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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – July 2019

Longitudinal changes in the gut microbiome of infants on total parenteral nutrition
Dahlgren AF, Pan A, Lam V, et al. *Pediatr Res.*

This is a prospective, longitudinal study looking at alterations in gut microbiome in infants >32 weeks receiving TPN over the first 4weeks of life. Weekly fecal samples were obtained from 47 infants (25 on TPN, 22 not on TPN) for gut microbiome composition using high throughput pyrosequencing of 16S rDNA. Results showed decreased fecal bacterial alpha diversity in the TPN group compared to controls at week 4 (p-value 0.03). The authors concluded that the use of TPN is associated with dysbiosis showing significant loss of biodiversity and changes to gut microbial colonization patterns.

Successful use of an artificial placenta to support extremely preterm ovine fetuses at the border of viability
Usuda H, Watanabe S, Saito M, et al. *Am J Obstet Gynecol.*

This study reports the use of ex-vivo uterine environment therapy using a membrane oxygenator to support preterm ovine fetuses at 95days of gestation (equivalent to 24wk human gestation) for 120hrs. Of the eight fetuses, seven completed the 120hr period (87.5%). There were no significant intergroup differences (P>.05) in key physiological variables when compared to normal controls euthanized at the same gestation. The study also measured absence of infection, brain injury as well as growth and cardiovascular patterns. The authors conclude that this could become a potential future option to improve outcomes in extremely preterm infants.

Understanding the pathobiology in patent ductus arteriosus in prematurity—beyond prostaglandins and oxygen
Hundscheid T, van den Broek M, van der Lee R, et al. *Pediatr Res.*

The authors review the physiology of ductal patency in fetal life, factors leading to closure after birth, and the effects of antenatal exposure to certain medications. Multiple pathways affecting ductal tone are described in detail including prostaglandin, oxygen, NO, CO, ion channels, and others. Targets for intervention in various pathways are illustrated, and the fetal to neonatal transition is described with respect to chemical mediators of ductal patency. Ductal tone is affected by antenatal use of MgSO4, indomethacin, and steroids as well as postnatal diazoxide, sulfonylurea, and furosemide.

Surfactant replacement therapy for respiratory distress syndrome in preterm infants: United Kingdom national consensus (PDF)
Banerjee S, Fernandez R, Fox GF, et al. *Pediatr Res.*

A United Kingdom consensus statement was developed for the use of surfactant in preterm infants with RDS. 5 key recommendations were included: (1) Each NICU should have an RDS management policy. (2) Early rescue therapy is preferred over prophylaxis. (3) Rescue surfactant should be given early in the disease process with oxygen need >30% as a reliable predictor of CPAP failure. (4) Weight-based dosing is recommended with occasional repeat dosing. (5) There is emerging evidence that LISA is superior to INSURE.

Topiramate plus cooling for hypoxic-ischemic encephalopathy: a randomized, controlled, multicenter, double-blinded trial
Nuñez-Ramiro A, Benavente-Fernández I, Valverde E, et al. *Neonatology.*

Therapeutic interventions to improve the efficacy of whole-body cooling for hypoxic-ischemic encephalopathy are desirable. Topiramate has been shown to be effective in reducing brain damage in experimental studies. Neonates were randomly assigned to topiramate or placebo at the initiation of hypothermia. Topiramate reduced seizures in patients achieving therapeutic levels in the first hours after treatment initiation; however, they represented only a part of the study population. Further studies with higher loading and maintenance dosing of topiramate are warranted.

Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes
Corsi DJ, Walsh L, Weiss D, et al. *JAMA.*

This population-based retrospective cohort study included 661,617 women aged 15 years and older in Ontario, Canada. Of these women, 9,427 (1.4%) reported cannabis use during pregnancy. In the matched cohort, reported cannabis exposure was significantly associated with preterm birth (RD of 2.98% [95% CI, 2.63%-3.34%] and RR of 1.41 [95% CI, 1.36-1.47]). Compared with no reported use, cannabis exposure was significantly associated with greater frequency of SGA (RR, 1.53 [95% CI, 1.45-1.61]), placental abruption (RR, 1.72 [95% CI, 1.54-1.92]), transfer to NICU (RR, 1.40 [95% CI, 1.36-1.44]), and 5-minute Apgar score less than 4 (RR, 1.28 [95% CI, 1.13-1.45]).

Genetically modified babies and a first application of clustered regularly interspaced short palindromic repeats (CRISPR-Cas9)
Rose BI and Brown S. *Obstet Gynecol.*

This commentary reviews CRISPR-Cas9 technology and describes how Dr. Jiankui attempted to prenatally delete a specific 32 base pair segment of the CCR5 gene (required by most strains of HIV to enter cells) in 18 retrieved embryos, ultimately leading to the birth of Lulu and Nina. The authors discuss the ethics of genetic modification, technologic challenges with mosaicism and heterogeneity, and off-target mutations that can result in unintended consequences.

Early acid suppression therapy exposure and fracture in young children
Malchodi L, Wagner K1, Susi A, et al. *Pediatrics.*

In this retrospective cohort study, the authors followed 851,631 children and evaluated risk of fractures in those that received early acid suppression therapy (AST) vs controls that did not receive AST. Risk of fractures with sub types of AST prescribed, including proton pump inhibitors (PPIs) and histamine H2-receptor antagonists (H2RAs) were also analyzed. The authors concluded that AST medication use during the first year of life was associated with increased fracture hazard in children. Fracture hazard increased with duration of AST use, which suggests a possible dose-dependent response, and with younger age of AST initiation with PPIs, alone or in combination with H2RAs.

Human cord blood-derived unrestricted somatic stem cell infusion improves neurobehavioral outcome in a rabbit model of intraventricular hemorrhage
Vinukonda G, Liao Y, Hu F, et al. Stem Cells Transl Med.

To determine if unrestricted somatic stem cells (USSCs) from human cord blood have reparative effects in animal models of brain and spinal cord injuries, the authors administered USSCs to premature rabbit pups with IVH and determined the effects on white matter integrity and neurobehavioral performance. They found that USSCs were functionally associated with attenuated microglial infiltration, less apoptotic cell death, fewer reactive astrocytes, diminished levels of key inflammatory cytokines, and anatomically with better preservation of myelin fibers, increased myelin gene expression, altered reactive astrocyte distribution, and improved locomotor function.

Cognitive and motor outcomes of children with prenatal opioid exposure: a systematic review and meta-analysis
Yeoh SL, Eastwood J, Wright IM, et al. JAMA Netw Open.

Since the association of Prenatal Opioid Exposure (POE) with long-term neurologic and physical development remains largely unknown, the authors performed a meta-analysis of 26 peer-reviewed cohort studies examining exposure and outcomes beyond 6 months of age. They found that POE was negatively associated with neurocognitive and physical development from age 6 months, and this association persisted until adolescence.

Pediatrics
Early acid suppression therapy exposure and fracture in young children
https://www.ncbi.nlm.nih.gov/pubmed/31175146
Infant deaths in sitting devices
https://www.ncbi.nlm.nih.gov/pubmed/31110162
A 2017 US reference for singleton birth weight percentiles using obstetric estimates of gestation
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A simpler prediction rule for rebound hyperbilirubinemia
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Neurologic outcome after prematurity: perspectives of parents and clinicians
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https://www.ncbi.nlm.nih.gov/pubmed/31248940
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https://www.ncbi.nlm.nih.gov/pubmed/31213519

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Mandated research peer review positively impacts research funding success rates for young investigators (PDF)
https://www.jpeds.com/article/S0022-3476(19)30601-8/pdf
So you want to give stem cells to babies? Neonatologists and parents' views to optimize clinical trials
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https://www.jpeds.com/article/S0022-3476(19)30392-0/pdf
A randomized trial of baby triple P for preterm infants: Child outcomes at 2 years of corrected age (PDF)
https://www.jpeds.com/article/S0022-3476(19)30052-6/pdf
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Maternal infection associated with autism and depression in their offspring (PDF)
https://www.jpeds.com/article/S0022-3476(19)30524-4/pdf

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Postnatal nutritional intakes and hyperglycemia as determinants of blood pressure at 6.5 years of age in children born extremely preterm
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Enhanced early prediction of clinically relevant neonatal hyperbilirubinemia with machine learning
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Effect of behavioral change intervention around new-born care practices among most marginalized women in self-help groups in rural India: analyses of three cross-sectional surveys between 2013 and 2016
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Optic nerve sheath diameter for preterm infants: a pilot study
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What do NICU fellows identify as important for achieving competency in neonatal intubation?
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Achieving procedural competency during neonatal fellowship training: can trainees teach us how to teach?
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Risk factors for late-onset sepsis in preterm infants: a multicenter case-control study
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Underdosing of surfactant for preterm babies with respiratory distress syndrome in clinical practice: A retrospective cohort study (PDF)
https://www.thieme-connect.com/products/ejournals/pdf/10.1055/s-0038-1675645.pdf
Association between the degree of twin birthweight discordance and perinatal outcomes
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Maternal Health, Neonatology and Perinatology

What topics should we teach the parents of admitted neonates in the newborn care unit in the resource-limited setting - a Delphi study
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6621949

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Impact of nonmedical factors on neurobehavior and language outcomes of preterm infants
https://neoreviews.aappublications.org/content/20/7/e372
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https://neoreviews.aappublications.org/content/20/7/e385
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Case 1: A blueberry muffin rash complicated by cardiomyopathy
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Case 2: dilated stomach in an infant with failure to thrive
https://neoreviews.aappublications.org/content/20/7/e412
Case 3: abdominal distention and bloody stools in a 2-week-old term neonate
https://neoreviews.aappublications.org/content/20/7/e415
Strip of the month: velamentous cord insertion
https://neoreviews.aappublications.org/content/20/7/e419
Legal briefs: head compression, ischemic encephalopathy, and adverse outcome
https://neoreviews.aappublications.org/content/20/7/e432
Visual diagnosis: a term infant with respiratory distress at birth
https://neoreviews.aappublications.org/content/20/7/e428

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Viewpoint: Screening for neonatal hyperbilirubinemia—First do no harm?
https://www.ncbi.nlm.nih.gov/pubmed/31107538
Aspirin for the prevention of preeclampsia and potential consequences for fetal brain development
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Severity of hypoxic ischemic encephalopathy and heart rate variability in neonates: a systematic review (PDF)
https://bmcpediatr.biomedcentral.com/track/pdf/10.1186/s12887-019-1603-7
Influence of prenatal and early-life exposures on food allergy and eczema in infancy: a birth cohort study (PDF)
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Growth of extremely low birth weight infants at a tertiary hospital in a middle-income country (PDF)
https://bmcpediatr.biomedcentral.com/track/pdf/10.1186/s12887-019-1568-6
Parental perspectives on retention and secondary use of neonatal dried bloodspots: a Dutch mixed methods study (PDF)
https://bmcpediatr.biomedcentral.com/track/pdf/10.1186/s12887-019-1590-8
The discovery BPD (D-BPD) program: study protocol of a prospective translational multicenter collaborative study to investigate determinants of chronic lung disease in very low birth weight infants (PDF)
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Viewpoints from families for improving transition from NICU-to-home for infants with medical complexity at a safety net hospital: a qualitative study (PDF)
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Effect of allopurinol in addition to hypothermia treatment in neonates for hypoxic-ischemic brain injury on neurocognitive outcome (ALBINO): study protocol of a blinded randomized placebo-controlled parallel group multicenter trial for superiority (phase III) (PDF)
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Ultrasound-guided femoral arterial cannulation in neonates undergoing cardiac surgery or catheterization: comparison of 0.014-inch floppy versus 0.019-inch straight guidewire
https://www.ncbi.nlm.nih.gov/pubmed/31013264
Population pharmacokinetics and dosing of milrinone after patent ductus arteriosus ligation in preterm infants
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Mortality rate-dependent variations in the timing and causes of death in extremely preterm infants born at 23–24 weeks' gestation
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We can do better for our tiniest babies
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Risk of severe intraventricular hemorrhage in the first week of life in preterm infants transported before 72 hours of age
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Screening for hepatitis B infection in pregnant women: updated evidence report and systematic review for the US Preventive Services Task Force
https://www.ncbi.nlm.nih.gov/pubmed/31334780
Breast milk for preemies
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Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes
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Self-reported medical and nonmedical cannabis use among pregnant women in the United States
https://www.ncbi.nlm.nih.gov/pubmed/31211824

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Health outcomes of young children born to mothers who received 2009 pandemic H1N1 influenza vaccination during pregnancy: retrospective cohort study
https://www.ncbi.nlm.nih.gov/pubmed/31292120

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Bacterial colonization of the hospitalized newborn: competition between Staphylococcus aureus and Staphylococcus epidermidis
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Impact of shifts to birth testing on early infant diagnosis program outcomes in KwaZulu-Natal, South Africa
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Reducing hematologic toxicity with short course postexposure prophylaxis with zidovudine for HIV-1 exposed infants with low transmission risk
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Neonatal group B streptococcal infection in a tertiary care hospital in Saudi Arabia
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Genetically modified babies and a first application of clustered regularly interspaced short palindromic repeats (CRISPR-Cas9)
https://www.ncbi.nlm.nih.gov/pubmed/31188312

Prevention of group B streptococcal early-onset disease in newborns: ACOG Committee Opinion Summary, Number 782
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Critical appraisal of the proposed defenses for planned home birth
https://www.ncbi.nlm.nih.gov/pubmed/30653945

Term cesarean delivery in the first pregnancy is not associated with an increased risk for preterm delivery in the subsequent pregnancy
https://www.ncbi.nlm.nih.gov/pubmed/30802437

Significant reduction in umbilical artery metabolic acidosis after implementation of intrapartum ST waveform analysis of the fetal electrocardiogram
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A contemporary amniotic fluid volume chart for the United States: The NICHD Fetal Growth Studies–Singletons
https://www.ncbi.nlm.nih.gov/pubmed/30790566

Successful use of an artificial placenta to support extremely preterm ovine fetuses at the border of viability
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Alobar holoprosencephaly detected in a 9-week embryo
https://www.ncbi.nlm.nih.gov/pubmed/30625294

Fresh in vitro fertilization cycles increase risk of small-for-gestational age; frozen cycles increase risk of large-for-gestational age: Which is worse?
https://www.ncbi.nlm.nih.gov/pubmed/30995459

Substance use disorders in pregnancy: clinical, ethical, and research imperatives of the opioid epidemic: a report of a joint workshop of the Society for Maternal-Fetal Medicine, American College of Obstetricians and Gynecologists, and American Society of Addiction Medicine

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BASIC SCIENCE SELECTIONS

Placental CpG methylation of inflammation, angiogenic, and neurotrophic genes and retinopathy of prematurity
Bulka CM, Dammann O, Santos HP Jr, et al. *Invest Ophthalmol Vis Sci.*
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Human cord blood-derived unrestricted somatic stem cell infusion improves neurobehavioral outcome in a rabbit model of intraventricular hemorrhage
Vinukonda G, Liao Y, Hu F, et al. *Stem Cells Transl Med.*
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Lung injury after asphyxia and hemorrhagic shock in newborn piglets: Analysis of structural and inflammatory changes
Weber B, Mendler MR, Lackner I, et al. *PLoS One.*
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Umbilical catheters as vectors for generalized bacterial infection in premature infants regardless of antibiotic use
Sobczak A, Klepacka J, Amrom D, et al. *J Med Microbiol.*
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Prevalence of permanent childhood hearing loss detected at the universal newborn hearing screen: systematic review and meta-analysis
Butcher E, Dezateux C, Cortina-Borja M, et al. *PLoS One.*
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Opioids affect the fetal brain: reframing the detoxification debate
Caritis SN and Panigrahy A. *Am J Obstet Gynecol.*
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Simulated amniotic fluid-like solution given enterally to neonates after obstructive bowel surgeries: A randomized controlled trial
El-Farrash RA, Gad GI, Abdelkader HM, et al. *Nutrition.*
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Embleton ND and van den Akker CHP. *Semin Perinatol.*
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Does early compared to late fortification of human milk for preterm infants improve clinical outcomes?
Godden B, Collins CT, Hilditch C, et al. *J Paediatr Child Health.*
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Cognitive and motor outcomes of children with prenatal opioid exposure: a systematic review and meta-analysis
Yeoh SL, Eastwood J, Wright IM, et al. *JAMA Netw Open.*
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Extended course of prednisolone in infants with severe bronchopulmonary dysplasia
Linafelter A, Cuna A, Liu C, et al. *Early Hum Dev.*

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