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c/o Mitchell Goldstein, MD
11175 Campus Street, Suite #11121
Loma Linda, CA 92354
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Indication

INOMAX is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

Important Safety Information

- INOMAX is contraindicated in the treatment of neonates dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOMAX may lead to increasing pulmonary artery pressure and worsening oxygenation.
- Methemoglobinemia and NO_2 levels are dose dependent. Nitric oxide donor compounds may have an additive effect with INOMAX on the risk of developing methemoglobinemia. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.
- In patients with pre-existing left ventricular dysfunction, INOMAX may increase pulmonary capillary wedge pressure leading to pulmonary edema.
- Monitor for PaO_2, inspired NO_2, and methemoglobin during INOMAX administration.
- INOMAX must be administered using a calibrated INOmax DSIR® Nitric Oxide Delivery System operated by trained personnel. Only validated ventilator systems should be used in conjunction with INOMAX.
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*INOmax Total Care is included at no extra cost to contracted INOMAX customers.

†Emergency deliveries of various components are often made within 4 to 6 hours but may take up to 24 hours, depending on hospital location and/or circumstances.

Reference: 1. Data on file. Hampton, NJ: Mallinckrodt Pharmaceuticals.

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INOmax Total Care®

INOmax® (nitric oxide gas)

Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Treatment of Hypoxic Respiratory Failure

INOmax® is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilator support and other appropriate agents.

CONTRAINDICATIONS

INOmax is contraindicated in neonates dependent on right-to-left shunting of blood.

WARNINGS AND PRECAUTIONS

Rebound Pulmonary Hypertension Syndrome following Abrupt Discontinuation

Wean from INOmax. Abrupt discontinuation of INOmax may lead to worsening oxygenation and increasing pulmonary artery pressure, i.e., Rebound Pulmonary Hypertension Syndrome. Signs and symptoms of Rebound Pulmonary Hypertension Syndrome include hypoxemia, systemic hypotension, bradycardia, and decreased cardiac output. If Rebound Pulmonary Hypertension occurs, reinstate INOmax therapy immediately.

Hypoxemia from Methemoglobinemia

Nitric oxide combines with hemoglobin to form methemoglobin, which does not transport oxygen. Methemoglobin levels increase with the dose of INOmax; it can take 8 hours or more before steady-state methemoglobin levels are attained. Monitor methemoglobin and adjust the dose of INOmax to optimize oxygenation.

If methemoglobin levels do not resolve with decrease in dose or discontinuation of INOmax, additional therapy may be warranted to treat methemoglobinemia.

Airway Injury from Nitrogen Dioxide

Nitrogen dioxide (NO_2) forms in gas mixtures containing NO and O_2. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.

If there is an unexpected change in NO_2 concentration, or if the NO_2 concentration reaches 3 ppm when measured in the breathing circuit, then the delivery system should be assessed in accordance with the Nitric Oxide Delivery System O&M Manual troubleshooting section, and the NO_2 analyzer should be recalibrated. The dose of INOmax and/or FiO_2 should be adjusted as appropriate.

Worsening Heart Failure

Patients with left ventricular dysfunction treated with INOmax may experience pulmonary edema, increased pulmonary capillary wedge pressure, worsening of left ventricular dysfunction, systemic hypotension, bradycardia and cardiac arrest. Discontinue INOmax while providing symptomatic care.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Controlled studies have included 325 patients on INOmax doses of 5 to 80 ppm and 251 patients on placebo. Total mortality in the pooled trials was 11% on placebo and 9% on INOmax, a result adequate to exclude INOmax mortality being more than 40% worse than placebo.

In both the NINOS and CINRGI studies, the duration of hospitalization was similar in INOmax and placebo-treated groups.

From all controlled studies, at least 6 months of follow-up is available for 278 patients who received INOmax and 212 patients who received placebo. Among these patients, there was no evidence of an adverse effect of treatment on the need for rehospitalization, special medical services, pulmonary disease, or neurological sequelae.

In the NINOS study, treatment groups were similar with respect to the incidence and severity of intracranial hemorrhage, Grade IV hemorrhage, periventricular leukomalacia, cerebral infarction, seizures requiring anticonvulsant therapy, pulmonary hemorrhage, or gastrointestinal hemorrhage.

In CINRGI, the only adverse reaction (>2% higher incidence on INOmax than on placebo) was hypotension (14% vs. 11%).

Based upon post-marketing experience, accidental exposure to nitric oxide for inhalation in hospital staff has been associated with chest discomfort, dizziness, dry throat, dyspnea, and headache.

DRUG INTERACTIONS

Nitric Oxide Donor Agents

Nitric oxide donor agents such as prilocaine, sodium nitroprusside and nitroglycerine may increase the risk of developing methemoglobinemia.

OVERDOSAGE

Overdosage with INOmax is manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO_2. Elevated NO_2 may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO_2 levels >3 ppm or methemoglobin levels >7% were treated by reducing the dose of, or discontinuing, INOmax.

Methemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation.

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Peer Reviewed

Tips for Medical Students and Non-Neonatologists on Physical Examination of the Newborn and Important Aspects of Early Newborn Care – An Irish Perspective

Aisling Smith, MD, Robert McGrath, MD, Naomi McCallion, MD, and Tom Clarke, MD

Abstract:

Appropriate physical examination technique of the newborn infant is vital to ensure the detection of pathology and the timely instigation of required management. No infant should be viewed as 'routine,' and all babies must have a comprehensive physical examination completed prior to discharge home. This paper will outline an Irish approach to good physical examination technique of the newborn for a number of the more challenging and error-prone aspects of the physical exam, which non-neonatal specialists and medical students may find helpful.

Introduction

Appropriate physical examination technique of the newborn infant is vital to ensure the detection of pathology and the timely instigation of required management or onward referral. Medical students are typically instructed on neonatal physical examination during their paediatric clerkships and may not receive any additional neonatal training prior to graduation. The duration of paediatric and neonatal medical student clerkships varies between Irish universities. Many medical specialties interact with neonatal patients besides neonatal or paediatric departments including ophthalmology, orthopaedics, general surgery, dermatology, and general practice. In particular, approximately 2,950 family doctors (general practitioners, GPs) in Ireland provide essential services for newborn care including 2 and 6 weeks checks, monitoring feeding, weight gain, head growth, and development. (1) Such visits provide a key window of opportunity for the early detection of pathology.

The curriculum of the School of Medicine at the Royal College of Surgeons in Ireland (RCSI) is designed to give medical students a sound knowledge of the science and art of medicine. RCSI medical students receive 7 weeks of training in paediatrics during their 4th of 5 years of medical school, of which one week is dedicated specifically to neonatal training in a tertiary maternity hospital. During their week of neonatal clerkship, correct physical examination technique of the newborn is emphasised. Students attend several tutorials detailing neonatal physical examination, have the opportunity to perform neonatal physical examination safely on well infants on the postnatal wards and also have access to online videos teaching comprehensive assessment of the neonatal cardiovascular system, head, face and neck, gastrointestinal system, neurological system, and hip examination. At the end of their paediatric rotations, the students' neonatal physical examination skills are thoroughly tested via a clinical examination of a well newborn, to ensure high standards of clinical practice and safety after graduation. One of the authors (TC), a professor of neonatology, has noted an improvement in the clinical examination skills of RCSI medical students at the end of their rotation assessments in recent years. The majority of neonatal medical student education is now provided by postgraduate paediatric and neonatal trainees who have taken time out of their specialist training schemes to pursue full-time research for higher degrees. It is probable that education delivered by those pursuing neonatology as a career improves the knowledge base of students regarding the newborn physical examination.

It is critically important that all professionals involved in newborn care, including junior doctors, surgeons, midwives, and advanced nurse practitioners are fully versed in the appropriate physical examination technique of the newborn. No infant should be viewed as 'routine,' and all babies must have a comprehensive physical examination completed prior to discharge home. This paper will outline the Irish approach to good physical examination technique of the newborn for a number of the more challenging and error-prone aspects of the physical exam, which non-neonatal specialists and medical students may find helpful.

"This paper will outline the Irish approach to good physical examination technique of the newborn for a number of the more challenging and error-prone aspects of the physical exam, which non-neonatal specialists and medical students may find helpful."

General Inspection of the Newborn

Doctors performing newborn examinations should position themselves so that they easily look at both the parents and baby and smile reassuringly, to all, as needed. Well trained doctors will quickly observe the colour, respiratory status, level of alertness, posture, movement, and nutrition status of the infant.

The normal baby is typically a pale pink colour. Skin colour should be observed for cyanosis, pallor, jaundice, and plethoric appearance. Central cyanosis should be assessed under the infant's tongue, is always an abnormal finding and may indicate a congenital heart lesion or lung pathology. Acrocyanosis, cyanosis of the extremities, particularly of the soles of the feet and palms of the hands, is a normal finding and typically caused by the infant being cold. Neonatal pallor warrants a prompt assessment for potential sepsis or anaemia. Neonatal jaundice is a common finding, particularly in breastfed infants. Jaundice which appears before 24 hours of age is pathological until proven otherwise, and appropriate investigations for immune-related haemolysis (Rhesus or ABO incompatibility), congenital infection, sepsis, and biliary obstruction should follow. A plethoric, or 'ruddy,' appearance to the baby is usually related to polycythaemia. Polycythaemia is defined as a central haematocrit > 65% and is commonly associated with maternal gestational diabetes mellitus, trisomy 21 and recipients of twin-to-twin transfusion.

General inspection of the baby's respiratory system includes observation for signs of respiratory distress, including tachypnoea (respiratory rate over 60 breaths per minute), nasal flaring, intercostal, and subcostal recession. Grunting, defined as forced expiration against a partially closed glottis, is a significant sign of respiratory distress as the baby is attempting to generate their own positive airway pressure.

The level of consciousness of the baby should be automatically assessed during the general inspection. There are 5 levels of

consciousness (LOC) that a newborn may assume; alert, hyperalert, lethargic, stuporous, and comatose. An 'alert' baby is a normal baby; the baby will assume a semi-flexed posture, move their limbs symmetrically and spontaneously, have spontaneous eye-opening, interact with their environment, and be consolable. A 'hyperalert' baby is baby hyperalert to environmental stimuli, often inconsolable, requires frequent soothing, has exaggerated primitive reflexes and feeding difficulties. A baby exhibiting signs of hyperalertness may potentially be withdrawing from maternal medication, prescribed or illicit, or developing central nervous system pathology such as meningitis or encephalitis. The decreased LOC states include lethargy, stuporous and comatose and always require immediate attention. A lethargic baby will be active on handling but will be quiet and non-responsive when not stimulated. A stuporous baby will only respond to noxious stimuli, such as firm sternal rub, while a comatose baby will not respond to noxious stimuli at all. The differential diagnosis for decreased LOC of the newborn is large and includes sepsis, hypoxic ischaemic encephalopathy, meningitis, encephalitis, hypoglycaemia, and inborn errors of metabolism.

Head Circumference (HC)

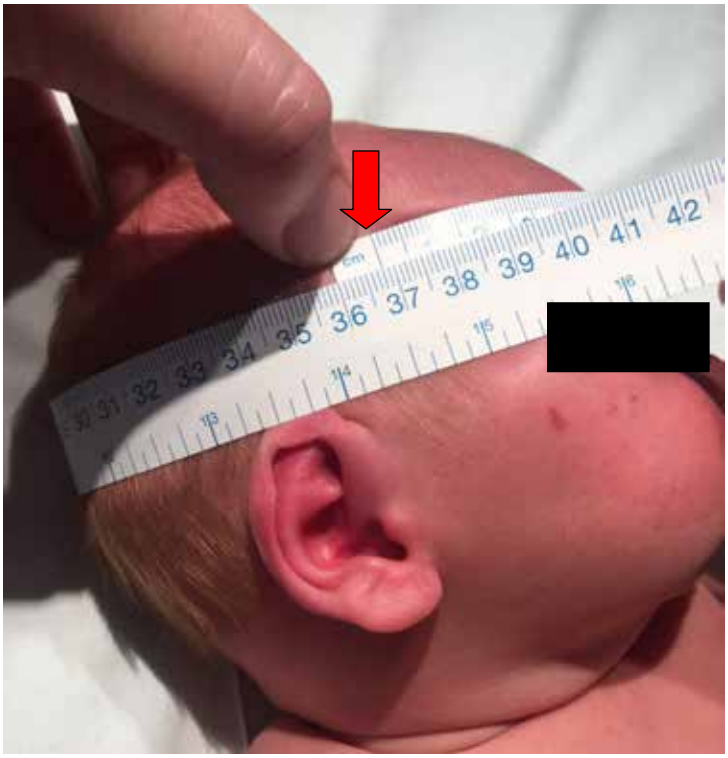

Figure 1: Measuring the Head Circumference

The head circumference should be measured at its maximum by positioning the measuring tape around the most prominent part of the forehead and the most prominent part of the occiput. The measuring tape should be tight, so as not to over-estimate the HC, with the numbers facing out. The HC should be taken at the intersection of the blue lines on the measuring tape, in this case, 36.8cm (Figure 1). The normal range of HC in a term infant is 32cm to 37 cm. The HC should be plotted on an appropriate centile chart and considered in tandem with the weight and length of the baby as well as its growth trajectory. The most common cause of macrocephaly is familial macrocephaly. However, rarer causes include hydrocephalus, Fragile X, and Sotos syndromes, mucopolysaccharidoses, and neurofibromatosis. Microcephaly is typically a more sinister entity, the differential diagnosis of which includes intrauterine growth restriction, congenital infection (TORCH infection, Zika virus), genetic abnormalities, metabolic disease, periventricular leukomalacia, neuronal migration disorders, and craniosynostosis. (2,3)

Eye Examination

Figure 2: Examination of the eye for the red reflex

The newborn eyes should be structurally assessed for the presence of hypertelorism, hypotelorism, epicanthic folds, and coloboma, all of which may form part of a dysmorphic phenotype. Of great importance for each newborn is examination with an ophthalmoscope to confirm the presence of bilateral red reflexes. The ophthalmoscope is held in the examiner's hand, and the baby's eye is gently opened with the other hand, as shown in Figure 2, to inspect for the red reflex. An absent red reflex indicates congenital cataract secondary to a congenital infection, genetic disorders including trisomy 21 or metabolic disease such as galactosemia.

(4) On very rare occasions, intraocular tumours may cause an absent red reflex.

Examination of the Cardiovascular System & Palpation of the Femoral Pulses

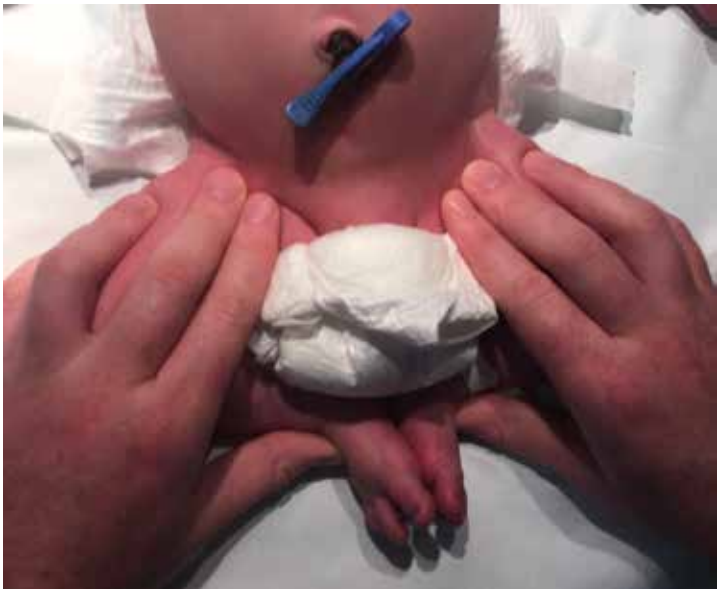

Figure 3: Palpation of the femoral pulses

> ***" Absent or weak femoral pulses are a concerning clinical sign and may indicate a left-sided obstructive heart lesion including a left hypoplastic heart, aortic coarctation, aortic stenosis or interrupted aortic arch. (5)"***

On examination of the cardiovascular system, the infants colour, respiratory status, capillary refill time, and precordial activity should be assessed. An active precordium may indicate the presence of left-to-right shunting. A thrill is a palpable murmur while palpation of a heave indicates right ventricular hypertrophy. Innocent, transient heart murmurs are often detected in the first days following delivery and are commonly related to the closure of the patent ductus arteriosus. On auscultation of a heart murmur, the murmur should be classified according to its grade, location, relation to systole, radiation, and whether the infant is symptomatic or asymptomatic. Clinical symptoms and signs associated with congenital heart disease include cyanosis, lethargy, tachypnoea, poor feeding, slow weight gain, hepatomegaly, and low oxygen saturations. Bilateral palpation of the femoral pulses forms an integral part of the neonatal cardiovascular examination. The femoral pulses are located halfway between the anterior iliac spine and the pubic symphysis. Palpation of the femoral pulses may be difficult when the baby is crying, tachypnoeic, or tensing their abdominal wall musculature. Placing the infant into a 'diamond' position, with both legs abducted and the soles of their feet opposed, as per Figure 3, can alleviate these issues and allow easier palpation of the femoral pulses. Absent or weak femoral pulses are a concerning clinical sign and may indicate a left-sided obstructive heart lesion including a left hypoplastic heart, aortic coarctation, aortic stenosis or interrupted aortic arch. (5)

Palpation of the liver

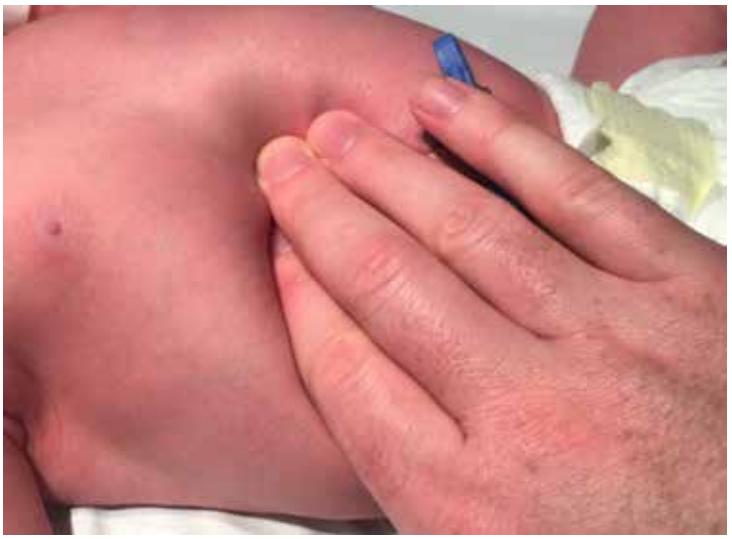

Figure 4: Palpation of the liver

Palpation of the neonatal liver should begin in the right iliac fossa and progress to the right costal margin. Steady pressure should be applied to the abdomen, and it is normal for up to 1cm of the liver edge to be palpable below the right costal margin. With the hand that is not being used for abdominal palpation, the abdomen can be relaxed by grasping the ankles and holding the legs at right angles to the abdomen. The abdomen should relax if you wait patiently in this position. Differential diagnosis of neonatal hepatomegaly includes congestive heart failure, congenital infection, haemolytic disease of the newborn, and metabolic disease. (6)

Palpation of the Testes

The testes are present in the scrotum in 98% of full-term male infants. The inguinal canal should be obliterated by placing the index finger over it during palpation of the testicle in the scrotum. This is to ensure that retractile testicles cannot ascend the inguinal canal during the examination. Failure of the testes to descend by 6 weeks of age is abnormal. (7) As per Haid et al., persistent undescended testes at 6 months of age in a term boy should be actively treated with orchidopexy performed to ensure the testes are in a scrotal position by 12 months of age. (8) Delayed management of undescended testes may promote future infertility with lower sperm concentrations inversely associated with the age of correction. (9)

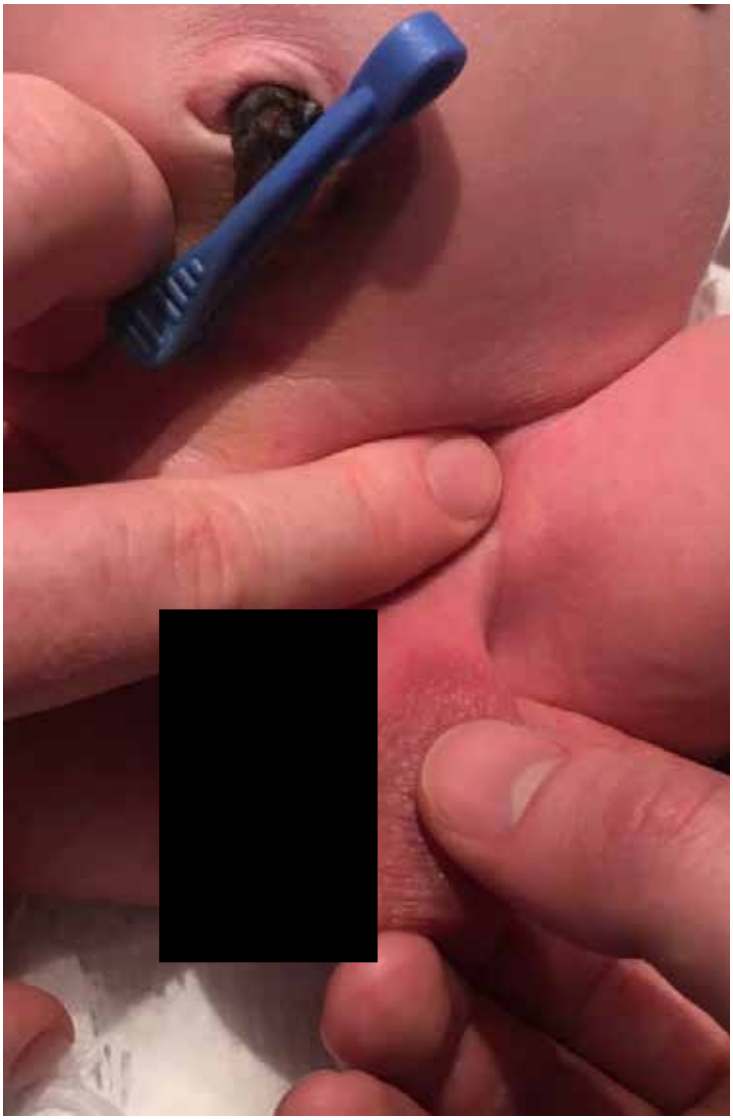

Figure 5: Palpation of the left testicle with obliteration of the left inguinal canal

Examination of the Hips

"If a baby is found to have a positive Barlow or Ortolani test, a hip ultrasound should be performed prior to discharge home to assess for dislocation. If risk factors for Developmental Dysplasia of the Hips (DDH) exist or a hip click is found on hip examination, a hip ultrasound should be arranged for the infant at 6 weeks corrected gestational age to determine hip subluxation vs. hip dysplasia."

Figure 6: Barlow Test (1): One hip is tested at a time (the left hip in this case). The pelvis is stabilised, and the knees and hips are flexed to 90 degrees

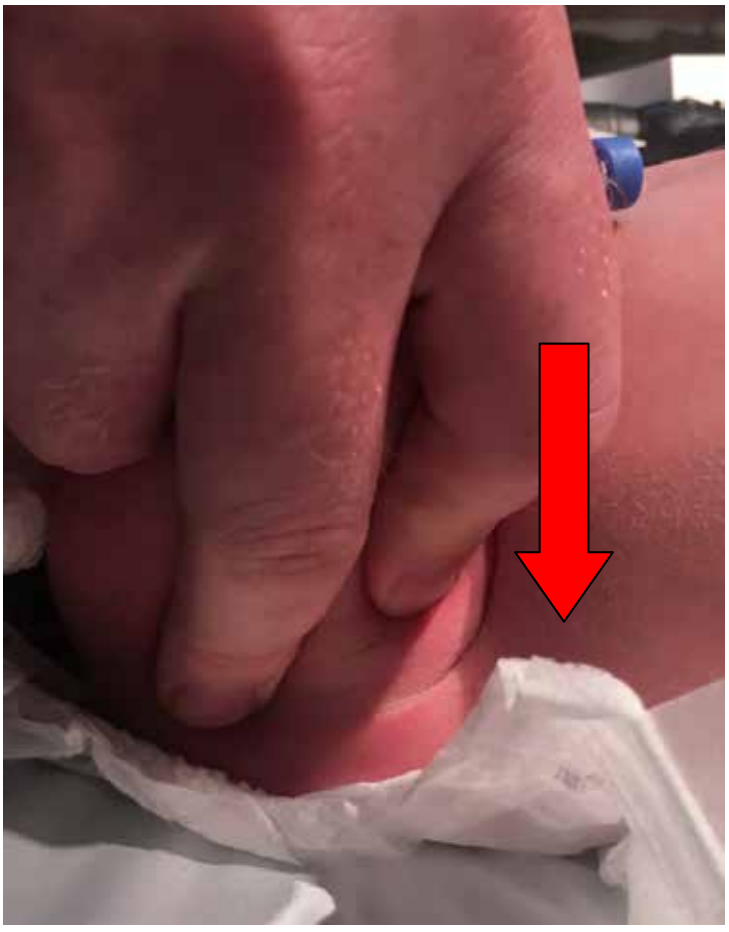

Figure 7: Barlow Test (2): The examiners fingers are placed over the femoral head and the hip is gently adducted downward to assess for hip dislocation

Figure 8: Ortolani Test: With their fingers still placed over the femoral head of the hip being assessed, the examiner gently abducts the thigh

The hips are examined for evidence of developmental dysplasia of the hip (DDH) with the Barlow and Ortolani manoeuvres. The Barlow test assesses whether the hip is dislocatable. To perform the Barlow manoeuvre the baby's knees and hips are flexed at 90 degrees, the pelvis is stabilised, and one hip is tested at a time (Figure 6). The examiner places their fingers over the femoral head of the hip to be tested and gently adducts it downward (Figure 7). Dislocation is palpable as the femoral head slips over the posterior lip of the acetabulum. (7) The Ortolani test examines if a dislocated femoral head, either congenitally dislocated or dislocated secondary to the Barlow test, may be reduced into the acetabulum. With their fingers still placed over the femoral head of the hip being assessed, the examiner gently abducts the thigh (Figure 8). The test is positive if the examiner senses reduction of the femoral head into the acetabulum by palpating a 'clunk' and movement forward of the femoral head. Risk factors for DDH include breech presentation, a positive family history in a first-degree relative, and fixed talipes. If a baby is found to have a positive Barlow or Ortolani test, a hip ultrasound should be performed prior to discharge home to assess for dislocation. If risk factors for DDH exist or a hip click is found on hip examination, a hip ultrasound should be arranged for the infant at 6 weeks corrected gestational age to determine hip subluxation vs. hip dysplasia.

Newborn Screening Assessments

All physicians involved in neonatal care should be fully versed on the newborn screening assessments in place for infants born in their jurisdiction, their utility, limitations, and appropriate management of babies with positive screens. Every baby in Ireland undergoes several newborn screening assessments prior to discharge home. The universal heel prick test screens for cystic fibrosis, congenital hypothyroidism, phenylketonuria, classical galactosaemia, glutaric aciduria type 1, medium-chain acyl-CoA dehydrogenase deficiency, homocystinuria, and maple syrup urine disease. (10) Early detection of these rare disorders is essential to instigate appropriate management and minimise associated morbidity. A newborn hearing screening programme (NHSP) was implemented in Ireland in April 2011 to detect permanent childhood hearing impairments and facilitate enrolment in early intervention programmes by 6 months of age. (11) Pulse oximetry to evaluate for the presence of congenital heart disease is performed on all Irish infants prior to discharge home, ideally after the first 24 hours of age. Although newborn pulse oximetry screening has a specificity of 99.9%, it is important to note that certain cardiac defects including coarctation of the aorta, interrupted aortic arch and some forms of total anomalous pulmonary venous return may not be detected by this screening tool. (12) Many Irish maternity hospitals also perform a transcutaneous bilirubin check prior to discharge home; this is especially relevant for those babies of African or Asian ethnicity where jaundice may be more challenging to assess visually.

Useful Advice for New Parents

The newborn physical examination is an excellent opportunity to form a good rapport with parents, provide advice for newborn care, answer questions, and provide reassurance. Breastfeeding should be encouraged, and the benefits of breastmilk promoted to parents; breastfeeding encourages maternal bonding with baby, provides natural and complete nutrition, prevents infection via maternal immunoglobulin and protects against future obesity. (13) The importance of appropriate sleeping practices should be emphasised. The 'Back to Sleep' campaign was launched in 1994, and since then, a reduction in over 50% of sudden infant death syndrome (SIDS) cases in the United States has been achieved. (14) As such, all infants should be placed on their backs when going to sleep, with their feet at the bottom of the cot, one breathable blanket to cover them and no pillows or toys in the cot around the baby. Smoking in the household should be discussed as a significant risk factor for SIDS and parents directed to appropriate supports for smoking cessation. Many neonatal units and maternity hospitals implement an infant 'car seat challenge' prior to discharge home to assess safe positioning of the infant in the car seat. This is especially relevant for infants born prematurely, who may experience apnoea, bradycardia, and oxygen desaturations if malpositioned in a car seat. (15) The newborn examination may also provide time to mention the value of immunizations, inform parents of the immunization schedule, and correct misconceptions they may have regarding vaccination.

In conclusion, a comprehensive physical examination of the newborn is essential. Appropriate training in neonatal physical examination technique for medical students and physicians working outside of neonatology is vital to ensure that newborns interacting with such services are examined thoroughly, and any pathology present promptly identified. We have outlined some of the more challenging aspects of the newborn physical exam, which are often performed incorrectly. We hope these tips may ameliorate such difficulties or errors in technique and be helpful for the non-neonatologist reviewing a newborn infant.

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Corresponding Author

Aisling Smith, MD
Department of Neonatology,
The Rotunda Hospital,
Parnell Square,
Dublin,
Ireland
E: smithai@tcd.ie
T: (01) 817 1700

Robert McGrath, MD,
Department of Neonatology,
The Rotunda Hospital,
Parnell Square,
Dublin,
Ireland

Naomi McCallion, MD
Department of Neonatology,
The Rotunda Hospital,
Parnell Square,
Dublin,
Ireland
School of Medicine,
Royal College of Surgeons in Ireland,
Dublin, Ireland

Tom Clarke, MD
Emeritus Consultant in Neonatology
The Rotunda Hospital,
Dublin. Ireland
tclarke347@gmail.com

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Who should attend:

Clinical and academic neonatologists, neonatal fellows, NICU nurses and other allied healthcare professionals who care for the neonatal patient are invited to attend.

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Commentary on Tips for Medical Students and Non-Neonatologists on Physical Examination of the Newborn and Important Aspects of Early Newborn Care– An Irish Perspective

T. Allen Merritt, MD

Examination of the newborn, as summarized by Irish neonatologists, should never be considered "routine." It must be done methodically and with competency; in performing the thorough examination of the newborn, the head to toe examination must be performed with skill and competence. In medical student education in Ireland, it is recognized that the vast majority of newborn examinations will be performed by non-neonatologists. This is also true in the U.S. where there is substantial variation in the amount of dedicated medical education focused on the newborn examination and care of the "normal" newborn. Other clinical rotations involving population medicine (1) provide mentorship for students. Pediatricians, Family physicians, Nurse Practitioners, and Physician's Assistants, Certified Nurse Midwives, and in some states licensed direct-entry midwives may examine the newborn. For the asymptomatic newborn, this examination may take place sometime within 24 hours after birth; however, infants who are symptomatic need attention immediately and not after office hours, or when rounds are completed. As mentioned by the author's in Ireland, the vast majority are examined by "general practitioners" with consultant Neonatologists available to assist and advise.

Thorough and detailed examination of each newborn from head to toe provides reassurance to parents that their newborn is "normal," but also has the potential to detect abnormalities requiring further diagnostic assessment or imaging that can be communicated to the parents with great sensitivity. Further appreciating the correct timing, positive and negative predictive values of newborn screening tests and their limitations (including hearing screening, an examination of eyes for pupillary symmetry and "red reflex" in both eyes) is essential. Understanding the limitations of upper and lower extremity oximetry targets in detecting congenital heart disease is vital for early referral for an echocardiogram and evaluation when needed by a pediatric cardiologist. Hearing screening is vitally important to recognize when retesting may be required, and when a referral for hearing augmentation is indicated for proper language development. As discussed by the author's metabolic screening evaluation of the newborn, with some metabolic screening more inclusive than others, will provide for detection of metabolic diseases, thyroid, and adrenal dysfunction or congenital infection such as cytomegalovirus that may need immediate interventions or further consultation.

Teaching newborn examination skills requires a full understanding of transitional physiology minor versus major anomalies, and recognition of often more subtle physical findings or symptoms. Our Irish colleagues have pointed out that these are best taught by Neonatal specialists who more frequently encounter abnormal findings at all gestational ages and who maintain up to date knowledge of the screening test limitations and appropriate interventions when abnormalities are detected. Together with videos and simulation, their teaching methods actually are "hands-on" examination of infants to gain expertise in both the correct techniques of every aspect of the newborn examination. Irish Neonatologists dedicate an entire week to teaching and demonstrating to medical students the finer points of the newborn examination and further discussion with the parents when referrals are needed. Providing anticipatory guidance regarding newborn care by their parents is critically important in both of our countries focused on breastfeeding, nutritional supplements when needed, correct positioning for sleep, use of car seats, and providing reassurance to new parents. In the U.S., the Stanford Medicine website offers an excellent array of photographs with commentary regarding findings on the newborn examination and provides guidance about common newborn conditions (2), and offers useful teaching for medical students, however, few photographs are as vivid as seeing these conditions firsthand.

In the U.S., too frequently, the electronic medical record (EMR) documents an examination using checkboxes or even a box indicating "all normal findings" in templated newborn exams that may abbreviate the detailed physical examination information needed to be conveyed to parents. Other "exams" may include repetitive "smart phrases" that may imply a detailed exam in the EMR with perhaps with only a space left for the practitioner to specify infant gender and the genital examination. The EMR implies a thoroughness of examination that is difficult to reconcile with the actual examination occurring of many newborns or may enter or omit critical findings of the examination in error with adverse patient consequences (3-4). Further, the information conveyed to pediatrician or family if they did not do the initial exam is often sketchy.

Substantial variation in training modules for newborn examination and care exists in pediatric programs in the U.S., and thus variation in the actual care of the newborns should be expected. The anticipated "normal" infant and their parents deserve careful examination and thoughtful anticipatory parenting guidance. Our Irish colleagues have placed high educational value on training medical students in the examination of newborns using multiple dimensions of teaching and with hand-on experience during their training. They provide an example of excellence in medical education about the newborn examinations to be emulated in many U.S. medical schools, and also those who care for the newborns who may be neither neonatologist nor pediatrician or family physician.

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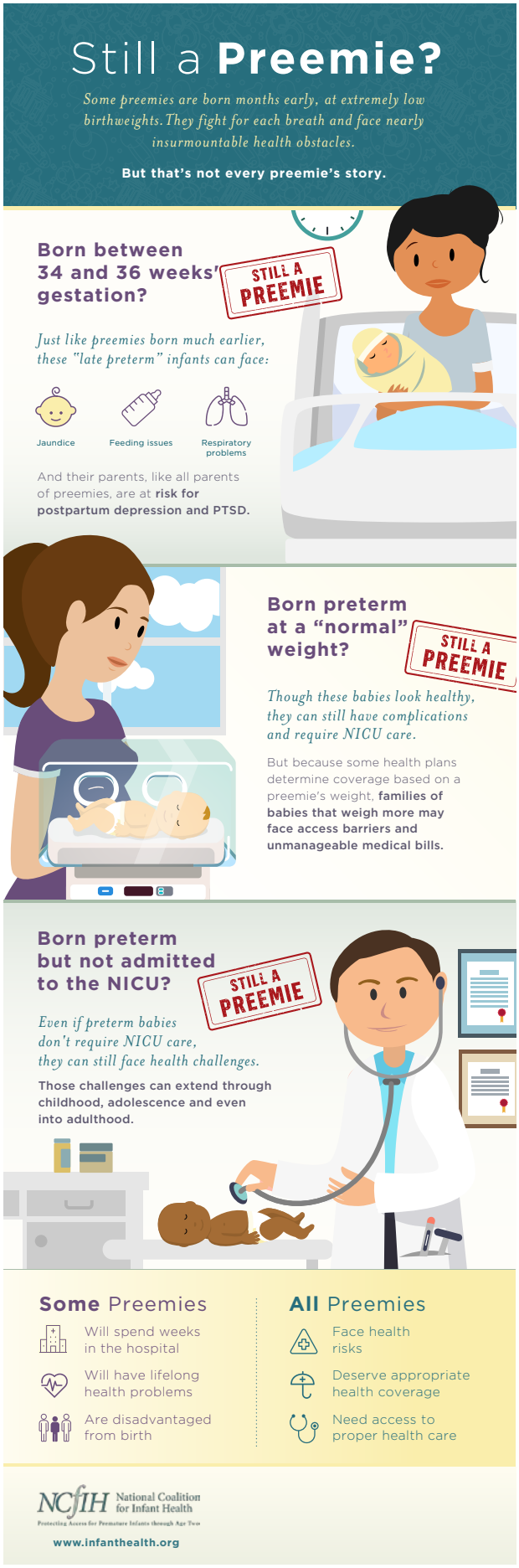
Corresponding Author

T.Allen Merritt, MD
Professor of Pediatrics
Loma Linda University School of Medicine
Division of Neonatology
Department of Pediatrics
tamerritt@llu.edu



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Parent-Child Attachment Disruption

Carolina Michel-Macías, MD, and Sandra Carrera-Muiños, MD

Abstract

Childbirth is a neurobiologically sensitive period, conceptualized as a developmental window during which a system displays high plasticity and vulnerability to shaping and attunement by environmental input. Healthcare professionals involved in perinatal services play a major role in the initiation of caregiver-child attachment by supporting practices that promote breastfeeding, immediate skin to skin contact, mother-child attachment, and father-child attachment. However, most of the facilities which provide maternity services promote policies that disrupt the establishment of attachment in spite of the recommendations of the World Health Organization (WHO). In México, only 3.7% of the births that occur in facilities, take place in a baby-friendly certified facility. For many private hospitals, to separate the mother from the infant in the first hour after birth is a strict policy and newborn permanence with her/his mother is denied even if requested by parents or healthcare professionals. This disruptive policy results in neuroendocrine alterations during a highly sensitive period.

"A disruption in these neuroendocrine events is likely to have not only a short-term impact on mother-child attachment but also long-term effects in the newborn, increasing the risk of behavioral alterations or mental health problems that may have not yet been causally related to a peripartal origin. (1)(2)"

Introduction

In humans like in other mammalian species, peripartal neuroendocrine events play an essential role in the initiation of the bonding of the newborn immediately after birth. (1)(2). A disruption in these neuroendocrine events is likely to have not only a short-term impact on mother-child attachment but also long-term effects in the newborn, increasing the risk of behavioral alterations or mental health problems that may have not yet been causally related to a peripartal origin. (1-2)

Childbirth is a neurobiologically sensitive period, conceptualized as a developmental window during which a system displays high plasticity and vulnerability to shaping and attunement by environmental input. (2)(3) According to Bowlby, attachment between the infant and his or her mother is an innate biological response that increases the probability of survival. (Bowlby, 1978). The attachment neurobiology develops early, beginning in utero and continues through preschool age. This is a complex process that involves the development of the HPA axis and reward system early on, followed by the development of the amygdala, followed by PFC development into adulthood. (2, 4)

Healthcare professionals involved in perinatal services play a major role in the initiation of caregiver-child attachment by supporting practices that promote breastfeeding, immediate skin to skin contact, mother-child attachment, and father-child attachment. However, most of the facilities which provide maternity services promote policies that disrupt the establishment of attachment in spite of the recommendations of the World Health Organization (WHO).

The Baby-Friendly Hospitals Initiative

The Baby-Friendly Hospital Initiative (BFHI) was launched in 1991 by the WHO and the United Nations Children's Fund (UNICEF), with the goal of protecting, promoting, and supporting breastfeeding in facilities that provide maternity services. Despite its proven benefits and relevance to current global health goals, the BFHI has suffered from waning political and financial support in recent years.

In México, only 3.7% of the births that occur in facilities take place in a baby-friendly certified facility. (10). According to INEGI (Instituto Nacional de Estadística y Geografía) 2, 234, 039 births occurred in 2017, of which 1,986,490 occurred in a health facility (1,672,295 [84.2%] took place in an official/ public facility, and 314,195 [15.8%] occurred in a private facility). Of note, births that occurred in a private facility have increased steadily for the last three years, and there is only one baby-friendly certified private facility in the entire country.

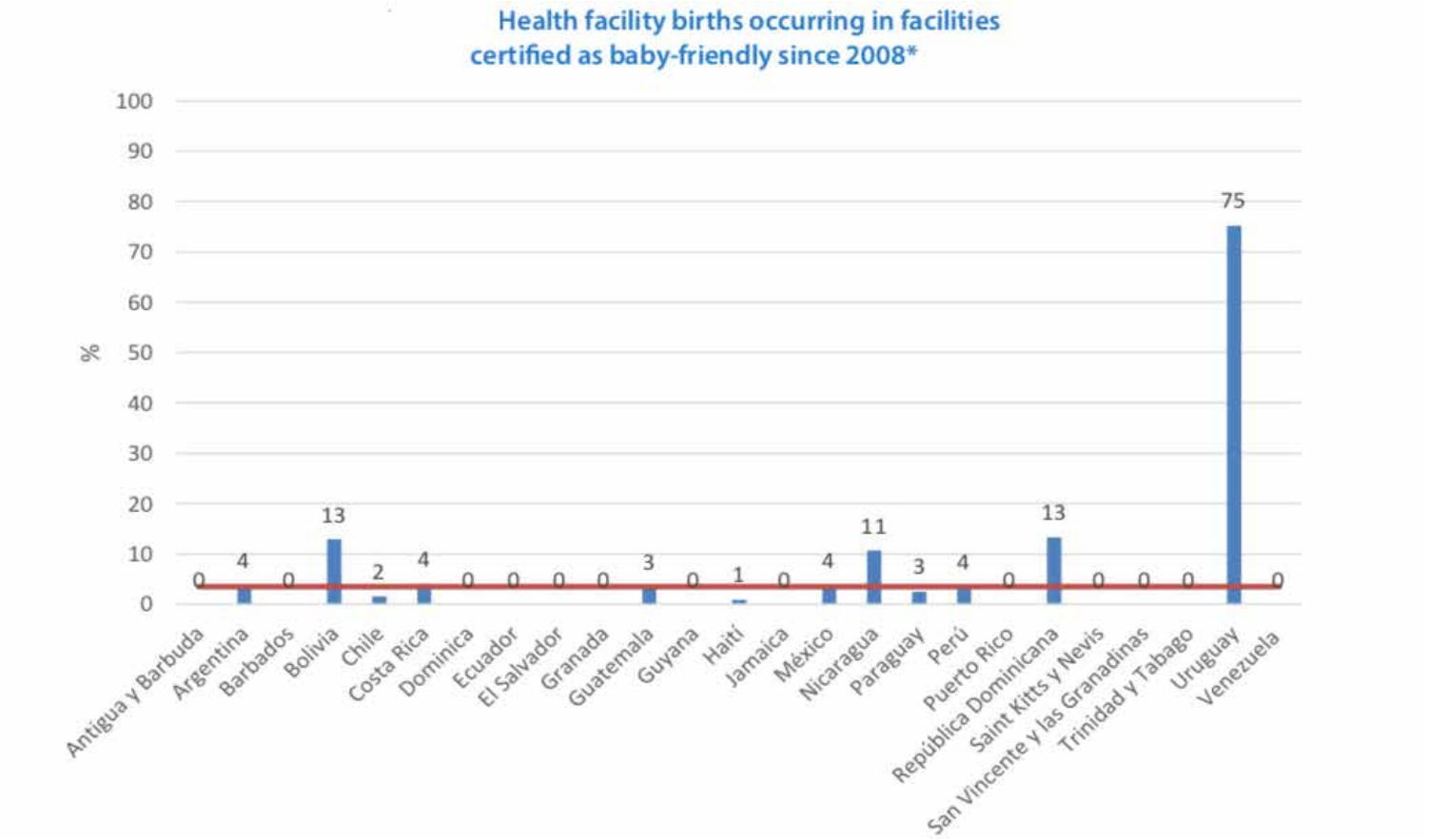
Rooming-in (allowing mothers and infants to remain together 24 hours a day) which is one of the Ten Steps for the promotion of successful breastfeeding, is a determinant for the establishment of caregiver-newborn attachment. However, in the majority of facilities, rooming-in for 24 hours a day is not routinely carried out, and it is implemented only when parents request it.

Moreover, routine separation occurs after cesarean section and even after vaginal delivery, so that the baby is placed in an isolette and vital signs are monitored for a variable number of hours. (Justified as surveillance of transitional period). During this period, infants are fed with formula and deprived of skin-to-skin contact from a caregiver.

For many private hospitals, to separate the mother from the infant in the first hour after birth is a strict policy and newborn permanence with her/his mother is denied even if requested by parents or healthcare professionals. This disruptive policy results in neuroendocrine alterations during a highly sensitive period.

It is important for healthcare professionals to understand that an infant separated from its mother should be cared for skin-to-skin with its father or another primary caregiver for the infant's well-being. (5)

From The Baby-Friendly Hospital Initiative in Latin America and the Caribbean: Current status, challenges, and opportunities, 2016. World



Health Organization.

Focusing on attachment

Birth outcomes have traditionally been measured in terms of maternal and neonatal morbidity in the short term. However, experiences during childbirth and in the first days of life can produce hypothetical changes in the brain, whose impact may only be manifested later in life. (1) Potential scenarios that can cause neurohormonal disruptions include elective cesarean section, intrapartum hormonal manipulations, preterm delivery, mother-infant postpartum separation, and bottle-feeding. (1)

Activation of the oxytocinergic system is inhibited during pregnancy, and its activation is necessary for parturition and for the onset of lactation and maternal behavior. (1)(2) Vaginal delivery results in increased levels of oxytocin not only in the periphery but also in the brain, as indicated by animal studies showing increased levels of the hormone at parturition in the cerebrospinal fluid and the paraventricular nucleus of sheep and in the brain of rats. (1)

The central increase in oxytocin levels may contribute to the generation of mother-infant bonding, which may be associated with increased activation of oxytocin and dopamine pathways in the brain. (1) In humans, the passage of the baby head through the birth canal is accompanied by a substantial activation of the sympathoadrenal axis and the enhanced release of noradrenaline, cortisol, and vasopressin. (1-2)

During natural childbirth, the odor of the mother is supposed to be the first biologically relevant odor that the newborn confronts. Therefore, the increase in noradrenaline levels caused by vaginal delivery may contribute to the identification of maternal odor and to the consequent establishment of the attachment of the newborns with their mothers. (1)

Right after delivery occurs the so-called sensitive period, a quiet alertness state that lasts for about two hours. (1-2) The sensitive neonatal period includes the spontaneous onset of breastfeeding in the first two hours of life. The first hours after birth are also a critical period for the development of attachment behavior. (1, 6) During this critical period for programming complex cognition and behavior, developmental perturbations can produce vulnerability to psychiatric disorders and maladaptive behaviors that reduce access to resources. (6)

Skin to skin contact immediately after delivery helps the baby to conserve energy, adjust acid-base balance and breathing and has a calming effect. (1) Skin to skin contact with both mothers and fathers reduces an infant's crying and promotes vocal communication between parent and newborns. (1). As a consequence of early skin to skin contact, infant regulation of emotions, stress reactivity, metabolic adaptation, social and cognitive development, and future interaction between mother and infant are promoted. (1-2)

In rats, maternal skin to skin contact increases central oxytocin in the pups, facilitating the induction of preference for maternal odor and the establishment of social affiliation. (1). The interaction of the mother with her pups seems to be necessary for the interaction of specific neuroplastic changes in the mother brain during the postpartum period. It is unknown if similar neuroplastic changes occur in the brain of human mothers. (1-2) Although the limited fMRI studies available suggest the existence of functional modifications in the hypothalamus, amygdala, and cerebral cortex in the brain of women during the postpartum period. (1) These functional modifications in the brain of postpartum women are influenced by the interaction with their infants. (1) The increase in intracerebral oxytocinergic signaling may mediate the association between breastfeeding and mother-child attachment. (6)

Early skin-to-skin contact with the mother has been shown as being important for the duration of breastfeeding, being even more important than early initiation of breastfeeding. (10). Breastfeeding might promote attachment, as one study showed that mother who breastfeed demonstrate greater activity in brain regions involved in bonding and

empathy in response to their own infant's cry. (7)

The work of Harlow and Harlow with rhesus monkeys clearly highlighted the importance of the infant's social interactions during a sensitive period in development since, without the caregiver, infants showed emotional and cognitive disabilities that were reminiscent of human children reared in adequate orphanages without an attachment figure. (2,4,6) For these reasons, not only breastfeeding but attachment to a caregiver must be enhanced and encouraged in all maternity facilities.

" For these reasons, not only breastfeeding but attachment to a caregiver must be enhanced and encouraged in all maternity facilities."

Father's role in the first days of life

During early life, the infant relies on the caregiver for the regulation of basic physiology, ranging from vital functions, such as heart rate and respiration, to emotional regulation. (6). Attachment between a child and a secure attachment figure is inherently biological and supersedes the existence of any genetic relationship. (7)

In situations of mother-child separation, healthcare professionals must recognize fathers as resources and primary caregivers for the infant immediately after birth. (5). In an experiment, Perry et al. reared infant pups with both their mother and father to test whether or not pups also displayed attachment to their father. Pups reared in these conditions showed similar approach levels to their mother's and father's natural odors, indicating high odor preference learning for both. (3)

Furthermore, the father's odor induced a neural signature similar to that of the maternal odor, suggesting that infant experiences with their fathers as a co-caregiver elicited infant attachment in a similar way to mothers. (5) In a study by Erlandsson, the fathers as primary caregivers during maternal-infant separation were the source of comfort and approach for the infant immediately following birth. (5)

Also, fathers can give the infant a chance to coordinate their pre-feeding behavior. (5) In situations of separation, when early skin-to-skin contact with the mother and initiation of breastfeeding is delayed fathers as primary caregivers, from the infant's perspective, can provide a calming skin-to-skin contact, an enhanced adaptation of breathing and a chance to pre-feed. (5)

Fathers supported for attachment process in infancy and through their presence in the delivery room have an increased possibility of developing secure attachment between themselves and their babies. (8). A strong father-infant attachment after childbirth serves as a good starting point for such a role. (8). Harrington et al interviewed with 1000 employed fathers to compare father's caregiver role. Only 30% of the fathers reported that they effectively participated in infant care. (8). According to a model of the parental brain by James Swain and colleagues, an infant's cry, smell, feel and appearance activate corticolimbic modules and trigger "reflexive caring impulses" (7), which might promote father's participation in infant's care.

Although father-child attachment remains understudied, it appears that attachment relationships can and do form in most father-child dyads. (9) Father-child attachment security has been implicated in numerous child outcomes, such that securely attached children show fewer behavior problems, greater sociability, and more reciprocated friendships. (9)

Besides the father, the entire family must be informed, supported, and enabled in order to take responsibility for the care of the newborn infant during periods of maternal-infant separation, after for example a cesarean section. (10)

The exceptionally strong influence of early experiences on brain architecture makes the early years a period of both great opportunity and great vulnerability for development. (10)

The reciprocal and dynamic interactions between the child and a caregiver are essential for healthy development and literally shape the architecture of the developing brain. (10)

Conclusion

Although healthcare professionals are aware of the benefits of early skin to skin contact and breastfeeding, the consequences of disrupting caregiver-infant attachment in the first hours of life seem to be unclear, as they may manifest at later ages.

As healthcare providers, we must enhance full and continuous child attachment to the mother or another primary caregiver in case of child-mother separation. Routine separation of the child from the mother without a medical indication is unacceptable, especially during the first hours after birth, when a sensitive period for attachment occurs.

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NT

Corresponding Author

Carolina Michel-Macías, MD
Neonatology. Instituto Nacional de Perinatología, México
Av. Río Churubusco 601 int. 1219. CP. 03330.
Colonia Xoco,
Delegación Benito Juárez.
Ciudad de México,
México.
Telephone: +1 52 5535 038968
Email: dra.carolinamichel@gmail.com

Sandra Carrera-Muiños, MD
Neonatology. Instituto Nacional de Perinatología, México
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Respiratory Report: To Grunt or Not To Grunt: That is the Question Considerations in the management of transient tachypnea of the newborn (TTN)

Rob Graham, R.R.T./N.R.C.P.

I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

Transient Tachypnea of the Newborn (TTN) is the most common respiratory condition seen in the newborn period with estimated occurrence in 0.5 to 4 percent of births. (1) It is a generally benign and self-limiting condition resulting from insufficient clearance of lung fluid during delivery. (2) Risk factors include birth by caesarian section (C/S) without labour, particularly if delivered before 39 weeks (doubles risk), gestational diabetes, small or large for gestational age infants, maternal asthma, perinatal asphyxia, male gender and prematurity. (3)

Clinically, TTN presents most commonly with exhalation against a partially closed glottis ("grunting," the infant's attempt to increase end-expiratory pressure), with or without retractions or nasal flaring. As severity increases, low oxygen saturation (SpO_2), respiratory acidosis, and finally, respiratory failure may occur without appropriate support and intervention. Treatment is supportive, the degree of which should be determined by how severely the infant presents.

In NICU's, it is sometimes said that "we make big babies sick." In my opinion, this stems from the tendency to over-treat these infants. Also, the fear of persistent pulmonary hypertension of the newborn (PPHN) may lead to interventions above and beyond what is required. Because of the severity of PPHN, it is hard to blame those at the bedside, however knowing risk factors ahead of time should lessen this fear. These include Cesarean section delivery, high maternal body mass index, maternal use of aspirin, nonsteroidal anti-inflammatory agents, and maternal diabetes mellitus are among the factors associated with an increased risk for PPHN.

Recent data suggest that maternal use of serotonin reuptake inhibitors might represent another important risk factor for PPHN. There appear to be no effective preventative strategies. (4) PPHN is, however, less likely to occur after 72 hours. (5) Further adding to the fear of PPHN is the fact that both birth by C/S and TTN are considered risk factors for PPHN, as well as RDS, post-term delivery, birth asphyxia, meconium aspiration, and sepsis. (6) That sepsis often first presents as mild respiratory distress compounds the dilemma of whether or not to escalate treatment and proper investigations to rule it out is prudent. Premature prolonged rupture of membranes (PPROM), particularly prior to 20 weeks gestation, also increases the risk of PPHN. (7)

Given the above risk factors and attending sequelae, it is not hard to see why so many clinicians immediately put these babies on some form of support, most notably CPAP; however, as benign as we believe CPAP is as a therapy, there are other forms of support available. Placing a baby on CPAP sets up a chain of events that may increase the length of stay unnecessarily, interfere with the establishment of oral feeding, and parental bonding. While, obviously, keeping a baby stable (and alive!) takes precedence over bonding, there are many babies who are well enough to simply monitor. Who might they be?

"One quick way to assess respiratory distress in a newborn is to offer them something to suck on, preferably their mother's breast. As a general rule, infants in significant respiratory distress will not suck or latch."

A baby who is grunting but otherwise well, in room air with SpO_2 95-100%, is clearly managing their pathology well themselves and, personally, I am reluctant to intervene. I believe these babies can, I believe, be safely watched without support as long as SpO_2 remains in that range, especially bigger full-term babies who have an adequate reserve. They can carry on this way for quite some time without tiring provided they do not become either hypothermic or hypoglycemic, (both of which can lead to secondary surfactant deficiency and respiratory distress syndrome), something those used to dealing with premature infants tend to forget. This is often a case of "less is more," but, the most difficult procedure in the NICU seems to be sitting on one's hands, what one of my mentors refers to as "skillful neglect."

One quick way to assess respiratory distress in a newborn is to offer them something to suck on, preferably their mother's breast. As a general rule, infants in significant respiratory distress will not suck or latch. Offering skin to skin contact with their mothers quite often works like magic. Prone positioning may also help. Skin to skin can also be initiated post C/S in the operating room. (8)

Should SpO_2 fall, supplementary oxygen may be given by nasal prongs, and support may be escalated to high flow nasal prongs with supplemental oxygen. (9) Another advantage of these less cumbersome therapies is that bigger babies tend not to like CPAP interfaces and are more comfortable with low flow or high flow prongs, and with larger babies, a "hands-off", minimal handling approach is best whenever possible. In my experience, they are also more likely to be offered kangaroo care or other parental contact and be fed orally. As well, there are attending costs associated with escalating treatment in terms of equipment and length of stay.

Knowing existing risk factors for more serious pathologies both on the maternal and infant side is essential when managing TTN less invasively, and waiting and watching does require close and careful monitoring, especially of SpO_2. A caveat here: the fear of a baby "flipping" into PPHN leads many clinicians to maintain SpO2 high with supplemental oxygen artificially. While well-intentioned, hyperoxia leads to increased formation of free radicals, one of which is a potent vasoconstrictor that will blunt the effect of inhaled nitric oxide or prevent it completely. (10) It is my practice to

set low SpO_2 alarms at 90-92% to prevent "falling off the cliff" on the oxygen desaturation curve but to not keep SpO_2 above 98% artificially.

Pneumothoraxes (particularly pneumomediastinum) may also present as grunting, and these should be ruled out before initiating nasal CPAP as these babies are best managed with supplemental oxygen and not positive pressure which may exacerbate the problem. Very often these will resolve on their own without intervention, although pneumothoraxes increase the risk of PPHN. The largest risk factors for spontaneous pneumothoraxes are birth by C/S, being male, higher birth weight and being large for gestational age. (11)

"July's column on MIST/LISA was inadvertently submitted missing two paragraphs, without which my view of the practice may be interpreted as overly negative. They are below, with apologies."

Addendum

July's column on MIST/LISA was inadvertently submitted missing two paragraphs, without which my view of the practice may be interpreted as overly negative. They are below, with apologies.

"There is also the endotracheal tube itself. Phthalates used in the production of PVC pose known health risks to humans, particularly to children, neonates being particularly at risk. These chemicals leach from the during the first 24 hours of placement.(12) PVC is used extensively in medication bags and tubing which are also used in the neonatal population thus isolating the effect of the ETT itself from a phthalate standpoint is impossible. Still, any reduction in phthalate exposure can only be a good thing. (13) Still, it is ostensibly what is done after the insertion of an ETT that creates the most harm, hence it is essential that clinicians have excellent knowledge of lung-protective ventilation strategies that are carried into practice as there are patients who will require intubation and mechanical ventilation.

Another factor to consider in very premature patients being managed with NIV is FiO_2. Until anti-oxidant production and supplementation are established, the premature infant has no protection from free radicals and is therefore very susceptible to oxidative stress. There seems to be great variance in clinical practice when it comes to just how high a safe FiO_2 is. I firmly believe less is best since FiO_2 is the barometer of pulmonary compliance. It is common practice to withhold surfactant replacement therapy until a threshold FiO_2 is reached, usually around 0.30. I do not embrace this practice, as there are consequences to delaying surfactant treatment. Increased length of exposure to higher FiO_2 in a patient lacking endogenous anti-oxidant protection and who's susceptibility to oxidative stress is increased is not, in my opinion, wise. Also, delayed treatment increases the risk of air leak, most notably pneumothorax. (14) (Please note I do not advocate waiting for FiO2 to be as high as this reference suggests. It is my practice to give intubated infants with any increased FiO_2 surfactant.) Any practice that reduces the reluctance of a clinician to give surfactant is a good thing in my mind."

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Disclosures: The author receives compensation from Bunnell Inc for teaching and training users of the LifePulse HFJV in Canada. He is not involved in sales or marketing of the device nor does he receive more than per diem compensation. Also, while the author practices within Sunnybrook H.S.C. this paper should not be construed as Sunnybrook policy per se. This article contains elements considered "off label" as well as maneuvers, which may sometimes be very effective but come with inherent risks. As with any therapy, the risk-benefit ratio must be carefully considered before they are initiated.

NT

Corresponding Author

Rob Graham, R.R.T./N.R.C.P.
Advanced Practice Neonatal RRT
Sunnybrook Health Science Centre
43 Wellesley St. East
Toronto, ON
Canada M4Y 1H1
Email: Rob Graham <rcgnrcp57@yahoo.ca>
Telephone: 416-967-8500

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Omegaven®

(fish oil triglycerides) injectable emulsion

Introducing a **Fish Oil** Lipid Emulsion for Pediatrics[1]

A source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC)

Patients receiving Omegaven achieved age appropriate growth

Omegaven treated patients experienced improvement in liver function parameters

OMEGAVEN (fish oil triglycerides) injectable emulsion, for intravenous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use Omegaven safely and effectively. Please see full prescribing information for Omegaven (fish oil triglycerides) injectable emulsion for intravenous use at www.fresenius-kabi.com/us.

INDICATIONS AND USAGE

Omegaven is indicated as a source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC).

Limitations of Use:

Omegaven is not indicated for the prevention of PNAC. It has not been demonstrated that Omegaven prevents PNAC in parenteral nutrition (PN)-dependent patients.

It has not been demonstrated that the clinical outcomes observed in patients treated with Omegaven are a result of the omega-6: omega-3 fatty acid ratio of the product.

DOSAGE AND ADMINISTRATION

Prior to administration, correct severe fluid and electrolyte disorders and measure serum triglycerides to establish a baseline level. Initiate dosing in PN-dependent pediatric patients as soon as direct or conjugated bilirubin levels are 2 mg/dL or greater. The recommended daily dose (and the maximum dose) in pediatric patients is 1 g/kg/day. Administer Omegaven until direct or conjugated bilirubin levels are less than 2 mg/dL or until the patient no longer requires PN.

CONTRAINDICATIONS

Omegaven is contraindicated in patients with known hypersensitivity to fish or egg protein or to any of the active ingredients or excipients, severe hemorrhagic disorders due to a potential effect on platelet aggregation, severe hyperlipidemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentrations greater than 1,000 mg/dL).

WARNINGS AND PRECAUTIONS

- Risk of Death in Preterm Infants due to Pulmonary Lipid Accumulation: Deaths in preterm infants after infusion of soybean oil-based intravenous lipid emulsions have been reported in medical literature. Autopsy findings in these preterm infants included intravascular lipid accumulation in the lungs. The risk of pulmonary lipid accumulation with Omegaven is unknown. Preterm and small-for-gestational-age infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion. This risk due to poor lipid clearance should be considered when administering intravenous lipid emulsions. Monitor patients receiving Omegaven for signs and symptoms of pleural or pericardial effusion.
- Hypersensitivity Reactions: Omegaven contains fish oil and egg phospholipids, which may cause hypersensitivity reactions. Signs or symptoms of a hypersensitivity reaction may include: tachypnea, dyspnea, hypoxia, bronchospasm, tachycardia, hypotension, cyanosis, vomiting, nausea, headache, sweating, dizziness, altered mentation, flushing, rash, urticaria, erythema, fever, or chills. If a hypersensitivity reaction occurs, stop infusion of Omegaven immediately and initiate appropriate treatment and supportive measures.

Please see continuation of Brief Summary of Prescribing Information for Omegaven on the reverse side.

ORDERING INFORMATION

Bottle Size	50 mL single-dose glass bottle	100 mL single-dose glass bottle
NDC Code	63323-205-50	63323-205-00
Bottle/Carton	10	10

FOR MORE INFORMATION ABOUT OMEGAVEN®:

Website: www.OmegavenUSA.com
To Order: 1.888.386.1300
Med Info phone: 1.800.551.7176 (option 4)
Med Info email: nutrition.medinfo.USA@fresenius-kabi.com

- Risk of Infections: The risk of infection is increased in patients with malnutrition-associated immunosuppression, long-term use and poor maintenance of intravenous catheters, or immunosuppressive effects of other conditions or concomitant drugs. To decrease the risk of infectious complications, ensure aseptic technique in catheter placement and maintenance, as well as in the preparation and administration of Omegaven. Monitor for signs and symptoms of early infections including fever and chills, laboratory test results that might indicate infection (including leukocytosis and hyperglycemia), and frequently inspect the intravenous catheter insertion site for edema, redness, and discharge.
- Fat Overload Syndrome: A reduced or limited ability to metabolize lipids accompanied by prolonged plasma clearance may result in this syndrome, which is characterized by a sudden deterioration in the patient's condition including fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations (e.g., coma).
- Refeeding Syndrome: Administering PN to severely malnourished patients may result in refeeding syndrome, which is characterized by the intracellular shift of potassium, phosphorus, and magnesium as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, closely monitor severely malnourished patients and slowly increase their nutrient intake.
- Hypertriglyceridemia: Impaired lipid metabolism with hypertriglyceridemia may occur in conditions such as inherited lipid disorders, obesity, diabetes mellitus, and metabolic syndrome. Serum triglyceride levels greater than 1,000 mg/dL have been associated with an increased risk of pancreatitis. To evaluate the patient's capacity to metabolize and eliminate the infused lipid emulsion, measure serum triglycerides before the start of infusion (baseline value), and regularly throughout treatment. If hypertriglyceridemia (triglycerides greater than 250 mg/dL in neonates and infants or greater than 400 mg/dL in older children) develops, consider stopping the administration of Omegaven for 4 hours and obtain a repeat serum triglyceride level. Resume Omegaven based on new result as indicated.
- Aluminum Toxicity: Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Preterm infants are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum. Patients with impaired kidney function, including preterm infants, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.
- Monitoring and Laboratory Tests: Routine Monitoring: Monitor serum triglycerides, fluid and electrolyte status, blood glucose, liver and kidney function, coagulation parameters, and complete blood count including platelets throughout treatment. Essential Fatty Acids: Monitoring patients for laboratory evidence of essential fatty acid deficiency (EFAD) is recommended. Laboratory tests are available to determine serum fatty acids levels. Reference values should be consulted to help determine adequacy of essential fatty acid status.
- Interference with Laboratory Tests: The lipids contained in Omegaven may interfere with some laboratory blood tests (e.g., hemoglobin, lactate dehydrogenase, bilirubin, and oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Lipids are normally cleared after a period of 5 to 6 hours once the lipid infusion is stopped.

ADVERSE REACTIONS

The most common adverse drug reactions (>15%) are: vomiting, agitation, bradycardia, apnea and viral infection.

Clinical Trials Experience

The safety database for Omegaven reflects exposure in 189 pediatric patients (19 days to 15 years of age) treated for a median of 14 weeks (3 days to 8 years) in two clinical trials.

Adverse reactions that occurred in more than 5% of patients who received Omegaven and with a higher incidence than the comparator group are: vomiting, agitation, bradycardia, apnea, viral infection, erythema, rash, abscess, neutropenia, hypertonia and incision site erythema. Patients had a complicated medical and surgical history prior to receiving Omegaven treatment and the mortality was 13%. Underlying clinical conditions prior to the initiation of Omegaven therapy included prematurity, low birth weight, necrotizing enterocolitis, short bowel syndrome, ventilator dependence, coagulopathy, intraventricular hemorrhage, and sepsis.

Twelve (6%) Omegaven-treated patients were listed for liver transplantation (1 patient was listed 18 days before treatment, and 11 patients after a median of 42 days [range: 2 days to 8 months] of treatment); 9 (5%) received a transplant after a median of 121 days (range: 25 days to 6 months) of treatment, and 3 (2%) were taken off the waiting list because cholestasis resolved.

One hundred thirteen (60%) Omegaven-treated patients reached DBil levels less than 2 mg/dL and AST or ALT levels less than 3 times the upper limit of normal, with median AST and ALT levels for Omegaven-treated patients at 89 and 65 U/L, respectively, by the end of the study.

Median hemoglobin levels and platelet counts for Omegaven-treated patients at baseline were 10.2 g/dL and 173 x 10^9/L, and by the end of the study these levels were 10.5 g/dL and 217 x 10^9/L, respectively. Adverse reactions associated with bleeding were experienced by 74 (39%) of Omegaven-treated patients.

Median glucose levels at baseline and the end of the study were 86 and 87 mg/dL for Omegaven-treated patients, respectively. Hyperglycemia was experienced by 13 (7%) Omegaven-treated patients.

Median triglyceride levels at baseline and the end of the study were 121 mg/dL and 72 mg/dL for Omegaven-treated patients respectively. Hypertriglyceridemia was experienced by 5 (3%) Omegaven-treated patients.

The triene:tetraene (Mead acid:arachidonic acid) ratio was used to monitor essential fatty acid status in Omegaven-treated patients only in Study 1 (n = 123). The median triene:tetraene ratio was 0.02 (interquartile range: 0.01 to 0.03) at both baseline and the end of the study. Blood samples for analysis may have been drawn while the lipid emulsion was being infused and patients received enteral or oral nutrition.

Postmarketing Experience

The following adverse reaction has been identified with use of Omegaven in another country. Life-threatening hemorrhage following a central venous catheter change was reported in a 9 month-old infant with intestinal failure who received PN with Omegaven as the sole lipid source; he had no prior history of bleeding, coagulopathy, or portal hypertension.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC, at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Prolonged bleeding time has been reported in patients taking antiplatelet agents or anticoagulants and oral omega-3 fatty acids. Periodically monitor bleeding time in patients receiving Omegaven and concomitant antiplatelet agents or anticoagulants.

USE IN SPECIFIC POPULATIONS

- Pregnancy: There are no available data on Omegaven use in pregnant women to establish a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with fish oil triglycerides. The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.
- Lactation: No data available regarding the presence of fish oil triglycerides from Omegaven in human milk, the effects on the breastfed infant, or the effects on milk production. Lactating women receiving oral omega-3 fatty acids have been shown to have higher levels of omega-3 fatty acids in their milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Omegaven, and any potential adverse effects of Omegaven on the breastfed infant.
- Pediatric Use: The safety of Omegaven was established in 189 pediatric patients (19 days to 15 years of age). The most common adverse reactions in Omegaven-treated patients were vomiting, agitation, bradycardia, apnea and viral infection.
- Geriatric Use: Clinical trials of Omegaven did not include patients 65 years of age and older.

OVERDOSE

In the event of an overdose, fat overload syndrome may occur. Stop the infusion of Omegaven until triglyceride levels have normalized and any symptoms have abated. The effects are usually reversible by stopping the lipid infusion. If medically appropriate, further intervention may be indicated. Lipids are not dialyzable from serum.

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1. Omegaven Prescribing Information, Fresenius Kabi USA, LLC. 2018.

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From the National Perinatal Association: The 7 Module Online Course "Caring for Babies and Families: Providing Psychosocial Support in the NICU"

Sue Hall, MD, MSW, FAAP; Sara Mosher, RN, MHA; Keira Sorrells, BCFCS

The National Perinatal Association (NPA) is an interdisciplinary organization that strives to be a leading voice for perinatal care in the United States. Our diverse membership is comprised of healthcare providers, parents & caregivers, educators, and service providers, all driven by their desire to give voice to and support babies and families at risk across the country.

Members of the NPA write a regular peer-reviewed column in Neonatology Today.

National Perinatal Association
Educate. Advocate. Integrate.

The National Perinatal Association is proud to announce the publication of a paper detailing the results of a study recently conducted in two Neonatal Intensive Care Units (NICUs) that demonstrates the efficacy of its NICU staff education course, "Caring for Babies and Their Families: Providing Psychosocial Support in the NICU." The paper, entitled "Improving Staff Knowledge and Attitudes towards Providing Psychosocial Support to NICU Parents through an Online Education Course," can be found online at this link (Hall, SL, ME Famuyide, SN Saxton, TA Moore, S Mosher, K Sorrells, CA Milford, and J Craig. 2019. "Improving Staff Knowledge and Attitudes towards Providing Psychosocial Support to NICU Parents through an Online Education Course." Advances in Neonatal Care epub in advance of print.)

An interprofessional collaborative group made up of members of the National Perinatal Association, Patient + Family Care, and the Preemie Parent Alliance formed My NICU Network (www.mynicunetwork.com) to develop this 7-hour continuing education course for NICU providers, including nurses, physicians, social workers, and more. The study of 114 NICU staff (primarily nurses) and showed that before taking the course, staff were aware of the importance of providing emotional support to families in their care, but did not feel they had either the confidence or strategies to provide that care successfully. After taking the course, staff achieved significant improvement in both knowledge and attitudes towards providing psychosocial support to parents, and improvements were sustained at a six-month follow-up evaluation. The course also eliminated differences between night and day shift staff, and between staff with less vs. more experience working in the NICU. In addition, the majority of staff agreed or strongly agreed that taking the course improved their knowledge (87.5%) and would change their practice (78%) and that they would recommend the course to their peers (90%).

"Research has shown that parents whose babies are hospitalized in a NICU undergo considerable stress, and have much higher risks for both postpartum depression and posttraumatic stress disorder compared with parents of healthy term babies."

Research has shown that parents whose babies are hospitalized in a NICU undergo considerable stress, and have much higher risks for both postpartum depression and posttraumatic stress disorder compared with parents of healthy term babies. NICU parents also view communication with providers as essential to their satisfaction with their experience. This comprehensive course aims to bring the emotional and communication needs of NICU parents to staff's awareness and to give evidence-based, practical, and trauma-informed approaches (Sanders, 2018) for meeting those needs. Involving NICU Parent Leaders in the creation of this course from development to instruction has been an essential way to enable providers to understand the challenges that NICU parents face; numerous parent stories, audios, and videos illustrate the learning points in the course.

The staff education course is based on the "Interdisciplinary Recommendations for Psychosocial Support in NICU Parents," published in the Journal of Perinatology in December, 2015. The core content areas covered in the course mirror the content areas of the "Recommendations," and include: Providing Emotional Support, Communication, Peer-to-peer Support, Family-Centered Developmental Care, Palliative and Bereavement Care, Discharge and Follow-up Care, and Supporting Staff as They Support Families.

The importance of supporting families, so that they can better bond with and support their sick or premature babies, has gained increasing recognition, as the model of NICU care has shifted to greater delivery of Family-Centered Care and now into Family-Integrated Care. When an entire NICU's staff takes the course at the same time, the NICU's culture can be transformed so that everyone sees the family - not just the baby - as the patient. It is hoped that by giving staff the tools they need to handle their expanded roles in involving parents in the care of their babies and supporting families, that infant developmental outcomes, parent mental health outcomes, and patient (parent) satisfaction will im-

prove. Additionally, the course focuses on the critical importance

"The course can be incorporated into unit-based quality improvement initiatives in a variety of ways. NICU staff can gather to jointly make an assessment of psychosocial support practices they currently have in place as well as to recognize areas that are lacking, using the NPA's NICU Self-Assessment tool (Hall, 2016)."

of supporting staff, so that they can support families, with a goal of reducing provider burnout rates—which can be over 50% in some NICUs (Profit, 2014)—and ultimately minimizing staff turnover.

The course can be incorporated into unit-based quality improvement initiatives in a variety of ways. NICU staff can gather to jointly make an assessment of psychosocial support practices they currently have in place as well as to recognize areas that are lacking, using the NPA's NICU Self-Assessment tool (Hall, 2016). As unit staff take the course together and share ideas on its Discussion Board, they can begin to identify and prioritize potentially better practices to implement either through the development of new policies and/or protocols or through traditional PDSA (Plan-Do-Study-Act) improvement cycles. A multitude of downloadable resources is shared in each content area to facilitate positive changes. A wrap-up staff discussion after taking the course can further illuminate the way forward. Some hospitals have elected to have staff take the course one content area at a time and then gather to discuss and process the information immediately thereafter.

What's Coming Next?

The team at My NICU Network is collaborating with a team from Stanford University Medical Center, led by Dr. Melissa Scala, Director of the Neonatology Fellowship Program, to study the efficacy of the course in Neonatal Fellows nationwide. For this research project, the course has been condensed with the content focused towards what physicians need to know about providing psychosocial support, and the research underpinning this knowledge base. This study, which is being funded by a grant from the Association of Pediatric Program Directors, will be launched soon.

The impetus for this study comes from the recently implemented directives put forth by both the American Board of Pediatrics (ABP) and the Accreditation Council for Graduate Medical Education (ACGME). In 2014, the ABP's Strategic Planning Committee identified the areas of behavioral and mental health as the highest priorities for the education of pediatric trainees, including Neonatal Fellows. This led to the development of their Roadmap Project, which advocates supporting "the resilience, emotional, and mental health of pediatric patients with chronic conditions and their families." The Roadmap's Key Drivers are to increase clinician awareness, knowledge, confidence, and clinical skill in providing support to patients and their families. And, effective July, 2019, the ACGME added the following requirements for Fellows in neonatal-perinatal medicine: "Fellows must demonstrate an understanding of the emotional impact on the family of having a child born prematurely or born with a life-threatening and/or chronic condition, and must demonstrate the communication skills necessary for encouraging dialogue." Our course for Neonatal Fellows will meet all of these requirements, as well as serve as an exemplar for similar courses in other pediatric subspecialties.

An Annual Refresher Course, which is a 2 CEU/CME review of key points in the original long-form course, will be ready to launch in 2020; it is to be used to maintain nursing competencies. And finally, My NICU Network will be adding My Perinatal Network in 2020, with a course for obstetric providers on how to provide psychosocial support to women during and after pregnancy ("Caring for Women and Their Families"). All of the courses, including both the NICU and obstetric courses, have a specific focus on the prevention, recognition, and mitigation of Perinatal Mood and Anxiety Disorders (PMADs), and all outline a trauma-informed approach to providing care.

Details about the Course

Usually, a NICU Nurse Manager, Clinical Nurse Educator, or NICU Medical Director will take the lead in identifying the value that this course can bring to their staff, and will put the process in play to bring the course to their unit. The course, which is available online and can also be accessed on smartphones, can be made available to a NICU for a period of several months, to give everyone a chance to complete it.

Cost for continuing education credits:

For nurses and neonatal nurse practitioners (NNPs): $10/CEU or $70 for the whole course

For physicians, licensed clinical social workers (LCSWs), licensed professional clinical counselors (LPCCs), licensed marriage and family therapists (LMFTs): $35/CME or $245 for the whole course.

Continuing education credits are provided by PAC/LAC, the Perinatal Advisory Council: Leadership, Advocacy, Consultation.

While CEUs are not yet available for licensed neonatal therapists (OT, PT, SLP or for RCPs), they are invited to take the course as part of an entire NICU staff, with the only charge being a $10/per-

son administrative fee for the 7-hour course.

While course modules can be taken individually, it is highly recommended that a NICU's staff goes through the entire course at the same time. For more information or to obtain quotes to bring the course to your NICU, please visit www.mynicunetwork.com, or email sara@mynicunetwork.com.

The email heading should read "I'm interested in your online course!" The body should read: "Please contact me with more information about your online NICU staff education course, "Caring for Babies and Their Families." I can be reached at _____."

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Disclosure: The National Perinatal Association www.nationalperinatal.org is a 501c3 organization that provides education and advocacy around issues affecting the health of mothers, babies, and families. www.nationalperinatal.org.

NT

Corresponding Author

Sue L. Hall, MD, MSW, FAAP
Neonatologist,
St. John's Regional Medical Center,
Oxnard, CA,

Keira Sorrells, BSFCS
Preemie Parent and Founder
Executive Director of the
NICU Parent Network,
Jackson, MS.

Sara Mosher, RN, MHA
NICU Nurse
Founder of Patient+Family Care,
Bend, OR.

My NICU Network

National Perinatal Association + Patient+Family Care + NICU Parent Network

Online NICU Staff Education Program

Caring for Babies and their Families:
Providing Psychosocial Support in the NICU

WWW.MYNICUNETWORK.COM

Looking to improve NICU staff skills in communicating with and supporting parents?

This educational program works!

Read the study by Hall et all in *Advances in Neonatal Care*, published online in 2019.

COMING SOON!

Ask us about our 2-lesson Annual Refresher Program, developed to maintain annual nursing competencies

Continuing education credits provided by

pac-lac

About the Program

- **WHO SHOULD TAKE THE PROGRAM?** This program is designed to educate, raise awareness, and increase the skill level of your entire NICU staff regarding providing comprehensive family support for parents. Individual learners are also welcome to take the program.

- **WHY TAKE THE PROGRAM?** Benefits to staff include improved skills in communicating with parents; improved teamwork, engagement and staff morale; reduced burnout, and reduced staff turnover. Benefits to families include improved parental resilience and mental health, and improved parent-baby bonding leading to better developmental outcomes for babies..

- **HOW DOES THE PROGRAM ACHIEVE ITS GOALS?** Our content is representative of Potentially Better Practices, engaging and story-driven, resource-rich, and developed by a unique collaboration of NICU professionals and NICU graduate parents. The program presents practical tips and an abundance of clinical information that together provide solutions to parents' emotional needs.

- **HOW WAS THE PROGRAM DEVELOPED?** This program was developed through collaboration among three organizations: a multidisciplinary group of professionals from the National Perinatal Association and Patient+Family Care, and NICU graduate parents from the NICU Parent Network. The seven courses offered represent the content areas of the "Interdisciplinary Recommendations for Psychosocial Support of NICU Parents."*

* Hall, SL, and MT Hynan, eds. 2015. "Interdisciplinary Recommendations for the Psychosocial Support of NICU Parents." Journal of Perinatology 35: Supplement

Program Objectives

- Describe elements of comprehensive family support.
- Describe principles and techniques of communication to help support NICU parents.
- Identify factors that put NICU parents at risk for Perinatal Mood and Anxiety Disorders.
- Describe the benefits of peer-to-peer for NICU parents.
- Define ways to involve and empower NICU parents in the care of their baby.
- Identify the benefits of palliative and bereavement care programs to families and staff.
- Define the ways that NICU parents can be supported during the discharge process.
- Define ways in which NICU caregivers can be supported by colleagues and supervisors, and engage in self-care.

Continuing education credits will be provided for physicians (neonatologists, neonatal fellows, pediatric residents), NICU nurses, neonatal nurse practitioners, social workers, psychologists, licensed marriage and family therapists. CEUs will be provided by Perinatal Advisory Council: Leadership, Advocacy, and Consultation.

In a recent survey of people who had taken the program, 90% said they would recommend the program to a colleague.

PROGRAM CONTENT

COMMUNICATION SKILLS

CEUs offered: 1

Enhance your communication skills with NICU parents. Learn to act as a coach and mentor to parents; best techniques for delivering bad news; involving parents in collaborative decision-making; principles of trauma-informed care and talking with parents in crisis; and provision of culturally competent care.

PROVIDING EMOTIONAL SUPPORT TO PARENTS

CEUs offered: 1

Recognize NICU parents' increased risk for perinatal mood and anxiety disorders, especially postpartum depression and post traumatic stress disorder; risk factors for these conditions; how to screen for them; and how to provide support to parents to mitigate their risks.

FAMILY-CENTERED DEVELOPMENTAL CARE

CEUs offered: 1

Identify key strategies for involving parents in the developmental care of their NICU baby; how to act as a coach and mentor to parents; how to empower parents; the importance of involving parents to decrease their risk for developing postpartum depression; and the critical importance of skin-to-skin care.

PEER-TO-PEER SUPPORT

CEUs offered: 1

Describe benefits to parents that peer support provides; different models for providing such support; how to start and sustain a peer support program; how to train and what to expect from peer mentors.

PALLIATIVE AND BEREAVEMENT CARE

CEUs offered: 1

Describe key differences between palliative and bereavement care; how and when palliative care should be offered as an alternative to intensive care; components of palliative care programs; and how to talk with parents when their baby is dying or has died.

DISCHARGE PLANNING AND FOLLOW-UP

CEUs offered: 1

Recognize the importance of discharge planning beginning with the NICU baby's admission; how parents can be provided with emotional support leading up to discharge and beyond; and how NICU staff can prepare parents and ease their family's transition to home.

SUPPORTING STAFF AS THEY SUPPORT FAMILIES

CEUs offered: 1

Identify risk factors for burnout, compassion fatigue and secondary traumatic stress syndrome and how to mitigate them; adverse effects of working in intensive care; elements of self-care; and how to create a supportive staff culture.

ABOUT THE PROGRAM

CEUs offered: 0

Optional: Information about program content creators, including our NICU parent graduates who are experts by experience, how the program was created, and what your NICU should do next.

Cost

- RNs and NNPs: $10/CEU; $70 for the full program
- Physicians, licensed clinical social workers (LCSWs), licensed professional clinical counselors (LPCCs) licensed marriage and family therapists (LMFTs): $35/CEU; $245 for the full program..
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- The program is available for entire NICU staffs to take at the same time, complete with an online Discussion Forum throughout all lessons. Contact sara@mynicunetwork.com to learn more.

Faculty

Jenene Craig, PhD, MBA, OTR/L, CNT
Program Director, Fielding Graduate University
Infant and Early Childhood Development Program (IECD) Board member, National Perinatal Association, Metro Atlanta, GA.

Cheryl Milford, EdS
Consulting NICU and Developmental Psychologist, Director of Development, National Perinatal Association, Huntington Beach, CA.

Sage N. Saxton, PsyD
Clinical Psychologist and Associate Professor of Pediatrics and Neonatology, Oregon Health and Science University, Portland, OR.

Sue L. Hall, MD, MSW, FAAP
Neonatologist, St. John's Regional Medical Center, Oxnard, CA,

Sara Mosher, RN, MHA
NICU Nurse and Founder of Patient+Family Care, Bend, OR.

Tiffany Moore, PhD, RN.
Assistant Professor, University of Nebraska Medical Center, College of Nursing, Omaha, NE.

Keira Sorrells, BSFCS
Preemie Parent and Founder and Executive Director of the NICU Parent Network, Jackson, MS.

CANCELLATIONS AND REFUNDS

- **For Individual Subscribers:**
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For Physicians: This activity has been planned and implemented in accordance with the Institute for Medical Quality and the California Medical Association's CME Accreditation Standards (IMQ/CMA) through the Joint Providership of the Perinatal Advisory Council: Leadership, Advocacy and Consultation (PAC/LAC) and the National Perinatal Association. PAC/LAC is accredited by the Institute for Medical Quality/California Medical Association (IMQ/CMA) to provide continuing education for physicians. PAC/LAC takes responsibility for the content, quality and scientific integrity of this CME activity. PAC/LAC designates this activity for a maximum of 7 AMA PRA Category 1 Credit(s)TM. Physicians should only claim credit commensurate with the extent of their participation in the activity. This credit may also be applied to the CMA Certification in Continuing Medical Education.

For Nurses: The Perinatal Advisory Council: Leadership, Advocacy and Consultation (PAC/LAC) is an approved provider by the California Board of Registered Nursing Provider CEP 5862. When taken as a whole, this program is approved for 8 contact hours of continuing education credit.

For CAMFT: Perinatal Advisory Council: Leadership, Advocacy, and Consultation (PAC/LAC) is approved by the California Association of Marriage and Family Therapists to sponsor continuing education for LMFTs, LCSWs, LPCCs, and LEPs. CE Provider #128542. PAC/LAC maintains responsibility for the program and its content. Program meets the qualifications for 7 hours of continuing education credit for LMFTs, LCSWs, LPCCs, and/or LEPs as required by the California Board of Behavioral Sciences.

For OT/PT/SLP: While CEUs are not yet available for licensed neonatal therapists (OT, PT, SLP or RCP), they are invited to take the program as individuals for $10/course. If taking as part of an entire NICU staff, the only charge is an administrative fee of $10/therapist for the entire program.

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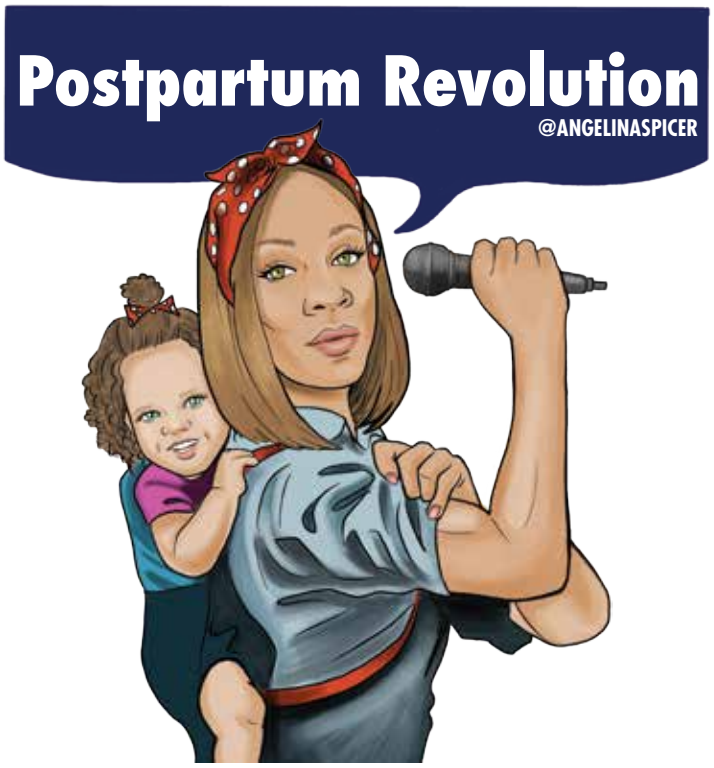

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Fellow's Column: An Extremely Premature Infant with Atypical Physical Characteristics

Maribel Martinez, MD, Sagar Patel, MD, Nitin Walyat, MD, Shabih Manzar, MD

Dr Martinez is a pediatric resident at Louisiana State University Health Sciences Center Shreveport. She and Dr. Patel are both Senior Residents in the program.

Case Report:

A premature infant born at 25 weeks and 6 days via urgent cesarean-section secondary to premature rupture of membranes and chorioamnionitis. Prenatal history was significant for poor prenatal care and perinatal ultrasound consistent with protruding abdominal wall mass suspecting omphalocele. At the time of delivery, resuscitation was required secondary to prematurity. Initial APGAR scores of 1, 5, 7 at 1, 5, and 10 minutes of life were given. After initial stabilization, including intubation and surfactant administration, he was admitted to the Neonatal Intensive Care Unit (NICU), and standard treatment was provided. Initial physical examination was significant for large for gestational age at 96.6% for weight (1.230 kilograms) head circumference at 81% for age (25.5cm), presence of small bilateral preauricular pits and 4-cm omphalocele with intact viable bowel. Omphalocele was surgically corrected. Infant continued to grow, and by 1 month of age, he was noted to have facial coarsening and macroglossia (protruding and prominent tongue). A renal ultrasound (US) was obtained secondary to oliguria, which revealed bilateral prominent hydronephrosis.

Final Diagnosis:

Due to omphalocele, macroglossia, and bilateral hydronephrosis genetic testing for Beckwith-Wiedemann (BWS) obtained via molecular analysis. Results were consistent with diagnosis of BWS showing hypomethylation of cyclin-dependent kinase inhibitor IC2 -LIT1 on chromosome 11p15.

"Prenatal history was significant for poor prenatal care and perinatal ultrasound consistent with protruding abdominal wall mass suspecting omphalocele."

Hospital Course:

The infant remained under the care of neonatology for 136 days. His course was complicated by multiple surgical procedures for corrections of omphalocele, bowel atresia with small bowel resection, and interventional drainage of an abdominal abscess. Other complications included large PDA with ibuprofen treatment, anemia requiring multiple transfusions, retinopathy of prematurity stage 3, microcolon and intraventricular hemorrhage grade 3 bilaterally. He was discharged on enteral feeds via gastrostomy tube feeds and on room air. The infant has since undergone multiple keyhole tongue reduction procedures. His last ultrasound showed normal liver and hyperechoic kidneys. He follows with pediatric gastroenterology, hematology, OMFS, and developmental clinic.

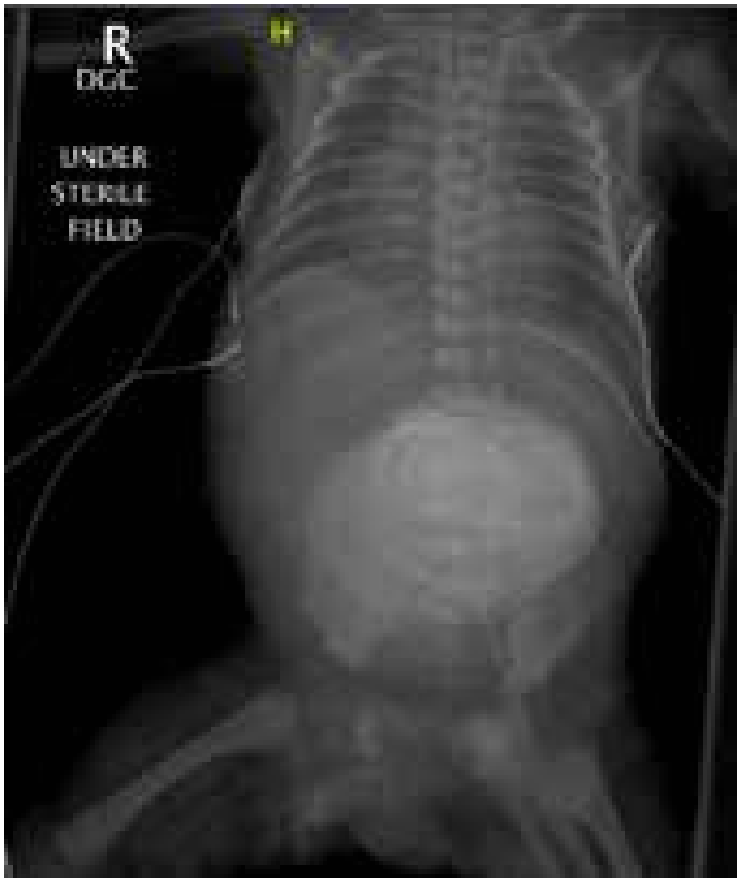

Figure 1 . Initial radiographic study of premature infant with ompahalocele

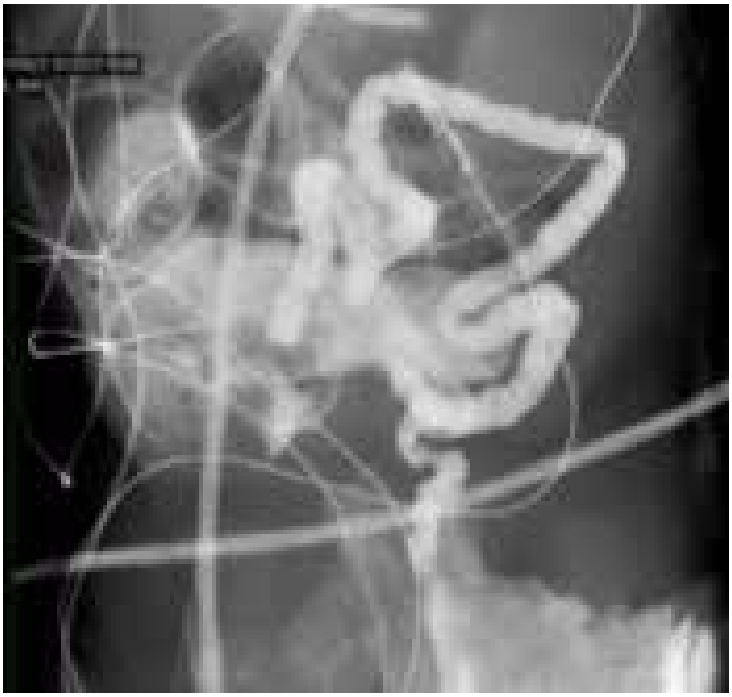

Figure 2. Image 2: Gastrointestinal study of our patient demonstrating microcolon

"Recognizing the classical findings can be a challenge when dealing with extremely premature infants. As demonstrated in this case report diagnosis may or may-not change acute management; however it is important to obtain genetic analysis due to the follow up medical care that is needed."

Discussion:

Beckwith-Wiedemann Syndrome is a rare pediatric genetic growth disorder associated with various physical and metabolic abnormalities. BWS individuals can display variability in clinical presentation. The classic physical findings include macrosomia, macroglossia, and hemihyperplasia 1. In the neonatal period, recurrent episodes of hypoglycemia and macroglossia are typically present 2. A literature review has a few documented cases of a neonatal diagnosis of BWS with no documented cases in extremely premature infants. Macroglossia and macrosomia are generally present at birth but may have postnatal onset 2,3. Our patient, unfortunately, born at 25-weeks gestation, the classical characteristics of BWS were initially masked. BWS leads to overgrowth stimulation due to epigenetic and genetic modifications in two regions of chromosome 11p15. The estimated prevalence of BWS is 1 in 13700, with an average of 300 children born per year.(1,4) The main areas affected include loss of methylation of maternal chromosome in imprinting center IC2, a gain of methylation on the maternal chromosome in imprinting center 1 (IC1) or paternal uniparental disomy for chromosome 11p15 (NCBI). These areas are involved in fetal growth and growth restriction via cyclin-dependent kinases. Cyclin-dependent kinases are involved in the regulation of cell cycle and require binding to cyclin to be active. (2,4-5) Inhibitors of these enzymes act to distort the binding leading to suppression of growth. In BWS, this regulation is lost, causing continued activation of kinase leading to the overgrowth phenomenon. The loss of inhibition also contributes to increased risk of developing tumors. Half of all affected individuals will have a loss of methylation at the IC2 region of the maternal chromosome, while up to 30% of patients have paternal uniparental disomy. (2,5-6) Another 5% of patients have a gain of methylation in the IC1 region of the maternal chromosome 5-8. Up to 85% of individuals with a diagnosis of BWS have no family history of this genetic disorder 8.

A clinical diagnosis of BWS can be made based on physical findings. However, it is recommended that patients undergo genetic testing to identify further the area affected. Treatment for BWS includes treating the manifestations when possible. Close monitoring for hypoglycemia, repairing the abdominal wall defects, and tongue reduction surgery to limit feeding and speech complications. (2) Surveillance for embryonic tumors via abdominal ultrasound is recommended every 3-6 months of age until 8 years of age. (2,9) A renal ultrasound should be performed at least once a year. Laboratory monitoring using alpha-fetoprotein (AFP) is recommended every 2-3 months until 4yrs of age aids in detecting hepatoblastomas. (2) Up to 8% of patients with BWS develop tumors during the first 8 years of life. (6,10) Genetic counseling should be offered to families of affected individuals.

Conclusion:

Diagnosis of BWS should be suspected when polyhydramnios, wall defects, and other organ anomalies are visualized on prenatal ultrasound or initial exam. (4,8) Recognizing the classical findings can be a challenge when dealing with extremely premature infants. As demonstrated in this case report diagnosis may or may-not change acute management; however it is important to obtain genetic analysis due to the follow up medical care that is needed.

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NT

Maribel Martinez, MD
Resident
Department of Pediatrics
College of Medicine
Louisiana State University of Health Sciences
Shreveport, LA

Sagar Patel, MD
Resident
Department of Pediatrics
College of Medicine
Louisiana State University of Health Sciences
Shreveport, LA

Nitin Walyat, MD
Attending
Department of Pediatrics
Division of Neonatology
College of Medicine
Louisiana State University of Health Sciences
Shreveport, LA

Corresponding Author

Shabih Manzar, MD
Attending
Department of Pediatrics
Division of Neonatology
College of Medicine
Louisiana State University of Health Sciences
1501 Kings Highway
Shreveport, LA 71130
Telephone: 318-626- 4374
Fax: 318-698-4305
Email: smanza@lsuhsc.edu

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- QI/QA work, case studies, or a poster from a scientific meeting may be submitted..
- Submission should be from a resident, fellow, or NNP in training.
- Topics may include Perinatology, Neonatology, and Younger Pediatric patients.
- No more than 7 references.
- Please send your submissions to:

Elba Fayard, MD
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lomalindapublishingcompany@gmail.com

FROM THE NATIONAL PERINATAL INFORMATION CENTER: *TRANSITIONS*

Janet H. Muri, MBA; Elizabeth Rochin, PhD, RN, NE-BC; and Jean Salera-Vieira, DNP, PNS, APRN-CNS, RNC

The National Perinatal Information Center (NPIC) is driven by data, collaboration and research to strengthen, connect and empower our shared purpose of improving patient care.

For over 30 years, NPIC has worked with hospitals, public and private entities, patient safety organizations, insurers and researchers to collect and interpret the data that drives better outcomes for mothers and newborns.

"Nothing endures but change" (Heraclitus) (1)

As summer wanes and we move back to our fall routines, many think about the fleeting warmth of summer or the relief from the summer heat. As is always the case, all perspectives are relative and how we manage expected or unexpected transitions depends on the nature of the event as well as our personal or collective mindset regarding change.

In our maternal/child health world, most transitions are expected and joyful—the birth of a healthy newborn. Unfortunately we also know that unexpected events happen, such as a traumatic birth experience or unexpected admission to a NICU - calling on the family and care team to manage a transition to a new reality that is sometimes immediate, heartbreaking and not always with a script on how to cope.

Caregivers are working hard to learn how best to support families through transitions - both positive and unfavorable. Clinicians find themselves within transitions frequently, and therefore find personal and professional satisfaction when they can assist others through these types of life transitions. Such an example of this work is supporting intended parents in their transition to parenthood.

Dr. Jean Salera-Vieira is a Perinatal Clinical Nurse Specialist in Rhode Island, and just completed her doctoral work examining postnatal supports for "intended parents", also known as commissioning parents; e.g. those who become parents through a surrogate or gestational carrier. Dr. Salera-Vieira identified a gap in postnatal support services for this population of parents who must manage their exciting and welcomed transition within a system that may not have a clearly defined place for them to receive support after the newborn arrives. (2) This gap was further identified through a mixed-methods survey of randomly chosen postpartum nurses who are members of the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN). In brief, the survey responses identified greater postnatal supports for mothers over fathers, and a gap in population-specific support services for intended parents. One qualitative response is representative of other responses, stating "We currently do not have any postnatal support services for intended parents."

Parents need support as they transition to parenthood. Hospitals may have programs that support more "traditional" parents through breastfeeding or postpartum support groups but may not have readily evident support systems in place for non-traditional intended parents. Intended parents may deliver in a community far from their home, or perhaps even their country, without their own support system within easy reach. Intended parents with an infant in the NICU face an additional challenge and will benefit from the same support systems as other parents, including referrals to community resources that will provide support after hospital discharge for both parents and infants. Recommendations from Dr. Salera-Vieira's work include exploration of current postnatal support programs, and then expanding those supports to include all parents.

Healthcare itself faces a multitude of transitions on an ongoing basis…new and innovative procedures; improved outcomes for conditions that were once considered impervious to treatment; electronic documentation and the list goes on. Transition and change are difficult, even when they represent a positive shift. Change and transition is always easier when there is an understanding of its purpose, and the intended outcomes that are expected. Dr. Afaf Meleis, a noted scholar and expert in transition theory, recognizes transitions that are both planned and unplanned, and consist of dynamic stages and milestones. (3) These stages and milestones, while unique between each individual, family, or community, are similar in nature, and provide a rich context for supporting those experiencing transition. Familiar transitions within neonatology are, and certainly not limited to:

1. Intrauterine to extrauterine life

2. Isolette to open crib
3. Intensive care to intermediate care
4. Step-down care to home

These types of transitions, despite being very positive for both providers and parents, can be stressful and difficult. How we approach these transitions provides the foundation for adaptation and growth. As providers and caregivers, we have an obligation to support transitions within our teams, organizations, and for the patients we serve and care for. And for the intended parents described in Dr. Salera-Vieira's work? We owe it to these families to provide stability, support and compassion through their transition to parenthood. Many of these families have fought for their right to parent, and we serve as a beacon of hope to them and their newfound parenthood.

As we close out this August column, we want to share NPIC's own exciting transition. On August 1st, Elizabeth Rochin, Ph.D., RN, assumed the presidency of the National Perinatal Information Center. Dr. Rochin, previously with the Association of Women's Health, Obstetric and Neonatal Nurses, is committed and dedicated to improving perinatal health and outcomes. With thirty years of nursing experience, including bedside care, education and administration, Dr. Rochin is well positioned to lead NPIC along throughout its own transitions, and into a new phase of innovation, development and growth. Having spent time researching patient engagement and activation through a population health lens, there are unique opportunities to leverage that knowledge and expertise within data analytics.

Dr. Rochin will take the lead on future columns supported by NPIC staff and, at times, guest columnists. Please feel free to reach out to Dr. Rochin at Elizabeth.Rochin@npic.org.

Resources

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The author has not indicated any disclosures.

NT

Corresponding Author

Janet H. Muri, MBA
Past President
National Perinatal Information Center
225 Chapman St. Suite 200
Providence, RI 02905
401-274-0650
inquiry@npic.org

Elizabeth Rochin, PhD, RN, NE-BC
President
National Perinatal Information Center
225 Chapman St. Suite 200
Providence, RI 02905

Jean Salera-Vieira, DNP, PNS, APRN-CNS, RNC
Perinatal Clinical Nurse Specialist
National Perinatal Information Center
225 Chapman St. Suite 200
Providence, RI 02905

An Update on Infants and Clinical Trials Diversity

Darby O'Donnell, JD
Alliance for Patient Access (AfPA) Government Affairs Team

The Alliance for Patient Access (allianceforpatientaccess.org), founded in 2006, is a national network of physicians dedicated to ensuring patient access to approved therapies and appropriate clinical care. AfPA accomplishes this mission by recruiting, training and mobilizing policy-minded physicians to be effective advocates for patient access. AfPA is organized as a non-profit 501(c)(4) corporation and headed by an independent board of directors. Its physician leadership is supported by policy advocacy management and public affairs consultants. In 2012, AfPA established the Institute for Patient Access (IfPA), a related 501(c)(3) non-profit corporation. In keeping with its mission to promote a better understanding of the benefits of the physician-patient relationship in the provision of quality healthcare, IfPA sponsors policy research and educational programming.

Earlier this summer, the Food and Drug Administration (FDA) issued draft guidance entitled, "Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry." This guidance was not focused on any one age group - and not specifically on the enrollment of the infant population - but about broadening eligibility criteria to improve retention of clinical trials patients and access to clinical trials.

Where are we now with infants and participation in clinical trials?

The NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development notes that four million infants are born each year in the United States. Of those, about 380,000 are born each year prematurely, per information available from the March of Dimes. This is important because premature birth (birth before 37 weeks of pregnancy) and its complications are the number one cause of death of babies in the United States. Yet, new treatment options for newborns are poorly lagging. In fact, the last currently available drug tested and approved specifically for newborns was approved about 20 years ago. (1)

In 2018, the Coalition for Clinical Trials Awareness (CCTA) dedicated its annual Clinical Trials Awareness Week (April 30-May 4, 2018) to the need for age diversity in research on new drugs. Andrew Rosenberg of the Newborn Health Initiative brought an economic perspective to the issue. About 200,000 newborns require admission to NICU for prematurity treatments, Rosenberg explained, costing about $26 billion each year. There are also some conditions for which drugs are needed in neonates that do not occur in older children and adults, he noted, heightening the need for new drug discovery, and thus clinical trials conducted specifically for infants. (2)

"About 200,000 newborns require admission to NICU for prematurity treatments, Rosenberg explained, costing about $26 billion each year. There are also some conditions for which drugs are needed in neonates that do not occur in older children and adults, he noted, heightening the need for new drug discovery, and thus clinical trials conducted specifically for infants. (2)"

Patient groups acknowledge the inherent difficulties in conducting clinical trials on infants, including "pharmaceutical companies and institutional review boards continue to shy away from studying infants because they are fragile, cannot spare many blood samples, and are vulnerable to permanent injuries — injuries that, in the past, have been awarded large malpractice verdicts." (3)

However, researchers and pediatricians in the health care community agree that there is no excuse not to study infants and proper dosage for this vulnerable population.

Infant-Focused Policy Solutions

One solution discussed has been components of the legislation "Promoting Life-Saving New Thera-pies for Neonates Act of 2017" (which has yet to be reintroduced in the 116th Congress). It pro-

posed to amend the Federal Food, Drug, and Cosmetic Act to require the FDA to award the sponsor of a new drug or biological product for the treatment of newborns a neonatal drug exclusivity voucher upon approval of the medication. A neonatal drug exclusivity voucher would be a transferable voucher for a one-year extension of all existing patents and marketing exclusivities for a brand name medication. (4)

Advocates generally support providing incentives such as exclusivity as a way to incentivize re-search that targets treatments tailored to difficult to reach populations - such as newborns.

Another Solution

The draft guidance also focuses in part on making trials less burdensome on participants. In the case of infants, this would have to apply to patients and their families. Trial designs and recruitment should focus on reimbursement of necessary expenses, travel times, locations, and frequency of visits, and further development of online tools to ease the burden of clinical trial participation. One often hears of families with newborns that require additional clinical care or hospitalization, while also managing childcare for multiple children and concerns with balancing a dual-income household. These considerations would provide both financial and logistical stability as families determine if clinical trial participation is right for their child and family.

Policies must be developed to encourage research in treatments for newborns, including finding ways to expand clinical trials targeting these patients. The status quo will have serious ramifications for the health care available to future generations.

Public comment to the FDA's draft guidance may still be submitted at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial.

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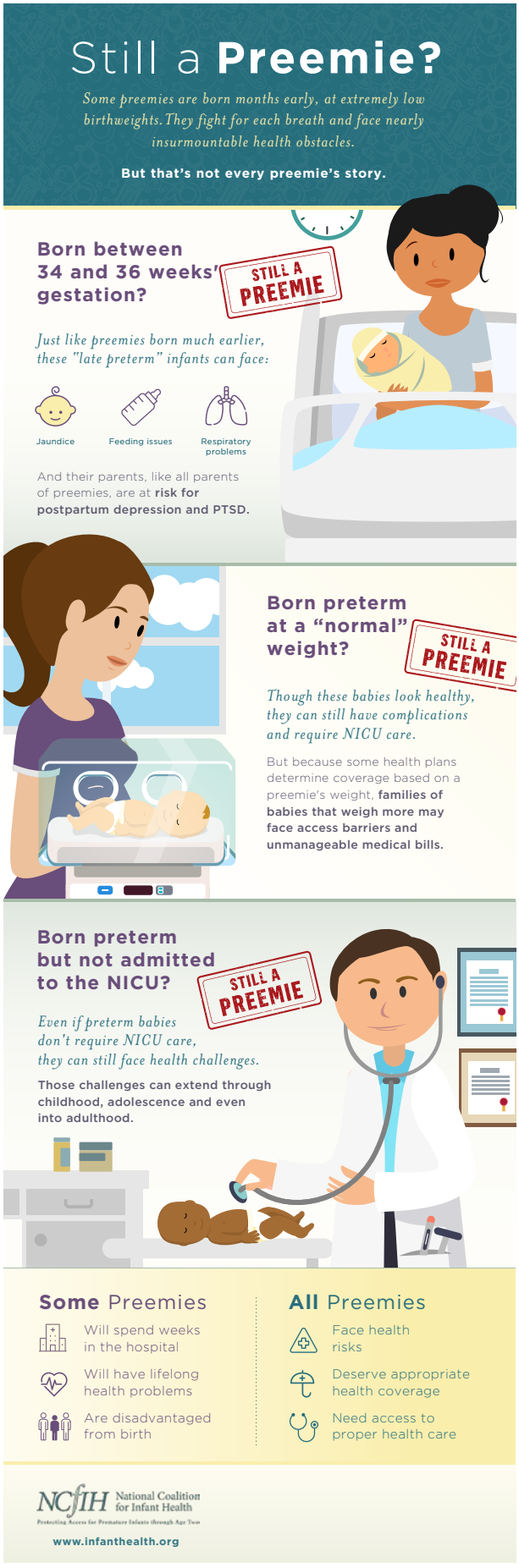

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The author has not indicated any disclosures.

NT

Corresponding Author

Darby O'Donnell, JD
Alliance for Patient Access (AfPA) Government Affairs Team
1275 Pennsylvania Ave. NW, Suite 1100A Washington, DC 20004-2417
202-499-4114
info@allianceforpatientaccess.org

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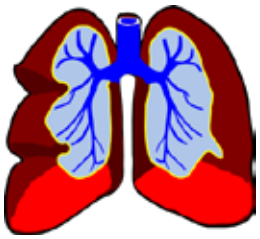

September 6, 2019
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Department of Pediatrics
Division of Neonatology

UR MEDICINE

Course Description

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- Discuss the principals of lung protective ventilatory strategies.
- Describe disease specific management of the neonatal patient
- Display a working knowledge of the technical aspects of the Bunnell Jet Ventilator, 3100A and 3100B ventilators.

Commercial Support Acknowledgment

This symposium and workshop is supported by a generous donation from Bunnell. ABG analyzers graciously provided by Siemens Diagnostics.

Continuing Education Credit

8.0 CEUs have been approved by the American Association for Respiratory Care (AARC) for continuing respiratory care education.

Location

The day will begin in the Center for Experiential Learning Rm # 2-7536/2-7544
University of Rochester Medical Center
601 Elmwood Ave
Rochester, NY 14642

Agenda

7:30-8 Welcome and Course Introduction
Patricia Chess, MD and Pamela Brown, RRT

8:00-8:55 History of Ventilation
Peter Papadakos, MD

9:00-10:00 Case review-Pediatric Cardiology
Joseph Kuebler, MD, MBA

Group A Lecture ~ Group B Animal Lab

*10:10-11:*00 and 2-*2:50*
Lung Protective Ventilation
Evan Richards, RRT

11:10-12:00 and 3-3:50
APRV Concepts
Joseph Manes, RRT

12:00-1:00 Lunch

1:00-2:00 High Frequency Oscillatory Ventilation in Brand New Baby Lung
Brian Jordan, MD, PHD

Group A Animal Lab ~ Group B Lecture

Reconvene in Lecture Hall

4:00-4:30 Closing and Discussion

Program Faculty

GOLISANO CHILDREN'S HOSPITAL

Brian Jordan, MD, PHD
Assistant Professor of Pediatrics, Division of Neonatology, School of Medicine
Oregon Health and Science University

Patricia Chess M.D.
Professor of Pediatrics and Biomedical Engineering
University of Rochester Medical Center

Peter Papadakos M.D.
Professor of Anesthesiology and perioperative medicine
University of Rochester Medical Center

Joseph Manes, RRT
Account Manager Hamilton Medical

Evan Richards, RRT
Critical Care Specialist
Bunnell Incorporated

Joseph Kuebler, MD, MBA
Assistant Professor of Pediatrics
University of Rochester Medical Center

Pamela Brown, RRT
Director of Respiratory Care
Golisano Children's Hospital
University of Rochester Medical Center

Acknowledgements

Jeff Wyatt, DVM, MPH, DACLAM
Professor & Chair Comparative Medicine

Dana LeMoine, DVM
Chief of Large Animal Medicine

Michael Barravecchia, LVT
Robin Westcott, LVT, LATG

Registration

Contact Pamela Brown 585-275-3830
Email
pamelap_brown@urmc.rochester.edu
Cost:
Respiratory Therapists—$150.00
Physicians— $200.00
Please make cheques payable to URMC
Registrant Information:

Name _____

Credentials_____

Hospital _____

Telephone _____

E-Mail _____

Address _____

Send Payment and Registration Form to:

Pamela Brown, RRT
University of Rochester Medical Center
BOX 317
601 Elmwood Ave
Rochester, NY 14642
585-275-3830
Fax Registration to: Respiratory Care
585-275-0120
Please register by August 25, 2019

A block of rooms have been reserved at the Staybridge Suites September 5th and 6th. Please phone 585-613-3400 for reservations and mention you are with the URMC HFV Symposium

Evening Reception

Please join us at the Genesee Brew House

25 Cataract Street, Rochester, NY 14605

September 5, 2019

4pm-7pm

Please take the Yellow elevators to the second floor and follow the signs.

If you need assistance please ask an Ambassador.

601 Elmwood Ave Box 317
Rochester, NY 14642
Phone 585-275-3830
Fax 585-275-0120
Email
pamelap_brown@urmc.rochester.edu

OPIOIDS and NAS

When reporting on mothers, babies, and substance use

LANGUAGE MATTERS

I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).

I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.

NAS is a temporary and treatable condition.

There are evidence-based pharmacological and non-pharmacological treatments for Neonatal Abstinence Syndrome.

My mother may have a SUD.

She might be receiving Medication-Assisted Treatment (MAT). My NAS may be a side effect of her appropriate medical care. It is not evidence of abuse or mistreatment.

My potential is limitless.

I am so much more than my NAS diagnosis. My drug exposure will not determine my long-term outcomes. But how you treat me will. When you invest in my family's health and wellbeing by supporting Medicaid and Early Childhood Education you can expect that I will do as well as any of my peers!

Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org

National Perinatal Association

NT

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Learn more about
Neonatal Abstinence Syndrome
at www.nationalperinatal.org

National Perinatal Association

Compiled and Reviewed by Mitchell Goldstein, MD Editor in Chief

Of Mice And Babies: New Animal Model Links Blood Transfusions to Dangerous Digestive Disease in Preemies

Johns Hopkins Medicine-led study also suggests likely mechanism, potential therapies

08/12/2019

Newsroom: A laboratory mouse feeds her newborn pups that are about the size of a quarter and weigh less than an ounce. A Johns Hopkins Medicine-led research team has overcome previous problems working with infant mice to develop a model for studying a devastating gastrointestinal disease that strikes premature babies with anemia. Credit: The Jackson Laboratory

Physicians have long suspected that red blood cell transfusions given to premature infants with anemia may put them in danger of developing necrotizing enterocolitis, or NEC, a potentially lethal inflammatory disease of the intestines. However, solid evidence for the connection has been difficult to obtain in part because of the lack of a practical animal model able to accurately represent what physically occurs when a baby gets NEC.

Now, researchers at Johns Hopkins Medicine report they have developed that model — believed to be the first of its kind — using infant mice, or pups, that are first made anemic and then given blood transfusions from neonates of a different mouse strain. The new method, the researchers say, mimics what happens when blood transfusions are given to human babies from a non-related donor.

A description of the mouse model, along with significant findings and potential benefits from its first uses, is published in a new paper in the journal Nature Communications.

"We needed a working live mouse model in order to learn if a blood transfusion alone leads to NEC or does it only happen if the transfusion is given when anemia is present," says Akhil Maheshwari, M.D., professor of pediatrics at the Johns Hopkins University School of Medicine, director of neonatology at the Johns Hopkins Children's Center, and senior author of the research paper.

Seen in approximately 10% to 12% of infants weighing less than 3.5 pounds at birth, NEC is a rapidly progressing gastrointestinal emergency in which bacteria invade the wall of the colon, causing inflammation that can ultimately destroy healthy tissue at the site. If enough cells are necrotized (killed) that a hole results in the intestinal wall, fecal material can enter the bloodstream and cause life-threatening sepsis.

Since 2004, Maheshwari says, research studies have repeatedly shown that babies born prematurely who are severely anemic — those with a proportion of red blood cells to total blood volume between 20% and 24% at birth — can develop NEC within 48 hours after receiving a red blood cell transfusion. By comparison, the American Academy of Pediatrics says that babies delivered at term normally have red blood cell volumes between 42% and 65%, dropping to between 31% and 41% at age 1.

CALL FOR ABSTRACTS

The 33rd Annual Gravens Conference on the Environment of Care for High Risk Newborns

March 4-7, 2020

Abstract due date is October 28, 2019. Late Abstracts will not be accepted.

The Gravens Conference is dedicated to providing a forum for the continuing education of NICU professionals. In particular, the conference focuses on the science of fetal and infant development, developmental care practices, NICU design, family support programs, and the influential role the NICU environment has on the neurodevelopment of the infant, and the well-being of families and staff.

The conference committee invites you to submit an abstract for a variety of presentation options: oral abstract session (20-ish minutes), workshop session (75 minutes), or poster presentation, regarding NICU design, the study of creative approaches to developmental and environmental issues of the NICU, care practices and/or programs to assist staff, parents and families. This conference offers an opportunity to share your work and experiences with colleagues.

The theme for the 2020 conference is *Biophysiology of Human Interaction.* However, the abstracts may be on any applicable NICU topic.

Abstracts should include the following sections, as applicable.

1. Abstract Title
2. Authors' names, degree(s), and institution
3. Background and Purpose: problem statement or hypothesis as appropriate
   What is the hypothesis, or what is the problem you are trying to solve, or what is your scientific question? Why is it important? State this in one or two sentences
4. Budget and Resources: cost of program and materials as appropriate
5. Program, Materials, or Methodology: also include any barriers to implementation and how they have been overcome
   What methods did you use to solve or research the problem? How did you collect your data? How big was your sample size? What were the main outcome measurements? This will probably be the longest part of your abstract.
6. Impact or Results: major accomplishment of program/materials; qualitative and quantitative data*; evidence-based results. *If providing data, it must exist; "data to be obtained by conference date" is no longer acceptable.
7. Bibliography: for oral presentations, at least 3 related references that support the program
8. Learner Objectives: 2-3

In the body of the email, please list the following:

1. Title of the abstract
2. Author's name, degree(s), credentials, and position title
3. Author's email address
4. Name of institution, city, and state. City and country if outside the US.
5. If the contact person is someone other than the author, please note that in the body of the email
6. Presentation preference: a) oral abstract session, b) workshop session, c) poster only, or d) no preference. (Please spell it out rather than provide just a lower case letter.)

Length of abstract: 1000 words maximum

Format: WORD, preference is Arial 12 pt, but font choice is optional.

Send abstract as an email attachment to Bobbi Rose at brose@health.usf.edu

You will get a reply within a day or two that the abstract was received. If you do not hear back, please call Bobbi Rose at (813) 974-6158, or send another email. Decisions by the abstract review committee for oral considerations are expected by early December 2019. Notification will be by email. **The conference does not provide any support for abstract presenters, regardless of presentation outcome. Abstract presenters must register to attend the conference.**

In search of a useful and practical mouse model, Maheshwari and his colleagues had to overcome a size problem.

"Newborn mouse pups are about the size of a quarter and weigh less than an ounce, so it's extremely difficult to remove enough blood from them for laboratories to analyze," Maheshwari says.

To get past that obstacle, a private medical diagnostic equipment company donated the use of its advanced blood analysis system that only requires a 5 microliter (5 millionths of a liter) sample instead of the 50 microliters — 60% of a mouse pup's total blood supply — that most testing labs require.

Next, the researchers designed a procedure to induce severe anemia in the pups by removing about half of their blood volume every other day for 10 days after birth. This dropped their red blood cell counts to levels approximating those in severely anemic newborn babies.

Seven days after birth, the researchers introduced bacteria that had been isolated and cultured from a premature infant with NEC. Finally, red blood cell transfusions were given on the 11th day after birth.

Over the next 48 hours, the researchers looked for development of NEC-like symptoms in their experimental group and three other sets of mouse pups: (1) a control group without any intervention, (2) a group without anemia that received transfusions and (3) a group with anemia but not transfused.

"Only the severely anemic pups who received blood transfusions showed intestinal damage that resembled human NEC with necrosis, inflammation and separation of the tissues supporting the lining of the colon," Maheshwari says. "The next step was to see if we could find a mechanism for why this occurred."

Examining the blood of the pups with NEC-like conditions after they were transfused, the researchers discovered that it contained three components not seen in the blood of the other test mice: (1) a large number of macrophages, the immune cells that engulf and digest cellular debris, bacteria and viruses, (2) freely circulating hemoglobin, the iron-based molecules that normally carry oxygen throughout the body when attached to red blood cells, and (3) elevated levels of inflammation-inducing proteins, indicating that the macrophages had been activated even without a biological threat to the intestine.

The researchers also observed that levels of haptoglobin, a protein that removes free hemoglobin from the blood, were extremely low.

"These findings suggest that anemia reduces the amount of haptoglobin in the neonate, preventing the free hemoglobin that comes in via transfusion from being properly removed as it normally would," Maheshwari says.

What apparently happens, he says, is that free hemoglobin attaches to a protein receptor on the intestinal wall that is the same site where bacterial poisons bind. As a result, the immune system mistakenly believes the intestine is being attacked and activates the macrophages.

Once those immune cells go to work, Maheshwari explains, they trigger release of the inflammatory proteins seen in the blood of the anemic, transfused mice. "That event starts a double whammy on the intestinal wall," he says. "First, the macrophage proteins inflame and weaken the tissues, making them vulnerable, and then, bacteria move in and produce endotoxins that kill the individual cells."

With evidence for a probable mechanism to explain the connection between anemia and transfusion in the development of NEC, the researchers next sought to confirm it by seeing if they could block two of its stages, and perhaps, advance the search for potential therapies.

"In one trial, we gave haptoglobin to our model anemic mice before transfusing them and blocked macrophage activation, so they did not develop NEC-like symptoms," Maheshwari says.

In another test, nanoparticles that Samuel Wickline, M.D., and his colleagues at the University of South Florida developed were used to deliver a genetic interruption — an RNA molecule known as a small interfering RNA, or siRNA — that blocks the chemical signal telling macrophages to start producing inflammatory proteins. The nanoparticles were tagged with a fluorescent dye to track their movement and included a non-toxic compound derived from honeybee venom.

Maheshwari says the macrophages in the blood of anemic mouse pups engulfed the nanoparticles and enclosed them within vacuoles. The bee venom derivative, he explains, broke open the vacuoles so that the siRNA could be released inside the macrophages.

The genetic signal blocker worked well, Wickline says, protecting the anemic mouse pups from intestinal inflammation after red blood cell transfusions.

"Because we showed that the inhibitory nanoparticles with siRNAs were able to control a master regulator of inflammation in NEC, perhaps this technology can one day be applied to not only treat or prevent NEC, but other diseases where inflammation plays a key role such as arthritis and atherosclerosis," he says.

Maheshwari says he hopes the new mouse model and the findings from the current study can be used to develop blood bio-

markers that could indicate which human newborns are most at risk of developing NEC.

Funding for this investigation came from National Institutes of Health (NIH) awards HL124078 and HL133022, and American Heart Association award 14GRNT20480307, given to Maheshwari; and NIH awards HL073646, DK102691 and AR067491, given to Wickline. Sysmex America donated the use of its automated veterinary hematology analyzer that made possible the mouse model developed in this study.

Collaborating on the study were researchers from the Johns Hopkins University School of Medicine, the Morsani College of Medicine at the University of South Florida, the Yale School of Medicine and the University of Alabama at Birmingham. Along with Maheshwari and Wickline, the team members included lead author Mohan Kumar Krishnan, Kopperuncholan Namachivayam, Tanjing Song, Byeong Jake Cha, Andrea Slate, Jeanne Hendrickson, Hua Pan, Joo-Yeun Oh, Rakesh Patel, Ling He and Benjamin Torres.

Media Contacts

Michael E. Newman
410-502-9463
mnewma25@jhmi.edu

Waun'Shae Blount
4109553195
wblount1@jhmi.edu

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American Academy of Pediatrics, Section on Advancement in Therapeutics and Technology

Released: Thursday 12/13/2018 12:32 PM, updated Saturday 3/16/2019 08:38

The American Academy of Pediatrics' Section on Advances in Therapeutics and Technology (SOATT) invites you to join our ranks! SOATT creates a unique community of pediatric professionals who share a passion for optimizing the discovery, development and approval of high quality, evidence-based medical and surgical breakthroughs that will improve the health of children. You will receive many important benefits:

- Connect with other AAP members who share your interests in improving effective drug therapies and devices in children.
- Receive the SOATT newsletter containing AAP and Section news.
- Access the Section's Website and Collaboration page – with current happenings and opportunities to get involved.
- Network with other pediatricians, pharmacists, and other health care providers to be stronger advocates for children.
- Invitation for special programming by the Section at the AAP's National Conference.
- Access to and ability to submit research abstracts related to advancing child health through innovations in pediatric drugs, devices, research, clinical trials and information technology; abstracts are published in Pediatrics.

AAP members can join SOATT for free. To activate your SOATT membership as an AAP member, please complete a short application at http://membership.aap.org/Application/AddSectionChapterCouncil.

The Section also accepts affiliate members (those holding masters or doctoral degrees or the equivalent in pharmacy or other health science concentrations that contribute toward the discovery and advancement of pediatrics and who do not otherwise qualify for membership in the AAP). Membership application for affiliates: http://shop.aap.org/aap-membership/ then click on "Other Allied Health Providers" at the bottom of the page.

Thank you for all that you do on behalf of children. If you have any questions, please feel free to contact:

Mitchell Goldstein, MD, FAAP, Section Chairperson, MGoldstein@llu.edu and

Christopher Rizzo, MD, FAAP, Membership Chairperson, crizzo624@gmail.com

Jackie Burke

Sections Manager

AAP Division of Pediatric Practice

Department of Primary Care and Subspecialty Pediatrics

630.626.6759

jburke@aap.org

Dedicated to the Health of All Children

# # #

The American Academy of Pediatrics is an organization of 67,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and

young adults. For more information, visit www.aap.org. Reporters can access the meeting program and other relevant meeting information through the AAP meeting website at http://www.aapexperience.org/

NT

Masimo Announces CE Marking of Neonatal Indication for Non-invasive, Continuous Hemoglobin Monitoring (SpHb®)

Non-invasive hemoglobin monitoring for neonates has received CE marking..

Neuchatel, Switzerland – August 5, 2019 – Masimo (NASDAQ: MASI) announced today the CE marking of SpHb®, noninvasive and continuous hemoglobin monitoring, for neonatal and infant patients (< 3 kg). With this clearance, the benefits of SpHb are available for patients of all ages in CE mark countries. SpHb for neonates and infants is provided on rainbow® sensors, which allow clinicians to simultaneously measure multiple additional noninvasive parameters alongside SpHb, including oxygen saturation (SpO2) and methemoglobin (SpMet®).

Masimo Root® with SpHb®and PVi®

Because of their small size, neonates and infants have less blood than older patients. In addition, their lack of bone marrow density makes them far less capable than adults of generating new red blood cells for approximately the first eight months of life. Current invasive methodologies for measuring hemoglobin can only provide intermittent, delayed results. By providing a continuous, noninvasive measurement, SpHb allows clinicians to more closely monitor neonatal hemoglobin status in real time by tracking the stability, or instability, of a patient's hemoglobin trend, providing visibility into changes, or lack of changes, in hemoglobin between invasive blood samples.

On adult patients, continuous monitoring with SpHb has been found to improve outcomes, such as reducing the percentage of patients receiving transfusions,1 reducing the units of red blood cells transfused per patient,2-3 reducing the time to transfusion,4 reducing costs,5 and even reducing mortality 30 days after surgery.6 In addition to hemoglobin, rainbow® sensors monitor SpO_2 using Masimo SET® Measure-through Motion and Low Perfusion™ technology, which has been shown in over 100 independent and objective studies to outperform other pulse oximetry technologies.7 Crucially for newborn health, SET® has been shown to help clinicians reduce severe retinopathy of prematurity in neonates8 and in multiple studies, including the largest critical congenital heart disease (CCHD) study to date, to improve CCHD screening in newborns.(9-10)

The rainbow® family of advanced noninvasive measurements also allows clinicians to use the same single sensor to monitor another physiological parameter particularly important to neonatal care: methemoglobin, using SpMet. SpMet helps clinicians noninvasively and continuously monitor methemoglobin levels in the blood.(11) In neonates and infants, inhaled nitric oxide (iNO) therapy and even topical anesthetics containing benzocaine or prilocaine can cause elevated levels of methemoglobin.(12-13)

Joe Kiani, Founder and CEO of Masimo, said, "We are thrilled to be able to bring the power of noninvasive hemoglobin monitoring with SpHb to the youngest, most fragile patients of all. We have long been dedicated to helping improve the lives of neonatal and infant patients, and this latest clearance significantly furthers that mission. SpHb is already used to monitor adult patients in more than 75 countries. We look forward to witnessing the impact that SpHb will now be able to have on neonatal and infant patients."
SpHb is not intended to replace laboratory blood testing. Clinical decisions regarding red blood cell transfusions should be based on the clinician's judgment considering among other factors: patient con-

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Leadership, Advocacy and Consultation

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- Certified Health Education Specialists (CHES)
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www.paclac.org

PAC/LAC's core values for improving maternal and child health have remained constant for over 30 years – a promise to lead, advocate and consult with others.

Leadership

Providing guidance to healthcare professionals, hospitals and healthcare systems, stimulating higher levels of excellence and improving outcomes for mothers and babies.

Advocacy

Providing a voice for healthcare professionals and healthcare systems to improve public policy and state legislation on issues that impact the maternal, child and adolescent population.

Consultation

Providing and promoting dialogue among healthcare professionals with the expectation of shared excellence in the systems that care for women and children.

dition, continuous SpHb monitoring, and laboratory diagnostic tests using blood samples.

Noninvasive, continuous SpHb has received FDA clearance for patients > 3 kg but is not currently indicated for patients < 3 kg in the US.

@MasimoInnovates || #Masimo

About Masimo
Masimo (NASDAQ: MASI) is a global medical technology company that develops and produces a wide array of industry-leading monitoring technologies, including innovative measurements, sensors, patient monitors, and automation and connectivity solutions. Our mission is to improve patient outcomes and reduce the cost of care. Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry, introduced in 1995, has been shown in over 100 independent and objective studies to outperform other pulse oximetry technologies.7 Masimo SET® has also been shown to help clinicians reduce severe retinopathy of prematurity in neonates,8 improve CCHD screening in newborns,9 and, when used for continuous monitoring with Masimo Patient SafetyNet™ in post-surgical wards, reduce rapid response team activations, ICU transfers, and costs.14-16 Masimo SET® is estimated to be used on more than 100 million patients in leading hospitals and other healthcare settings around the world,17 and is the primary pulse oximetry at 9 of the top 10 hospitals listed in the 2018-19 U.S. News and World Report Best Hospitals Honor Roll.18 Masimo continues to refine SET® and in 2018, announced that SpO2 accuracy on RD SET™ sensors during conditions of motion has been significantly improved, providing clinicians with even greater confidence that the SpO2 values they rely on accurately reflect a patient's physiological status. In 2005, Masimo introduced rainbow® Pulse CO-Oximetry technology, allowing noninvasive and continuous monitoring of blood constituents that previously could only be measured invasively, including total hemoglobin (SpHb®), oxygen content (SpOC™), carboxyhemoglobin (SpCO®), methemoglobin (SpMet®), Pleth Variability Index (PVi®), RPVi™ (rainbow® PVi), and Oxygen Reserve Index (ORi™). In 2013, Masimo introduced the Root® Patient Monitoring and Connectivity Platform, built from the ground up to be as flexible and expandable as possible to facilitate the addition of other Masimo and third-party monitoring technologies; key Masimo additions include Next Generation SedLine® Brain Function Monitoring, O3® Regional Oximetry, and ISA™ Capnography with NomoLine® sampling lines. Masimo's family of continuous and spot-check monitoring Pulse CO-Oximeters® includes devices designed for use in a variety of clinical and non-clinical scenarios, including tetherless, wearable technology, such as Radius-7® and Radius™ PPG, portable devices like Rad-67™, fingertip pulse oximeters like MightySat® Rx, and devices available for use both in the hospital and at home, such as Rad-97™. Masimo hospital automation and connectivity solutions are centered around the Iris® platform, and include Iris Gateway™, Patient SafetyNet, Replica™, Halo ION™, UniView™, and Doctella™. Additional information about Masimo and its products may be found at www.masimo.com. Published clinical studies on Masimo products can be found at www.masimo.com/evidence/featured-studies/feature/.

ORi and RPVi have not received FDA 510(k) clearance and are not available for sale in the United States.

The use of the trademark Patient SafetyNet is under license from University HealthSystem Consortium.

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Forward-Looking Statements
This press release includes forward-looking statements as defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, in connection with the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, among others, statements regarding the potential effectiveness of Masimo SpHb®. These forward-looking statements are based on current expectations about future events affecting us and are subject to risks and uncertainties, all of which are difficult to predict and many of which are beyond our control and could cause our actual results to differ materially and adversely from those expressed in our forward-looking statements as a result of various risk factors, including, but not limited to: risks related to our assumptions regarding the repeatability of clinical results; risks related to our belief that Masimo's unique noninvasive measurement technologies, including Masimo SpHb, contribute to positive clinical outcomes and patient safety; as well as other factors discussed in the "Risk Factors" section of our most recent reports filed with the Securities and Exchange Commission ("SEC"), which may be obtained for free at the SEC's website at www.sec.gov. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we do not know whether our expectations will prove correct. All forward-looking statements included in this press release are expressly qualified in their entirety by the foregoing cautionary statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of today's date. We do not undertake any obligation to update, amend or clarify these statements or the "Risk Factors" contained in our most recent reports filed with the SEC, whether as a result of new information, future events or otherwise, except as may be required under the applicable securities laws.

Evan Lamb
Masimo
Phone: (949) 396-3376
Email: elamb@masimo.com

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SHHS Media Briefing on the Safe Importation Action Plan

FDA has a plan for safe importation of drugs in shortage.

Speech by
Norman E. "Ned" Sharpless, MD
Acting Commissioner of Food and Drugs - Food and Drug Administration

Remarks Prepared for FDA Acting Commissioner Ned Sharpless, M.D.

As Prepared for HHS Media Briefing on the Safe Importation Action Plan July 31, 2019; 8:45 a.m. ET

Good morning. I'm Ned Sharpless, Acting Commissioner for the U.S. Food and Drug Administration. It's a privilege and an honor to serve in this post and represent the FDA's dedicated workforce around the globe, all working in their own unique ways to advance our mission to protect and promote the health of the American public.

As you may know, prior to joining the FDA, I served as director of the National Cancer Institute at NIH since 2017. Before that, I was a cancer researcher and cancer doctor, treating patients with hematologic malignancies for nearly 20 years. Helping patients live better lives is why I got into medicine, it's what drove me to study the molecular mechanisms of cancer and aging, and it's what has now brought me into public service.

We know that increasing drug prices present real challenges for patients and their families. The President and Secretary Azar have been deeply committed to exploring all potential solutions to combat drug prices that protect patient safety, are effective at delivering lower prices, and respect choice, innovation and access. While the FDA doesn't regulate drug prices, we have made a concerted effort to examine our policies and explore ways we can help address this challenge.

But FDA has a unique role to play in promoting competition that in turn can help reduce drug prices and improve access to medicine for Americans and we support the President and Secretary's efforts.

Early on, I vowed that the guiding principles that will steer my priorities as Acting Commissioner are a commitment to science-based decision-making and prioritizing our efforts for the benefit of the public health.

Today's announcement fits within that commitment. The Safe Importation Action Plan we're describing today is the result of the hard work by the dedicated staff of the FDA, in close collaboration with HHS and the White House, to identify potential pathways we can pursue to support the safe importation of certain prescription drugs. We've been keenly focused on ensuring the importation approaches we've outlined would pose no additional risk to the public's health and safety.

Specifically, the Safe Importation Action Plan outlines the government's intention to pursue two pathways to allow safe importation of drugs originally intended for foreign markets:

First, through a notice of proposed rulemaking (NPRM), HHS and FDA would propose to rely on the authority under current federal law that would, when the rule is finalized, authorize pilot (or demonstration) projects developed by states, wholesalers or pharmacists and submitted for HHS review, outlining how they would import certain drugs from Canada that are versions of FDA-approved drugs manufactured consistent with the FDA approval. The NPRM would include conditions to ensure the importation poses no additional risk to the public's health and safety and that the demonstration projects would achieve significant cost savings to the American consumer.

Secondly, in draft guidance, FDA would describe recommendations to manufacturers of FDA- approved drugs who seek to import into the U.S. versions of those drugs they sell in foreign countries. Under this pathway, manufacturers would use a new National Drug Code (NDC) for those products, potentially allowing them to offer a lower price than what their current distribution contracts require. To use this pathway, the manufacturer would establish with the FDA that the foreign version is the same as the U.S. version and appropriately label the drug for sale in the U.S.

Rest assured that protecting patients is the highest priority of the FDA, and Americans can be confident that any efforts in this space will not sacrifice patient safety.

We recognize there are many operational challenges and questions that we need to overcome before these policies can be implemented. We look forward to sharing greater detail on these proposals and we welcome questions as we work through these policies. HHS and FDA will continue to work through these questions and look forward to announcing the NPRM and draft guidance for public comment in the coming months.

We know there will be hurdles ahead of us. In addition to advancing the two pathways we're describing in the Action Plan, we'll also continue our important and successful work through our Drug Competition Action Plan to increase competition and reign in prescription drug costs through advances in our generic drug and biosimilars programs.

Thank you..

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Inquiries

Media:
Sandy Walsh
301-796-4669

Consumer:
888-INFO-FDA

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Online compendium helps navigate neonatal abstinence syndrome care

AAP helps navigate neonatal abstinence syndrome

8/8/2019

ITASCA, IL – Every 15 to 20 minutes, a baby with neonatal abstinence syndrome (NAS) is born in the U.S.

As the opioid crisis grows, the AAP Section on Neonatal-Perinatal Medicine Trainees and Early Career Neonatologists (TECAN) is stepping up efforts to help those who are taking care of mothers and infants affected by NAS.

Navigating NAS, https://aap.org/navigatingnas, is a comprehensive online resource that provides educational materials for clinical practice, resources for families, webinars and social media outreach. Information is provided on opioids and public policy, pregnancy and substance use, caring for the mother-infant dyad with NAS and living with NAS beyond infancy to adolescence.

Pregnant mothers who are addicted to opioids face stigma, guilt and societal judgment, and need support from pediatricians, said TECAN Chair Ashley M. Lucke, M.D., FAAP. Some states press child abuse charges against pregnant women who use opiates or other illicit substances.

“A mom who’s smoking tobacco isn’t having her baby taken away from her after birth because she smoked tobacco during the pregnancy,” she said. “It takes only five pills before you can have an increased propensity for becoming dependent on opioids. This (could happen to) anybody who has had a dental procedure or a car accident.”

Pregnant mothers with an opioid use disorder are at greater risk of sexually transmitted infections, poor nutrition and legal issues. Babies are at higher risk of being born prematurely and having neurodevelopmental disabilities, difficult temperaments and other special needs that will affect all stages of their development.

Navigating NAS connects pediatricians to the latest information for their care.

Legal and advocacy resources are available for those supporting bills, educating legislators, providing testimony and developing action plans.

Dr. Lucke encourages AAP members to speak up for “the moms who really feel so stigmatized and as though they don’t have a voice anymore, but also the babies who are counting on us to help give them the best shot that they have to be healthy and successful and thrive.”

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The American Academy of Pediatrics is an organization of 67,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults. For more information, visit www.aap.org or follow us on Twitter @AmerAcadPeds.

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Depression is the single largest predictor of substance use during pregnancy

Substance use in pregnancy is associated with depression.

Released: 8-Aug-2019 3:05 PM EDT
University of Western Ontario

Newswire - It is well known that tobacco, alcohol, and cannabis use during pregnancy are associated with poor birth outcomes, yet many women continue to use these substances during pregnancy.

Researchers at Western University and its affiliate Brescia University College have now shown that depression is the single largest driver of substance use during pregnancy, highlighting the need for greater supports for the mental health of pregnant mothers.

The research team analyzed health and geographical data gathered through Lawson Health Research Institute from more than 25,000 pregnant women in Southwestern Ontario.

"Pregnant women who were depressed were 2.6 times more likely to use cannabis and twice as likely to smoke cigarettes and use alcohol while pregnant," said Jamie Seabrook, PhD, and Associate Professor at Brescia and Western's Schulich School of Medicine & Dentistry, and Scientist at Children's Health Research Institute, a Lawson program. "We don't know when the substance use first began but we do know that it was continuing during pregnancy and that is a big risk factor for poor maternal and infant health outcomes."

The study, published in the Journal of Neonatal-Perinatal Medicine, is the first Canadian study with a sample size this large to show that depression during pregnancy is the primary risk factor for cannabis, tobacco and alcohol use, and is more important than education, income, or age.

"This really highlights the importance of programming for mental health, including mental health promotion strategies, psychotherapy and safe and proper medication for mental health during pregnancy," said Rachel Brown, an MSc candidate and first author on the paper. "The research shows that there is an effect later on in life as well with infants that are born preterm or low birth weight. To intervene or advocate for mental health programs for the mom, the idea is that it sets up the health of the infants later on in life."

The research team points out that this research is especially important in Canada with the recent legalization of recreational cannabis.

"Let's help women with their mental health to improve their overall health and in do-

ing so, improve the health of their baby," said Seabrook.

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MEDIA CONTACT: Crystal Mackay, Media Relations Officer, Schulich School of Medicine & Dentistry, Western University, t. 519.661.2111 ext. 80387, c.519.933.5944, crystal.mackay@schulich.uwo.ca @CrystalMackay

ABOUT WESTERN

Western University delivers an academic experience second to none. Since 1878, The Western Experience has combined academic excellence with life-long opportunities for intellectual, social and cultural growth in order to better serve our communities. Our research excellence expands knowledge and drives discovery with real-world application. Western attracts individuals with a broad worldview, seeking to study, influence and lead in the international community.

ABOUT BRESCIA UNIVERSITY COLLEGE

Brescia University College, Canada's women's university college, is affiliated with Western University. The 1,500 women registered as either full- or part-time students at Brescia study a wide variety of subjects in the Schools of Behavioural & Social Sciences, Food & Nutritional Sciences, Humanities and Leadership & Social Change in an empowering, compassionate, student-centred and invigorating environment. Degrees are granted by Western. The Catholic University College welcomes students from all backgrounds and values diversity.

ABOUT LAWSON HEALTH RESEARCH INSTITUTE:

As the research institute of London Health Sciences Centre and St. Joseph's Health Care London, and working in partnership with Western University, Lawson Health Research Institute is committed to furthering scientific knowledge to advance health care around the world.###

Despite Improvement, Preterm Black Infants Still Face Gaps in Care and Health Outcomes

Black infants outcomes are still not optimal

8/12/2019

U.S. Neonatal Intensive Care Units (NICUs) have reduced some of the race-based gaps in health outcomes and care provided for very preterm infants, according to new research in the September 2019 Pediatrics. However, findings showed that black infants born at least 10 weeks early remain less likely to receive certain treatments and more likely to die or experience some serious health outcomes than their white counterparts. For the National Institutes of Health-funded

study, "Racial and Ethnic Differences Over Time in Outcomes of Infants Born Less Than 30 Weeks' Gestation," researchers analyzed 2006-2017 data for 224,297 infants drawn from the Vermont Oxford Network, a voluntary worldwide network including 789 NICUs in the U.S. focused on quality improvement. The infants were born between 22 to 29 weeks' gestation. The researchers discovered a narrowing gap during the 12-year-study period in the rate for some evidence-based care practices, such as the use of antenatal corticosteroids to help a premature baby's lungs function, as well as mortality (defined as death before discharge) and complications such as hypothermia and late-onset sepsis among black infants. However, by the end of the study period, black infants still had lower rates of vital care practices and higher rates of mortality, hypothermia, necrotizing enterocolitis, late-onset sepsis, and severe intraventricular hemorrhage than white infants. Study authors said the quality deficit among minority infants for several care practice measures, and potentially modifiable health outcomes suggests a critical role that quality improvement initiatives can play if tailored to hospitals serving minority populations. They encourage continued research to assess care and outcome trends for preterm infants to ensure that infants of all racial and ethnic backgrounds benefit equally from medical developments.

Editor's note: The solicited commentary, "Improving Quality of Care Can Mitigate Persistent Disparities," accompanies this study.

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Advances in Therapeutics and Technology

Formerly:
High-Frequency Ventilation of Infants, Children & Adults

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Palliative Medicine, Good Days, and the Angel of Death

Shelly Haug, MD

I walked in the large, wooden front door and took my shoes off as the family requested. The attending pediatric palliative physician and I traded pleasantries with the family as we walked across the hardwood floor to sit on the soft, beige couch in the family den. My attention was quickly drawn to the hallway where I watched the team nurse walk in hugging baby Ellie in her arms. Ellie's mother, Gloria, paused in our conversation. Of course, I cannot be sure what her exact thoughts were, but Gloria's contented smile as she watched Ellie giggle spoke volumes to me.

"Of course, I cannot be sure what her exact thoughts were, but Gloria's contented smile as she watched Ellie giggle spoke volumes to me."

I sat in quiet astonishment. Ellie had a diagnosis with little hope for many Good Days, yet here she was…giggling and snuggling with Gloria at home, her 3 brothers energetically running around the room. The home was filled with happy, rambunctious chaos. Ellie was 15 months old at the time with a diagnosis of severe lissencephaly, and I was able to witness one of Ellie's Good Days.

Gloria told us about Ellie's recent, not-so-good days the week prior. How Ellie had cried in pain with her back arching due to severe muscle spasms. A small increase in symptom management with methadone had subsequently changed Ellie's whole world for the better. The conversation naturally led to the palliative team's role. A discussion surrounding how to maintain the number of Good Days for Ellie.

This is exactly what palliative medicine does. It may not always be a seemingly simple increase in opioid medication that creates an improved quality of life. Palliative medicine is there in the home to help decipher needs and manage symptoms as well as aid in communication. The team is also there to talk to those families in need through the inevitable decline in Good Days if the patient nears the end of life.

I did not imagine I would ever be working in palliative medicine, yet life-altering experiences happen to us all. We have personal events or patient encounters that seem to change our physician identity completely. In my neonatology fellowship, I had many valuable yet tough experiences in life and death. My perspective on palliative medicine morphed with each experience. Subsequently, I had a bit of permanent ink placed to mark some of these encounters. I chose these marks of remembrance not as a reminder of the babies I could not save, but as a resounding symbol of change these patients brought me.

The moment I decided to complete another fellowship was, in fact, while talking with one such patient family. Baby Allen's family. He had just spent two weeks on ECMO due to acute respiratory failure, and his heart was now failing, getting worse by the day. There were moments of extensive communication failures that happened over the course of one particular day. The very bad news was shared insensitively, hallway conversations were accidentally overheard and misinterpreted which should never have happened in a hallway, to begin with, the list went on. Despite the mishaps, we knew time was running short – we were not sure how much longer baby Allen's heart would continue to beat. A family meeting to discuss the transition of care was a must.

I sat with his parents and grandparents after the family meeting. Anger and a heavy, ineffable sadness filled the room. This day was an unfathomable, unending nightmare for the family.

We talked extensively about what they wanted their last moments with baby Allen to be like. As I turned to leave the room, I hesitated. The grandfather was still staring angrily at the floor. I thought I understood why. No family should have to overhear bad news in the hallway or be told their son has life-threatening heart failure by a rushed specialist walking out of a room. I slowly turned around, faced the grandfather, and extended my hand to offer an apologetic handshake. It felt like several painstaking minutes before he looked at my face or acknowledged my apologies for…well, everything. I shook his hand and promised I would do everything I could to ensure baby Allen's final moments were peaceful. The Grandfather finally reached out to return my handshake speaking words of appreciation as well as a final, surprising request. Would I do whatever it took to ensure other families have a better experience in the life and death of their loved ones? For me, my mind solidified in that moment. Yes, I would – and for me, that promise meant palliative medicine was the next step.

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I have seen everything from bewildered looks of misunderstanding to shocked shouts of anger for the recommendation that palliative medicine should be consulted. This is true in the neonatal world, adult medicine, and even geriatric practice. These heart-wrenching outcries have come equally from medical colleagues, families, and even personal friends. I finished

my pediatric palliative fellowship by working with a physician doing outpatient home visits. Home palliative and hospice visits reminded me why all physicians, nurses, and team members should take a moment to reflect and possibly adjust our perspective.

"How does a doctor who took the Hippocratic oath and is trained to save lives identify with palliative medicine? To me, palliative medicine is an essential part of whole-person care. "

How does a doctor who took the Hippocratic oath and is trained to save lives identify with palliative medicine? To me, palliative medicine is an essential part of whole-person care. I make the case that every single physician can identify with at least a small piece of palliative and even hospice medicine. Palliative medicine is not giving up the fight to the Angel of Death and just ensuring good care surrounding end of life. (1) Palliative medicine is relieving suffering. Palliative medicine is ensuring as many Good Days for the patient and family as possible. Palliative medicine is helping families make informed and extremely difficult decisions. (2) Palliative medicine is a resource to help patients and families through a life-threatening medical diagnosis. As Robert Frost once said, "Hope is not found in a way out but in a way through."

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Corresponding Author:

Shelly Haug, MD, FAAP
Neonatology Attending Physician
Mountain States Neonatology, Mednax
Email: Shelly_Haug@mednax.com


Survey Says: RSV
RESPIRATORY SYNCYTIAL VIRUS, or RSV, is a dangerous virus that can lead to:
Hospitalization
Lifelong health complications
Death
for infants and young children
ACCORDING TO A NATIONAL SURVEY,
Specialty Health Care Providers say:
They treat RSV as a priority, "often" or "always" evaluating their patients
RSV is the "most serious and dangerous" illness for children under four
Barriers to access and denials from insurance companies limit patients' ability to get preventive RSV treatment
But Parents are Unprepared.
Only 18% know "a lot" about RSV
Only 22% consider themselves "very well" prepared to prevent RSV
RSV EDUCATION & AWARENESS CAN HELP
After parents learned more about RSV, they were:
65% "More concerned" about their child contracting the disease
67% Likely to ask their doctor about RSV
NCIFIH National Coalition for Infant Health
Learn More about RSV at www.infantshealth.org/RSV


Why PREMATURE INFANTS Need Access to an EXCLUSIVE HUMAN MILK DIET
In the United States, more than 1 IN 10 BABIES ARE BORN PREMATURE.
Very low birthweight babies are born severely premature, weighing less than 1,250 grams.
VERY LOW BIRTHWEIGHT BABIES are at risk for Necrotizing Enterocolitis (NEC), which:
Damages intestinal tissue
Causes distended abdomen, infection, low blood pressure and shock
Threatens infants' lives
NEC occurrence increases when a preemie consumes non-human milk products.
When that happens:
17%
12%
5%
1%
30%
HOW TO HELP PREVENT NEC:
EXCLUSIVE HUMAN MILK DIET
What is an Exclusive Human Milk Diet?
NO cow's milk
NO sheep's milk
NO goat's milk
NO formula
mother's milk
human donor milk
human milk-based fortifier
Why Is An Exclusive Human Milk Diet Important?
When a very low birthweight baby can access an EXCLUSIVE HUMAN MILK DIET:
HUMAN MILK = MEDICINE
LEARN MORE
NCIFIH National Coalition for Infant Health

Frequently Asked Questions, Part II
More about Copy number variants (CNVs), Variants of Uncertain Significance (VUS) in Chromosome Microarrays, with a special focus on Congenital Heart Defects (CHDs)

Robin Clark, MD

How common are genetic disorders in children with CHDs?

Congenital heart defects are the most common form of birth defects, affecting almost 1% of all newborns. Genetic factors play a role in most CHDs, which are typically isolated and nonsyndromic, and inherited as multifactorial traits, in which gene-environmental interactions contribute to the etiology. However, about 30% of all CHDs, including some of the isolated and many of the syndromic forms, are caused by single-gene disorders or chromosomal anomalies, such as aneuploidy or CNV.

Is chromosome microarray a first-line test for CHD?

Conventional chromosome analysis can detect aneuploidies like Trisomy 21 or Turner syndrome in about 10% of children with CHDs. However, smaller CNVs or microdeletions and microduplications, are beyond the resolution of the microscope used for traditional chromosome analysis. Because chromosome microarray can detect these smaller CNVs, it has become the preferred first test, in most situations, for children with congenital anomalies of all types, including heart defects.

When is chromosome analysis, rather than microarray, the preferred test?

Chromosome analysis is a better first-line test when an aneuploidy is suspected or when there is a family history of multiple miscarriages or infertility when a balanced translocation is suspected. Both conventional chromosome analysis and microarray testing can detect aneuploidy. However, microarrays, which analyze DNA rather than whole chromosomes, cannot identify translocations, inversions or other structural chromosome rearrangements, whereas, in conventional cytogenetics, the microscopic analysis of banded chromosomes examines explicitly the shape and morphology of chromosomes.

How common are CNVs in children with CHD?

Children with CHDs and other extracardiac congenital anomalies account for 20-30% of all CHDs. In this group, 15-20% have pathogenic CNVs. Children with apparently isolated CHDs also have more pathogenic or likely pathogenic CNVs when compared with the general population. The number of CNVs in this group is 4-10% depending on the study. Both *de novo* and familial CNVs are more common in children with CHD. It is important to understand that a CNV can act as one of many contributory traits in a multi-hit model, or it can be the principal cause of a CHD.

"Both de novo and familial CNVs are more common in children with CHD. It is important to understand that a CNV can act as one of many contributory traits in a multi-hit model, or it can be the principal cause of a CHD. "

Can the same pathogenic CNV be associated with more than one type of cardiac defect?

Several recurrent de novo CNVs are associated with more than one type of CHD. Example: The classic 3Mb deletion of 22q11.2 that includes TBX1 is seen in >10% of Tetralogy of Fallot, 35% of truncus arteriosus, and 50% of interrupted aortic arch type B. However, some CNVs are specific to one type of cardiac defect. For instance, large CNVs on the X-chromosome are found in males with coarctation of the aorta.

Can a CNV in the same chromosome region cause CHD both as a microduplication and as a microdeletion?

Yes. Dosage sensitivity for critical genes may work both ways, as copy number gain or loss may disturb the same pathway.

Example: Microduplications and microdeletions for the same regions of 1q21.1 (*GJA5)*, 3p24.1 (*TGFBR2*), 8p23.1 (*GATA4*) and 22q11.2 (*TBX1*) have been reported in CHDs.

Are recurrent CNVs seen in both isolated and syndromic CHDs?

The same recurrent CNVs are seen in children with both isolated and syndromic CHD. It may be that the syndromic forms of CHDs have a wider phenotype, including milder forms, that we are just starting to appreciate, or it may be that other modifying factors may contribute to the range of phenotypes that are expressed by a CNV in a given gene or chromosome region.

Why is a CNV diagnosis important in the care of children with CHDs?

Outcomes for CHDs vary with the type and severity of the cardiac defect, the presence or absence of associated anomalies and with the underlying cause. Early identification of genetic diagnosis can alter the clinical course of a child with a CHD. Children with CHD caused by a pathogenic CNV have more complications and a less favorable prognosis than their similarly affected peers without CNVs. Identifying these children early gives medical providers the chance to offer more appropriate care.

"Early identification of genetic diagnosis can alter the clinical course of a child with a CHD. Children with CHD caused by a pathogenic CNV have more complications and a less favorable prognosis than their similarly affected peers without CNVs."

Practical applications:

1. Recognize that recurrent CNVs associated with CHDs include important genes for cardiogenesis.
   a. Patients with isolated CHDs can have the same CNVs that are responsible for syndromic cardiac defects.
2. Utilize online resources (OMIM, www.omim.org; DECIPHER, rarechromo.org) for more information about recurrent and novel CNVs and the genes within them.

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Corresponding Author

Robin Clark, MD
Professor, Pediatrics
Loma Linda University School of Medicine
Division of Genetics
Department of Pediatrics
rclark@llu.edu

Perinatal Substance Use

5 ways you can improve care during pregnancy and beyond

Pregnancy presents unique opportunities for patients to make positive changes in their substance use. When you become an informed provider you empower patients to make those changes.

Educate Yourself

Learn more about the pharmacology of substance use. Promote evidence-based care by communicating with patients in a way that separates fact from fiction. Understand the cycles of sobriety and relapse so that you can help patients plan for their recovery. Advise on the risks associated with polysubstance use.

Use the Right Words

Know the difference between substance use, substance misuse, and Substance Use Disorders (SUDs). Recognize that substance use is stigmatized and that stigma is a barrier to seeking care. Reject language that shames. Embrace the principles of Harm Reduction as a way to support any positive change.

Screen Every Patient

Talking about substance use should be a routine part of everyone's medical care. Get comfortable discussing it. Ask questions and listen to what your patients have to say. You may be the first person to ever ask.

Get Trained to Offer MAT

Medication-Assisted Treatment is the Standard of Care during pregnancy, but there are not enough providers. Contact SAMHSA to become an OTP*. Make naloxone available to all your patients who use opioids.

*opioid treatment program

End the Stigma and Criminalization of Drug Use

Embrace people who use substances. Meet them where they are. Abide by your medical ethics. Practice beneficence. Promote public health. Advocate for decriminalization.

Your Advocacy Matters

Learn more at
www.nationalperinatal.org

National Perinatal Association

TOP 10

RECOMMENDATIONS FOR THE PSYCHOSOCIAL SUPPORT OF NICU PARENTS

SUPPORT 4 NICU PARENTS

Essential evidence-based practices that can transform the health and well being of NICU families and staff

based on the National Perinatal Association's
Interdisciplinary Recommendations for Psychosocial Support of NICU Parents

1 PROMOTE PARTICIPATION

Honor parents' role as primary caregiver. Actively welcome parents to participate during rounds and shift changes. Remove any barriers to 24/7 parental involvement and avoid unnecessary separation of parents from their infants.

2 LEAD IN DEVELOPMENTAL CARE

Teach parents how to read their baby's cues. Harness your staff's knowledge, skills, and experience to mentor families in the principles of neuroprotection & developmental care and to promote attachment.

3 FACILITATE PEER SUPPORT

Invest in your own NICU Parent Support program with dedicated staff. Involve veteran NICU parents. Partner with established parent-to-parent support organizations in your community to provide continuity of care.

4 ADDRESS MENTAL HEALTH

Prioritize mental health by building a team of social workers and psychologists who are available to meet with and support families. Provide appropriate therapeutic interventions. Consult with staff on trauma-informed care - as well as the critical importance of self-care.

5 SCREEN EARLY AND OFTEN

Establish trusting and therapeutic relationships with parents by meeting with them within 72 hours of admission. Follow up during the first week with a screening for common maternal & paternal risk factors. Provide anticipatory guidance that can help normalize NICU distress and timely interventions when needed. Re-screen prior to discharge.

6 OFFER PALLIATIVE & BEREAVEMENT CARE

Support families and NICU staff as they grieve. Stay current with best practices in palliative care and bereavement support. Build relationships with service providers in your community.

7 PLAN FOR THE TRANSITION HOME

Set families up for success by providing comprehensive pre-discharge education and support. Create an expert NICU discharge team that works with parents to find specialists, connect with service providers, schedule follow-up appointments, order necessary medical supplies, and fill Rx.

8 FOLLOW UP

Re-connect with families post-discharge. Make follow-up calls. Facilitate in-home visits with community-based service providers, including Early Intervention. Partner with professionals and paraprofessionals who can screen families for emotional distress and provide timely therapeutic interventions and supports.

9 SUPPORT NICU CARE GIVERS

Provide comprehensive staff education and support on how to best meet families' psychosocial needs, as well as their own. Acknowledge and address feelings that lead to "burnout."

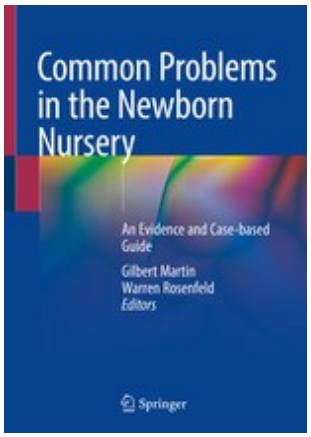
10 HELP US HEAL

Welcome the pastoral care team into your NICU to serve families & staff.

SUPPORT4NICUPARENTS.ORG

Springer
science+business media

Editors: **Martin**, Gilbert, **Rosenfeld**, Warren (Eds.)



Common Problems in the Newborn Nursery
An Evidence and Case-based Guide

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A False Tubing Alarm for Hospitals & Preemies

Susan Hepworth and Mitchell Goldstein, MD

NCfIH National Coalition for Infant Health

Protecting Access for Premature Infants through Age Two

The National Coalition for Infant Health is a collaborative of more than 180 professional, clinical, community health, and family support organizations focused on improving the lives of premature infants through age two and their families. NCfIH's mission is to promote lifelong clinical, health, education, and supportive services needed by premature infants and their families. NCfIH prioritizes safety of this vulnerable population and access to approved therapies.

The trade organization for manufacturers of tubing systems used to deliver nutrition, medicine or fluids to patients recently informed hospitals that their existing devices would be "phase[d] out" starting July 1, 2020. The organization's statement explained that the phase-out would make way for a new series of tubing connectors known as ENFit. The change in technology (the trade organization noted) was meant to "comply" with regulatory guidance and to increase patient safety.

"The trade organization for manufacturers of tubing systems used to deliver nutrition, medicine or fluids to patients recently informed hospitals that their existing devices would be "phase[d] out" starting July 1, 2020."

Patient safety is a critical concern. New connectors were designed to reduce dangerous tubing mix-ups, where connectors for enteral nutrition or medicine get swapped, sending the wrong substance to the wrong part of the body. But attempted solutions can actually produce new risks for premature infants.

Before hospitals overhaul their tubing technology, several points are worth considering.

1. ENFit isn't for everyone. As pointed out by the National Coalition for Infant Health, ENFit can present some serious issues for premature infants. Medication can linger in the

area around the syringe barrel, inadvertently increasing the medication dose. If the moat is not fully cleared when the syringe is inserted into the feeding tube, a premature infant may receive up to 30 percent more medicine than intended. (1)

This places the baby at risk for overdose and adverse drug reactions. The design also increases the risk for infection if residual breast milk or formula remains in the moat and the connector is then attached to the feeding tube.

2. Safe, FDA-compliant options still exist. Not all legacy tubing systems are phasing out. For instance, manufacturer Vygon issued a statement explaining that it was neither discontinuing nor "ramp[ing] down" production of its tubing system. Becton Dickinson, another manufacturer of tubing connectors, continues to produce its products as well, while NeoChild and York's Medical Solutions also both have systems that are compliant with international standards.

The Global Enteral Device Supplier Association may want hospitals and health care providers to plan for a "full conversion to ENFit connectors," but hospitals and health care providers who have concerns about ENFit shouldn't be alarmed.

"Other safe, FDA-approved options continue to be available. Each hospital should weigh the risks and benefits of tubing systems carefully before determining whether a transition is right for its patients."

Other safe, FDA-approved options continue to be available. Each hospital should weigh the risks and benefits of tubing systems carefully before determining whether a transition is right for its patients.

References:

1. *A Victory For Nicu Patient Safety - Alliance For Patient .., https://allianceforpatientaccess.org/a-victory-for-nicu-patient-safety/ (accessed August 09, 2019).*

Disclosures: The author does not have any relevant disclosures.

NT

Corresponding Author

Susan Hepworth
Director
National Coalition for Infant Health
1275 Pennsylvania Ave. NW, Suite 1100A
Washington, DC 20004
info@infanthealth.org

Mitchell Goldstein, MD
Professor of Pediatrics
Loma Linda University School of Medicine
Division of Neonatology
Department of Pediatrics
mgoldstein@llu.edu

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National Coalition for Infant Health Values (SANE)

Safety. Premature infants are born vulnerable. Products, treatments and related public policies should prioritize these fragile infants' safety.

Access. Budget-driven health care policies should not preclude premature infants' access to preventative or necessary therapies.

Nutrition. Proper nutrition and full access to health care keep premature infants healthy after discharge from the NICU.

Equality. Prematurity and related vulnerabilities disproportionately impact minority and economically disadvantaged families. Restrictions on care and treatment should not worsen inherent disparities.

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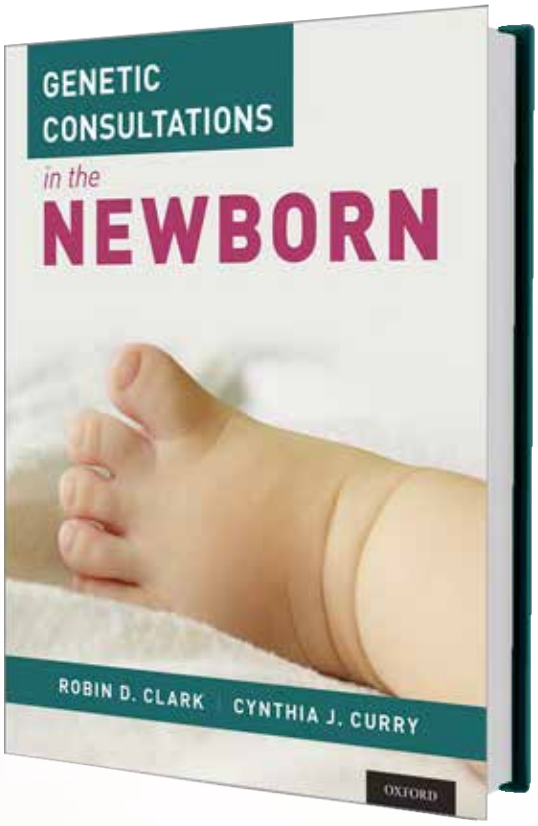

Robin D. Clark | Cynthia J. Curry

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Comprising of more than 60 chapters organized by system and symptom, *Genetic Consultations in the Newborn* facilitates fast, expert navigation from recognition to management in syndromes that manifest during the newborn period. Richly illustrated and packed with pearls of practical wisdom from the authors' decades of practice, it empowers readers to recognize the outward signs and symptoms crucial for an effective diagnosis.

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OXFORD

RSV AWARENESS:
A National Poll of Parents & Health Care Providers

Respiratory syncytial virus, or RSV, is far from the common cold. It can lead to hospitalization, lifelong health complications or even death for infants and young children. **In fact, it is the leading cause of hospitalization in children younger than one.**

Yet a national poll of parents and specialty health care providers reveals a startling divide in attitudes toward the virus. While both groups acknowledge RSV as a significant concern, the two populations vary widely in their reported ability to meet RSV's threat head-on. Health care providers vigilantly monitor for the virus, which they report seeing regularly in their practices. Parents, however, feel unequipped to protect their young children.

Meanwhile, specialty health care providers overwhelmingly report that health plan rules and insurance denials block vulnerable infants' access to preventive RSV treatment. Such barriers can put unprepared parents at a double disadvantage. The survey does suggest, however, that education can embolden parents to seek more information about RSV and take steps to protect their children.

KEY FINDINGS

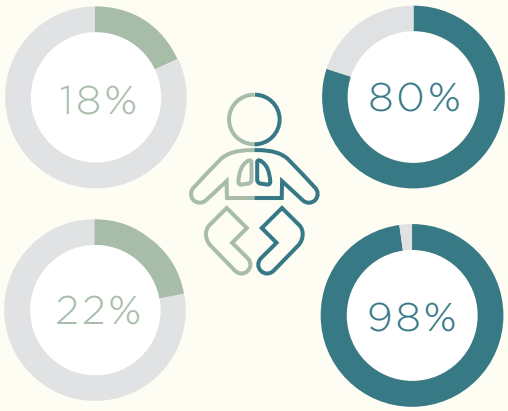
Preparedness

Parents of children age four and under report that understanding of RSV is lacking. That leaves them less than fully prepared to prevent their young children from catching the virus.

Specialty health care providers reiterated these concerns; 70% agreed that parents of their patients have a low awareness of RSV. Meanwhile, specialty health care providers themselves actively monitor for RSV. They reported that:

PARENTS

Only 18% said parents know "a lot" about RSV, reflecting an awareness level that's roughly half that of the flu



Only 22% of parents consider themselves "very well prepared" to prevent RSV.

SPECIALTY HEALTH CARE PROVIDERS

They treat RSV as a priority, "often" or "always" evaluating their patients (80% doctors; 78% nurses)

During RSV season, they are especially vigilant about monitoring patients for symptoms or risk factors for RSV (98%).

Peer Reviewed

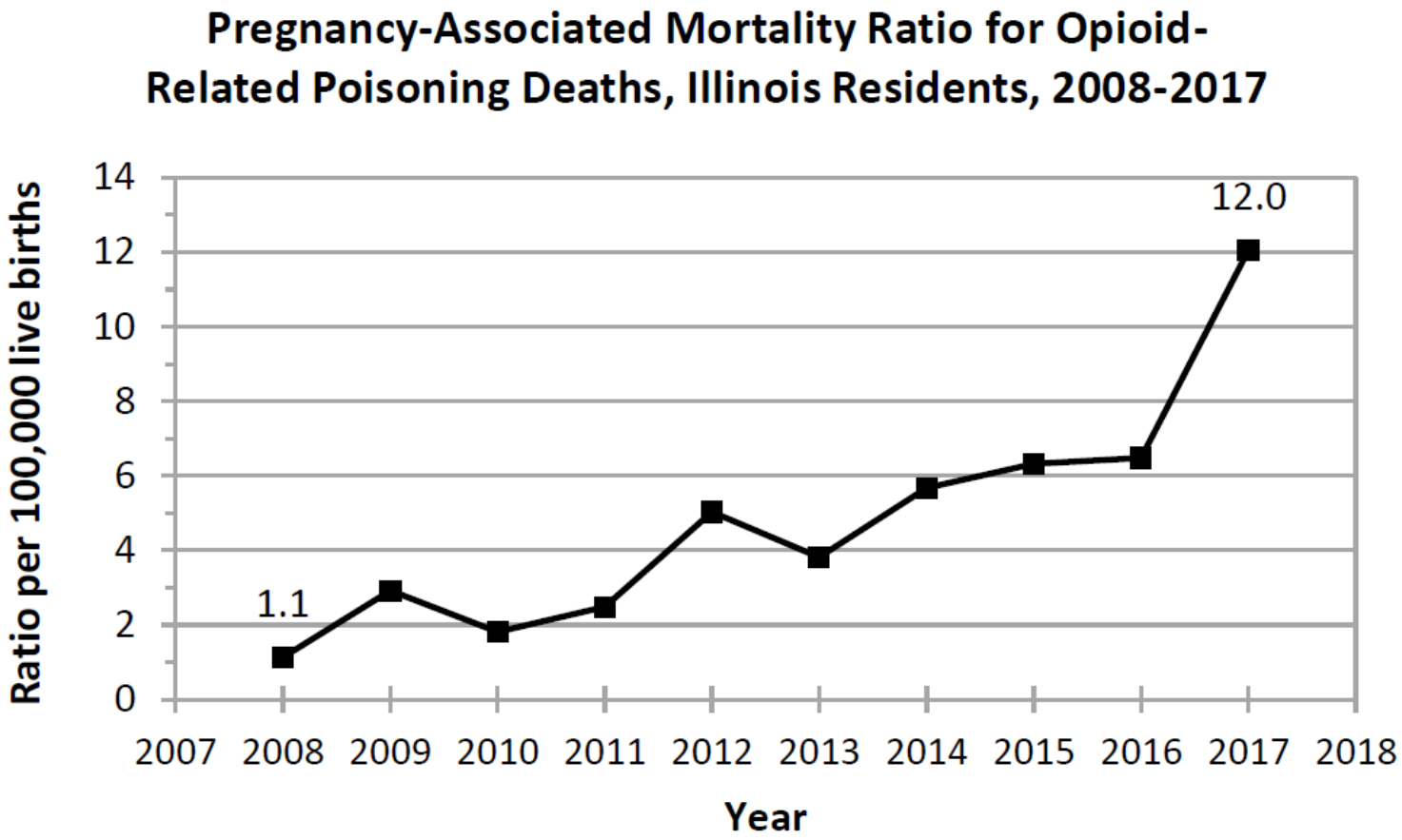
Potentially Preventable: Maternal Deaths Secondary to Opioid Use Disorder (OUD) Following Delivery of Their Infants

Joseph R Hageman, MD, Patricia Ann Lee King, MSW, Ann Borders, MD

I just attended the Illinois Perinatal Quality Collaborative (ILPQC) Face-to-Face Meeting last week in Springfield, IL, and was again overwhelmed by the presentation during which maternal death due to drug poisoning was discussed. In 2017, Pregnancy-associated deaths related to opioid poisoning increased 10-fold over a 9- year period. The pregnancy-associated mortality ratio related to opioid poisonings nearly doubled in just one year from 2016 to 2017. (1)

" In 2017, Pregnancy-associated deaths related to opioid poisoning increased 10-fold over a 9- year period. The pregnancy-associated mortality ratio related to opioid poisonings nearly doubled in just one year from 2016 to 2017. (1)"

The goals of the ILPQC Mothers and Newborns affected by Opioids – Obstetric (MNO-OB) quality improvement (QI) initiative are to identify pregnant women with opioid use disorder (OUD) prenatally or during delivery admission, link them to medication-assisted treatment (MAT) and behavioral health counseling/ recovery services, and utilize the OUD clinical care checklist. Women with OUD receiving MAT and recovery services reduces maternal overdose deaths, improves pregnancy outcomes, and increases the number of women who can parent their infants. Hospital teams participating in the MNO-OB initiative are working on active clinical culture change to help clinical care teams recognize that OUD is an urgent obstetric issue and a life-threatening chronic disease with lifesaving treatment available with benefit to both pregnant and postpartum women and their infants. In addition, the neonatal teams working on the MNO-Neonatal Initiative are focused on improving care of opioid exposed newborns by better engaging pregnant, and postpartum women with OUD, including breastfeeding, active involvement of women in the non-pharmacological care of their infants should the baby develop neonatal abstinence syndrome (NAS), and engagement in coordinated discharge planning for mother and infant. Recent



***Data Source**: Illinois death certificates, 2008-2017*

***Chart Source**: Data Snapshot: Opioid Poisoning Deaths among Illinois Women of Reproductive Age, IDPH Office of Women's Health and Family Services, March 2019*

studies have demonstrated that newborn infants born to women with OUD receiving MAT have a significantly less severe NAS clinical course compared with newborns born to women with OUD who are not on MAT. (2,3)

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1. *http://www.dph.illinois.gov/sites/default/files/publications/opioid-deaths-among-women-repro-age.pdf*
2. *Zedler BK, Mann AL, Kim MM et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: A systematic review and meta-analysis in the mother, fetus, and child. Addiction 2015; 111:2115-2128.*
3. *Kraft WK, Adeniyi-Jones SC, Chervoneva I, Greenspan JS et al. Buprenorphine for the treatment of the neonatal abstinence syndrome. New Eng Jl Med. 2017; 376:2341-2348.*

The author has identified no conflicts of interest.

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Corresponding Author

Joseph R. Hageman, MD
Senior Clinician Educator
Pritzker School of Medicine
University of Chicago
MC6060
5841 S. Maryland Ave.
Chicago, IL 60637
Phone: 773-702-7794
Fax: 773-732-0764
jhageman@peds.bsd.uchicago.edu

Patricia Lee King, PhD, MSW,
State Project Director and Quality Lead,
Illinois Perinatal Quality Collaborative and Senior Research Associate,
Center for HealthCare Studies,
Feinberg School of Medicine,
Northwestern University
Chicago, IL

Ann Borders, MD, MSc, MPH,
Executive Director and Obstetric Lead,
Illinois Perinatal Quality Collaborative
Clinical Associate Professor
Maternal Fetal Medicine,
NorthShore University HealthSystem
Chicago, IL

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May begin with a brief case summary or example.

Summarize the pearl for emphasis.

No more than 7 references.

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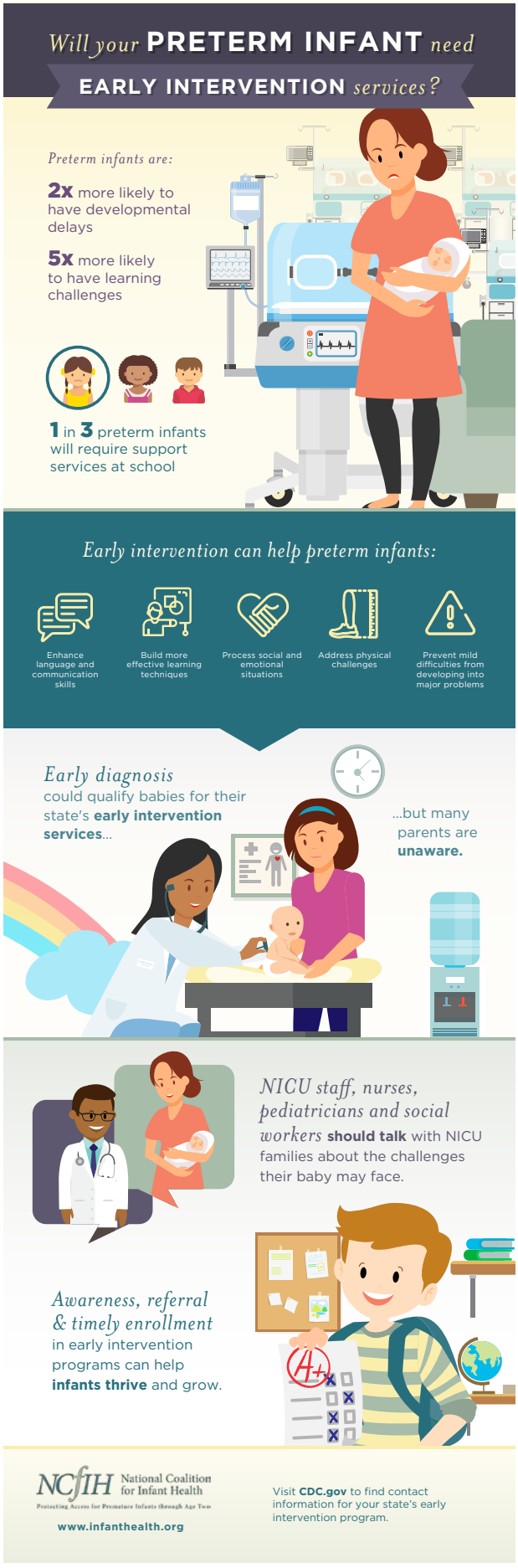
Will your PRETERM INFANT need
EARLY INTERVENTION services?
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2x more likely to have developmental delays
5x more likely to have learning challenges
1 in 3 preterm infants will require support services at school
Early intervention can help preterm infants:
Enhance language and communication skills
Build more effective learning techniques
Process social and emotional situations
Address physical challenges
Prevent mild difficulties from developing into major problems
Early diagnosis could qualify babies for their state's early intervention services...
...but many parents are unaware.
NICU staff, nurses, pediatricians and social workers should talk with NICU families about the challenges their baby may face.
Awareness, referral & timely enrollment in early intervention programs can help infants thrive and grow.
NCfIH National Coalition for Infant Health
Protecting Access for Premature Infants through Age Two
www.infanthealth.org
Visit CDC.gov to find contact information for your state's early intervention program.


Survey Says: RSV
RESPIRATORY SYNCYTIAL VIRUS, or RSV, is a dangerous virus that can lead to:
Hospitalization
Lifelong health complications
Death
for infants and young children
ACCORDING TO A NATIONAL SURVEY,
Specialty Health Care Providers say:
They treat RSV as a priority, "often" or "always" evaluating their patients
RSV is the "most serious and dangerous" illness for children under four
Barriers to access and denials from insurance companies limit patients' ability to get preventive RSV treatment
But Parents are Unprepared.
Only 18% know "a lot" about RSV
Only 22% consider themselves "very well" prepared to prevent RSV
RSV EDUCATION & AWARENESS CAN HELP
After parents learned more about RSV, they were:
65% "More concerned" about their child contracting the disease
67% Likely to ask their doctor about RSV
NCfIH National Coalition for Infant Health
Learn More about RSV at www.infanthealth.org/RSV

Abstracts from the Advances in Therapeutics and Technology: Critical Care of Neonates, Children, and Adults Conference March 26-30, 2019, Snowbird, Utah

Donald Null, MD, Mitchell Goldstein, MD, and Arun Pramanick, MD

The 36th Annual Advances in Care Conference – Advances in Therapeutics and Technology: Critical Care of Neonates, Children, and Adults (formerly: High-Frequency Ventilation of Infants, Children & Adults) presented high quality education and networking opportunities to healthcare professionals who provide care for critically ill neonatal, pediatric, and adult patients with a focus on advances in therapeutics and technologies. Along with featured speakers, the conference includes abstract presentations on research on advances in these areas:

Abstracts Table of Contents:

ATT2019-1
Effects of soft PVC foam in reducing nasal skin breakdown in preterm neonates receiving non-invasive ventilation via RAM nasal cannula

Vita Boyar, M.D., F.A.A.P , WCP, F.A.B.W.H

Director, Neonatal Wound Service
Co-lead of Neonatal ECMO program
Co-lead Pressure Injury Task Force for Northwell Health
Neonatal-Perinatal Medicine, Cohen Children's Medical Center of NY
Northwell Health
Assistant Professor of Pediatrics
Hofstra University School of Medicine
Northwell Health
718-470-3440
Cell 516-606-6231

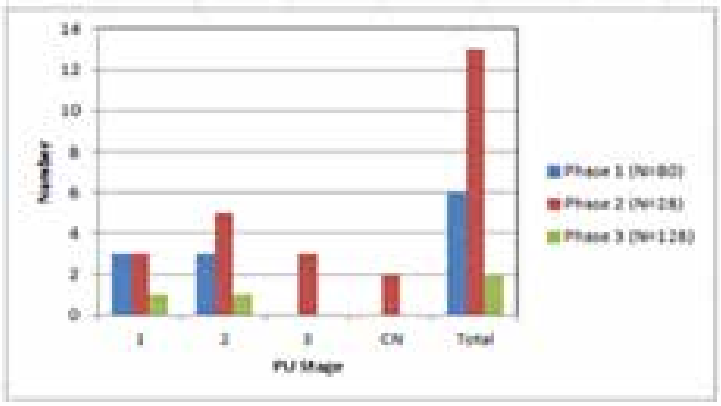
Background: Neonates rely on non-invasive ventilation (NC-PAP) for survival. Due to unique anatomical and physiological characteristics of neonatal columella area, bi-nasal prongs can lead to nasal trauma. Small bony maxillary spine, inadequate SQ and dermal tissue fail to off-load transmitted pressure, leading to deformation of skin layers, poor blood flow and ischemia. Lack of robust stratum corneum, increased heat and humidity delivered via prongs alter microclimate. Rates of neonatal nasal pressure injury (PI) range between 5 to 40%. NPUAP/EPUAP has recommended use of barrier products in all patients at risk for medical device related PI (MDRPI). The RAM Nasal Cannula is a simple cannula connected to ventilator capable of transmitting CPAP/O2. Manufacturer explains its theoretical advantage due to softer material, thinner walled prongs, and larger inner diameter prong resulting in lower resistance which may reduce nasal trauma. They recommend its use without offloading barrier device.

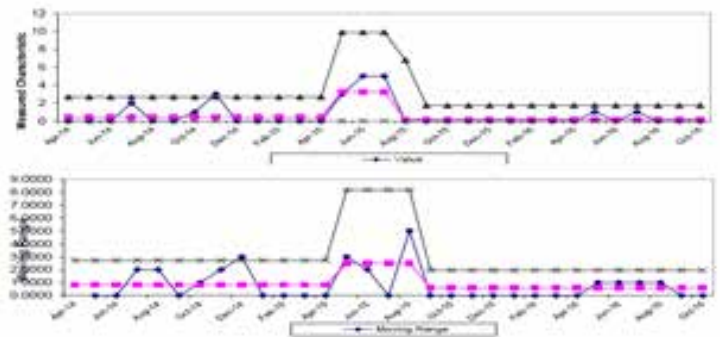
Objectives: Assess the incidence and severity of nasal pressure injury in premature infants receiving CPAP via RAM cannula and efficacy of PVS foam, Neoseal in reducing these injuries.
Method: Study conducted 04/2014-10/2016. All infants under 28 6/7 wks. GA requiring NCPAP. RAM cannula was set up accord-

ing to manufactures instructions. Soft PVC foam-Neoseal™ was placed on the bi-nasal prongs, without touching patients nasal skin and leaving 30-40% leak between nostrils and prongs. 3 time periods were compared. Period 1(04/2014- 04/2015)- RAM cannula plus Neoseal. Period 2(05/2015-07/2015) RAM and No Neoseal. Period 3(08/2015-10/2016) –RAM plus Neoseal™
Statistics: Fisher exact test confirmed statistical differences in PI rate with and without Neoseal (P<0.0001) and in severity.

Results: Of 236 neonates, 80 evaluated during period1. (RAM +Neoseal). 6 PI were identified (3 –stage 1 and 3 stage 2) with rate of nasal injury 7.5%. 27 infants qualified during period 2(RAM only); 13 PI were identified (Stage1-3; stage2-5, stage 3-3 and columella necrosis-2) with the rate of 48%. PI rate had risen 6 times during Period 2, with 18% out of 48% staged as St 3 PI and columella necrosis. Period 3(RAM +Neoseal) -128 neonates, 2 PI-1.5 %(1-St1&1-St2). There were no significant differences (T-test) in the patient characteristics between 3 groups.

Conclusion: Unique anatomy of columella area, need for precise fit to deliver pressure and poor tolerability of device repositioning contributes to nasal MDRPI via sustained pressure and friction. RAM cannula, without a barrier is a significant risk factor for PI. Microclimate (increased moisture, temperature) generated by nasal cannula increases skin susceptibility. Younger and smaller babies, with prolong PEEP application are at risk for more severe injuries. We demonstrated clinically significant benefit in applying prophylactic soft PVC foam on RAM cannula in effort to prevent nasal injuries. To our knowledge this is the first study addressing incidence of nasal injuries in preterm neonates receiving non-invasive ventilation via RAM cannula. We conclude that preventative products must be used in conjunction with PEEP-delivering devices, including RAM nasal cannula.





ATT2019-2

Determining an Optimal Weaning Method of Nasal Continuous Positive Airway Pressure (CPAP) in Preterm Neonates

Venkatakrishna Kakkilaya, (1) Sheron Wagner, (2) Judy Ridpath, NNP, 2John Ibrahim, MD, (1) L. Steven Brown, (2) and Charles R. Rosenfeld (1)

(1) UT Southwestern Medical Center, Dallas, TX
(2) Parkland Hospital and Health Systems

Background: Despite the wide adoption of CPAP for the respiratory support of preterm infants, optimal weaning strategy is not well established. While low level of CPAP (3 cm H_20) can help decrease apnea of prematurity and work of breathing, its benefits in weaning process has not been adequately evaluated.
Objective: To compare between stopping CPAP from a lower level after gradual pressure wean and discontinuation from standard therapeutic level.

Design/Methods: Single center, unblinded, prospective randomized control trial involving preterm infants born 23-32 week GA between October 2014 and February 2018. Infants meeting eligibility criteria were enrolled in the study after obtaining informed consent. Stability criteria to initiate weaning and failure criteria to restart CPAP were established a priori. CPAP was stopped at 5 cm H_2O (Group1) or pressure was weaned stepwise and stopped at 3 cm H_2O (Group 2). Primary outcome of interest was total CPAP days. 113 infants per group were required to achieve a 25% reduction in the primary outcome (Alpha 0.05, Power 0.8). Computer generated randomization sequence stratified by GA categories were placed in sealed opaque envelopes. ClinicalTrials.gov identifier NCT02064712.

Results: Of the 226 infants enrolled in the study, 116 infants belonged to Group 1 and 110 to Group 2 (Figure 1). In the intention to treat analysis, there were no differences in the baseline charac-

teristics between groups. Although CPAP was stopped earlier and at lower post- menstrual age in Group 1, primary outcome was not different between two groups. Higher proportion of infants in Group 1 failed initial attempt to stop CPAP (43% vs 27%, P 0.01) compared to Group 2. In the subgroup analysis, primary outcome was shorter among 30-32 week GA infants in Group 1 compared to Group 2 (P<0.01). Higher proportion of <30 week GA infants failed initial attempt to stop CPAP (54% vs 34%, P 0.02) and had ≥2 failed discontinuation attempts (26% vs 6%, P <0.01) in Group 1 compared to Group 2. Logistic analysis showed that Group 2 method is twice as likely to result in successful discontinuation of CPAP at first attempt compared to Group 1 [adjusted odds ratio 2.1 (1.2, 3.7)].

Conclusion: Stopping CPAP from standard therapeutic level is beneficial in decreasing duration of therapy among 30-32 week GA infants. Among <30 week GA infants, stopping CPAP from low level after gradual pressure wean can help achieve successful discontinuation at first attempt without prolonging the duration of therapy

ATT2019-3
The effects of altitude and definition on bronchopulmonary dysplasia and the role of the NRN BPD prediction algorithm

K. Gulliver, B. Yoder

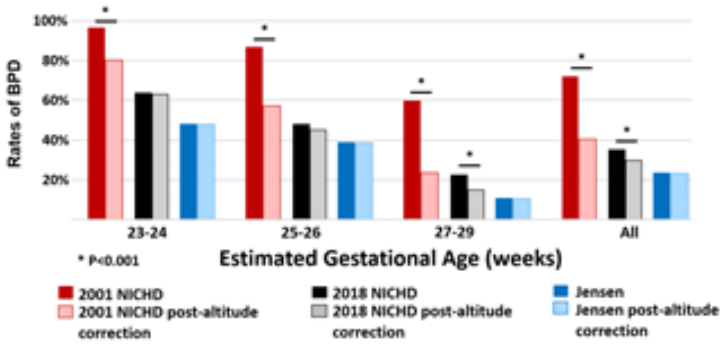
University of Utah, Salt Lake City, UT, United States

Purpose: Newer definitions for bronchopulmonary dysplasia (BPD) were developed to include current respiratory support strategies. We previously reported increased BPD rates at high altitude that normalized with altitude correction. The Neonatal Research Network developed a BPD prediction model for neonates 23-30 weeks gestational age (GA) with birth weight 501-1249g at various postnatal ages (Laughon, Am J Respir Crit Care Med, 2011) validated against the 2001 NICHD BPD definition. Our objective was to assess the effect of altitude correction on BPD rates and assess the validity of the NRN BPD prediction tool when using 3 different BPD definitions.

Methods: This is a retrospective review of neonates <30 weeks gestational age (GA) at University of Utah NICU from 1/2010 – 12/2017. BPD was defined using the following definitions: 2001 NICHD Consensus (Jobe, Am J Respir Crit Care Med, 2001), 2018 NICHD Consensus (Higgins, J Pediatr, 2018), and Jensen (PAS 2018). Effective FiO2 was determined at 36 weeks PMA (Benaron, Arch Pediatr Adolesc Med, 1994). Altitude correction was performed via the ratio of average barometric pressure (BP) in our unit of 640 mmHg (BP at 5000 feet) to 760 mmHg (BP at sea level). Probability of death and/or moderate-severe BPD was calculated at 14 days of age using the NRN BPD outcome estimator (https://neonatal.rti.org). Area under the curve (AUC) analysis and positive predictive values (PPV) were determined.

Results: 697 infants were identified (GA 27.0+1.9 weeks, BW 959±303g). BPD rates were inversely proportional to GA (Figure). BPD rate significantly decreased following altitude correction for all gestational ages (P<0.001) using 2001 NICHD definition and for the 27-29 week subgroup and overall (P<0.001) by the 2018 NICHD definition. There was no need for altitude correction with the Jensen definition. Post-altitude correction, 2001 NICHD BPD rates were significantly higher for all gestational ages (P<0.001) compared to 2018 NICHD and Jensen BPD definitions. Probability risk of BPD or death calculated at 14 days of age was similar by AUC for the 3 BPD definitions. PPV for BPD or death varied based on the BPD definition used (Table) and increased as the percentage risk of BPD or death increased.

Conclusion: Moderate to severe BPD rates differ based on the definition used. Altitude has less of an effect with the proposed 2018 NICHD BPD definition and no effect by the Jensen model, and may not need correction for altitude. With correction of FiO2 for altitude, the NRN BPD outcome estimator at 14 days of age remains a valid tool in predicting the risk of moderate-severe BPD or death in our NICU population when using recently proposed BPD definitions. Remodeling the BPD outcome estimator algorithm for newer BPD definitions may improve predictive properties.



Predictive Risk at 14 days	2001 NICHD	2018 NICHD	Jensen
≥50%	76%	61%	51%
≥60%	80%	65%	55%
≥70%	84%	70%	59%
≥80%	85%	76%	61%
≥90%	90%	86%	71%

Figure: Rates of moderate-severe BPD pre- and post-altitude correction based on definition used

Table: PPV of predicted risk at 14 days of age for 3 different BPD definitions

ATT2019-4
Decreasing the 3100A Inspiratory Percent as an Alternate to Increasing Hertz during Weaning

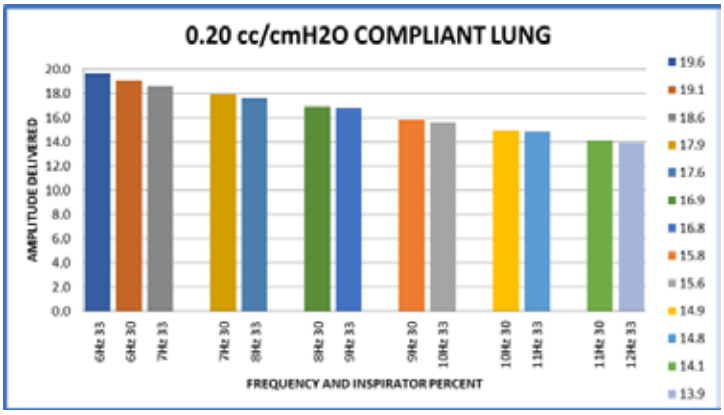
Jeffrey Wright BSRT, RRT-NPS, M. Parker ASRT, RRT, Brittanie Smith ASRT, RRT,

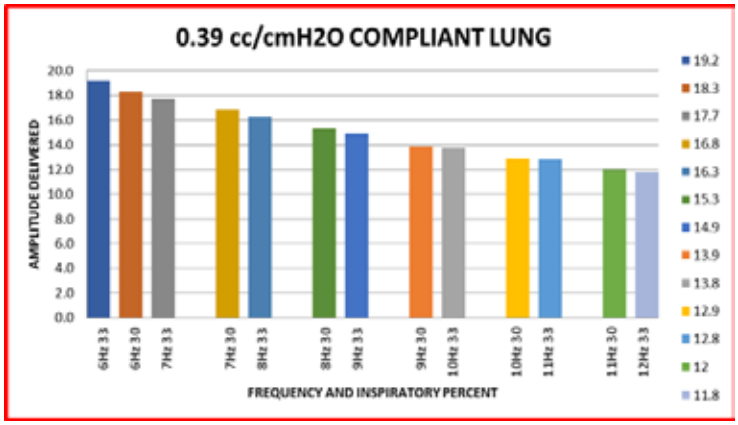
100 N Mario Cepecchi Way, Primary Children's Hospital, Salt Lake City, Utah, 84113.

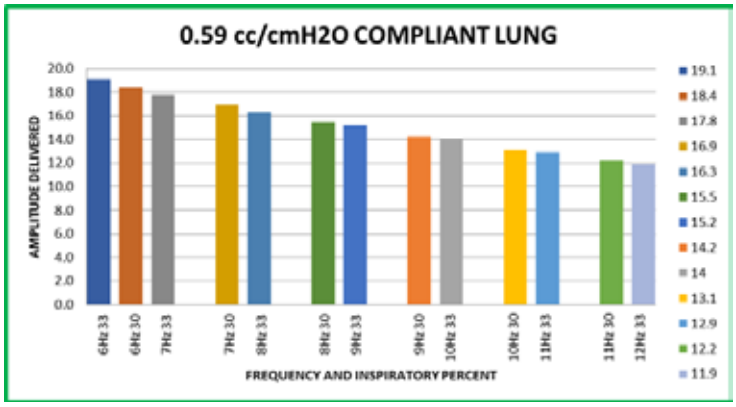
Introduction: This study looks at the relationship of the delivered Amplitude (amp) and Tidal Volume (Vt) using an inspiratory percent(I%) of 30 at one Hertz (Hz) vs the next greater HZ with an I% of 33 using a Sensor Medics 3100A High Frequency Oscillatory Ventilator (HFOV). Increasing HFOV Hz is an accepted method of weaning the HFOV ventilated patient. By increasing the Hz, you decrease the inspiratory time. The expiratory time in turn is then decreased. There is then an increased possibility of inadequate expiratory time for exhalation. The resulting consequence can be air trapping. The trapping of the expiratory gasses can result in hyper-expansion of the lungs. The hyper-expansion can impair gas exchange, increase shunting, and in some cases impair cardiac function if the hyper-expansion is severe enough. This study looks at the delivered amp's and Vt's to help understand if decreasing the I % is a viable choice in weaning the HFOV.

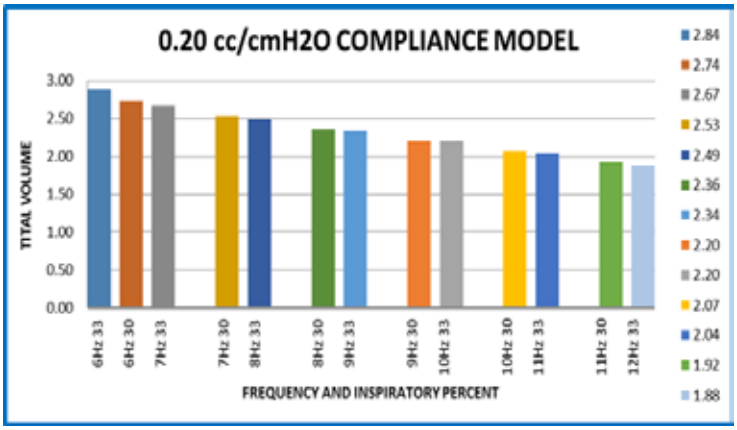
Method: A calibrated HFOV was connected to one of the three test lungs using a full-length endotracheal tube. The lung compliances and ETT's used were; 0.20cc/cmH2O with a 2.5 ETT, 0.39cc/cmH2O with a 3.0 ETT, and 0.59cc/cmH2O using a 3.5 ETT. The HFOV bias flow was maintained at 15 lpm throughout all testing. The MAP was set to 14 cmH2O (+- 0.1). As each parameter was set. The amp was measured from within the test lungs using a TSI Certifier. The Vt was measured using a Dragger VN 500 BabyLog ventilator as a volume monitor. The HFOV frequencies tested were 6Hz thru 12Hz. The I% was set to 30 and 33 for each frequency, except 12 Hz which ran at 33 I%, only. The amplitudes tested were; 16, 18, 20, 22, 24, 26, 28, and 30. Once the data was collected it was placed into a category. A category consisted of the averaged measured values from all eight Amp's tested from a single Hz frequency at a given I%. The categories were then paired. The pairing was a category of a Hz at 30 I% with the category of the next higher Hz at 33 I% (see graphs 1 thru 6). The Vt categories were then stratified further using the coefficient of the gas transport equation [(f * Vt2) / Kg] (see graphs 7, 8, and 9). Where the test lungs could not be assigned a patient weight, the weight aspect of the equation was not completed.

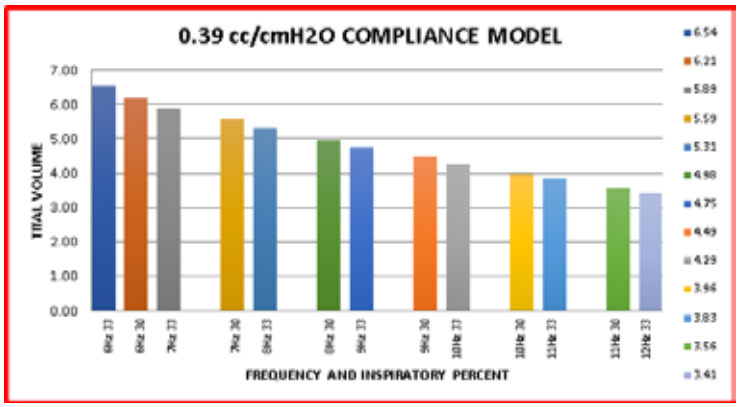
Conclusion: By decreasing the I% to 30 there is a demonstrated reduction in the delivered amp and Vt. The paired categories results are similar. The 30 I% values are slightly larger than the 33% measurements, except for a few examples. Where 30 I% values are larger you may expect that the change would be a lesser wean. However, when the Vt categories are stratified using the coefficient of the gas transport equation the data would suggest the Hz at 30 I% change would be a marginally greater wean than increasing the Hz at 33 I%. Only clinical application/trial will determine if these assumptions are correct.

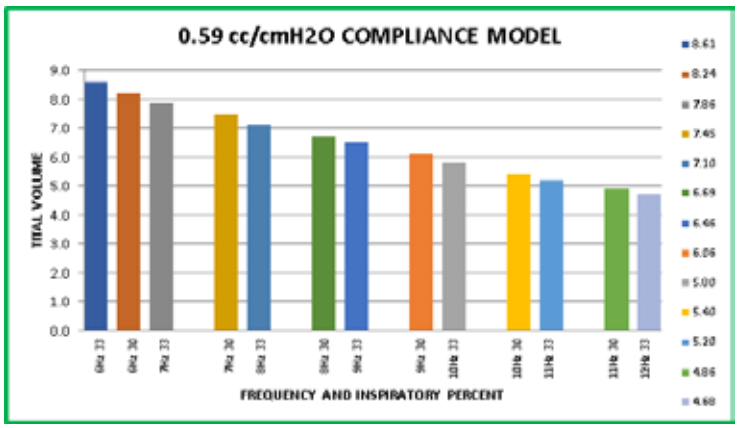


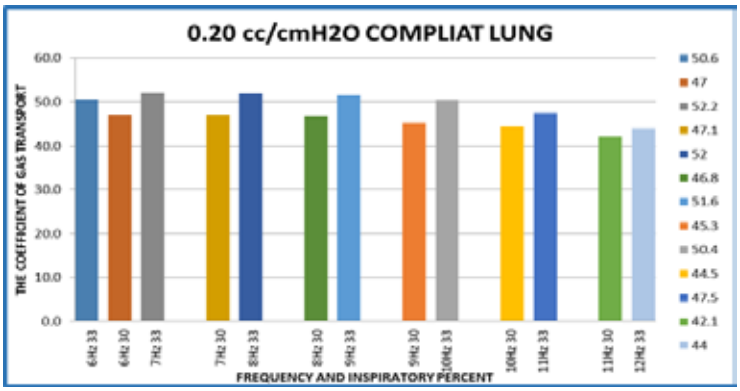


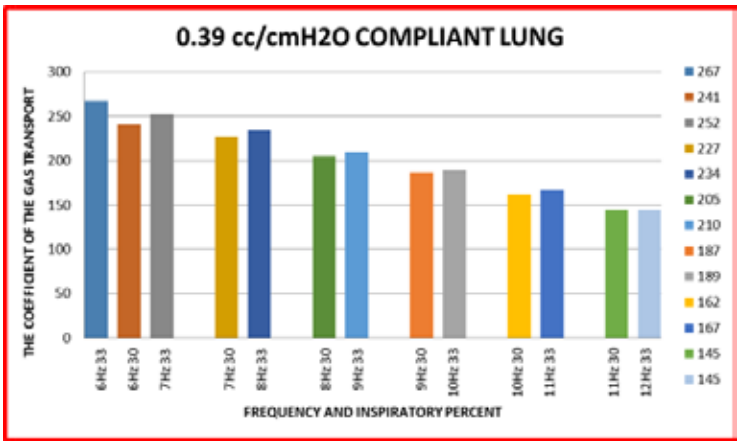


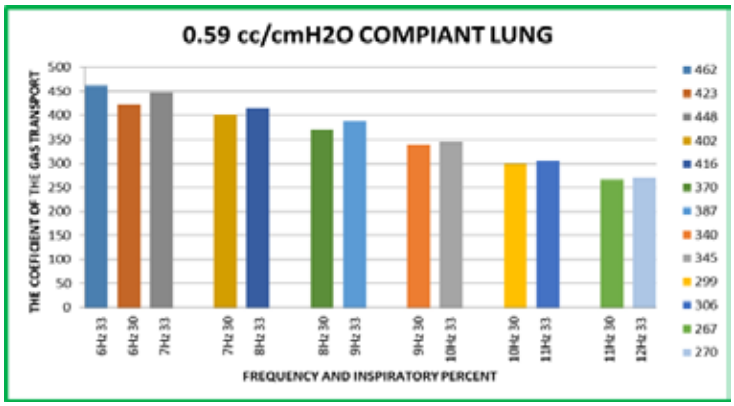












ATT2019-5

HFOV Tidal Volumes with Inspiratory Percent at 30 vs 33 at The Next Higher Hertz

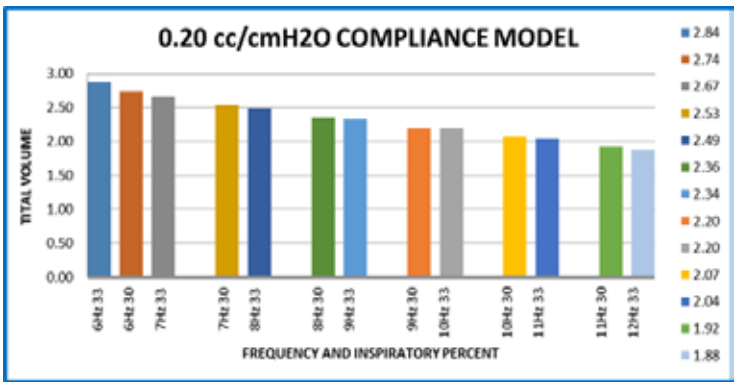
Jeffrey Wright BSRT, RRT-NPS, Brittanie Smith ASRT, RRT,

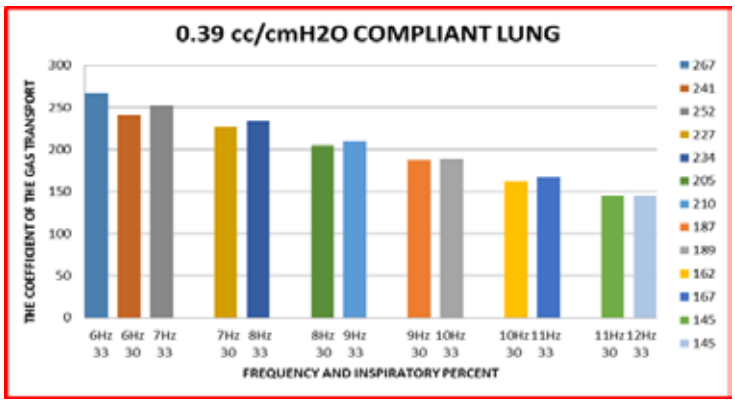
100 N Mario Cepecchi Way, Primary Children's Hospital, Salt Lake City, Utah.

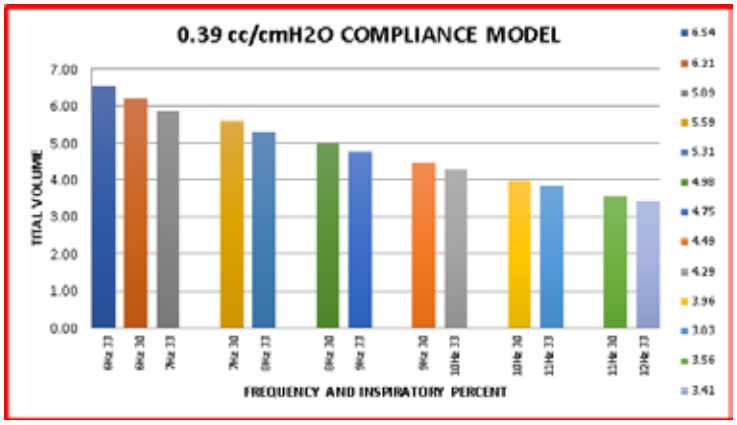
Introduction: This study looks at the relationship of the delivered Tidal Volume (Vt) using an inspiratory percent(I%) of 30 at one Hertz (Hz) vs the next greater HZ with an I% of 33 using a Sensor Medics High Frequency Oscillatory Ventilator (HFOV). In clinical care, increasing HFOV Hz is an accepted method of weaning the HFOV to increase the PCO_2 in the mechanically ventilated patient. The idea is by increasing the Hz you decrease the inspiratory time and it is assumed the Vt to the patient. The concern is increasing the Hz increases the possibility of inadequate expiratory time for exhalation. Air trapping can be a consequence. The trapping of ventilation gasses can result in hyper-expansion of the lungs. The hyper-expansion can impair gas exchange, shunting, and in some cases impair cardiac function if the hyper-expansion is severe enough. The goal of this study is to determine if decreasing the I% could deliver a similar out come as seen when the Hz in increased while at 33 I%, but with lowering the risk of air trapping. This study will look at the delivered Vt's to see if the assumption is correct.

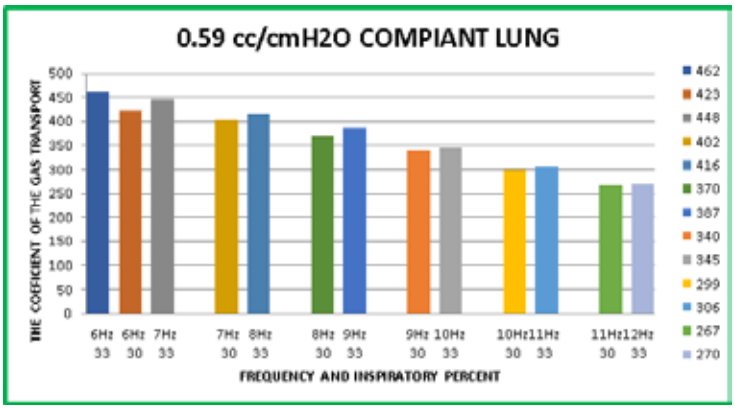
Method: A calibrated HFOV was connected to one of the three test lungs using a full-length endotracheal tube. The HFOV bias flow was maintained at 15 lpm throughout all testing. The MAP was set to 14 cmH_2O (+- 0.1). As each parameter was set the Vt were measured using a Dragger VN 500 BabyLog ventilator. The VN 500 became a volume monitor by placing its' flow sensor between the HFOV circuit and ETT. The lung compliances and ETT's used were; 0.20cc/cmH_2O using a 2.5 ETT, 0.39cc/cmH_2O using 3.0 ETT, and 0.59cc/cmH_2O using a 3.5 ETT. The HFOV frequencies tested were 6Hz thru 12Hz. The I% was set to 30 and 33 for each frequency, except 12 Hz which ran at 33 I% only. The amplitudes tested were; 16, 18, 20, 22, 24, 26, 28, and 30. Once the data was collected it was placed into a category. A category consisted of the averaged measured Vt's delivered from all Amp's, from a single Hz frequency at a given I%. The categories were then paired. The pairing was a category of a Hz at 30 I% with the category of the next higher Hz at 33 I% (see graphs 1, 2, and 3).

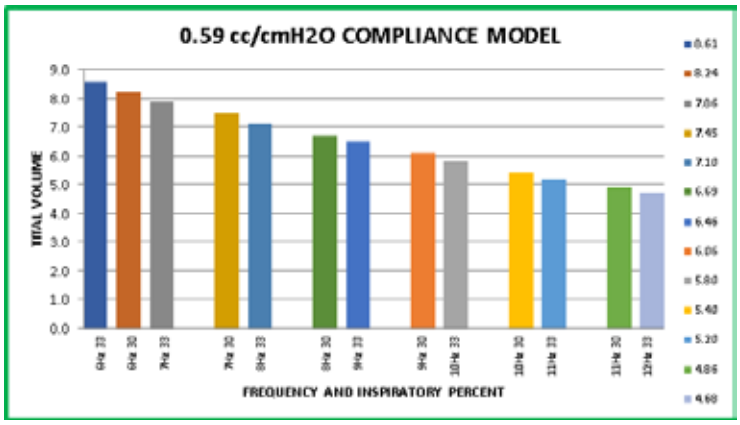
Conclusion: By decreasing the I% to 30 there is a demonstrated reduction in the delivered Vt. When looking at the paired categories they are very similar. If you only look at the delivered Vt you would think it is highly likely in a clinical setting if the I% were reduced to 30, rather that increasing the Hz on 33 I% the lab values would yield similar results. Only clinical application/trial will determine if either of these assumptions are correct.

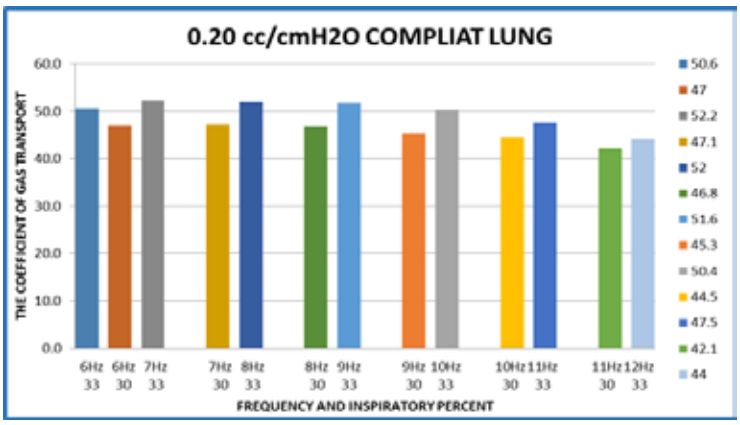












ATT2019-6

Delivered HFOV Amplitudes At 30 vs 33 Inspiratory Percent

Jeffrey Wright BSRT, RRT-NPS, M. Parker ASRT, RRT,

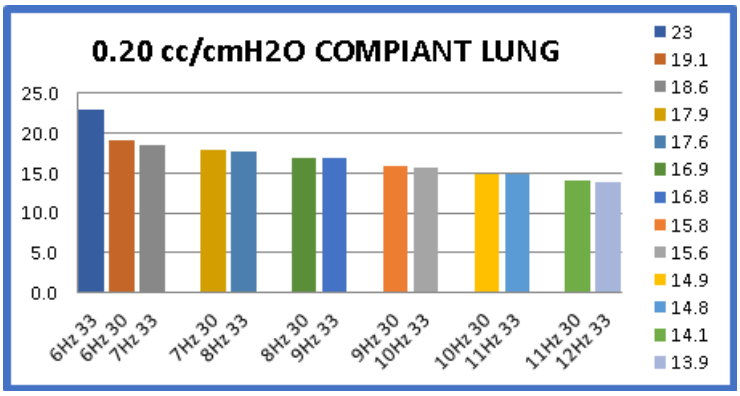
Primary Children's Hospital, Salt Lake City, Utah.

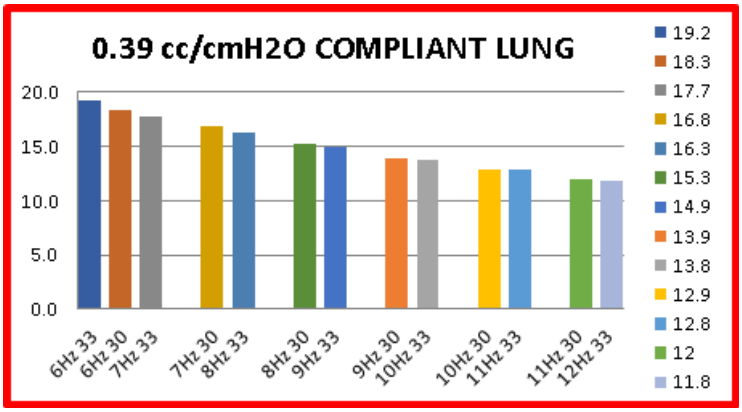
Introduction: This study looks at the relationship of the delivered amplitude using an inspiratory percent of 30 at one Hertz (Hz) vs the next greater HZ with an inspiratory of 33 using a Sensor Medics High Frequency Oscillatory Ventilator (HFOV). In clinical care, increasing HFOV Hz is an accepted method of weaning the HFOV to increase the PCO_2 in the mechanically ventilated patient. Increasing the Hz can have a negative effect in some patients. Air trapping is a common negative side effect. The trapping of ventilation gasses can result in hyper-expansion of the lungs, shunting, impair adequate gas exchange, and in some cases cause reduced cardiac function if the hyper-expansion is severe enough. The goal of this study is to determine if decreasing the inspiratory percent could deliver a similar out come as seen in increasing the Hz, but with a reduced possible air trapping in the lung.

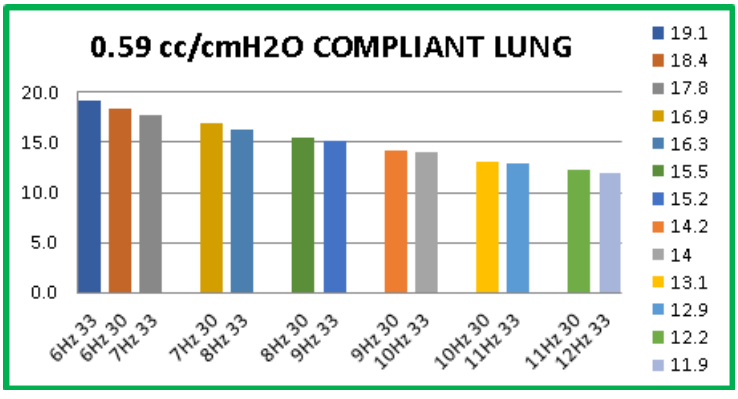
Method: A calibrated HFOV was connected to one of the three test lungs using a full-length endotracheal tube. The HFOV bias flow was maintained at 15 lpm throughout all testing. The MAP was set at 14 cmH2O (+- 0.1). Each parameter was set, and the pressures were measured within the test lungs using a TSI Certifier. The lung compliances and ETT's used were; 0.20 cc/cmH_2O using a 2.5 ETT, 0.39 cc/cmH_2O using a 3.0 ETT, and 0.59 cc/cmH_2O using a 3.5 ETT. The HFOV frequencies tested were 6 Hz thru 12 Hz. The inspiratory percent was set to 30 and 33 for each frequency, with exception of the 12 Hz which was only ran at an inspiratory percent of 33. The amplitudes tested were; 16, 18, 20,

22, 24, 26, 28, and 30. Once the data was collected it was placed in a category and then averaged. A category consists of a specific Hz frequency at a single inspiratory percent, and all 8 amplitudes studied averaged. The categories were then paired. The pairing consisted of a Hz category at an inspiratory percent at 30 with the next higher Hz category inspiratory percent set at 33.

Results/Conclusion: By decreasing the inspiratory percent to 30 there was a demonstrated reduction in the delivered amplitude to the test lungs (see graphs). When comparing the categories, the findings are very similar to each other. It is highly likely in a clinical setting if the inspiratory percent were to be reduced to 30, rather that increasing the Hz at an inspiratory percent of 33 the lab value differences would be minorly different. Only a clinical trial/application will determine if this assumption is correct.







ATT2019-7

Assessment of the number of neuronal progenitor cells in the brain of preterm lambs.

Nabi A*, Pettet L, Rebentisch A, Wang Z, Dawson E, Dahl M, Yoder B, Null D, Albertine K.

University of Utah, Salt Lake City, UT and University of California at Davis, Davis, CA

Purpose of Study: Although brain injury happens in chronically ventilated preterm infants, pathogenic mechanisms remain to be identified in part because brain tissue is not typically part of clinical material for study. We showed that preterm lambs supported by invasive mechanical ventilation (IMV) have more apoptosis, and less proliferation, of neurons and glial subtypes compared to non-invasive respiratory support (NRS). These results suggest that cell survival may be decreased in the brain of preterm lambs that are managed by IMV. Disruption might lead to shift to more progenitor cells as a compensatory response. Neural stem cells give rise to neuronal progenitor cells, which are identifiable by doublecortin. We hypothesized that decreased neuron survival during IMV may increase the number of neuronal progenitor cells in the brain.

Methods Used: Preterm lambs, treated with antenatal steroids and postnatal surfactant, were managed by IMV or NRS for either 3d or 21d (n=4/group). We use NRS (high-frequency nasal support) as the positive gold-standard for alveolar formation in the lung. At the end of 3d or 21d of respiratory management, cortical brain tissue from the temporal lobe was fixed. We used immunohistochemistry to localize doublecortin-positive neuronal progenitor cells. We used stereology to quantify numerical density of doublecortin-positive neurons in Layer II, using systematic, uniform, random sampling.

Summary of Results: We found a statistically significant difference in numerical density of doublecortin-positive neuronal progenitor cells in cortical layer II of the temporal lobe at 21d between the two modes of respiratory support. Numerical density was significantly lower for the 21d IMV group (0.021±0.002/cm3) compared to the 21d NRS group (0.027±0.005/cm3; $p<0.05$). No difference was detected at 3d between the two groups (3d IMV 0.024±0.003/ cm3 versus 3d NIS 0.029±0.005/ cm3, respectively). Conclusions: We conclude that 21d of IMV reduces the number of neuronal progenitor cells in layer II of temporal lobe gray matter compared to 21d of NRS. We speculate that the better outcome after NRS may lead to better neurodevelopmental outcomes later in life. Supported by R01 HL110002 and Division of Neonatology.

ATT2019-8

Mask resuscitation and continuing noninvasive respiratory support leads to better alveolar formation compared to invasive mechanical ventilation resuscitation and continuing invasive mechanical ventilation of preterm lambs.

LRebentisch A*, Dahl M, Johnson O, Bradford C, Dawson E, Dellaca' R, Lavizzari A, Null D, Yoder Y, Albertine K.

University of Utah, Salt Lake City, UT, Politecnico di Milano, Milan, Italy, Ospedale Maggoire Policlinico, Milano, Italy, and UC Davis, Davis, CA.

Purpose of Study: Chronic lung disease of prematurity is histopathologically characterized by alveolar simplification. We showed, using our preterm lamb model, that 3d of invasive mechanical ventilation (IMV) leads to thicker and less secondary septated distal airspace walls, both being indices of alveolar simplification, compared to preterm lambs supported by 3d of noninvasive respiratory support (NRS). An unknown is whether preterm lambs that are not endotracheally intubated, and therefore not supported by IMV, will have improved architectural formation of alveoli. Therefore, the aim of this study was to develop a preterm lamb model in which lambs were resuscitated noninvasively by facial mask.

Methods Used: Preterm lambs (delivered by Cesarean-section at 128d gestation; term ~150d; equivalent to ~28w gestation in humans) were either (1) intubated at birth, resuscitated by IMV, and continued on IMV ("IMV" group; n=4; control group) for 3d or (2) resuscitated by facial mask and continued with NRS ("NRS" group; n=5) for 3d. The NRS group was supported noninvasively by nasal cannula. All lambs were given surfactant prior to delivery and caffeine citrate after delivery. Both groups received two sustained lung inflations (35sec). Quantitative histology was used to measure indices of alveolar formation.
Summary of Results: IMV-managed preterm lambs had significantly thicker distal airspace walls (2.5±0.2 μm) compared to the NRS preterm lambs (2.0±0.1 μm; $p<0.05$ by unpaired t-test). Volume density of secondary septa was not significantly different for the IMV group (4.8±1.6%; $p=0.6$) compared to the NRS group (8.3±1.8%) of preterm lambs.

Conclusions: Noninvasive resuscitation and continuing noninvasive respiratory support leads to more rapid thinning of distal airspace walls compared to IMV resuscitation and continuing IMV of preterm lambs. Supported by R01 HL110002 and Division of Neonatology

ATT2019-9
Balance between proliferation and apoptosis of interstitial cells remains constant in the lung of former preterm lambs, regardless of the mode of respiratory support after preterm birth of preterm lambs.

Cutler B*, Rebentisch A, Wang Z, Dawson E, Dahl M, Yoder B, Null D, Albertine K.

University of Utah, Salt Lake City, UT and University of California at Davis, Davis, CA

Purpose of Study: Alveolar simplification is the characteristic histopathology for bronchopulmonary dysplasia. We showed, using our chronically ventilated preterm lamb model, that days or weeks of invasive mechanical ventilation (IMV) leads to thicker distal airspace walls, an index of alveolar simplification, compared to noninvasive respiratory support (NRS). We also showed that the increased thickness is related to disproportionate proliferation of mesenchymal cells compared to their apoptosis. Our new former preterm lamb studies indicate that their lungs have alveolar walls that are persistently thicker at 5 months corrected postnatal age (cPNA) compared to unventilated term lambs matched for PNA. An unknown is whether the former preterm lambs have persistently disrupted proliferation versus apoptosis of alveolar wall interstitial (mesenchymal) cells.

Methods Used: Preterm lambs (delivered by Cesarean-section at 128d gestation; term ~150d; equivalent to ~28w gestation in humans) were either (1) intubated at birth, resuscitated by IMV, and continued on IMV for 6d ("IMV" group; n=6) or (2) resuscitated noninvasively by facial mask and continued NRS for 6d ("NRS" group; n=4). Both groups were weaned from all respiratory support and lived for ~6 months (former preterm (FPT) lambs; ~5 months corrected postnatal age; ~6y human). Control term lambs were not ventilated and lived 5 months. Quantitative immunohistochemistry was used to quantify proliferation and apoptosis.
Summary of Results: FPT lambs managed by IMV or NRS during their first week of postnatal life had comparable proliferation index (0.87±0.49 and 0.97±0.18, respectively; mean±SD; not different) and apoptotic index (apoptotic interstitial cells/total epithelial cells; 0.85±0.70 and 0.60±0.25, respectively; not different). These indices were comparable to those for control term lambs (0.64±0.41 for apoptotic index and 0.99±0.51 for proliferation index).

Conclusions: Our results suggest that the persistently thicker alveolar walls of FPT lambs that were managed by IMV for ~6d during their first week of postnatal life (Dahl, 2018) occurs without persistent disruption of the balance between proliferation and apoptosis of interstitial (mesenchymal) cells in alveolar walls. We speculate that the persistently thicker alveolar walls may be the result of reduced turnover of interstitial cells and/or excess accumulation of extracellular matrix (Pierce, Am J Physiol - Lung 1997). Supported by R01 HL110002 and Division of Neonatology

ATT2019-10
Jet 58: HFJV and Confessions of a NICU Mom

Kuljit Minhas RRT, BSc, Ashely Durance NICU Mother

Royal Columbian Hospital (Fraser Health Authority), New Westminster, BC Canada

Kuljit.Minhas@fraserhealth.ca 604-319-5565
AshleyLdurance@gmail.com

To discuss the process of starting the HFJV program at our site and increase awareness on family centered care in the NICU thru the eyes of a NICU family.

Initiating a new ventilation program can be challenging. It involves multiple stakeholders who need to understand the therapy and also agree on strategies, techniques and management. The impact of these interventions on patients and families must be considered as well.

In this presentation we will discuss the implementation of the HFJV program at Royal Columbian Hospital and the learnings along the way. This includes the creation of a ventilation standard, appropriate timing of the intervention, and subsequent modifications with complementary strategies to allow skin to skin on the HFJV (construction of a "jet arm" for the patient box).

In addition, we will present the story of Baby girl Hazel. We will hear her journey of 6 months in the NICU from her mother and the multi-disciplinary clinicians that cared for her. We will share her 58 day "flight" on HFJV with multiple Respiratory interventions including, unique "outside of the box" events. Family experience from

admission to discharge will be highlighted including knowledge of the NICU environment, feedback on improvements from family, and post discharge.

ATT2019-11

Implementing the Use of Early Lung Recruitment for Newborn Respiratory Management in a Level II Nursery.

Julia Thomas [mailto:Julia.Thomas@imail.org]

3rd year DNP-NNP student
Creighton University

Background: Newborn infants experience many physiologic changes at birth to enable transition to extra-uterine life. Newborns are at risk for respiratory distress due to many factors. A standardized ELR CPAP protocol in level two NICUs for newborns in respiratory distress, could improve quality of care, reduce the severity of respiratory distress during the immediate newborn period, and potentially reduce treatment duration.

Purpose: The purpose of this quality improvement project was to implement a standardized extended early lung recruitment (ELR/CPAP) protocol for infants who exhibit symptoms of respiratory distress within the immediate newborn period (within 10-120 minutes of life) for respiratory management. Specific aims were to improve respiratory management of newly born infants, increase the rate of infants transitioned to the mother-baby unit, promote maternal-infant proximity, and decrease the transfers to higher level III NICU.

Methods:

1. Education of ELR practice was provided to all staff who attend deliveries
2. Assessment of the process continued throughout administration of ELR/CPAP to ensure correct application/practice of the protocol.

Results:

Data collected suggests ELR/CPAP is beneficial for a specific patient population, the patients who were able to transition to the mother/baby unit after an extended transition period, who would have otherwise been transported to a higher level of care for ongoing respiratory management. This project provides a baseline for future studies to explore ELR in neonates.

ATT2019-12

Is Conventional Ventilation Actually High-Frequency Ventilation in Disguise?

Mitchell Goldstein, MD, Carter Tong, RRT, Munaf Kadri, MD, Anamika Banerji, MD, Elba Fayard, MD, Ricardo Peverini, MD.

Division of Neonatology, Department of Pediatrics, Loma Linda University Children's Hospital, Loma Linda, CA

Introduction: Neonatal ventilation has been traditionally divided into two different categories. Conventional ventilation consists of tidal ventilation using a "conventional" ventilation rate typically less than 60 breaths per minute. High-frequency ventilation has been defined as ventilation in excess of 2.5 Hz or 150 breaths per minute. From earlier studies on high-frequency ventilation, we were able to demonstrate that high-frequency ventilation gives rise to harmonics of yet higher frequency waveforms. Some of these frequencies may have a clinically significant effect on ventilation.

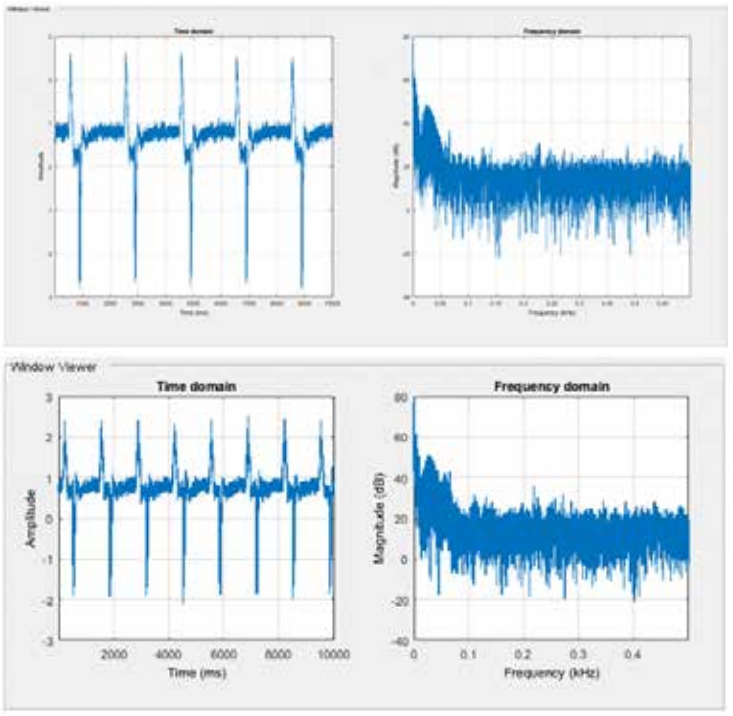
Purpose: We asked whether conventional ventilation produces harmonics that are in the high-frequency range.

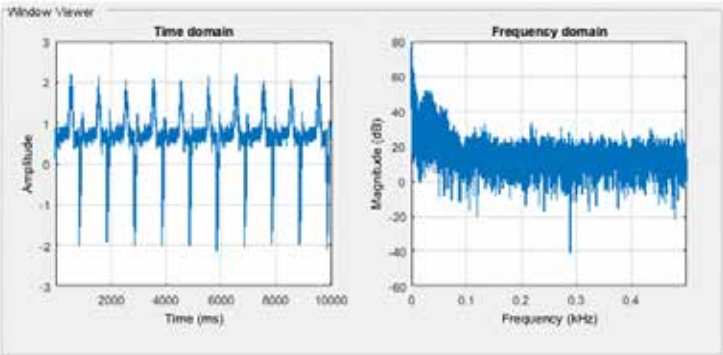
Methods: We used the Maquet SERVO-n Neonatal Ventilator (MAQUET Holding B.V. & Co., Rastatt, Germany) and the RD020 from Fisher and Paykel (Huntington Beach, CA) as our artificial lung for this study. The ventilator was set at a rate of 30, 45, and 60 BPM with pressures of 25/4 and an inspiratory time of 0.35. We studied different flow and pressure dynamics at each setting. Easy Sense UPC2100 software from Validyne (Northridge, CA) was used to obtain our measurements. Sampling was at 1000 Hz. 10 seconds of data or 10,000 measurements were taken at each of these settings. Data were analyzed using MATLAB (R2015B) and mapped in time and frequency domains.

Results: As noted in the Graphics below (30, 45, 60 bpm). In all samples, the frequency domain indicated substantial magnitude waveforms in the high-frequency range (i.e., a substantial bump in magnitude in the harmonics in the < 0.1 KHz range).

Discussion: Although the debate continues as to whether "conventional" or high-frequency ventilation is superior in the ventilation of neonates, it is readily apparent that the differences are not as well defined as previously described. There is a substantial component of high-frequency ventilation in conventional ventilation patterns. Ventilator dynamics and patient factors may affect the degree to which this effect is clinically significant, but it is clear that "conventional ventilation" also produces significant harmonics.

Conclusion: "Conventional" ventilation may, in fact, be high-frequency ventilation in disguise. Further research is indicated to define the precise operational frequencies.





ATT2019-13
Neonatology Today: Statistics, Logistics, and You

Mitchell Goldstein, MD.

Division of Neonatology, Department of Pediatrics, Loma Linda University Children's Hospital, Loma Linda, CA.

Last February, Neonatology Today was acquired by Loma Linda Publishing Company, a Delaware 501-C3 Not-For-Profit operating as a Public Charity. In the 12 months since the journal has been under new ownership, we have initiated the following plan:

- All manuscripts submitted will be peer-reviewed. We plan to add additional reviewers as needed to accommodate the demand. Our commitment will be to provide feedback on any submission in fewer than 14 business days.
- We will continue to commit to not charge authors any fees whatsoever for publication of their manuscripts.
- We will continue to provide the journal for free to our readers.
- We will actively solicit and publish case reports that provide insights into the management of complex conditions confronting practicing neonatologists. Although many journals have discouraged case report submission, it is our feeling that these provide a way of disseminating meaningful academic information that may not otherwise see the light of day.
- We will be making Neonatology Today a multidisciplinary publication, open to all professionals who engage in academic pursuits in the fields of Neonatology, Perinatology, and Pediatrics.
- We hope to increase our readership by striving to be first to report on innovative new concepts in all of the associated specialties.
- We will expand our readership by adding an international component to our board.
- We are highlighting the work of the patient and provider advocacy community including organizations like the National Coalition for Infant Health (NCfIH),(infanthealth.org).
- We will have open conference calls to improve the journal content.
- We will have a dedicated message line for questions, concerns, and comments.
- We aim to provide CME's for our reviewers.

Since NT 's acquisition, the page count has tripled. We have added additional distribution models, increasing our circulation to 15,000 readers/month with a peak readership of 100,000 for the 12 month period. EBSCO and CiteFactor have indexed our journal. We are continuing to look for new content and new members of our editorial board. Please consider NT for your publication plans

ATT2019-14
Prongs and Velocities - Unraveling the Vapotherm Flow Dynamics

Rivera L., Agrawal P., Tong C., Goldstein M.

Division of Neonatology, Department of Pediatrics, Loma Linda University Children's Hospital, Loma Linda, CA.

Background:
The use of high flow therapy (HFT) is growing rapidly, particularly in the neonatal intensive care setting. Vapotherm (VT) is a HFT modality that was developed as a method for humidifying and warming inhaled gas, allowing for flow to be delivered in a way that is less traumatic to the nasal mucosa.

The VT cannula is not uniform in its diameter. The recommended cannula size will vary depending on the patient's weight, inner diameter of the nares and the outer diameter of the cannula prongs in use. VT cannulas were developed with the impression that their small size will increase gas velocity to more efficiently flush the nasal extra-thoracic dead space and therefore flush CO_2 at lower, more comfortable flows. This ability to flush the extra-thoracic dead space is important for the management of respiratory distress and hypercapnia.

Objective:
We evaluated the effect of varying the nasal cannula opening size in a typical VT cannula application, on the exit velocity of gas based on different flow rates.

Design/Methods:
Outer diameters of 1.5, 1.9, 2.7 and 4.8 mm were selected based on the cannula opening sizes provided by the Vapotherm manufacturer. Using the preselected recommended flow rate for each cannula, the exit flow velocity from the nasal cannula was calculated using known relationships between flow and velocity.

Results:
Decreasing cannula opening sizes and increasing flow rate lead to significant increases in nasal cannula velocity.

Conclusion(s):
High flow cannulas can vary considerably based on the diameter of the cannula opening. Smaller cannula size and increased flow allow for propagation of flow at higher velocities, theoretically influencing hypoxia, hypercapnia and work of breathing in patients with respiratory distress. It is important to be cognizant about the effect of weaning flow to the nasal cannula on the velocity of gas delivered. Clinicians should also take into account the size of prongs as this contributes significantly to the delivered velocity to the patient.

Velocity (m/s) at Given Flow Rate and Cannula Size				
	Cannula Size in mm			
	1.5	1.9	2.7	4.8
Liter per minute (LPM) Flow to Cannula				
1	9.4	5.9	2.9	0.9
2	18.9	11.7	5.8	1.8
3	28.3	17.6	8.7	2.8
4	37.7	23.5	11.6	3.7
5	47.2	29.3	14.5	4.6
6	56.6	35.2	17.4	5.5
7	66.0	41.1	20.3	6.5
8	75.5	46.9	23.2	7.4
10	94.3	58.7	29.0	9.2
20	188.6	117.3	58.0	18.4
30	283.0	176.0	87.1	27.7
40	377.3	234.6	116.1	36.9

NT

Corresponding Author

Donald Null, MD
Professor of Pediatrics
Division of Neonatology
Department of Pediatrics
University of California, Davis
'Donald M Null' <dnull@ucdavis.edu>

Mitchell Goldstein, MD
Professor of Pediatrics
Division of Neonatology
Department of Pediatrics
Loma Linda University School of Medicine
mgoldstein@llu.edu

Arun Pramanik, MD
Professor of Pediatrics
Division of Neonatology
Department of Pediatrics
Louisiana State University

How to Care for a Baby with NAS

Use the Right Words

I was exposed to substances in utero. I am not an addict. And my mother may or may not have a Substance Use Disorder (SUD).

Treat Us as a Dyad

Mothers and babies need each other. Help my mom and me bond. Whenever possible, provide my care alongside her and teach her how to meet my needs.

Support Rooming-In

Babies like me do best in a calm, quiet, dimly-lit room where we can be close to our caregivers.

Promote Kangaroo Care

Skin-to-skin care helps me stabilize and self-regulate. It helps relieve the autonomic symptoms associated with withdrawal and promotes bonding.

Try Non-Pharmacological Care

Help me self-soothe. Swaddle me snugly in a flexed position that reminds me of the womb. Offer me a pacifier to suck on. Protect my sleep by "clustering" my care.

Support Breastfeeding

Breast milk is important to my gastrointestinal heath and breast feeding is recommended when moms are HIV-negative and receiving medically-supervised care. Help my mother reach her pumping and breastfeeding goals.

Treat My Symptoms

If I am experiencing withdrawal symptoms that make it hard for me to eat, sleep, and be soothed, create a care plan to help me wean comfortably.

Learn more about
Neonatal Abstinence Syndrome
at www.nationalperinatal.org

National Perinatal Association

Letters to the Editor

[EXTERNAL] Letter to the Editor

Monday, July 08, 2019 09:31

Dear Dr. Goldstein,

When an infant transport has been requested for a higher level of care such as a Level II requesting a transfer of an infant to a Level III or IV unit because an infant is assessed to be ill, and determined to need treatments beyond the usual treatments offered at the facility of origin, who assumes the medical decision maker role and legal responsibility for the infant after the transport team arrives--the Neonatologist at the Level III or IV facility who has accept the transport and transfer of the infant, or the pediatrician or other care provider requesting transport to a higher level of care until the infant and transport team arrives back at the tertiary or higher level of care?

T. Allen Merritt, MD MHA

Dear Dr. Merritt,

This is an excellent question. The location and local laws may impact the decision. In my training, I had always been taught that the patient was my responsibility from the moment I arrived at the hospital to pick up the patient until the time the patient was safety back to the home base. This arrangement worked well. The referring physician had the reassurance of knowing that the patient was under the auspices of the higher level of care from the point in time that the ambulance or the helicopter arrived, the parents were given the assurance that the transport team was an extension of the higher level of care, and the hospital and its staff were reassured that they had a "contracted" arrangement with a responsible facility.

At some point in time, things changed. One anonymous source that I discussed this with blamed EMTALA (a United States law) that requires any center with a highly level of care accept an patient that they could potentially provide care for regardless of capacity, bed space, staffing, or other issues. This law mainly applies to emergency room transfers but has applicability to hospitals that provide birthing services and neonatal intensive care. So it appears that if I am situated in Alaska or Maine, and I want to transfer a patient needing a higher level of care to some place in Southern California, that hospital would have to accept the transfer regardless of the distance and the availability of other applicable hospitals and levels of care located along the route. It should come as no surprise that this problem is not a concern for most centers. However, for those centers with a national or international reputation, this problem has occurred with some frequency.

There are extreme liability concerns beyond risks to patient safety. And one solution to this concern is to place the referring physician at risk. As the representative of risk management for a hospital in our local area explained, this condition of referral was spelled out in the transport agreement that the hospital signed with each of its referral partners. A referring physician and hospital would have to acknowledge their full responsibility for medical care occurring on the transport performed by the receiving facility. Malpractice plans here in the United States are predicated on acts committed by the insured provider and not those delegated through relations with other parties. If a problem occurred on transport, the responsible physician would not have been managing the actions of the team. Under the terms of such an arrangement, our hospital and physician group pulled back from arranging transports by the transport team of this particular facility until the language was changed under considerable duress.

Dr. Merritt's question is very apropos because there was no announcement of this changed policy prior to implementation. The contract had been represented to medical administration as business as usual. The subtle change involving millions of dollars in potential liability was not recognized for what it was. And we were not alone; many other hospitals in the same area had similar agreements in place. No one had recognized the change in the directionality of transport liability.

It is critically important to read your transport agreements thoroughly, make sure patient responsibility, liability, and other care issues are carefully spelled out before a potential problem occurs.

Sincerely,
Mitchell Goldstein, MD

Editor in Chief

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Loma Linda Publishing Company
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c/o Mitchell Goldstein, MD
11175 Campus Street, Suite #11121
Loma Linda, CA 92354
Tel: +1 (302) 313-9984
LomaLindaPublishingCompany@gmail.com

www.NeonatologyToday.net
Twitter: www.Twitter.com/NeoToday

Mitchell Goldstein, MD
Professor of Pediatrics
Loma Linda University School of Medicine
Division of Neonatology
Department of Pediatrics
mgoldstein@llu.edu

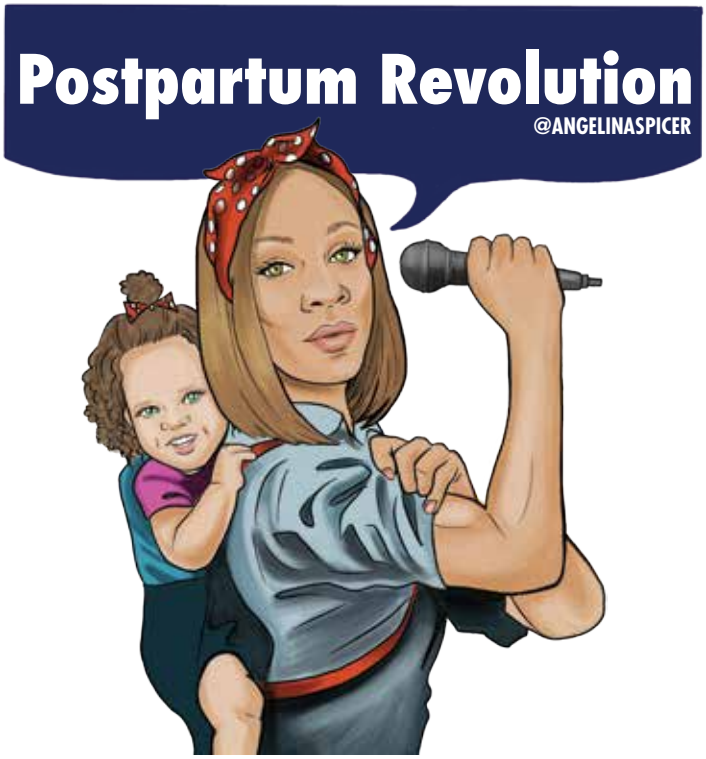
Neonatology Today welcomes your editorial commentary on previously published manuscripts, news items, and other academic material relevant to the fields of Neonatology and Perinatology.

Please address your response in the form of a letter. For further formatting questions and submissions, please contact Mitchell Goldstein, MD at LomaLindaPublishingCompany@gmail.com.

Erratum (Neonatology Today July, 2019)

Neonatology Today has identified an erratum affecting the July, 2019 edition. Rob Grahan's Respiratory Report was missing two paragraphs. These are included as an addendum to the August column

Corrections can be sent directly to LomaLindaPublishingCompany@gmail.com. The most recent edition of Neonatology Today including any previously identified erratum may be downloaded from www.neonatologytoday.net.



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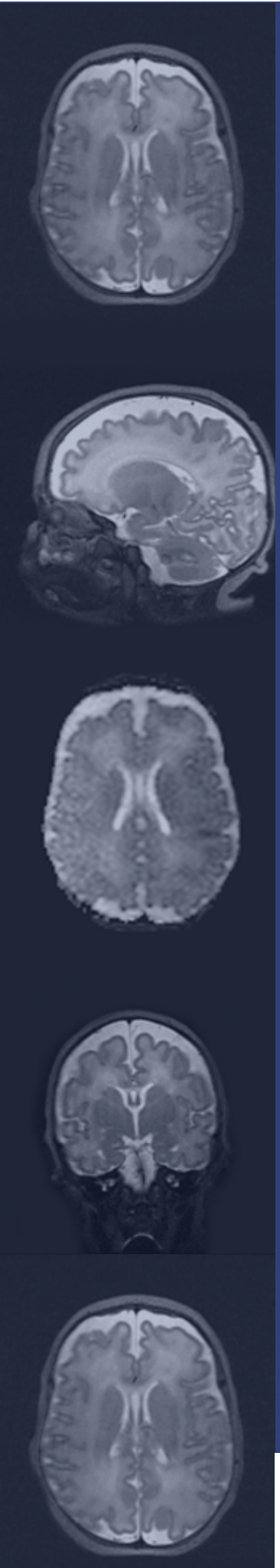

California NICU Professionals

You are invited!

NEONATAL MRI:
THE WHO? WHY? WHEN AND HOW?

Dear Colleagues,
You are invited to a dinner presentation and networking event with the renowned neonatologist Dr. Terrie Inder.

NETWORKING.
WINE RECEPTION.
DINNER.
PRESENTATION.

In this case-based presentation, Dr. Inder will review the state of science on the use of neonatal MRI for both term and preterm infants at risk for brain injury.

She will share an evidence-based approach to developing a neonatal neuro-imaging protocol for your NICU and take a deep dive into the most common misconceptions about the use of MRI for preterm infants at term-age equivalents.

As an early adopter of in-NICU MRI scanners, she will be sharing her experiences from blueprints to their first year of use.

Two Dates to Choose From

Thursday, Sept 19th
5:30pm - 8:30pm
Hyatt Regency SFO Airport
1333 Old Bayshore Hwy
Burlingame, CA 94010

Monday, Sept 23rd
5:30pm - 8:30pm
Sheraton Park Hotel
1855 S Harbor Blvd
Anaheim, CA 92802

Register at rsvp.synapsecare.com *

** Please note that seating for dinner is limited. Please register as soon as possible to secure a spot.*

This event sponsored by Aspect Imaging

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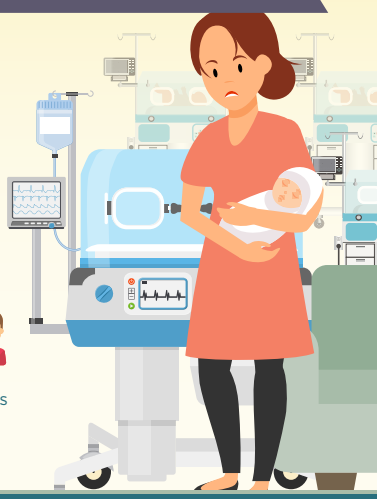
Will your **PRETERM INFANT** *need* **EARLY INTERVENTION** *services?*

Preterm infants are:

2x more likely to have developmental delays

5x more likely to have learning challenges

1 in **3** preterm infants will require support services at school

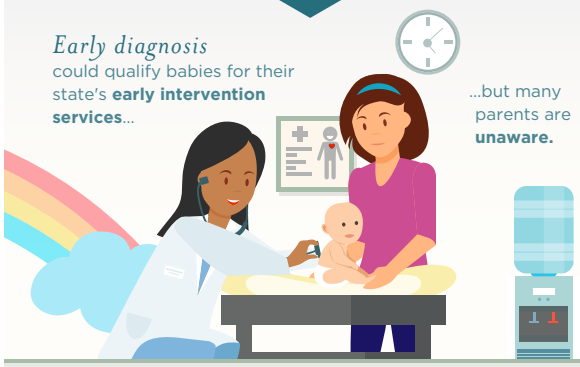


Early intervention can help preterm infants:

- Enhance language and communication skills
- Build more effective learning techniques
- Process social and emotional situations
- Address physical challenges
- Prevent mild difficulties from developing into major problems

Early diagnosis could qualify babies for their state's **early intervention services**...

...but many parents are **unaware.**



NICU staff, nurses, pediatricians and social workers **should talk** with NICU families about the challenges their baby may face.

Awareness, referral & timely enrollment in early intervention programs can help **infants thrive** and grow.

NCFIH National Coalition for Infant Health

Protecting Access for Premature Infants through Age Two

www.infanthealth.org

Visit **CDC.gov** to find contact information for your state's early intervention program.

Las nuevas mamás necesitan acceso a la detección y tratamiento para **LA DEPRESIÓN POSPARTO**

1 DE CADA **7** MADRES AFRONTA LA DEPRESIÓN POSPARTO, *experimentando*

- Llanto incontrolable
- Sueño interrumpido
- Ansiedad
- Desplazamientos en los patrones de alimentación
- Ideas de hacerse daño a sí mismas o al bebé
- Distanciamiento de amigos y familiares

Sin embargo, sólo el 15% recibe tratamiento[1]

LA DEPRESIÓN POSTPARTO **NO TRATADA** PUEDE AFECTAR:

- *La salud de la madre*
- *El sueño, la alimentación y el comportamiento del bebé a medida que crece*[2]
- *La capacidad para cuidar de un bebé y sus hermanos*

PARA AYUDAR **A LAS MADRES A ENFRENTAR LA DEPRESIÓN POSPARTO**

LOS ENCARGADOS DE FORMULAR POLÍTICAS PUEDEN:

- Financiar los esfuerzos de despistaje y diagnostico
- Proteger el acceso al tratamiento

LOS HOSPITALES PUEDEN:

- Capacitar a los profesionales de la salud para proporcionar apoyo psicosocial a las familias... **Especialmente aquellas con bebés prematuros, que son 40% más propensas a desarrollar depresión posparto**[3,4]
- Conectar a las mamás con una organización de apoyo

NCFIH National Coalition for Infant Health

www.infanthealth.org

[1] American Psychological Association. Accesible en: http://www.apa.org/pi/women/resources/reports/postpartum-depression.aspx

[2] National Institute of Mental Health. Accesible en: https://www.nimh.nih.gov/health/publications/postpartum-depression-facts/index.shtml

[3] Journal of Perinatology (2015) 35, 529–536; doi:10.1038/jp.2015.147.

[4] Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. Vigod SN, Villegas L, Dennis CL, Ross LE BJOG. 2010 Apr; 117(5):540-50.

Upcoming Medical Meetings

Quantum Caring for NICU Clinicians
Summerlin Hospital.png
August 24th, 2019, 8:30am - 5:00pm
Summerlin Hospital Medical Center, Las Vegas NV
https://www.caringessentials.net/quantum-caring-for-clinicians-workshop

7th International Conference on Neonatal Care
October 10-11, 2019
Airport Hotel Okecie, Warsaw, Poland
www.neonatus.org

8th Annual Scientific Sessions of the Cardiac Neurodevelopmental Outcome Collaborative
October 11-13, 2019;
Hospital for Sick Children, Toronto, Ontario, Canada
www.cardiacneuro.org/upcoming/

NANN's 35th Annual Conference
Savannah Convention Center
Savannah, GA
October 9-12, 2019
http://nann.org/education/annual-meeting

The AAP Experience
National Convention and Exhibition
New Orleans, LA
October 25-29, 2019.
http://aapexperience.org/

International Lactoferrrin Conference
Lima, Peru
November 4-8, 2019
http://www.lactoferrinconference2019.com/index.html
Chair: Dr. Theresa Ochoa, Theresa.J.Ochoa@uth.tmc.edu

Miami Neonatology 43rd Annual International Conference 2019
November 10-13, 2019
November 13, 2019
Loews Miami Beach Hotel
Miami, Florida
http://pediatrics.med.miami.edu/neonatologyMillennium

Neonatology: Building a Better Pathway for Preemies
November 16, 2019
8 a.m. to 5 p.m.
Women & Infants Hospital
Malcolm and Elizabeth Chace Education Center
101 Dudley Street, Providence, RI
For More Information
Please contact:
Mary Tucker mtucker@wihri.org or Brenda Vecchio bvecchio@wihri.org
/international-neonatal-conference

Hot Topics in Neonatology®
National Harbor, MD
December 8-11, 2019
http://www.hottopicsinneonatology.org/

NEO
The Conference for Neonatology
Coming February 2020
San Diego, CA
http://www.neoconference.com/

The 37th Annual Advances in Therapeutics and Technologies Conference
March 24-28, 2020
Snowbird, UT
http://paclac.org/advances-in-care-conference/

Pediatric Academic Societies 2020 Meeting
April 29 – May 6, 2020
Philadelphia, PA
https://2020.pas-meeting.org/

For up to date Meeting Information, visit NeonatologyToday.net and click on the events tab.

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Mitchell Goldstein, MD
Loma Linda Publishing Company
11175 Campus Street
Suite #11121
Loma Linda, CA 92354
www.NeonatologyToday.net
Tel: +1 (302) 313-9984
LomaLindaPublishingCompany@gmail.com

Editorial and Subscription
Mitchell Goldstein, MD
Neonatology Today
11175 Campus Street
Suite #11121
Loma Linda, CA 92354

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Academic Neonatologist Opportunity in Southern California

Loma Linda University Faculty Medical Group, Department of Pediatrics, Division of Neonatology, is seeking board certified or board eligible Neonatologists to join their team.

The Neonatal Intensive Care Unit (NICU) at Loma Linda University Children's Hospital is committed to providing the highest quality of family-centered medical care with our skilled, multi-disciplinary neonatal team. Our unit has 84 licensed beds for the most critically ill babies. As one of the few level 4 tertiary centers in Southern California, we are equipped to provide the highest level of care for newborns with the most complex disorders. Our facility has the largest Level IV NICU in California, serving approximately 25 percent of the state.

We have subspecialists in all medical and surgical areas that are available at all times and are supported by hospital staff with technical, laboratory, and service expertise. Pediatric neurologists work together with us in our NeuroNICU to diagnose, treat and monitor babies with neurologic injury or illness and we focus on providing neuroprotective, developmentally appropriate care for all babies in the NICU. Very specialized care is given in our Small Baby Unit to babies born at less than 30 weeks gestation. Babies at risk for developmental delay are followed up to 3 years in our High-Risk Infant Follow-up Clinic. Genetics specialists are available for evaluation and consultation.

Our Children's Hospital is designated as a Baby Friendly Hospital that supports breastmilk feeding for both term and preterm babies. Neonatal Social Workers and Child Life Specialists are important members of our team. It is our goal to support babies and families in culturally sensitive ways as our patients come from many different ethnic and religious backgrounds.

Loma Linda is located in the center of Southern California. A sunny climate augments the cultural benefits of Los Angeles and Palm Springs and the year-round recreational opportunities of nearby mountains, deserts and beaches.

This opportunity is not eligible for a J1 Waiver.

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Elba Fayard, MD
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efayard@llu.edu

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The Neonatal Intensive Care Unit (NICU) at Loma Linda University Children's Hospital is committed to providing high-quality, family-centered care with our highly skilled, multi-disciplinary neonatal team. Our unit has 84 licensed beds for the most critically ill infants and a new Tiny Baby Program focusing on improving survival and outcomes of extremely low birth weight infants (<1000g at birth). As one of the only level 3 tertiary centers in Southern California, we are equipped to provide the highest level of care for the most complex disorders. We have subspecialists in all medical and surgical areas that are available at all times and are supported by hospital staff with technical, laboratory, and service expertise.

At Loma Linda University Health, we combine the healing power of faith with the practices of modern medicine. We consist of a University, a Medical Center with four hospitals, and a Physicians Group. These resources have helped us become one of the best health systems in the nation.

Contact Us

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Editorial Board

Neonatology and the Arts

This section focuses on artistic work which is by those with an interest in Neonatology and Perinatology. The topics may be varied, but preference will be given to those works that focus on topics that are related to the fields of Neonatology, Pediatrics, and Perinatology. Contributions may include drawings, paintings, sketches, and other digital renderings. Photographs and video shorts may also be submitted. In order for the work to be considered, you must have the consent of any person whose photograph appears in the submission.

Works that have been published in another format are eligible for consideration as long as the contributor either owns the copyright or has secured copyright release prior to submission.

Logos and trademarks will usually not qualify for publication.

We are stuck on "birds" for this month once again. Larry Tinsley, MD shares a photograph of a pink flamingo. When asked where he found such an elusive bird, Dr. Tinsley replied, " We saw this one rare bird on our Alaska cruise. I hear there is an endangered species breeding program in Miami, Florida." Our Editor in Chief Dr. Goldstein provided further clarification, "The breeding program is actually in the Florida Keys. They have had considerable success since the sub-species *lawnae ornamentus* has no natural predators native to the region." The birds continue to rule.

Herbert Vasquez, MD

Associate Neonatologist
Queen of the Valley Campus
Citrus Valley Medical Center
West Covina, CA
VasquezH1@gmail.com

Manuscript Submission: Instructions to Authors

1. Manuscripts are solicited by members of the Editorial Board or may be submitted by readers or other interested parties. Neonatology Today welcomes the submission of all academic manuscripts including randomized control trials, case reports, guidelines, best practice analysis, QI/QA, conference abstracts, and other important works. All content is subject to peer review.

2. All material should be emailed to: LomaLindaPublishingCompany@gmail.com in a Microsoft Word, Open Office, or XML format for the textual material and separate files (tif, eps, jpg, gif, ai, psd, or pdf) for each figure. Preferred formats are ai, psd, or pdf. tif and jpg images should have sufficient resolution so as not to have visible pixilation for the intended dimension. In general, if acceptable for publication, submissions will be published within 3 months.

3. There is no charge for submission, publication (regardless of number of graphics and charts), use of color, or length. Published content will be freely available after publication (i.e., open access). There is no charge for your manuscript to be published under open access

4. The title page should contain a brief title and full names of all authors, their professional degrees, their institutional affiliations, and any conflict of interest relevant to the manuscript. The principal author should be identified as the first author. Contact information for the principal author including phone number, fax number, e-mail address, and mailing address should be included.

5. A brief biographical sketch (very short paragraph) of the principal author including current position and academic titles as well as fellowship status in professional societies should be included. A picture of the principal (corresponding) author and supporting authors should be submitted if available.

6. An abstract may be submitted.

7. The main text of the article should be written in formal style using correct English. The length may be up to 5,000 words. Abbreviations which are commonplace in neonatology or in the lay literature may be used.

8. References should be included in standard "Vancouver" format. Bibliography Software should be used to facilitate formatting and to ensure that the correct formatting and abbreviations are used for references.

9. Figures should be submitted separately as individual separate electronic files. Numbered figure captions should be included in the main file after the references. Captions should be brief.

10. Only manuscripts that have not been published previously will be considered for publication except under special circumstances. Prior publication must be disclosed on submission. Published articles become the property of the Neonatology Today and may not be published, copied or reproduced elsewhere without permission from Neonatology Today.

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