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American Academy of Pediatrics
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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – June 2019

Development of nationwide recommendations to support prenatal counseling in extreme prematurity
Geurtzen R, Van Heijst AFJ, Draaisma JMT, et al. *Pediatrics.*

The authors sought to develop a nationwide, evidence-based framework to support prenatal counseling in extreme prematurity. A nationwide multicenter RAND-modified Delphi method study was performed between November 2016 and December 2017 in the Netherlands. A total of 101 recommendations were included in the framework, including tools to support personalization. A nationwide, evidence-based framework for prenatal counseling in extreme prematurity was developed containing recommendations and tools for personalization in the domains of organization, decision-making, content, and style of prenatal counseling.

Effect of early versus delayed cord clamping in neonate on heart rate, breathing and oxygen saturation during first 10 minutes of birth - randomized clinical trial (PDF)
Ashish KC , Nalini Singhal, Jageshwor Gautam, et al. *Maternal Health, Neonatology, and Perinatology*

The authors sought to evaluate the effect of delayed (≥180 s) versus early (≤60 s) cord clamping on peripheral blood oxygenation and heart rate up to 10 min after birth on term and late preterm infants. Spontaneously breathing babies subjected to DCC have higher oxygen saturation up to 10 min after birth compared to those who have undergone ECC. Spontaneously breathing babies with DCC have lower heart rates compared to ECC until 390 s. Spontaneously breathing babies receiving DCC have early establishment of breathing compared to ECC.

Mild neonatal brain hypoxia-ischemia in very immature rats causes long-term behavioral and cerebellar abnormalities at adulthood
Sanches EF, Van de Looij Y, Toulotte A, et al. *Front Physiol*.

In order to evaluate long-term impact of hypoxia-ischemia (HI) the authors measured behavior, alterations in vivo 1H magnetic resonance spectroscopy (1H MRS) and molecular changes to the cerebellum in adult rats after mild early postnatal HI. They found that HI induces hyperactivity toward adulthood, long-lived neuro-metabolic change, and substantial decreases of expression of neuronal and

myelin markers in the cerebellum of adult rats. Taken together, the data provides in vivo evidence of long-term neurologic changes in the cerebellum following mild neonatal HI.

Prophylactic postnatal corticosteroids: early hydrocortisone
Baud O and Watterberg KL. *Semin Fetal Neonatal Med.*

The authors review and summarize four randomised clinical trials enrolling almost 1000 extremely preterm infants, treated prophylactically with low-dose hydrocortisone. These studies show significantly decreased BPD and mortality, reduced need for medical treatment for the PDA, no increase in GI perforation in the absence of indomethacin, but an increase in late-onset sepsis. They conclude that the effects of early low-dose hydrocortisone make a strong case for its use in extremely preterm infants at high risk for BPD.

Oxygen desaturations in the early neonatal period predict development of bronchopulmonary dysplasia
Fairchild KD, Nagraj VP, Sullivan BA, et al. *Pediatr Res.*

This is a single-center retrospective descriptive study quantifying bradycardia (HR <100 for ≥ 4 seconds), desaturation (SpO2 <80% for ≥ 10 seconds) events, and percent time spent in events in VLBW infants (23-33wks) in the first 4weeks of life. The study tested logistic regression models of clinical risks to estimate the risks of BPD or death and secondary outcomes. The primary outcome of BPD was noted in 187 of 502 infants (37%). The study concluded that oxygen desaturations in the first four weeks of life are associated with increased risk of BPD as well as other comorbidities (severe IVH, ROP, prolonged length of stay).

Prolonged duration of early antibiotic therapy in extremely premature infants
Greenberg RG, Chowdhury D, Hansen NI, et al. *Pediatr Res.*

This is a multicenter cohort study of prolonged early antibiotic use (≥5days, started ≤72hrs of age) in preterm infants 22-28wk gestation (birth weight 401-1000g) from 13 centers during 2008–2014 and survived ≥5 days without culture-confirmed infection, NEC, or spontaneous intestinal perforation. Among 5730 infants who met inclusion criteria, prolonged antibiotic use declined from 49% in 2008 to 35% in 2014. The study showed that prolonged early antibiotics were not significantly associated with increased odds of death ($p = 0.07$) or NEC. The authors concluded that significant center variation persists with prolonged early antibiotic use.

Cost effectiveness of neonatal resuscitation at 22 weeks of gestation
Yieh L, Dukhovny D, Zhou CG, et al. *Obstet Gynecol.*

A decision-analytic model was used to evaluate the cost of care of infants born at 22 weeks in the United States. Three resuscitation strategies were compared: universal resuscitation, selective resuscitation, or no resuscitation. Outcomes of death and survival with and without impairment were compared over the infant's predicted lifetime with cost data including healthcare costs and estimated quality of life for mother and child. In a one-year model of 22-week births, a predicted cohort of 5,176 neonates receiving universal resuscitation would result in 365 additional survivors at a cost of $465 million over no resuscitation. Selective resuscitation would also increase survival by 70 at a cost of $130 million. Both universal and selective resuscitation increased neonatal quality of life but decreased

maternal quality of life. The authors conclude that no resuscitation is currently the most cost-effective strategy for 22-week births.

Effects of a new device for automated closed loop control of inspired oxygen concentration on fluctuations of arterial and different regional organ tissue oxygen saturations in preterm infant
Gajdos M, Waitz M, Mendler MR, et al. *Arch Dis Child Fetal Neonatal Ed.*

The authors tracked oxygen saturation for 12 VBLW babies in a crossover study to assess the effectiveness of an integrated automated oxygen control on the Sophie Infant Ventilator compared to manual oxygen adjustment by the bedside staff. 2 babies were intubated, 3 were on non-invasive PPV, and 7 were on CPAP. Infants were randomly assigned to automated or manual control for 24 hours; then each patient crossed over to the opposite arm for 24 hours. Automated control increased the time spent within target saturation range, decreased hypoxemia, decreased the number of prolonged (>60s) hypoxemic events, and decreased the number of manual adjustments. Regional tissue oxygenation was unaffected.

Physiological-based cord clamping in preterm infants using a new purpose-built resuscitation table: a feasibility study
Brouwer E, Knol R, Vernooij ASN, et al. *Arch Dis Child Fetal Neonatal Ed.*

This single-center observational study included 37 infants born less than 35 weeks' gestational age. Infants were stabilized on a purpose-built resuscitation table (Concord) and cord clamping was performed when the infant was stable (HR >100 bpm, spontaneous breathing on CPAP with tidal volumes >4 mL/kg, SpO2 ≥25th% and FiO2<0.4). Physiologic-based cord clamping was successful in 33 infants (89.2%) and resulted in median (IQR) cord clamping time of 4:23 (3:00-5:11) min after birth. There were no maternal or neonatal adverse events. The authors concluded that physiologic-based cord clamping is feasible in preterm infants

Hyperglycemia and glucose variability are associated with worse brain function and seizures in neonatal encephalopathy: a prospective cohort study
Pinchefsky EF, Hahn CD, Kamino D, et al. *J Pediatr.*

In a prospective cohort study of 45 infants, the authors investigated the correlation between glucose abnormalities measured using continuous interstitial glucose monitors and aEEG in the first 3 days in infants with neonatal encephalopathy. Several episodes of hypoglycemia (≤50 mg/dL; ≤2.8 mmol/L) and hyperglycemia (>144 mg/dL; >8.0 mmol/L) were identified. Epochs of hypoglycemia were not associated with aEEG changes. Compared with epochs of normoglycemia, epochs of hyperglycemia were associated with worse aEEG background scores, less sleep-wake cycling and more EEG seizures after adjusting for severity. The authors concluded that in neonates with encephalopathy, epochs of hyperglycemia were temporally associated with worse global brain function and seizures, either reflecting severe brain damage or by causing direct neuronal injury.

[Donor human milk and risk of surgical necrotizing enterocolitis: A meta-analysis]
Silano M, Milani GP, Fattore G, et al. *Clin Nutr.*

Several published meta- analysis have evaluated the protective effect of donor banked milk (DM) on overall incidence of NEC, but none so far focused on the risk of surgical NEC in infants receiving DM. In this meta-analysis, the authors identified 4 relevant manuscripts. Estimates were pooled using random-effects. Study quality was assessed by GRADE score and risk of bias by the Review Manager software tool. They concluded that DM did not exert a clear protective effect on risk of preventing surgical NEC compared to formula.

Pediatrics

An early infant HIV risk score for targeted HIV testing at birth.
https://www.ncbi.nlm.nih.gov/pubmed/31101703
Development of nationwide recommendations to support prenatal counseling in extreme prematurity.
https://www.ncbi.nlm.nih.gov/pubmed/31160512
Food insecurity during pregnancy and breastfeeding by low-income Hispanic mothers.
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Associations of preeclampsia with expiratory airflows in school-age children born either at <28 weeks or weighing <1000 g
https://www.ncbi.nlm.nih.gov/pubmed/30871797
Neonatal intensive care variation in medicaid-insured newborns: a population-based study
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Recommendations for the design of therapeutic trials for neonatal seizures
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Prolonged early antimicrobials in ELBWs: too much for too little
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Diffuse optical tomography for the detection of perinatal stroke at the cot side: a pilot study
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Origins of neonatal leptin deficiency in preterm infants
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Deferred consent for the enrolment of neonates in delivery room studies: strengthening the approach
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Targeting glucose control in preterm infants: pilot studies of continuous glucose monitoring
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Randomised cross-over study of automated oxygen control for preterm infants receiving nasal high flow
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Diagnostic accuracy of imaging studies in congenital lung malformations
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High-frequency oscillatory ventilation with volume guarantee: a single-centre experience
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Risk-adjusted mortality of VLBW infants in high-volume versus low-volume NICUs
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Parental opinion of consent in neonatal research
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Epidemiological study on intestinal volvulus without malrotation in VLBW infants
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Academic trajectories of very preterm born children at school age
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Proton magnetic resonance spectroscopy lactate/N-acetylaspartate within 2 weeks of birth accurately predicts 2-year motor, cognitive and language outcomes in neonatal encephalopathy after therapeutic hypothermia
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Continuous infusion versus intermittent bolus doses of fentanyl for analgesia and sedation in neonates: an open-label randomised controlled trial
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Heart rate assessment using NeoTapAdvancedSupport: a simulation study
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Understanding the principle biophysics concepts of pulmonary surfactant in health and disease
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Exome sequencing in the assessment of congenital malformations in the fetus and neonate
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White chalky dermatitis in a very preterm neonate with fungal skin infection
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Respiratory management during therapeutic hypothermia for hypoxic-ischemic encephalopathy
https://www.ncbi.nlm.nih.gov/pubmed/30858610
Antecedents of epilepsy and seizures among children born at extremely low gestational age
https://www.ncbi.nlm.nih.gov/pubmed/30918341
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Early transpyloric vs gastric feeding in preterm infants: a retrospective cohort study
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Dysnatremia in extremely low birth weight infants is associated with multiple adverse outcomes

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Infant feeding practices and perceived optimal breastfeeding interventions among low-income women delivering at a baby-friendly hospital
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Trial characteristics that affect parental consent in neonatal drug trials
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Effect of early versus delayed cord clamping in neonate on heart rate, breathing and oxygen saturation during first 10 minutes of birth - randomized clinical trial (PDF)
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Infectious episodes during pregnancy, at particular mucosal sites, increase specific IgA1 or IgA2 subtype levels in human colostrum (PDF)
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Facility readiness in low and middle-income countries to address care of high risk/ small and sick newborns (PDF)
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Severe combined immunodeficiency: a review for neonatal clinicians.
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Hematopoietic stem cell transplantation: a neonatal perspective.
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Case 1: bilious vomiting in a term neonate.
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Case 2: infant with early direct hyperbilirubinemia.
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Case 3: hypermetabolic state in an infant.
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Strip of the month: decreased fetal movement.
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Effect of gastric residual evaluation on enteral intake in extremely preterm infants a randomized clinical trial
https://www.ncbi.nlm.nih.gov/pubmed/31034045
Association of perceived maternal stress during the perinatal period with electroencephalography patterns in 2-month-old infants
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Decision-making at the limit of viability: the Austrian neonatal choice context (PDF)
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A clinical scoring system to predict the need for extensive resuscitation at birth in very low birth weight infants (PDF)
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Probiotics may not prevent the deterioration of necrotizing enterocolitis from stage I to II/III (PDF)
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Low head circumference during early childhood and its predictors in a semi-urban settlement of Vellore, Southern India (PDF)
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Head ultrasound, CT or MRI? The choice of neuroimaging in the assessment of infants with congenital cytomegalovirus infection (PDF)
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Baseline cardiac output and its alterations during ibuprofen treatment for patent ductus arteriosus in preterm infants (PDF)
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Prediction of mortality in newborn infants with severe congenital diaphragmatic hernia using the chest radiographic thoracic area
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Subpopulations are vulnerable to fetal alcohol spectrum disorder
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Pattern of antimicrobial resistance in bloodstream isolates from Chinese neonates
https://www.ncbi.nlm.nih.gov/pubmed/30672894
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Screening echocardiography and brain natriuretic peptide levels predict late pulmonary hypertension in infants with bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/30937503
Nicardipine for the treatment of neonatal hypertension during extracorporeal membrane oxygenation
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Dysmaturation of premature brain: importance, cellular mechanisms, and potential interventions
https://www.ncbi.nlm.nih.gov/pubmed/30975474

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Maternal and neonatal morbidity associated with early term delivery of large-for-gestational-age but nonmacrosomic neonates
https://www.ncbi.nlm.nih.gov/pubmed/31135729
Cost effectiveness of neonatal resuscitation at 22 weeks of gestation
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Recorded diagnoses of depression during delivery hospitalizations in the united states, 2000–2015
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Immune tolerance attenuates gut dysbiosis, dysregulated uterine gene expression and high-fat diet potentiated preterm birth in mice
https://www.ncbi.nlm.nih.gov/pubmed/30790568
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Can in utero fetal pacing cause cardiac complications?
https://www.ncbi.nlm.nih.gov/pubmed/30885771

BASIC SCIENCE SELECTIONS

Changing expression profiles of mRNA, lncRNA, circRNA, and miRNA in lung tissue reveal the pathophysiological of bronchopulmonary dysplasia (BPD) in mouse model
Wang J, Yin J, Wang X, et al. *J Cell Biochem.*
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Torres-Cuevas I, Corral-Debrinski M and Gressens P. *Free Radic Biol Med.*
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Li B, Saka R, Takama Y, et al. *Surg Today.*
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Mild neonatal brain hypoxia-ischemia in very immature rats causes long-term behavioral and cerebellar abnormalities at adulthood
Sanches EF, Van de Looij Y, Toulotte A, et al. *Front Physiol.*

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Donor human milk and risk of surgical necrotizing enterocolitis: A meta-analysis
Silano M, Milani GP, Fattore G, et al. *Clin Nutr.*
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Intravenous fish oil containing lipid emulsion attenuates inflammatory cytokines and the development of bronchopulmonary dysplasia in very premature infants: A double-blind, randomized controlled trial
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