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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – July 2022

Sleep-related infant deaths: updated 2022 recommendations for reducing infant deaths in the sleep environment
Rachel Y Moon, Rebecca F Carlin and Ivan Hand. *Pediatrics*

The American Academy of Pediatrics published updated recommendations for a safe sleep environment to reduce the risk of all sleep-related deaths. These include supine positioning, use of a firm, non-inclined sleep surface; room sharing without bed sharing; and avoidance of soft bedding and overheating. Additional recommendations include human milk feeding; avoidance of exposure to nicotine, alcohol, marijuana, opioids, and illicit drugs; routine immunization; and use of a pacifier. This report discusses several new recommendations, rationale and strength of underlying evidence, including non-inclined sleep surfaces, short-term emergency sleep locations, use of cardboard boxes as a sleep location, bed sharing, substance use, home cardiorespiratory monitors, and tummy time.

Breast milk vs 24% sucrose for procedural pain relief in preterm neonates: a non-inferiority randomized controlled trial
Pradeep Kumar Velumula, Faesal Elbakoush, Carl Tabb, et al. *J Perinatol.*

This randomized, single-blinded, non-inferiority trial compared the pain scores in preterm neonates undergoing automated heel lance for blood draws between the two groups, breast milk (BM; 2ml given in an oral syringe) and 24% sucrose. Pain scores were measured using Premature Infant Pain Profile-Revised (PIPP-R) in infants born 30 1/7weeks - 36 6/7 weeks of gestation. Two investigators assigned pain scores at baseline, during the procedure, 30-, 60-, 90-, and 120-seconds post-procedure. Baseline characteristics were not significantly different between groups. PIPP-R scores were not statistically significant between groups. The authors concluded that BM is not inferior to 24% sucrose in providing analgesia during heel lance.

A randomized, controlled trial to investigate the efficacy of nebulized poractant alfa in premature babies with respiratory distress syndrome
Carlo Dani, Gyula Talosi, Annalisa Piccinno, et al. *J Pediatr.*

In this multicenter RCT, nebulized poractant alfa given with nasal CPAP was compared to CPAP alone. The study enrolled 129 infants born at 28-32 weeks with mild to moderate RDS diagnosed by x-ray or ultrasound between 1 and 12 hours after birth. All patients were on nCPAP 5-8cm H2O with FiO2 0.25-0.40. Surfactant groups were treated either with 200mg/kg or 400mg/kg. The primary outcome was the need for intubation in the first 72 hours, and this was not different among groups. There were also no differences in secondary outcomes including respiratory failure prior to discharge, use of mechanical ventilation, duration of non-invasive support, use and duration of supplemental oxygen, and BPD at 36

weeks. There were no adverse events or increased morbidities associated with treatment. The study was stopped early after the Independent Safety Monitoring Board determined there was likely a negligible effect of treatment.

Diabetes mellitus, maternal adiposity, and insulin-dependent gestational diabetes are associated with COVID-19 in pregnancy: the INTERCOVID study
Brenda Eskenazi, Stephen Rauch, Enrico Iurlaro, et al. *Am J Obstet Gynecol.*

This is a prospective observational study of >2000 pregnant women looking at maternal comorbidities (diabetes, overweight, obesity) that may be risk factors for COVID-19. Gestational diabetes alone did not increase the risk of COVID-19, but GDM with insulin did (Normal weight aRR 1.79, 95% CI 1.06-3.01; BMI ≥25 kg/m2 aRR 1.77, 95% CI 1.28-2.45). Both preexisting DM (aRR 1.97, 95% CI 1.55-2.42) and BMI ≥25 kg/m2 (aRR1.20, 95% CI 1.06-1.37) were found to be risk factors for COVID-19 infection during pregnancy. The highest risk of COVID-19 was found among women with pre-existing DM with BMI ≥25 (aRR 2.32, 95% CI 1.82-2.97). Among all patients diagnosed with COVID-19, women with BMI ≥25 were more likely to report symptomatic infection (RR 1.06, 95% CI 1.01-1.11). There are no data on COVID-19 severity. The authors conclude that pre-existing DM, GDM with insulin, and BMI ≥25 are risk factors for COVID-19 infection during pregnancy, and BMI ≥25 is a risk factor for symptomatic infection. These high-risk women should be encouraged to accept COVID-19 vaccination.

Trial of erythropoietin for hypoxic–ischemic encephalopathy in newborns
Yvonne W Wu, Bryan A Comstock, Fernando F Gonzalez, et al. *N Engl J Med.*

Erythropoietin has been hypothesized to have neuroprotective effects in infants with hypoxic-ischemic encephalopathy, but its effects on neurodevelopmental outcomes when given in conjunction with therapeutic hypothermia are unknown. In this multicenter, double-blind, randomized, placebo-controlled trial, the authors assigned 501 infants born at 36 weeks or more of gestation with moderate or severe hypoxic-ischemic encephalopathy to receive erythropoietin or placebo, in conjunction with standard therapeutic hypothermia. They found that the administration of erythropoietin to newborns undergoing therapeutic hypothermia for hypoxic-ischemic encephalopathy did not result in a lower risk of death or neurodevelopmental impairment than placebo and was associated with a higher rate of serious adverse events.

Effect of various preterm infant milk formulas on NEC-like gut injury in mice
Karishma Rao, Alain Cuna, Susana Chavez-Bueno, et al. *Front Pediatr.*

Formula feeding is a risk factor for the development of necrotizing enterocolitis in preterm infants. The authors demonstrate that feeding newborn mouse pups with various preterm formulas resulted in differing effects on intestinal inflammation, apoptosis, and activation of the pro-inflammatory transcription factor NFkappaB. Formula feeding with EleCare and Similac Special Care caused greater intestinal injury compared to NeoSure. Pre-treatment with Lactobacillus rhamnosus GG ameliorated severity of intestinal injury from EleCare and Similac Special Care.

Long-term neurodevelopmental outcome in preterm infants with intraventricular haemorrhage
Nele Legge, Tracey Lutz, Crista Wocadlo, et al. *J Paediatr Child Health.*

Intraventricular hemorrhage (IVH) is a risk for long-term neurodevelopmental issues in preterm infants, yet controversy remains over the impact low-grade IVH has on these outcomes. This retrospective cohort analysis describes the long-term neurodevelopmental impact of Grade I and II IVH in infants born at <30 weeks gestation. When comparing infants with mild IVH to those with normal cranial ultrasounds, there was no significant difference in cognitive, motor and academic outcomes at 5- and 8-year follow-up.

Neurodevelopmental outcomes of preterm infants after randomisation to initial resuscitation with lower (FiO2 <0.3) or higher (FiO2 >0.6) initial oxygen levels. An individual patient meta-analysis
Ju Lee Oei, Vishal Kapadia, Yacov Rabi, et al. *Arch Dis Child Fetal Neonatal Ed.*

In a meta-analysis of three randomized controlled trials, looking at 543 children less than 32 weeks gestation, it was found that initial FiO2 was not associated with difference in risk of disability /death at 2 years of age. Substantial benefit or harm could not be excluded. Five minute SpO2 > 80% was associated with decreased disability/death and cognitive scores > 85. Larger randomized studies accounting for patient differences are needed.

Randomised crossover trial comparing algorithms and averaging times for automatic oxygen control in preterm infants
Christoph E Schwarz, Karen B Kreutzer, Lukas Langanky, et al. *Arch Dis Child Fetal Neonatal Ed.*

In an unblinded, randomized controlled crossover study, 2 (automatic control) SPOC algorithms and 2 (pulse oximeter) SpO2 averaging times in random order: 12 hours SPOCnew and 12 hours SPOCold (averaging time 2 s or 8 s for 6 hours each) were compared with 6-hour RMC (routine manual control). Target% was higher with both SPOC algorithms compared to RMC. Despite limiting the maximum FiO_2, $SPOC_{new}$ remained significantly better at maintaining SpO_2 within target range compared to RMC.

Levetiracetam or phenobarbitone as a first-line anticonvulsant in asphyxiated term newborns? an open-label, single-center, randomized, controlled, pragmatic trial
Sukena Susnerwala, Amol Joshi, Laxmikant Deshmukh, et al. *Hosp Pediatr.*

This open-label randomized controlled trial included 82 term asphyxiated infants with seizures in the first 48 hours of life. Infants received either levetiracetam (20 mg/kg) (n=44) or phenobarbitone (20 mg/kg) (n=38). Clinical seizure control with the primary drug and maintenance of the same for 24 hours was observed in 29 infants (65.9%) in the levetiracetam group and 13 infants (34.2%) in the phenobarbitone group (P < .05, relative risk 0.52, 95% confidence interval 0.32-0.84). Of the infants in the phenobarbitone group who did not respond, 57.8% were controlled after adding levetiracetam. This study supported the effectiveness of Levetiracetam as a first- and second-line drug in asphyxiated term infants

OTHER NOTEWORTHY PUBLICATIONS – July, 2022

COVID-19
Maternal vaccination and risk of hospitalization for COVID-19 among infants
https://pubmed.ncbi.nlm.nih.gov/35731908/
Editorial: COVID-19 vaccination during pregnancy — two for the price of one
https://pubmed.ncbi.nlm.nih.gov/35731898/
COVID-19 MRNA vaccine booster during pregnancy increases maternal and fetal antibodies
https://pubmed.ncbi.nlm.nih.gov/35731542/
Among young infants with uncomplicated COVID-19: should we broaden diagnostic tests for infectious causes of apnea?
https://pubmed.ncbi.nlm.nih.gov/35389947/
Impact of the COVID-19 pandemic on the diagnosis of congenital cytomegalovirus infection in Spain
https://pubmed.ncbi.nlm.nih.gov/35363648/
Association of COVID-19 vaccination during early pregnancy with risk of congenital fetal anomalies
https://www.ncbi.nlm.nih.gov/pubmed/35377399
Multisystem inflammatory syndrome in a neonate with severe hemophilia - a diagnostic challenge in COVID times: a case report (PDF)
https://bmcpediatr.biomedcentral.com/track/pdf/10.1186/s12887-022-03463-3.pdf

Diabetes mellitus, maternal adiposity, and insulin-dependent gestational diabetes are associated with COVID-19 in pregnancy: the INTERCOVID study
https://pubmed.ncbi.nlm.nih.gov/34942154

Pediatrics

Family educational attainment and racial disparities in low birth weight
https://pubmed.ncbi.nlm.nih.gov/35757969/
Palivizumab use in the NICU: 1999–2020
https://pubmed.ncbi.nlm.nih.gov/35730329/
Maternal high-dose DHA supplementation and neurodevelopment at 18–22 months of preterm children
https://pubmed.ncbi.nlm.nih.gov/35652296/
Validating a sclera-based smartphone application for screening jaundiced newborns in Ghana
https://pubmed.ncbi.nlm.nih.gov/35656782/
Policy Statement: Breastfeeding and the Use of Human Milk
https://pubmed.ncbi.nlm.nih.gov/35921640/
Sleep-related infant deaths: updated 2022 recommendations for reducing infant deaths in the sleep environment
https://pubmed.ncbi.nlm.nih.gov/35726558/
Machine learning prediction models for neurodevelopmental outcome after preterm birth: a scoping review and new machine learning evaluation framework
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Journal of Pediatrics

Timing neonatal hypoxic-ischemic encephalopathy (PDF)
https://www.jpeds.com/article/S0022-3476(22)00433-4/pdf
Prematurity is a chronic disease (PDF)
https://www.jpeds.com/article/S0022-3476(22)00591-1/pdf
Implications of an elevated nucleated red blood cell count in neonates with moderate to severe hypoxic-ischemic encephalopathy
https://www.ncbi.nlm.nih.gov/pubmed/35430249
Longitudinal analysis of amplitude-integrated electroencephalography for outcome prediction in hypoxic-ischemic encephalopathy (PDF)
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Rates and determinants of home nasogastric tube feeding in infants born very preterm
https://www.ncbi.nlm.nih.gov/pubmed/35301017
Perinatal inflammatory biomarkers and respiratory disease in preterm infants (PDF)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9264338/pdf/nihms-1820080.pdf
A randomized, controlled trial to investigate the efficacy of nebulized poractant alfa in premature babies with respiratory distress syndrome (PDF)
https://www.jpeds.com/article/S0022-3476(22)00175-5/pdf
Brain volumes and abnormalities in adults born preterm at very low birth weight (PDF)
https://www.jpeds.com/article/S0022-3476(22)00189-5/pdf
The clinical and cost utility of cardiac catheterizations in infants with bronchopulmonary dysplasia
https://www.ncbi.nlm.nih.gov/pubmed/35430250
Do pediatricians and nurses recommend vaccines for preterm infants? A survey in Italy
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Neonatal intensive care unit network neurobehavioral scale profiles in full-term infants: associations with maternal adversity, medical risk, and neonatal outcomes
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Dopamine and neonatal pulmonary hypertension—pressing need for a better pressor?
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Molecular mechanisms contributing to the etiology of congenital diaphragmatic hernia: a review and novel cases
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A standardized definition of neonatal opioid withdrawal syndrome (PDF)
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Reply (PDF)
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Pediatric Research
Systemic Review: Remote ischemic postconditioning for neuroprotection after newborn hypoxia–ischemia: systematic review of preclinical studies
https://pubmed.ncbi.nlm.nih.gov/34282277
Review Article: Neonatal hyperbilirubinemia and bilirubin neurotoxicity in hospitalized neonates: analysis of the US Database
https://pubmed.ncbi.nlm.nih.gov/34429513
Retinopathy of prematurity shows alterations in Vegfa164 isoform expression
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Elevated circulating endothelial microparticles (EMPs) in prepubertal children born preterm
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Spontaneous preterm delivery is reflected in both early neonatal and maternal gut microbiota
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Postnatal glucocorticoid use impacts renal function in VLBW neonates
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The new normal: parental use of online health communities in the NICU
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Language lateralization in very preterm children: associating dichotic listening to interhemispheric connectivity and language performance
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Is it time for routine probiotic use in UK neonatal units? (PDF)
https://fn.bmj.com/content/fetalneonatal/107/4/344.full.pdf
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Resuscitation decisions in fetal myelomeningocele repair should center on parents' values: a counter analysis
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Part 6: Essentials of Neonatal–Perinatal Medicine fellowship: program administration
https://pubmed.ncbi.nlm.nih.gov/35082429/
Call to action: gender equity in neonatology
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Neonatology
Multisystemic inflammatory syndrome in neonates: a systematic review (PDF)
https://www.karger.com/Article/Pdf/524202
Development and validation of a mortality prediction model in extremely low gestational age neonates (PDF)
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Caffeine: some of the evidence behind its use and abuse in the preterm infant
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Melatonin administration from 2000 to 2020 to human newborns with hypoxic-ischemic encephalopathy
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Risk factors and predictors of rebound hyperbilirubinemia in a term and late-preterm infant with hemolysis
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Mechanisms underlying abnormal expression of LNCRNA H19 in neonatal hypoxic–ischemic encephalopathy
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What are the factors affecting total sleep time during video polysomnography in infants?
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Charge nurses taking charge, challenging the culture of culture-negative sepsis, and preventing central-line infections to reduce NICU antibiotic usage
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Shifting provider attitudes and institutional resources surrounding resuscitation at the limit of gestational viability
https://www.ncbi.nlm.nih.gov/pubmed/33111279
Code blue events in the neonatal and pediatric intensive care units at a tertiary care children's hospital
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Birth tourism is associated with fewer neonatal intensive care unit admissions: a healthy migrant effect?
https://www.ncbi.nlm.nih.gov/pubmed/33167040
Neonatal preterm respiratory care in Ukraine: an observational study of outcomes in relation to timing and methods of surfactant treatment
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Rooming-in for infants at risk for neonatal abstinence syndrome: outcomes 5 years following its introduction as the standard of care at one hospital (PDF)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9270102/pdf/10-1055-s-0040-1719182.pdf
Perinatal outcomes of subjects enrolled in a multicenter trial with a waiver of antenatal consent (PDF)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8788902/pdf/nihms-1670308.pdf

Journal of Neonatal-Perinatal Medicine
No new content

Maternal Health, Neonatology and Perinatology
Evidence based recommendations for an optimal prenatal supplement for women in the US: vitamins and related nutrients
https://pubmed.ncbi.nlm.nih.gov/35818085/

Neoreviews
Ventilator-associated pneumonia in the neonatal intensive care unit
https://pubmed.ncbi.nlm.nih.gov/35773508/
Immune-mediated neonatal thrombocytopenia
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Multimodal assessment of systemic blood flow in infants
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Prematurity and congenital heart disease: a contemporary review
https://pubmed.ncbi.nlm.nih.gov/35773510/
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https://pubmed.ncbi.nlm.nih.gov/35773509/
Presumed aspiration pneumonia in a term newborn infant
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