very low birth weight infants: Bayley scores at 18–38 months of age
Jordan D Reis, Kristine Tolentino-Plata, Maria Caraig, et al. *J Perinatol.*

This is a follow up study of a double-blinded RCT that initially assessed the effect of type of human milk supplementation on growth in neonates <29wks GA and those <35wks GA who were SGA. Infants were randomized to receive optimized nutrition (i.e., feeding adjustments based on growth and serial measurements of serum nutrients, n=58) or individualized nutrition (based on serial measurements of macronutrients in mother's own milk (MOM), experimental group, n=62). This follow up study assessed Bayley scores in 91/114 (80%) infants at 18-38 months of age. The two groups had similar frequencies of low cognitive, motor and language Bayley scores and similar age-adjusted Bayley scores. The initial study had no difference in nutrient intake and growth prior to discharge from the NICU between the two groups. Therefore, this study suggests that individualized nutrition may not improve growth and neurodevelopment compared to infants already receiving optimized nutrition.

A prospective, longitudinal, case–control study to evaluate the neurodevelopment of children from birth to adolescence exposed to COVID-19 in utero
Rachel A Hill, Atul Malhotra, Vathana Sackett, et al. *BMC Pediatr.*

This paper outlines the designs and methodology for a prospective, case-controlled study aimed to investigate the long-term impacts of SARS-CoV2 exposure on children exposed in utero. Women infected with SARS-CoV-2 during pregnancy are being recruited from two centers in Melbourne, Australia and Londrina, Brazil. Cases are matched 2:1 with women who gave birth in the same month of

delivery, are of similar age but did not contract SARS-CoV-2 during their pregnancy. The study aims to collect developmental data at various time-points from birth to 15 years of life as well as biospecimens.

Cerebral regional tissue Oxygen Saturation to Guide Oxygen Delivery in preterm neonates during immediate transition after birth (COSGOD III): multicentre randomised phase 3 clinical trial
Gerhard Pichler, Katharina Goeral, Marlene Hammerl, et al. *BMJ.*

This multicenter randomized controlled phase 3 trial assessed whether monitoring of cerebral tissue oxygen saturation using near infrared spectroscopy in addition to routine monitoring combined with defined treatment guidelines during immediate transition and resuscitation increases survival without cerebral injury of premature infants <32 weeks' gestation compared with standard care alone. Neonates were randomly assigned to either standard care or standard care plus monitoring of cerebral oxygen saturation with a dedicated treatment guideline during immediate transition (first 15 minutes after birth) and resuscitation. The primary outcome was a composite of survival without cerebral injury. In the near infrared spectroscopy, delivery room Fio2 was titrated based on cerebral regional tissue oxygen saturation (crSO2) in addition to SpO2. 607 infants (304 and 303, respectively) were included in the final analysis. The incidence of delivery room interventions within the first 15 minutes after birth did not differ between the groups except for a significantly higher number of neonates receiving intravenous fluids in the near infrared spectroscopy group (12 (4.0%) v 2 (0.7%), P=0.007; table 2). CrSO2 values at each minute during the first 15 minutes after birth did not differ between the groups. FiO2 was slightly higher in the near infrared spectroscopy group than control group in the first minutes after birth, and SpO2 values during the first 15 minutes after birth were similar in both groups. Overall, 252 (82.9%) out of 304 neonates in the near infrared spectroscopy group survived without cerebral injury compared with 238 (78.5%) out of 303 in the control group (relative risk 1.06, 95% confidence interval 0.98 to 1.14). Monitoring of cerebral tissue oxygen saturation in combination with dedicated interventions in preterm neonates (<32 weeks' gestation) during immediate transition and resuscitation after birth did not result in substantially higher survival without cerebral injury compared with standard care alone.

Levetiracetam versus phenobarbital for neonatal seizures: a retrospective cohort study
Linda Bättig, Corinne Dünner, Dorottya Cserpan, et al. *Pediatr Neurol.*

The authors compared the safety and efficacy of levetiracetam (LEV) and phenobarbital (PB) as first-line antiseizure medication (ASM) for neonatal seizures by conducting a retrospective cohort study of 108 neonates with EEG-confirmed seizures treated with first-line LEV or PB in 2012 to 2020. Their study suggests a potential noninferiority and a more acceptable safety profile for LEV, which may thus be a reasonable option as first-line ASM for neonatal seizures in place of PB. Treatment should be initiated as early as possible since higher seizure frequencies predispose to less favorable responses

Neuroprotective effect of lipopolysaccharides in a dual-hit rat pup model of preterm hypoxia-ischemia
Da Lu, Angelina V Evangelou, Krithika Shankar, et al. *Neurosci Lett.*

The authors show that administering a single injection of LPS (0.1 mg/kg) to postnatal-day-2 rat pups 14 h before inducing HI effectively protects the brain from HI-associated damage. The LPS-treated HI rat pups have significantly less histopathology compared to the saline-treated HI rat pups. Apoptotic deaths were dramatically curtailed in both the neocortex and white matter when evaluated at 2 days of recovery. One mechanism through which LPS pre-treatment appears to be preventing injury is through the AKT-endothelial nitric oxide synthase (eNOS) pathway as LPS induced an increase in both the expression and phosphorylation of eNOS. Altogether these data show that the neocortex, as well as the white matter sustain damage after HI at this timepoint in forebrain development and that acutely activating the immune system can protect the brain from brain injury.

Fetal growth restriction impairs lung function and neurodevelopment in an early preterm rabbit model
Ignacio Valenzuela, Katerina Zapletalova, Marnel Greyling, et al. *Biomedicines.*

The authors hypothesize that FGR (fetal growth restriction) has a detrimental effect on prematurity in both pulmonary function and neurodevelopment. FGR was induced at gestational day (GD) 25 by placental underperfusion, accomplished by partial uteroplacental vessel ligation in one uterine horn. Rabbits were delivered by cesarean section at GD 29, and placentas were harvested for histology. Neonates underwent neurobehavioral or pulmonary functional assessment at postnatal day 1. FGR was associated with higher perinatal mortality, lower birth and placental weight, and a similar brain-to-body weight ratio compared to controls. Placental underperfusion decreased labyrinth and junction zone volumes in FGR placentas. FGR impaired pulmonary function, depicted by higher parenchymal resistance, damping, and elastance. Neurobehavioral tests showed motoric and sensorial impairment in FGR rabbits. In FGR brains, cell density was globally reduced, with higher apoptosis in selected areas.

Early amino acids in extremely preterm infants and neurodisability at 2 years
Frank H Bloomfield, Yannan Jiang, Jane E Harding, et al. *N Engl J Med.*

In this multicenter, parallel-group, double-blind, randomized, placebo-controlled trial, 434 infants were enrolled with birth weights less than 1000 gms at 8 NICUs. It was found that extra parenteral amino acids at a dose of 1 g per day for 5 days after birth did not increase the number who survived free from neurodisability at 2 years.

Age at first extubation attempt and death or respiratory morbidities in extremely preterm infants
Wissam Shalish, Martin Keszler, Lajos Kovacs, et al. *J Pediatr.*

This subanalysis of a multicenter observational study included 250 infants with birth weights of 1250 g or less and intubated within 24 hours of birth. Of the infants included, 129 (52%) were extubated within 7 days, 93 (37%) between 8 and 35 days, and 28 (11%) beyond 35 days of life. The authors found that only early and successful extubation was independently associated with lower death/BPD rates compared with early failure (OR, 0.13; 95% CI, 0.04-0.40) and late failure (OR, 0.19; 95% CI, 0.04-1.00). Early and successful extubation was also independently associated with lower BPD among survivors compared with early failure (OR, 0.18; 95% CI, 0.05-0.6), late success (OR, 0.26; 95% CI, 0.07-0.97), and late failure (OR, 0.12; 95% CI, 0.02- 0.72).

Association of survival at 22 weeks' gestation with use of antenatal corticosteroids and mode of delivery in the United States
Ramesh Vidavalur, Zeenat Hussain and Naveed Hussain. *JAMA Pediatr.*

This cross-sectional study utilized the US Centers for Disease Control and Prevention-Wide-Ranging Online Data for Epidemiological Research to evaluate the association of antenatal corticosteroid use and cesarean delivery with birth-linked survival at birth certificate reporting. From 2016 to 2020, there were 5713 births at 22 weeks' gestational age reported to the CDC. The authors found an increasing trend of median-1 year survival, from 11.6% in 2017 to 16.7% in 2019. Of particular note, there were higher survival rates for infants delivered via cesarean birth (OR, 4.2; 95% CI, 3.6-5.0, $p<0.001$) and a more than 3-fold increase in the odds of survival when antenatal steroids were used (OR, 3.5; 95% CI. 3.0-4.1; $p<0.001$

OTHER NOTEWORTHY ARTICLES – JANUARY, 2023

COVID-19
A prospective, longitudinal, case–control study to evaluate the neurodevelopment of children from birth to adolescence exposed to COVID-19 in utero
https://pubmed.ncbi.nlm.nih.gov/36717903/
Clinical characteristics, transmission rate and outcome of neonates born to COVID-19-positive mothers: a prospective case series from a resource-limited setting

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Why monitor the neonatal brain—that is the important question
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Granulocyte-macrophage colony-stimulating factor suppresses induction of type I interferon in infants with severe pneumonia
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Immunomodulatory therapy using a pediatric dialysis system ameliorates septic shock in miniature pigs
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What's new in the management of neonatal early-onset sepsis?
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Journal of Neonatal-Perinatal Medicine
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Maternal Health, Neonatology and Perinatology
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Pediatric Infectious Disease Journal
Incidence of group b streptococcus disease in infants in China: an updated systematic review and meta-analysis
https://pubmed.ncbi.nlm.nih.gov/36476529/

Hearing outcome and virologic characteristics of children with congenital cytomegalovirus infection in relation to antiviral therapy: a retrospective cohort study
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Pediatric Cardiology

The prevalence of congenital anomalies of the airway or lung in infants with hypoplastic left heart syndrome and differences in midterm outcomes: a national pediatric cardiology quality improvement collaborative registry analysis
https://pubmed.ncbi.nlm.nih.gov/35731252
Surgical outcomes of congenital heart disease in Down syndrome: tertiary center experience—focus on the electrical conduction system
https://pubmed.ncbi.nlm.nih.gov/36260102
Tricuspid valve blood cysts mimicking thrombus or vegetation on echocardiogram in a neonate
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Pediatric Neurology

Partial efficacy of vigabatrin in an infant with West syndrome due to pyruvate dehydrogenase complex deficiency: a case report
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Distribution of intrathalamic injury according to nuclei and vascular territories in children with term hypoxic-ischemic injury
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Levetiracetam versus phenobarbital for neonatal seizures: a retrospective cohort study
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Measures of racism and discrimination in preterm birth studies
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Timing of maternal smoking cessation and newborn weight, height, and head circumference
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American Journal of Obstetrics & Gynecology

Lactogenesis and breastfeeding after immediate vs delayed birth-hospitalization insertion of etonogestrel contraceptive implant: a noninferiority trial
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Reduced fetal growth velocity and weight loss are associated with adverse perinatal outcome in fetuses at risk of growth restriction
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Noninvasive prediction models of intra-amniotic infection in women with preterm labor
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Long-term childhood outcomes for babies born at term who were exposed to antenatal corticosteroids
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General health in a cohort of children conceived after assisted reproductive technology in the United Kingdom: a population-based record-linkage study
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Effect of pentaerythritol tetranitrate (PETN) on the development of fetal growth restriction in pregnancies with impaired uteroplacental perfusion at midgestation—a randomized trial
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Telemedicine improves rate of successful first visit to nicu follow-up clinic
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Quality improvement through nurse-initiated kaiser sepsis calculator at a county hospital
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Assessing and validating a model of study completion for a prospective cohort of healthy newborns
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Safe or sorry? risk reduction and humanism in newborn medicine
https://pubmed.ncbi.nlm.nih.gov/36458410/

BASIC SCIENCE SELECTIONS

Genome-wide exploration of a pyroptosis-related gene module along with immune cell infiltration patterns in bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/36685920

Evaluation of a plant-based infant formula containing almonds and buckwheat on gut microbiota composition, intestine morphology, metabolic and immune markers in a neonatal piglet model
https://www.ncbi.nlm.nih.gov/pubmed/36678256

Involvement of HIF1 stabilization and VEGF signaling modulated by Grx-1 in murine model of bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/36640422

Neuroprotective effect of lipopolysaccharides in a dual-hit rat pup model of preterm hypoxia-ischemia
https://www.ncbi.nlm.nih.gov/pubmed/36574812

Development of a peripheral blood transcriptomic gene signature to predict bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/36472344

Longitudinal measurement of histidine-rich glycoprotein levels in bronchopulmonary dysplasia: a pilot study
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Lung ultrasound of the dependent lung detects real-time changes in lung volume in the preterm lamb
https://www.ncbi.nlm.nih.gov/pubmed/35750468

PAR2 overexpression is involved in the occurrence of hyperoxygen-induced bronchopulmonary dysplasia in rats
https://www.ncbi.nlm.nih.gov/pubmed/36657618

Fetal growth restriction impairs lung function and neurodevelopment in an early preterm rabbit model
https://www.ncbi.nlm.nih.gov/pubmed/36672647

Inhibition of ERK/CREB signaling contributes to postoperative learning and memory dysfunction in neonatal rats
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MSC EXO and tempol ameliorate bronchopulmonary dysplasia in newborn rats by activating HIF-1alpha
https://www.ncbi.nlm.nih.gov/pubmed/36650825

Beta-glucan protects against necrotizing enterocolitis in mice by inhibiting intestinal inflammation, improving the gut barrier, and modulating gut microbiota
https://www.ncbi.nlm.nih.gov/pubmed/36627673

IL-33-ST2 pathway regulates AECII transdifferentiation by targeting alveolar macrophage in a bronchopulmonary dysplasia mouse model
https://www.ncbi.nlm.nih.gov/pubmed/36573439

ADDITIONAL JOURNAL SELECTIONS

Neonatal systemic hypertension across the PHIS database: An update
https://www.ncbi.nlm.nih.gov/pubmed/36682689

The effect of hopelessness on depressive symptoms in mothers of infants hospitalized at neonatal intensive care unit: the mediating role of anxiety
https://www.ncbi.nlm.nih.gov/pubmed/36688831

Interventions for the management of pain and sedation in newborns undergoing therapeutic hypothermia for hypoxic-ischemic encephalopathy: a systematic review
https://www.ncbi.nlm.nih.gov/pubmed/36481984

Brain injury patterns in hypoxic ischemic encephalopathy of term neonates
https://www.ncbi.nlm.nih.gov/pubmed/36164277

The prognostic value of neonatal conventional-EEG monitoring in hypoxic-ischemic encephalopathy during therapeutic hypothermia
https://www.ncbi.nlm.nih.gov/pubmed/35711160

Role of systemic inflammatory indices in the prediction of moderate to severe bronchopulmonary dysplasia in preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/36681603

Impact of delayed time to antibiotics in medical and surgical necrotizing enterocolitis
https://www.ncbi.nlm.nih.gov/pubmed/36670710

Oxygenation index in the first three weeks of life is a predictor of bronchopulmonary dysplasia grade in very preterm infants
https://www.ncbi.nlm.nih.gov/pubmed/36639768

Lung transplantation for bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/36610665

Pharmacokinetics of l-citrulline in neonates at risk of developing bronchopulmonary dysplasia-associated pulmonary hypertension
https://www.ncbi.nlm.nih.gov/pubmed/36316628

Feasibility of implementing a modified SENSE program to increase positive sensory experiences for preterm infants in the neonatal intensive care unit (NICU): a pilot study
https://www.ncbi.nlm.nih.gov/pubmed/35903855

Hypocarbia is associated with adverse outcomes in Hypoxic Ischemic Encephalopathy (HIE)
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Longer duration of initial invasive mechanical ventilation is still a crucial risk factor for moderate-to-severe bronchopulmonary dysplasia in very preterm infants: a multicentrer prospective study
https://www.ncbi.nlm.nih.gov/pubmed/36604390

Maternal smoking during pregnancy negatively affects brain volumes proportional to intracranial volume in adolescents born very preterm
https://www.ncbi.nlm.nih.gov/pubmed/36684830

Late vitreoretinal complications of regressed retinopathy of prematurity: retinal break, vitreous hemorrhage, and retinal detachment
https://www.ncbi.nlm.nih.gov/pubmed/35843486

Assisted reproductive technology and neonatal intensive care unit: A retrospective observational study from a single center
https://www.ncbi.nlm.nih.gov/pubmed/36283401

Behavioral outcome of very preterm children at 5 years of age: Prognostic utility of brain tissue volumes at term-equivalent-age, perinatal, and environmental factors
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Development of necrotizing enterocolitis after blood transfusion in very premature neonates

https://www.ncbi.nlm.nih.gov/pubmed/36227506
Hypothermia combined with neuroprotective adjuvants shortens the duration of hospitalization in infants with hypoxic ischemic encephalopathy: Meta-analysis
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Risk factors for hypoxic-ischemic encephalopathy or neonatal death in placental abruption
https://pubmed.ncbi.nlm.nih.gov/36336280/