ARTICLES OF INTEREST – April 2019

**Early postnatal growth failure in preterm infants is not inevitable**

In this original article, in a five year sample cohort of 396 preterm infants <32wks, the authors described postnatal growth approximating birth centiles after the introduction of improved nutritional guidelines. Patients were grouped according to their gestational age at birth. Growth lines were constructed for weight, HC and length in each gestational age group from the median measures and compared with reference centile lines. The authors conclude that postnatal growth failure is not inevitable and extra-uterine weight gain can be achieved closer to centerline.

**Nebulised surfactant to reduce severity of respiratory distress: a blinded, parallel, randomised controlled trial**

This is a single center double blind, randomized control trial of using nebulized surfactant (Poractant alfa) in preterm infants 290-336 weeks gestation within the first 4 hours of life. Surfactant was nebulized using a customized vibrating membrane nebulizer (eFlow neonatal). 64 infants were randomized to two groups (bubble CPAP only & Bubble CPAP + nebulized surfactant; n=32/group). The primary outcomes were requirement for intubation and duration of mechanical ventilation at 72 hours with intention to treat. The results showed reduced need for intubation in the first 72 hours, primarily in infants >32weeks.

**Prognostic value of electroencephalography in hypothermia-treated neonates with hypoxic-ischemic encephalopathy: a meta-analysis**

Electroencephalography (EEG) background activity is associated with neurological outcome in neonates with hypoxic-ischemic encephalopathy. The authors sought to determine the prognostic value of EEG background activity after hypothermia was introduced. Eighteen studies with 940 neonates were included in this meta-analysis. EEG background activity is predictive of long-term neurological outcome in hypothermia-treated neonates with hypoxic-ischemic encephalopathy. Burst suppression, low voltage, and flat trace are potential predictors of death or neurodevelopmental impairment.
Combined antenatal and postnatal steroid effects on fetal and postnatal growth, and neurological outcomes in neonatal rats

To determine if combined antenatal and postnatal glucocorticoids (GC) have long-lasting adverse effects on fetal and neonatal growth, growth factors, and neurological outcomes the authors administered a single IM dose of betamethasone or dexamethasone to pregnant dams late in pregnancy and pups with betamethasone or dexamethasone in the newborn period. At 3 weeks of age, all GC groups were growth suppressed, but only the postnatal Dex group had deficits in brain weight and abnormal brainstem function. At 6 weeks, sustained reductions in body and brain weight occurred all combined antenatal and postnatal GC groups. IGF-I, GH and insulin levels were elevated at all ages with Dex. Combined antenatal and postnatal GCs have persistent detrimental lasting effects on growth, growth factors, neurological outcomes, and HPA axis activity.

Optimal oxygenation and role of free radicals in PPHN

Management of neonates with PPHN includes ventilation of the lungs with supplemental oxygen to correct hypoxemia. Optimal oxygenation should meet oxygen demand to the tissues and avoid hypoxic pulmonary vasoconstriction (HPV) while preventing oxidative stress. Oxidant stress can be due to free radical generation from underlying lung disease or from free radicals generated by supplemental oxygen. Free radicals act on the nitric oxide pathway reducing cGMP and promoting pulmonary vasoconstriction. This review highlights the need for additional studies to mitigate the impact of oxidative stress in the lung and pulmonary vasculature in PPHN.

Left ventricular cardiac output is a reliable predictor of extracorporeal life support (ECLS) in neonates with congenital diaphragmatic hernia (CDH)

The authors conducted a single center retrospective chart review from 2012 to 2018 of 27 patients with CDH of which 6 (22%) required ECLS. They found a statistically significant decrease in LV cardiac index, 1.33 L/min/m² vs 1.80 L/min/m² for patients requiring ECLS and non-ECLS respectively. No significant difference was found between the 2 groups with regards to vasoactive medication use, surfactant use, iNO use, severity of pulmonary hypertension, or right ventricular (RV) function.

Comparative effectiveness of drugs used to constrict the patent ductus arteriosus: a secondary analysis of the PDA-TOLERATE trial (NCT01958320)

In this secondary analysis of the multicenter randomized PDA-Tolerate trial, the authors evaluated and compared effectiveness of acetaminophen, indomethacin and ibuprofen in constricting the ductus arteriosus in newborns <28 weeks gestation. Drugs were randomized to center and their relative effectiveness was determined by comparing to spontaneous constriction. Indomethacin had the greatest effectiveness for ductus constriction (relative risk compared with conservative treatment (RR, (95% CI) = 3.21, (2.05–5.01)), followed by ibuprofen (2.03, (1.05–3.91)) and acetaminophen (1.33, (0.55–3.24). The authors concluded that acetaminophen was less effective than indomethacin when used as early initial drug treatment for ductal constriction in infants <28 weeks gestation.
Early total enteral feeding versus conventional enteral feeding in stable very-low-birth-weight infants: a randomised controlled trial

This was an unblinded randomized controlled trial to evaluate the effect of early total enteral feeding (ETEF) to conventional enteral feeding (CEF) in hemodynamically stable VLBW infants. ETEF group received 80 mL/kg with expressed breast milk or low-birth-weight (LBW) hydrolyzed formula on day 1 with no IV fluids unless hypoglycemic. In the CEF group, feeding was initiated with 20 mL/kg of expressed breast milk or LBW formula with IV fluids to make up the rest. Primary outcome was postnatal age at attaining full enteral feeds while secondary outcomes measured were episodes of feed intolerance, incidence of sepsis and necrotizing enterocolitis (NEC), and duration of hospital stay. The authors concluded that ETEF in stable VLBW infants resulted in earlier attainment of full feeds and decreased the duration of hospital stay without any increased risk of feed intolerance or NEC.

Effect of prophylaxis for early adrenal insufficiency using low-dose hydrocortisone in very preterm infants: an individual patient data meta-analysis

4 randomized controlled trials were evaluated looking at prophylactic low-dose hydrocortisone therapy in very preterm infants for adrenal insufficiency. Treatment for 10-15 days was associated with a significant increase in survival without BPD (OR, 1.45; 95% CI, 1.11-1.90; P = .007), as well as with decreases in medical treatment for patent ductus arteriosus (OR, 0.72; 95% CI, 0.56-0.93; P = .01) and death before discharge (OR, 0.70; 95% CI, 0.51-0.97; P = .03). The therapy was associated with an increased risk of spontaneous gastrointestinal perforation (OR, 2.50; 95% CI, 1.33-4.69; P = .004) when hydrocortisone was given in association with indomethacin exposure. The incidence of late-onset sepsis was increased in infants exposed to hydrocortisone (OR, 1.34; 95% CI, 1.02-1.75; P = .04).

Low cerebral oxygenation in preterm infants is associated with adverse neurodevelopmental outcome

In an observational cohort study conducted from 2006 to 2013 in infants <32 weeks of gestation, regional cerebral oxygenation (rScO2) data for the first 72 hours was compared with neurocognitive outcomes assessed at 15 to 24 months. Associations with an unfavorable cognitive outcome in multivariable analysis were comparable for time spent with a rScO2 below 55% and -1.5 SD (according to published reference values), with an OR of 1.4 (CI 1.1-1.7) for 20% of time below either threshold. This suggests the use of a threshold of rScO2 <55% for future clinical studies when using adult near-infrared sensors (rScO2 <65% for neonatal sensors, approximately).

OTHER NOTEWORTHY PUBLICATIONS – April, 2019

Pediatrics
Maternal smoking before and during pregnancy and the risk of sudden unexpected infant death

Neonatal herpes simplex virus infection among medicaid-enrolled children: 2009–2015

Expressions of gratitude and medical team performance

Commentary: neonatal herpes simplex virus infections: new data, old conundrum

Severe fetal hemolysis and cholestasis due to high-titer maternal IgG anti-A antibodies
https://www.ncbi.nlm.nih.gov/pubmed/30872329

Multilocus heterotopic gastric mucosa of ileum masquerading as vesiobd in a newborn
Journal of Pediatrics
Analysis of the seasonal trend of congenital heart defects
A comparison of developmental outcomes of adolescent neonatal intensive care unit survivors born with a congenital heart defect or born preterm
Low cerebral oxygenation in preterm infants is associated with adverse neurodevelopmental outcome
Living with severe bronchopulmonary dysplasia—parental views of their child’s quality of life
Beyond a seat at the table: the added value of family stakeholders to improve care, research, and education in neonatology
Black race is associated with a lower risk of bronchopulmonary dysplasia
Effect of prophylaxis for early adrenal insufficiency using low-dose hydrocortisone in very preterm infants: an individual patient data meta-analysis
The association of hydrocortisone dosage on mortality in infants born extremely premature
Prematurity does not increase early childhood fracture risk
Increased congenital hypothyroidism detection in preterm infants with serial newborn screening
Expired tidal volume variation in extremely low birth weight and very low birth weight infants on volume-targeted ventilation

Pediatric Research
Addressing rural health disparities in neonatal abstinence syndrome: population-based surveillance and public policy
Future perspectives on the use of deformation analysis to identify the underlying pathophysiological basis for cardiovascular compromise in neonates
Capturing the statewide incidence of neonatal abstinence syndrome in real time: the West Virginia experience
Genetic variation in CRHR1 is associated with short-term respiratory response to corticosteroids in preterm infants at risk for bronchopulmonary dysplasia.
Altered in utero kidney development in newborns with congenital heart disease.
Accuracy of preterm infant weight gain velocity calculations vary depending on method used and infant age at time of measurement
Dried blood spot compared to plasma measurements of blood-based biomarkers of brain injury in neonatal encephalopathy
Mediators of racial and ethnic disparity in mother’s own milk feeding in very low birth weight infants
Urinary acute kidney injury biomarkers in very low-birth-weight infants on indomethacin for patent ductus arteriosus

The relationship between IGF-I and -II concentrations and body composition at birth and over the first 2 months

Maternal preeclampsia and respiratory outcomes in extremely premature infants

Maternal hypertension and survival in singletons and twins born at 23–29 weeks: not just one answer

Fetal inflammation is associated with persistent systemic and hippocampal inflammation and dysregulation of hippocampal glutamatergic homeostasis

MIF inhibition enhances pulmonary angiogenesis and lung development in congenital diaphragmatic hernia

Angiotensin inhibition in the developing kidney; tubulointerstitial effect

Archives of Disease in Childhood - Fetal & Neonatal Edition

Early postnatal growth failure in preterm infants is not inevitable

Premature small for gestational age infants fed an exclusive human milk-based diet achieve catchup growth without metabolic consequences at 2 years of age

Early-onset neonatal infections in Australia and New Zealand, 2002–2012

Outcomes following antenatal identification of hydrops fetalis: a single-centre experience from 2001 to 2012

Visual attention on a respiratory function monitor during simulated neonatal resuscitation: an eyetracking study

Gastrointestinal sequelae after surgery for necrotising enterocolitis: a systematic review and meta-analysis

Hypoxemic and hyperoxemic likelihood in pulse oximetry ranges: NICU observational study

Patient-ventilator asynchrony in preterm infants on nasal intermittent positive pressure ventilation

Hypothermia for perinatal asphyxia: trial-based resource use and costs at 6–7 years

Epidemiology of infections and antimicrobial use in Greek Neonatal Units

Blood pressure intervention levels in preterm infants: pilot randomised trial

Impact of breast milk intake on body composition at term in very preterm babies: secondary analysis of the Nutritional Evaluation and Optimisation in Neonates randomised controlled trial

Nebulised surfactant to reduce severity of respiratory distress: a blinded, parallel, randomised controlled trial
3D airway model to assess airway dead space

Challenges and opportunities for antibiotic stewardship among preterm infants

Milk feed osmolality and adverse events in newborn infants and animals: a systematic review

Staff matter too: pilot staff support intervention to reduce stress and burn-out on a neonatal intensive care unit

Parental smoking and support in the NICU

Intrathoracic renal ectopia with congenital diaphragmatic hernia

TPNoma: an unusual complication of umbilical venous catheter malposition

Optimising nutrition during therapeutic hypothermia

Is preterm nutrition a trade-off between head and heart?

Journal of Perinatology

Comparative effectiveness of drugs used to constrict the patent ductus arteriosus: a secondary analysis of the PDA-TOLERATE trial (NCT01958320)

Fetal heart rate, heart rate variability, and heart rate/movement coupling in the Safe Passage Study

The Relationship between blood pressure parameters and left ventricular output in neonates

Cardiac mechanics in infants with Down syndrome in the early neonatal period

Who’s counting? Assessing the effects of a simulation-based training intervention on the accuracy of neonatal heart rate auscultation

Adrenal insufficiency in neonates undergoing cardiopulmonary bypass and postoperative hypothalamic-pituitary-adrenal function after prophylactic glucocorticoids

Left ventricular cardiac output is a reliable predictor of extracorporeal life support in neonates with congenital diaphragmatic hernia

Comparison of early postnatal prediction models for survival in congenital diaphragmatic hernia

In-hospital outcomes of neonates with hypoxic-ischemic encephalopathy receiving extracorporeal membrane oxygenation

Sutureless closure: a versatile treatment for the diverse presentations of gastroschisis

Association of chorioamnionitis and its duration with neonatal morbidity and mortality

Correction: Association of chorioamnionitis and its duration with neonatal morbidity and mortality
Hospital-acquired viral respiratory infections in neonates hospitalized since birth in a tertiary neonatal intensive care unit
Diagnosis of congenital/perinatal infections by neonatologists: a national survey
Trends in the incidence, mortality, and cost of neonatal herpes simplex virus hospitalizations in the United States from 2003 to 2014
Differential effects of the retinopathy of prematurity exam on the physiology of premature infants
https://www.ncbi.nlm.nih.gov/pubmed/30755719
Outcomes of preterm infants conceived with in vitro fertilization
Tidal volume transmission during non-synchronized nasal intermittent positive pressure ventilation via RAM® cannula
Use of very low tidal volumes during high-frequency ventilation reduces ventilator lung injury
Association between maternal serious mental illness and adverse birth outcomes
Neonatal postgraduate training program for physician assistants: meeting a need in neonatal care
Is early caffeine therapy safe and effective for ventilated preterm infants?
Should we target higher or lower oxygen saturation targets in the preterm infant?

Neonatology
Understanding and improving diagnostic tests: the clinician perspective
Low renal oxygen saturation at near-infrared spectroscopy on the first day of life is associated with developing acute kidney injury in very preterm infants
Inadvertent migration of umbilical venous catheters often leads to malposition
Milk curd obstruction in human milk-fed preterm infants
Neurotoxicity of unconjugated bilirubin in mature and immature rat organotypic hippocampal slice cultures
Cerebral blood flow measured by phase-contrast magnetic resonance angiography in preterm and term neonates
Does a good quality breastfeed improve the blood glucose concentration in hypoglycaemic babies?
Alert newborn infants are ready to feed and raise their glucose concentration
The neonatal acute bilirubin encephalopathy registry (naber): background, aims, and protocol
Seizures in premature infants born at less than 28 weeks’ gestation
Early total enteral feeding versus conventional enteral feeding in stable very-low-birth-weight infants: a randomised controlled trial

A multicenter lung ultrasound study on transient tachypnea of the neonate

Perinatal iron deficiency: implications for mothers and infants

Neonatal autopsy: a 21st century approach?

Commentary on ‘lower versus higher oxygen concentrations titrated to target oxygen saturations during resuscitation of preterm infants at birth’
https://www.ncbi.nlm.nih.gov/pubmed/30986782

**American Journal of Perinatology**

Pregnancy outcomes after early amniotomy among class III obese gravidas undergoing induction of labor
https://www.ncbi.nlm.nih.gov/pubmed/30396229

Assessing maternal and fetal risks associated with prolonged induction of labor

Neuropathology of early sudden infant death syndrome—hypoplasia of the pontine Kolliker-Fuse nucleus: a possible marker of unexpected collapse during skin-to-skin care

Occult placenta accreta: risk factors, adverse obstetrical outcomes, and recurrence in subsequent pregnancies

Survey of ventilation practices in the neonatal intensive care units of the United States and Canada: use of volume-targeted ventilation and barriers to its use

The difference in sibling birthweight and neonatal death: a population-based cohort study

Increased frequency of skin-to-skin contact is associated with enhanced vagal tone and improved health outcomes in preterm neonates

Cord blood erythropoietin and hepcidin reflect lower newborn iron stores due to maternal obesity during pregnancy

Interpregnancy body mass index changes: distribution and impact on adverse pregnancy outcomes in the subsequent pregnancy

Diagnosis discordance and neonatal transport: a single-center retrospective chart review

Identification of a pivotal period in the oral feeding progression of preterm infants

Stillbirth and live birth at periviable gestational age: a comparison of prevalence and risk factors

Apgar scores at 10 minutes and outcomes in term and late preterm neonates with hypoxic-ischemic encephalopathy in the cooling era

**Journal of Neonatal-Perinatal Medicine**

The relationship of cervical microbiota diversity with race and disparities in preterm birth
Transitional fetal hemodynamics and gas exchange in premature postpartum adaptation: immediate vs. delayed cord clamping

International perspectives: implementation of the Korean neonatal network
Prevention of bronchopulmonary dysplasia: a summary of evidence-based strategies
Neonatal respiratory support on transport
Approaches to noninvasive respiratory support in preterm infants: from CPAP to NAVA
Case 1: Vomiting and bradycardia in a newborn infant
Case 2: Rapidly growing neck mass in an extremely preterm infant with pulmonary hypertension
Case 3: A rare cause of respiratory distress and excessive salivation in a term infant
Strip of the month: Premature preterm rupture of membranes and fetal decelerations
Legal briefs: Was the adverse outcome from Goldenhar syndrome or hypoxic-ischemic events?
Visual diagnosis: bilateral lacrimal sac swelling in a newborn

Preventing perinatal depression to improve maternal and child health—a health care imperative
Associations of maternal diabetes and body mass index with offspring birth weight and prematurity
Association between in vitro bleeding time and bleeding in preterm infants with thrombocytopenia

Prevalence, risk factors and outcome of congenital anomalies among neonatal admissions in OGBOMOSO, Nigeria (PDF)
Delayed appearance of mature ganglia in an infant with an atypical presentation of total colonic and small bowel aganglionosis: a case report (PDF)
An atypical case of Klippel-Trénaunay syndrome presenting with crossed-bilateral limb hypertrophy and postaxial polydactyly: a case report (PDF)
Prospective audit and feedback on antibiotic use in neonatal intensive care: a retrospective cohort study (PDF)
Heterozygous familial hypercholesterolaemia in a pair of identical twins: a case report and updated review (PDF)
Lethal perinatal hypophosphatasia caused by a novel compound heterozygous mutation: a case report (PDF)
Enterostomy complications in necrotizing enterocolitis (NEC) surgery, a retrospective chart review at Odense university hospital (PDF)
Anthropometric measurements can identify small for gestational age newborns: a cohort study in rural Tanzania (PDF)
Respiratory severity score as a predictive factor for severe bronchopulmonary dysplasia or death in extremely preterm infants (PDF)
Prenatal diagnosis of congenital megalourethra with imperforate anus (PDF)
First clinical experience with the Kora pacemaker system in congenital complete heart block in newborn infants (PDF)
Predictive value of the aspartate aminotransferase to platelet ratio index for parenteral nutrition associated cholestasis in extremely low birth weight infants (PDF)
The various clinical spectra of juvenile xanthogranuloma: imaging for two case reports and review of the literature (PDF)
Follow-up study of neurodevelopment in 2-year-old infants who had suffered from neonatal hypoglycemia (PDF)
Drug related problems in the neonatal intensive care unit: incidence, characterization and clinical relevance (PDF)
Etiology of neonatal seizures and maintenance therapy use: a 10-year retrospective study at Toulouse Children’s hospital (PDF)

Pediatric Critical Care Medicine
Avoiding furosemide ototoxicity associated with single-ventricle repair in young infants
Fluid management practices after surgery for congenital heart disease: a worldwide survey

New England Journal of Medicine
Lentiviral gene therapy combined with low-dose busulfan in infants with SCID-X1
Molecular genetic anatomy and risk profile of Hirschsprung’s disease
"Is it safe?" - The many unanswered questions about medications and breast-feeding.
**Lancet**
Growth trajectories of breastfed HIV-exposed uninfected and HIV-unexposed children under conditions of universal maternal antiretroviral therapy: a prospective study
Transmission of CMV, HTLV-1, and HIV through breastmilk

**JAMA**
Association of state medicaid expansion status with low birth weight and preterm birth
The right to grieve (PDF)
https://jamanetwork.com/journals/jama/fullarticle/2731182
Wireless vital signs monitoring for the NICU (PDF)
https://jamanetwork.com/journals/jama/fullarticle/2730089

**BMJ**
Learning from birthing stories on Twitter
Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study
Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study

**Pediatric Infectious Disease Journal**
Transient tachypnea of the newborn is associated with an increased risk of hospitalization due to respiratory syncytial virus bronchiolitis (PDF)
https://journals.lww.com/pidj/Fulltext/2019/04000/Transient_Tachypnea_of_the_Newborn_Is_Associa
ted.19.aspx
Combination of nasal and expanded skin swabs enhances the detection rate of staphylococcus aureus colonization in premature infants
Invasive pneumococcal disease in neonates prior to pneumococcal conjugate vaccine use in South Africa: 2003–2008 (PDF)
https://journals.lww.com/pidj/Fulltext/2019/04000/Invasive_Pneumococcal_Disease_in_Neonates_Prio
to.22.aspx

**Pediatric Cardiology**
Complications of transthoracic intracardiac and central venous lines in neonates undergoing cardiac surgery
Recurrent congenital heart diseases among neonates born to mothers with congenital heart diseases
https://www.ncbi.nlm.nih.gov/pubmed/30830281
Umbilical vein catheter protruding through a pulmonary vein in a patient with an infracardiac type total abnormal pulmonary venous drainage
**Pediatric Neurology**
Prognostic value of electroencephalography in hypothermia-treated neonates with hypoxic-ischemic encephalopathy: a meta-analysis

**Obstetrics and Gynecology**
Safety assessment of a large-scale improvement collaborative to reduce nulliparous cesarean delivery rates
Neonatal and maternal morbidity among low-risk nulliparous women at 39–41 weeks of gestation
Association of a delayed cord-clamping protocol with hyperbilirubinemia in term neonates

**American Journal of Obstetrics & Gynecology**
Trial of labor after cesarean delivery in twin gestations: systematic review and meta-analysis
Threshold of metabolic acidosis associated with newborn cerebral palsy: medical legal implications
From population reference to national standard: new and improved birthweight charts
Time from neuraxial anesthesia placement to delivery is inversely proportional to umbilical arterial cord pH at scheduled cesarean delivery
Unexpected term NICU admissions: a marker of obstetrical care quality?
Association between gestational age and severe maternal morbidity and mortality of preterm cesarean delivery: a population-based cohort study

**BASIC SCIENCE SELECTIONS**
Combined antenatal and postnatal steroid effects on fetal and postnatal growth, and neurological outcomes in neonatal rats

Epigenome-wide analysis identifies genes and pathways linked to neurobehavioral variation in preterm infants

Fetal growth restriction is associated with an altered cardiopulmonary and cerebral hemodynamic response to surfactant therapy in preterm lambs

Preterm lung exhibits distinct spatiotemporal proteome expression at initiation of lung injury
CXCR2 blockade mitigates neural cell injury following preclinical chorioamnionitis

ADDITIONAL JOURNAL SELECTIONS
Optimal oxygenation and role of free radicals in PPHN

Emerging roles of miRNAs in brain development and perinatal brain injury

Long-term effects of postnatal corticosteroids to prevent or treat bronchopulmonary dysplasia: balancing the risks and benefits
Cheong JLY and Doyle LW. *Semin Fetal Neonatal Med.*

Early extubation is not associated with severe intraventricular hemorrhage in preterm infants born before 29 weeks of gestation. Results of an EPIPAGE-2 cohort study

Gestational age at birth and mortality from infancy into mid-adulthood: a national cohort study

Children's hospital of Philadelphia score to predict severe retinopathy in Indian preterm infants
Doshi S, Desai S, Nanavati R, et al. *Eye (Lond).*

Improved feeding tolerance and growth are linked to increased gut microbial community diversity in very-low-birth-weight infants fed mother's own milk compared with donor breast milk