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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.
- The most common adverse reaction is hypotension.

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Please visit inomax.com/PI for Full Prescribing Information.

Visit inomax.com/totalcare to find out more about what's included in your contract.

*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.

Mallinckrodt Pharmaceuticals

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.

INOMAX® is a registered trademark of a Mallinckrodt Pharmaceuticals company.

 US-1800236 August 2018

Peer Reviewed

Addressing the Microvillus Inclusion Disease Knowledge Gap: A Comprehensive Case Analysis

Billy Chang, Nelson Chang, Ronak Patel, Christina McGrath, Dmitry V. Kravtsov, M.D., and Ludmila Kvochina, Ph.D., M.D.

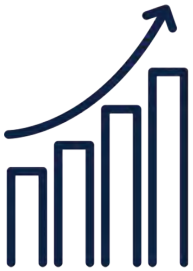
Abstract:

Many children affected by the genetic intestinal disorder known as microvillus inclusion disease (MVID) may not live to see their third birthday. Given MVID's rarity, it can be difficult for doctors, researchers, and parents confronted with the devastating disease to locate necessary data related to the disorder, presenting challenges with research, diagnosis, and the development of treatment strategies.

To address this knowledge gap, this paper summarizes data trends compiled from all known literature published globally on the disease and includes a comprehensive review of the outcome of treatment methods employed.

$451k

estimated annual treatment costs for an MVID patient on total parenteral nutrition (TPN)



147%

increase in reported MVID cases from the 5-yr. period 2006 - 2010 to the period 2011- 2015

0

number of accessible, reliable long-term MVID treatment options

Microvillus inclusion disease (MVID)

Microvillus inclusion disease (MVID) is an exceedingly rare intestinal disease presenting early in the neonatal period, with affected infants developing intractable diarrhea within hours, days, or months after birth. The severity of diarrhea in MVID patients is such that patients are unable to absorb fluids, nutrients, or electrolytes; thus malnutrition and dehydration are inevitable and often lethal if the condition is not appropriately treated.

The inherently small population of patients with MVID presents challenges regarding the breadth of scientific and medical knowledge pertaining to the disease. This means that diagnosis can require long-distance travel to visit multiple hospitals and specialists over the course of several months. In areas without medical expertise of the disease, families and doctors of MVID patients often conduct their own research to better understand the disease.

Given the rarity of MVID, most case reports are either single reports or compilations of previous cases. Individual characteristics and data trends related to the disease have not previously been compiled. This paper includes the first comprehensive analysis of all known literature published globally on MVID since the first case report (356 reports total, spanning from 1978 to 2017) - aggregating data related to patient location, gender, disease onset, and outcomes of the various treatment strategies employed.

Additionally, this paper analyzes the mechanism behind attempted treatment strategies demonstrating any degree of positive outcome, concluding that no effective long-term treatment strategies currently exist outside of total parenteral nutrition (TPN) and small bowel transplantation. This indicates a need for the accelerated development of new medicine to improve the quality of life and extend the lifespan of MVID patients.

"This indicates a need for the accelerated development of new medicine to improve the quality of life and extend the lifespan of MVID patients. "

What is MVID?

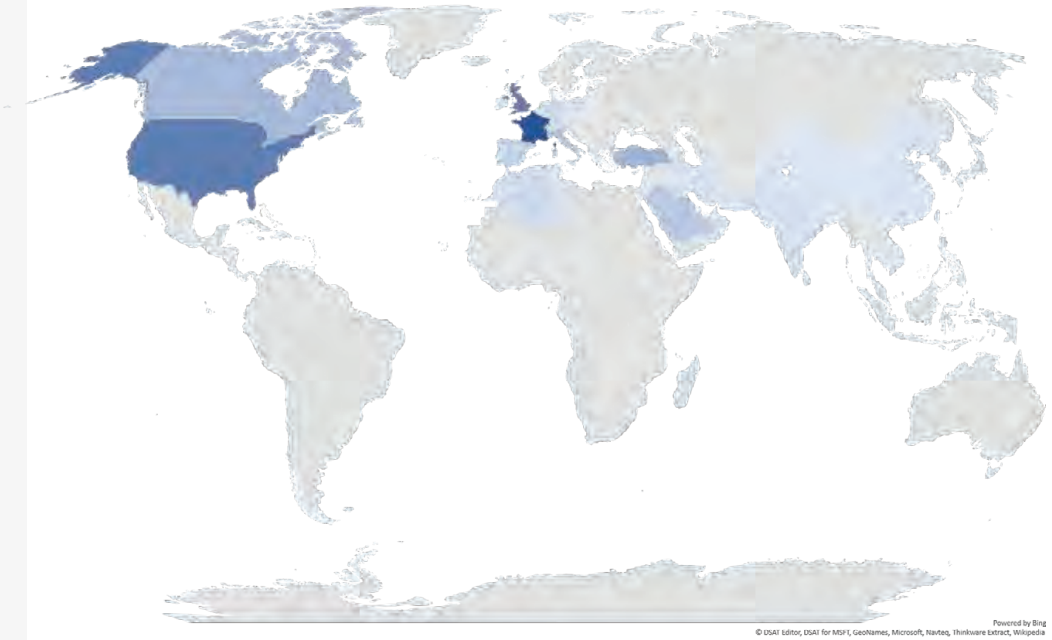
MVID is a rare, hereditary enteropathy presenting in neonates; characterized by life-threatening volumes of watery diarrhea. MVID is an autosomal- recessive congenital disease affecting predominantly intestinal epithelial cells, caused by a mutation in the MYO5 gene that limits the growth and function of these cells.

The intestine of an MVID patient is out of balance. It severely and continuously secretes much more than it absorbs because the genetic defect of MVID impairs proper development of cells and ion channels, which would normally drain or absorb fluid from the gut. Instead, the cells are frozen in an immature state where their main task is to secrete fluids into the intestine. This causes the intestine to overflow, resulting in serious diarrhea. Critical nutrients, water, and electrolytes are lost in the stool; and therefore not absorbed into the body when the infant eats or drinks. Because of this imbalance, an infant with MVID can lose up to one

Figure 1

Global Distribution of MVID Cases

Darker hue indicates a higher number of reported cases.



third of his or her body weight each day.

Diagnosis

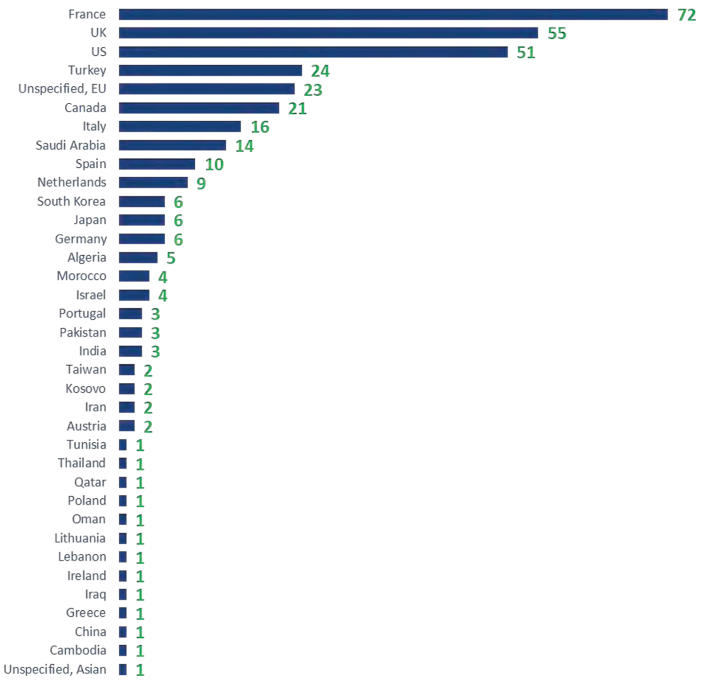
MVID is very difficult to diagnose; the reason for this is two-fold. First, the disease is extremely rare and therefore largely unknown to the pediatric community. Second, confirmation of MVID requires sophisticated diagnostic techniques such as electron microscopy of intestinal biopsies. The combination of the necessary equipment to perform the confirmatory electron microscopy, and the highly-trained personnel to conduct the procedure is not readily available in most hospitals around the world. A simple, effective, and readily-available means to diagnose the disease does not currently exist.

Affected infants typically spend the first months of their lives in the hospital and receive a diagnosis within two to three months. It is common for patients to travel to two or more hospitals seeking diagnosis and an appropriate course of treatment. A well-known and accessible test to diagnose MVID could improve doctors' ability to determine a treatment strategy earlier in these infants' lives – a factor that could make all the difference given the short length of their estimated lifespans.

Geographic Distribution of Reported Patient Population

Figure 2

Distribution of MVID Cases by Country



> ***"A well-known and accessible test to diagnose MVID could improve doctors' ability to determine a treatment strategy earlier in these infants' lives – a factor that could make all the difference given the short length of their estimated lifespans."***

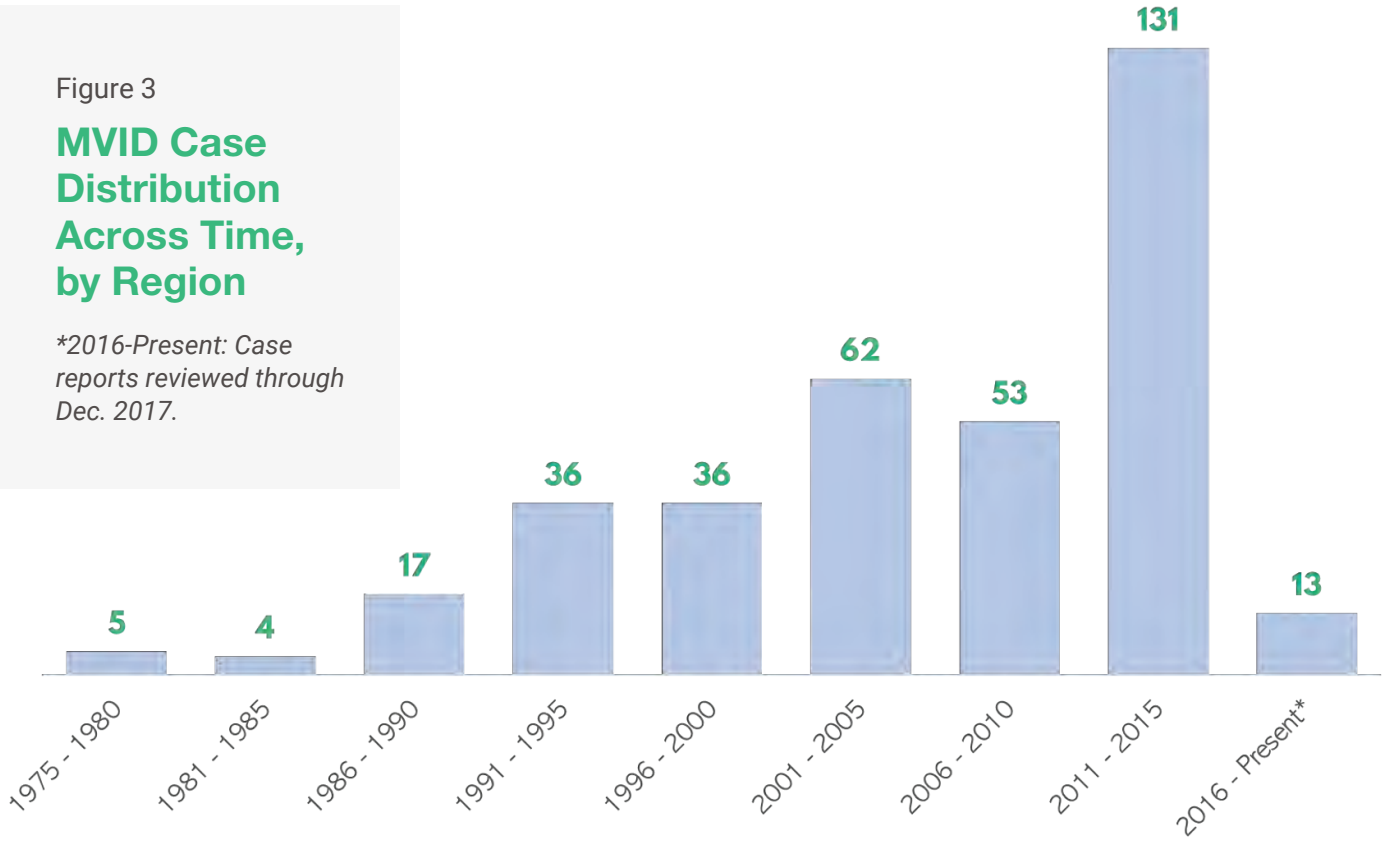
Treatment

The current standard treatment for MVID is total parenteral nutrition (TPN), in which fluids and nutrients are delivered directly to the bloodstream of the patient up to 24-hours a day via IV. Dependence on TPN contributes to a poor quality of life and can result in infection, damage to the veins, and liver failure. Patients who have unmanageable complications due to TPN ultimately seek a small bowel and/or liver transplant; a process which comes with many challenges and risks of its own.

Figure 3

MVID Case Distribution Across Time, by Region

**2016-Present: Case reports reviewed through Dec. 2017.*



Geographic Distribution of Reported Patient Population

356 cases of microvillus inclusion disease were reported globally from 1978 to 2017. Most of these reports originated from Europe and North America – from Europe, 202 individual cases, or 57% of all known cases, were reported in 43 publications.

Of the 202 European cases, France and the United Kingdom represent 72 (20% of all cases worldwide) and 55 (15% worldwide) cases respectively. For North America, 72 individual cases were reported in 28 publications, representing 20% of the worldwide distribution. Of these 72 cases, 51 (14% worldwide) were reported in the United States and 21 (6%) in Canada. Following France, the UK, and the US, the country with the next highest incidence is Turkey, with 24 reported cases (7%). The remaining cases were scattered among 19 countries and one unspecified Asian region. Plotting the clinical case reports on the world map reveals that the highest concentration of countries with reported cases of MVID is in the Western hemisphere.

Case Distribution Across Time

Since the initial classification of the disease, the number of cases reported has increased substantially throughout the years. Relatively few new cases were reported in the ten-year period from 1975 through 1985. However, in the next five-year period (1986-1990) there were over four times as many cases reported at 17 worldwide; over the subsequent five-year period (1991 – 1995), this number more than doubled to 36 cases. Cases remained relatively high from 1991 through 2015, with a notable spike of 147% more cases (over the previous five-year period) from 2011 through 2015.

For the period January 2016 through December 2017, 13 cases were reported at the time of this publication. Given that this period spans two calendar years, rather than the five years represented in all other categories in Figure 3, and factoring in an anticipated gap between disease diagnosis and published case report (i.e., it is not likely that all known cases from 2016– 2017 have been published at the time of this analysis), this number should be excluded

Figure 4

MVID Case Distribution Across Time, by Region

2016-Present: Case reports reviewed through Dec. 2017.

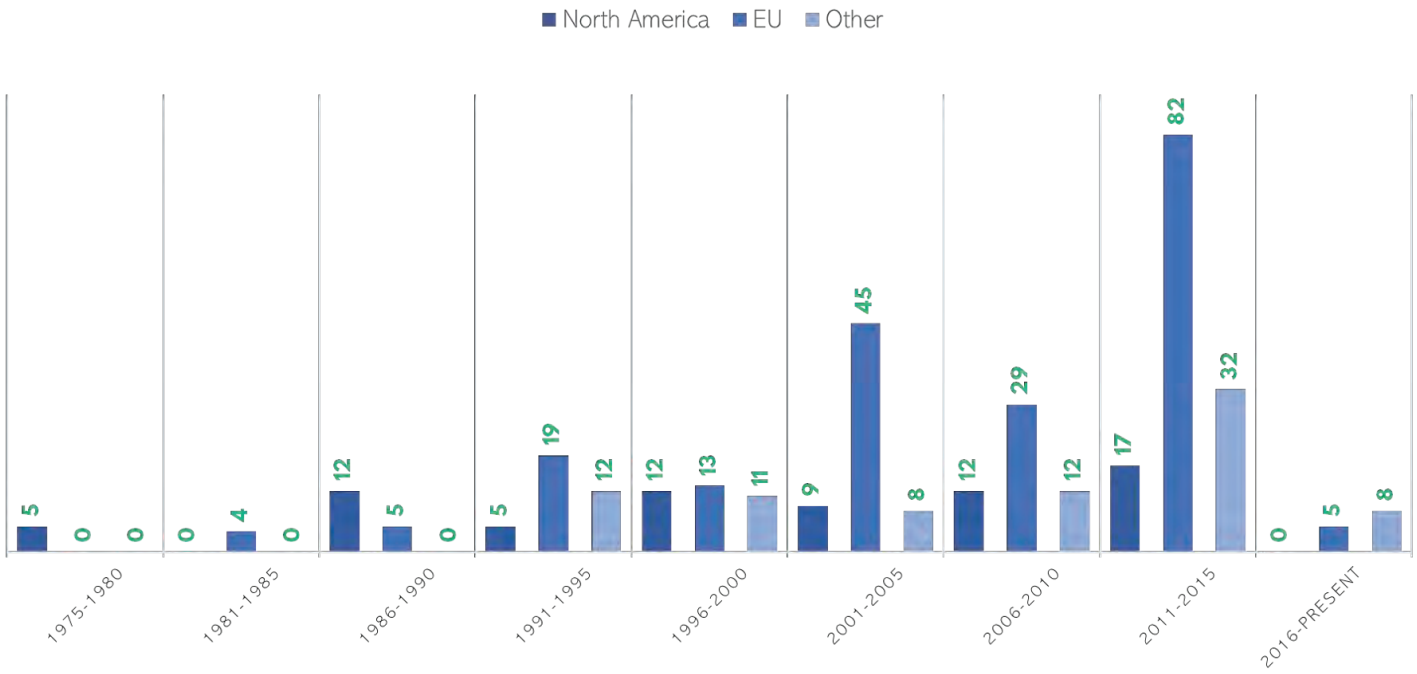


Figure 5

Gender Distribution of MVID Cases

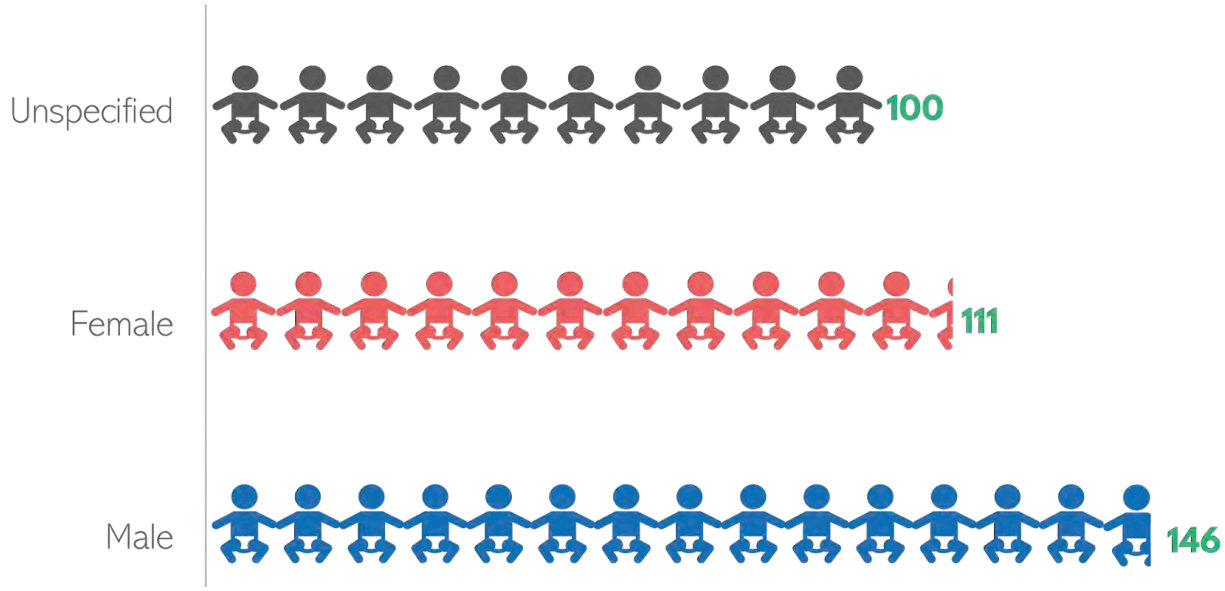
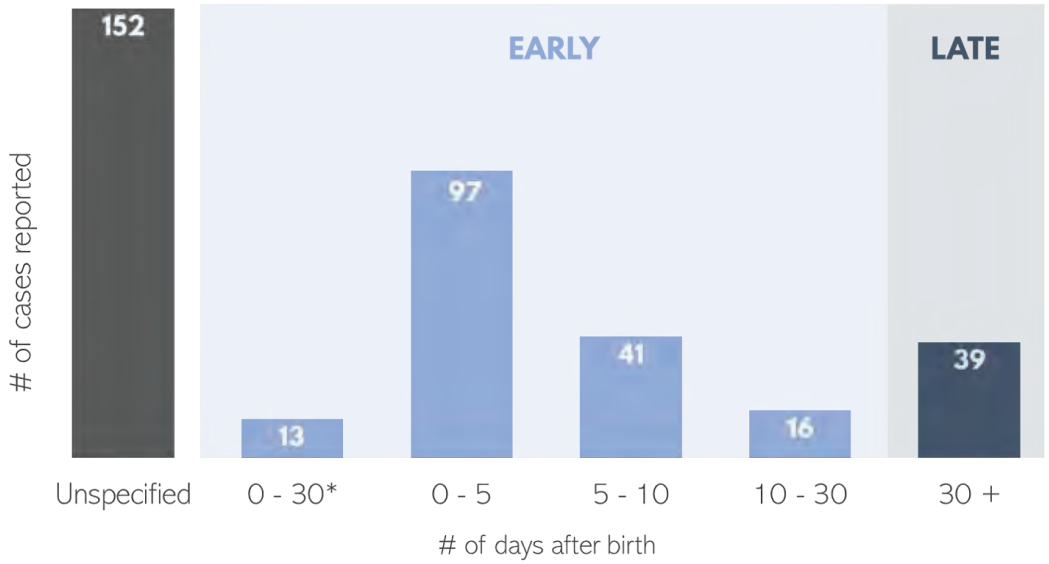


Figure 6

Onset of MVID

*Cases in the "0-30" days category indicate this range was provided, but exact day of onset was not further specified.



from consideration of the overall upward trend in number of cases reported across time.

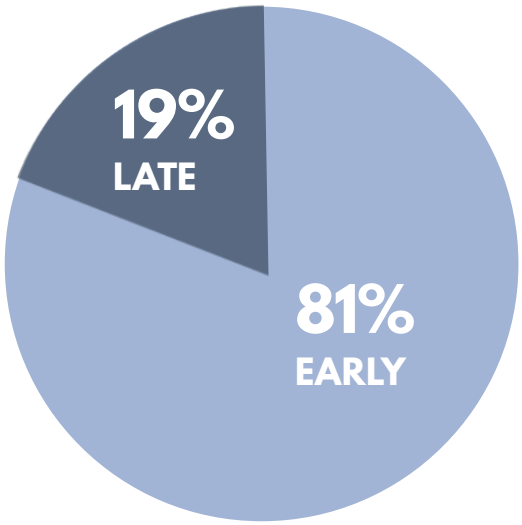
Case Distribution Across Time, by Region

For purposes of this analysis, case reports have been divided into three categories: Europe, North America, and Other, which encompasses the remaining 20 countries/regions with reported cases. This division was made based on the distribution of cases, with Europe representing 57% (202 cases) of all worldwide cases and North America representing 20% (72 cases). The remaining 23% of cases (82 cases) were scattered around the world.

This distribution is likely due in part to patients being transferred to major hospital centers from smaller countries, seeking a diagnosis and appropriate course of care. The absence of an adequate and accessible screening test around the world contributes to this imbalance towards major systems in Europe and North America, and to misdiagnosis of the disease altogether.

Figure 7

Onset of MVID, Unspecified Cases Excluded



Disease Onset

"Early onset" of the disease is defined by the National Institutes of Health (NIH) as MVID symptoms presenting within the first 30 days of an affected infant's life. All cases in which symptoms present at any point after these first 30 days are defined as "late onset." Of the 356 cases reviewed, 152 reports did not specify disease onset.

Of the 206 cases with a reported date of onset, 81% were found to be early, and 19% late. Further, it was found that in almost half (47%) of these cases, onset occurred within the first 5 days after the affected infant was born; in 20% of cases, onset occurred between 5 and 10 days; and in 8% of cases, onset occurred between 10 and 30 days. An additional 6% of cases were reported as "early onset," but the exact day of first appearance was not further specified.

Cost of Treatment

Treatment of MVID is extremely expensive – in 2008, one MVID patient's family reported racking up medical bills totaling $1M USD within the first 8 months of their child's life. Raper et al. reported in 2002 that the average annual cost for "multi-compartment, 'big bag' total parenteral nutrition in an ICU" was around $182,000 (~ $255,000 when adjusted for inflation, according to the U.S. Bureau of Labor Statistics); with TPN patients encountering around $140,000 (~ $196,000, adjusted for inflation) in additional expenses associated with hospitalization. This equates to a total of $322,000 each year (~ $451,000, adjusted for inflation).

The estimated price of intestinal/small- bowel transplantation, considered to be the most effective long-term method of treatment for MVID, was reported by Bentley et al. in 2017 to be around $1.6

Cost of Treatment

million, with an additional annual expense of $40,000 for ongoing immunosuppression.

The significant costs associated with MVID are shared both by families of MVID patients and the healthcare financial support systems of their given countries.

Treatment Methods

Since the identification of MVID in 1978, most reported cases were treated with TPN and small bowel transplantation; some have included trials of enteral (oral) nutrition, which has been found to aggravate the condition further. Anti-diarrheal pharmaceuticals have been attempted in many cases as well, often with little to no observed therapeutic response. While there is currently no cure for MVID, there have been four isolated cases of spontaneous recovery from the illness (Perry et al., 2014).

Total Parenteral Nutrition (TPN)

The most common method for managing MVID is total parenteral nutrition (TPN), in which fluids and nutrients are delivered directly to the bloodstream of the patient via IV, and no nutrition is ingested. Due to the severity of diarrhea experienced by MVID patients, TPN is often administered continuously for 20 to 24 hours a day. Dependence on TPN contributes to poor quality of life; and can result in infection, damage to the veins, and liver failure.

Small Bowel Transplantation

Patients who have unmanageable complications due to TPN will ultimately seek a small bowel and/or liver transplantation, a process which comes with many challenges and risks of its own. Small-bowel transplantation is considered at present to be the most effective method of treatment for MVID. Halac et al. conducted a study from 1995 to 2009, analyzing 24 MVID patients, 13 of which underwent small-bowel transplantation. Of the patients studied, it was found that over this 14-year period, the survival rate without small-bowel transplantation was 63%, and the survival rate with transplantation was 77%; the subsequent term of life for patients that underwent transplantation ranged from 0.4 to 14 years (Halac et al., 2011). In many cases, small-bowel transplantation can be unattainable given the high costs associated with the procedure and/or the difficulty of locating an appropriate donor.

Treatment Methods

Anti-diarrheal Pharmaceuticals

Treatment with anti-diarrheal pharmaceuticals has been attempted in many cases, often with no observed therapeutic response. In rare cases, patients have experienced a somewhat positive response to anti-diarrheals, showing reduced stool volume outputs.

A summary of all known anti-diarrheal treatments attempted for MVID, and the reported outcome for each is provided in Table 1.

[table]

As indicated in Table 1, some of the anti-diarrheals listed led to reduced stool output to varying extents and, in the case of EGF/Urogastrone, increased microvillus population. However, it is important to note that in all cases, any positive effect observed was minimal or transient, and no treatment attempted was successful to the extent that the need for TPN was eliminated. A summary of anti-diarrheal treatments with reported positive outcomes is included in Table 2.

[table]

Reported Lifespan and Cause of Death

From the data reviewed, it is not possible to definitively analyze MVID survival rate or lifespan as cases have been reviewed from as early as 1978; and up-to-date information on patient status following publication is not available. Of the 356 cases reviewed, 101 patients were reported to be deceased at the time of case report publication, and lifespan was not reported for 39 of the 101 patients. The reported lifespan of the deceased is summarized in Figure 8.

Table 1

Attempted Anti-diarrheal Treatments and Reported Outcomes

Antidiarrheal	Outcome	Halted TPN?	Reference
ACTH	No response	No	Phillips et al., 1985
	No response	No	Davidson et al., 1978; Bell et al., 1991; Rhoads et al., 1991; Phillips and Schmitz, 1992; Beck et al., 2001; Ukarapol et al., 2001
Cholestyramine	Variable efficiency	No	Girard et al., 2014
	Reduced stool output from 150g/kg/day to 50g/kg/day	No	Beck et al., 1997
Chlorpromazine	No response	No	Phillips and Schmitz, 1992
Cisapride	No response	No	Phillips and Schmitz, 1992
Cimetidine	No response	No	Phillips and Schmitz, 1992
Clonidine	Negative response	No	Rhoads et al., 1991
EGF / Urogastrone	No response	No	Walker-Smith et al., 1985; Drumm et al., 1988; Cutz et al., 1989; Phillips and Schmitz, 1992
	Increased microvillus population, but no effect on villus atrophy	No	Beck et al., 1997
Glucocorticoids (hydrocortisone, prednisolone)	No response	No	Davidson et al., 1978; Phillips et al., 1985; Drumm et al., 1988; Cutz et al., 1989; Bell et al., 1991; Phillips and Schmitz, 1992; Herzog et al., 1996
Loperamide	No response	No	Phillips et al., 1985; Bell et al., 1991; Tran et al., 2017
	Partial reduction in stool output	No	Phillips and Schmitz, 1992; Pohl et al., 1999
Octreotide	No response	No	Rhoads et al., 1991; Herzog et al., 1997; Beck et al., 1997; Ukarapol et al., 2001; Mendes et al., 2014
Oral disodium chromoglycate	No response	No	Phillips et al., 1985
Pentagastrin	No response	No	Davidson et al., 1978; Cutz et al., 1989
Probiotics	No response	No	Ukarapol et al., 2001
Ranitidine	No response	No	Burgis et al., 2013
Racecadotril	Transient reduction in stool output and frequency. The effect was replicated to a lesser degree after the treatment paused.	No	Tran et al., 2017
Somatostatin	No response	No	Cutz et al., 1989; Bell et al., 1991; Schoffield et al., 1992; Pohl et al., 1999
	Reduction or minor reduction in stool output	No	Phillips and Schmitz, 1992 (2 cases); Groisman et al., 1993

Table 2

Attempted Anti-diarrheal Pharmaceuticals with Reported Positive Outcomes

Antidiarrheal	Outcome	Halted TPN?	Reference
	Variable efficiency	No	Girard et al., 2014
Cholestyramine	Reduced stool output from 150g/kg/day to 50g/kg/day	No	Beck et al., 1997
EGF / Urogastrone	Increased microvillus population, but no effect on villus atrophy	No	Beck et al., 1997
Loperamide	Partial reduction in stool output	No	Phillips and Schmitz, 1992; Pohl et al., 1999
Racecadotril	Transient reduction in stool output and frequency. The effect was replicated to a lesser degree after the treatment paused.	No	Tran et al., 2017
Somatostatin	Reduction or minor reduction in stool output	No	Phillips and Schmitz, 1992 (2 cases); Groisman et al., 1993

Of the 101 reported cases in which the patient was deceased at the time of publication, only 44 specified a cause of death. The limited available data implies that the leading primary cause of death for MVID patients is sepsis (61% of reported cases) followed by liver failure (14%).

Conclusion

In areas without medical expertise of microvillus inclusion disease, families and doctors of patients will often seek research to understand the disease better. Given MVID's rarity, it can be difficult for doctors, researchers, and parents confronted with the disease to locate necessary data; presenting challenges with research, diagnosis, and development of treatment strategies. This resource was compiled to provide the first comprehensive analysis of existing literature on MVID; analyzing 95 articles containing 356 original case reports from 1978 to 2017. It should be noted that any statements made within this paper have been deduced based on the known clinical case reports publicly available online, and that single cases recorded in multiple reports (i.e., cohort studies) cannot be identified or accounted for given the confidentiality of clinical cases.

Since MVID was established as a disease in 1978, global reports have grown substantially, with Europe experiencing the highest level of growth compared to other regions of the world. This may be due in part to a general increase in awareness of the relatively new rare disease.

Additionally, patients are often drawn to major centers from smaller regions, as diagnosis can require long-distance travel to visit multiple hospitals and specialists. A well-known and accessible test to diagnose MVID could improve doctors' ability to both identify the disease and determine a treatment strategy (or appropriate center for treatment) earlier in affected infants' lives, despite location or specialization.

Other data compiled in this analysis indicated that slightly over half of affected patients are male, and that MVID typically presents within the first 30 days of an infant's life. While it is not possible to definitively analyze survival rate or lifespan from the information collected, data on those reported deceased at the time of case publication implied that most patients pass away before reaching two years of age.

The treatment methods currently considered to be the most effective for the management of MVID are total parenteral nutrition (TPN) and small bowel transplantation. It is generally understood that the methods are accompanied by health issues and poor quality of life and this analysis further confirmed the serious com-

Figure 8

Lifespan of MVID patients reported deceased

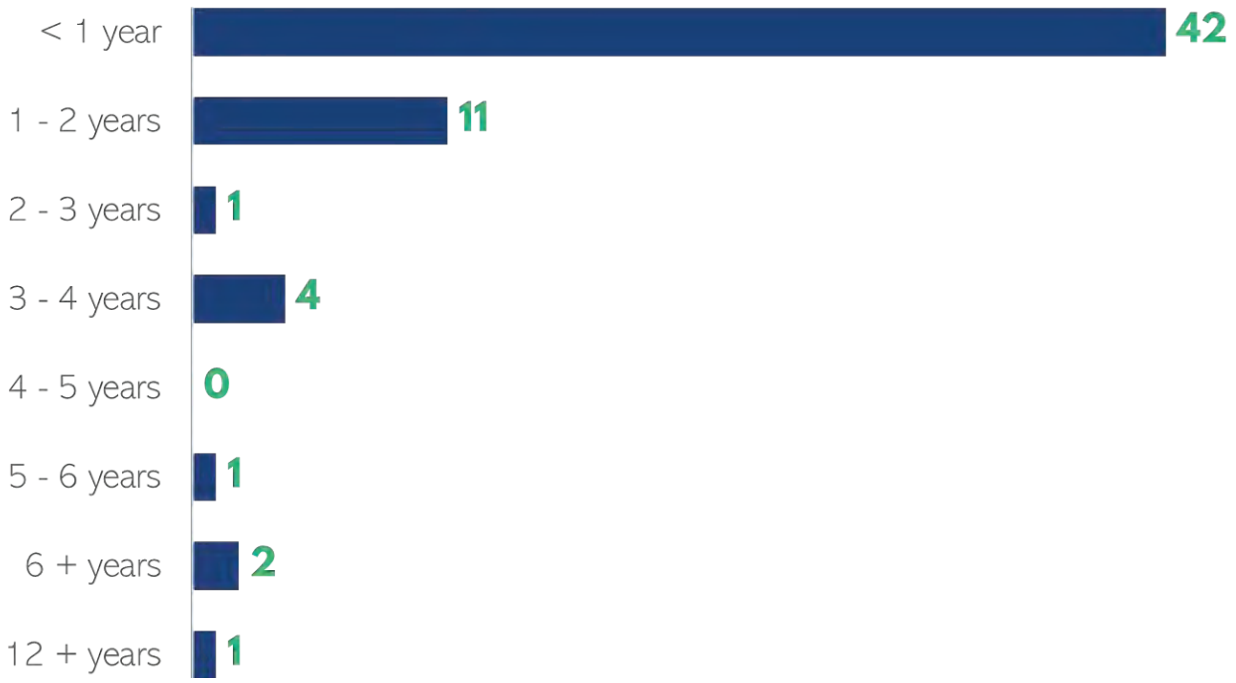
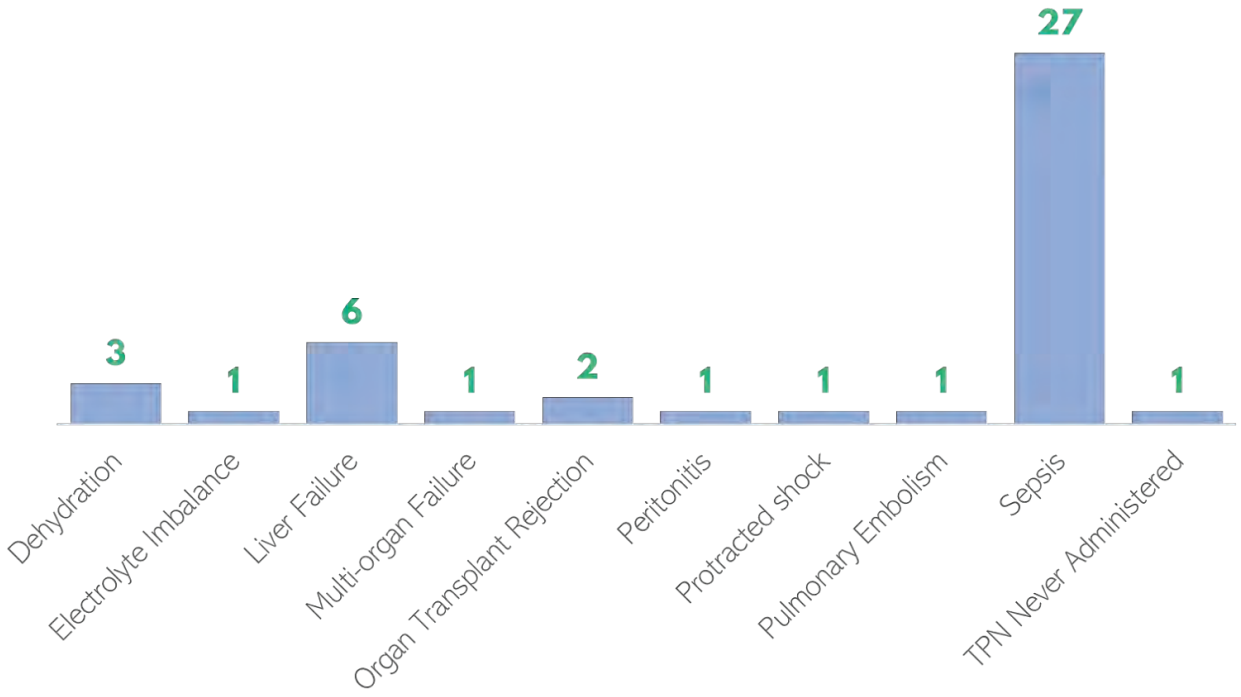


Figure 9

Reported primary cause of death



plications of these treatment strategies by indicating that the primary known causes of death in MVID patients are infection, liver failure, and transplant rejection – all outcomes associated with the preferred treatment options available.

This paper also analyzed attempted alternative (anti-diarrheal) treatment strategies. Of all cases reviewed, a handful of alternative methods led to a reduction in stool output; however, any positive outcome was minimal or transient. No alternative methods attempted have resulted in the elimination of TPN-dependence for any patient. This - coupled with the poor prognosis associated with the standard treatment methods - further underscores the need for the accelerated development of new medicine to improve the quality of life and extend the lifespan of MVID patients.

The Future for MVID Patients

The first step towards a brighter future for MVID patients would be the development of an effective, easily available, and easily- administered diagnostic test. This would greatly improve the ability for doctors to recognize the disease early, and therefore begin work to either determine the best course of treatment for the patient or to determine the best facility to provide specialized treatment. The current diagnostic limitations are likely leading to under-diagnosis and misdiagnosis, and given the demanding treatment needs of this disease, there is no time to waste when it comes to caring for MVID patients.

As far as treatment is concerned, the development of new medicine is required for long-term management of MVID. The current methods – total parenteral nutrition and small bowel transplantation – have proven to be riddled with potentially lethal health complications and require strict, difficult, and expensive maintenance.

Gene therapy could be a distant possibility, but it is not currently under consideration for this disease. Although none of the alternative anti-diarrheal remedies that have been attempted for treatment of MVID have been effective to the extent that the need for TPN was eliminated, doctors and researchers are taking positive steps towards an effective treatment by targeting different mechanisms of action of the disease. A future possibility may be a treatment focused on "turning on" the pathways in those intestinal cells which are not impacted by the genetic mutation, allowing the MVID intestine to function as a healthy intestine would. Regardless of the exact mechanism of treatment, children affected by MVID are desperately in need of new, alternative options that will improve their quality of life and extend their life expectancy.

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Our hearts go out to all families impacted by this difficult disease. The strength exhibited by both the families of children affected by MVID, and by the patients themselves, is commendable and beyond compare.

A list of hospitals, diagnostic centers, and non-profits that support patients and their families can be found at mvid.vanessaresearch.com/patient-resources.

Appendix A:

Mechanism of action for anti-diarrheal pharmaceuticals used in attempted treatment of MVID, with the appearance of positive outcome

Cholestyramine is a resin that prevents re-absorption of bile by binding it in the gastrointestinal tract. It is an ion exchange resin, meaning it can exchange its chloride anions with anionic bile acids in the gastrointestinal tract. It has the functional center and a quaternary ammonium group (which is attached to an inert styrene-divinylbenzene copolymer). Cholestyramine resin absorbs the bile acids in the intestine forming an insoluble complex which is excreted in the feces (Drugbank, 2018).

EGF, known as Urogastrone, is a protein with size 6-kDa (Harris RC, 2003) and consists of 53 amino acid residues and three intramolecular disulfide bonds (Carpenter G, 1990). It stimulates cell proliferation, growth and differentiation by binding to its specific binding site, receptor, EGFR and activating GTP/MAPK cascade. Human EGF exerts trophic effects on the internal intestine surface and may be involved in maintaining normal intestinal structure and function. Consequently, it is important in cases in which nutrients are administered parenterally, as parenteral nutrition can result in intestinal hypoplasia and hypofunction.

Loperamide acts as the μ-opioid receptor agonist/calcium channel antagonist along the small and large intestine to decrease circular and longitudinal muscle activity through the neural mechanism in the peripheral nervous system (Drugbank, 2018). Loperamide exerts its anti-diarrheal action by causing an increase in the time fecal matter stays in the intestine, allowing more water to be reabsorbed. (US Government, 1993).

Racecadotril is a peripherally acting enkephalinase inhibitor (Matheson, 2000). Unlike other opioid medications which treat diarrhea by reducing intestinal motility, racecadotril reduces the secretion of water and electrolytes into the intestine (Matheson, 2000), resulting in an anti-secretory effect. Racecadotril's active metabolite, thiorphan, inhibits the enzyme neutral endopeptidase (NEP) and increases exposure of cells to NEP substrates such as enkephalins and atrial natriuretic peptide (ANP). Endogenous enkephalines are active on both μ- and δ- opioid receptors (Huighebaert et al., 2003). NEP inhibition will also increase exposure of cells to endogenous neuropeptide Y and, possibly, peptide YY, both of which have strong anti-secretory effects in the gut (Playford and Cox, 1996).

Somatostatin is a peptide hormone that is considered to be an anti-secretory. It acts on neurotransmission and cell proliferation via interaction with G protein-coupled somatostatin receptors. Somatostatin, also known as a growth hormone–inhibiting hormone (GHIH), regulates the endocrine system and inhibits the release of secondary hormones. It acts as a powerful inhibitor of intestinal Cl− secretion and inhibits one kind of basolateral K+ channels in human intestinal crypt cells via a G protein- dependent mechanism, which may result in a loss of the Ca2+sensitivity caused by K+ channels. (Sandle, 1999).

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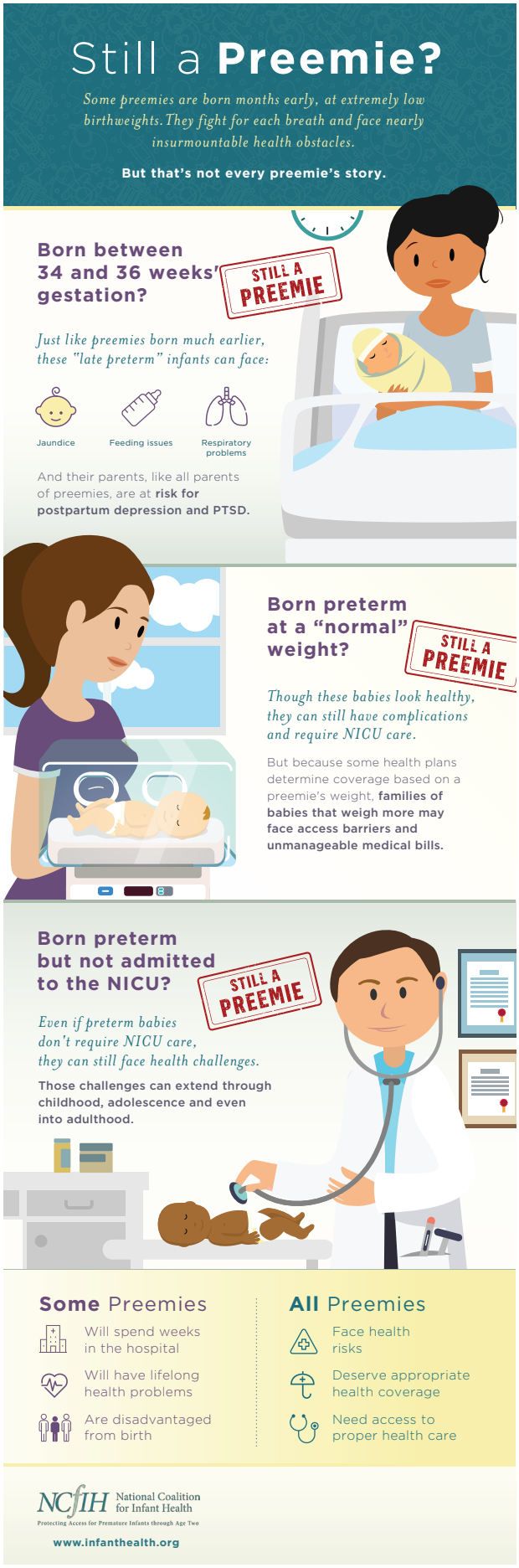


Case Report: Prune Belly Syndrome- With An Unusual Presentation

Anwar Khan, MBBS, MD, Muzammil Hafeez, MBBS, DCH, MRCPCH (UK), Wasim Khan, MBBS, DCH, MRCPCH (UK)

Prune belly syndrome (PBS) is also known as Eagle – Barret syndrome.

It is classically characterized by

- Deficient development of abdominal muscles that causes the skin of the abdomen to wrinkle like a prune.
- Bilateral cryptorchidism.
- Abnormalities of the urinary tract such as bilateral gross hydronephrosis, megaureter and megacystis. (1)

Our case had an unusual presentation with a hugely distended abdomen with smooth, shiny skin due to the presence of massive urinary ascites.

Case:

A 30 weeks gestational age male preterm infant was born by Cesarean section to a 33 year old Para 3 mother. Antenatal ultrasound scan showed megacystis, and dysplastic kidneys the bladder was filled with hyperechoic shadows with suspected vesicoenteric fistula. Initially, there was anhydramnios but later normal amount of amniotic fluid was noted. Abdomen showed evidence of ascites on the antenatal scan. A large mass compressed the chest with evidence of pulmonary hypoplasia. (fig 1 and 2)

After birth, the baby required ventilator support due to severe respiratory distress and lung hypoplasia. He was extubated at 62 days of life after several attempts of failed extubation.

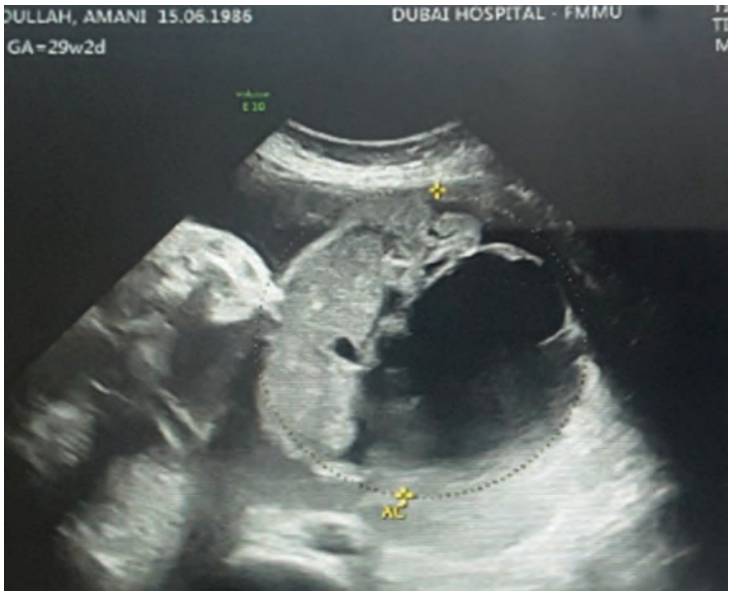


Fig 1 – Figure showing evidence of ascites on antenatal scan

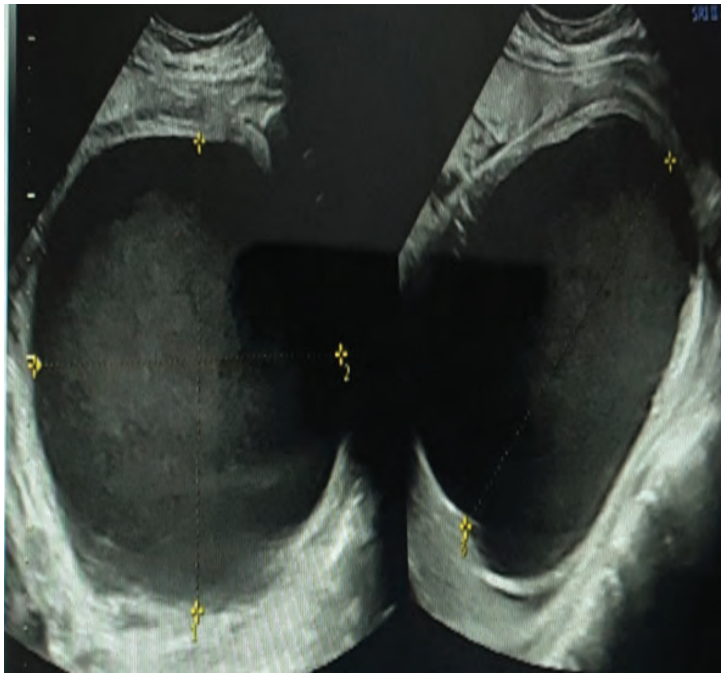


Fig 2- Figure showing antenatal megacystis

His systemic examination at birth showed a narrow thorax, severely distended abdomen with shiny skin (Figure 3 and Figure 4), palpable bladder, male genitalia with bilaterally undescended testes, and imperforate anus. His cardiovascular examination was normal.

> ***"Our case had an unusual presentation with a hugely distended abdomen with smooth, shiny skin due to the presence of massive urinary ascites. "***

Postnatal ultrasound showed hydronephrosis of both kidneys with bilateral megaureter. Paracentesis was performed postnatally, and 450 ml of urine was drained. The pediatric surgeon deflated the ureters by inserting bilateral ureteral drains and draining 750 ml of urine. A urinary catheter was also inserted.

The abdominal distension decreased, and skin became wrinkled, showing evidence of absent anterior abdominal wall muscles (Figure 5 and Figure 6).

Later, laparotomy was performed revealing a large thick walled urinary bladder occupying the whole of the lower abdomen with vesicoenteric fistula. The Vesicoenteric fistula was resected, and vesicostomy was

completed with fixation of the bladder catheter. Colostomy bypassed the imperforate anus.

The baby is passing good amount of urine through the vesicostomy and his renal Ultrasound scan done post surgery shows small right kidney and left kidney with mild dilatation of the renal pelvis. Both ureters are not visualized now.

The vesicostomy tube was removed on day 118 of life and kept as free drainage into the pamper, with clean intermittent catheterization

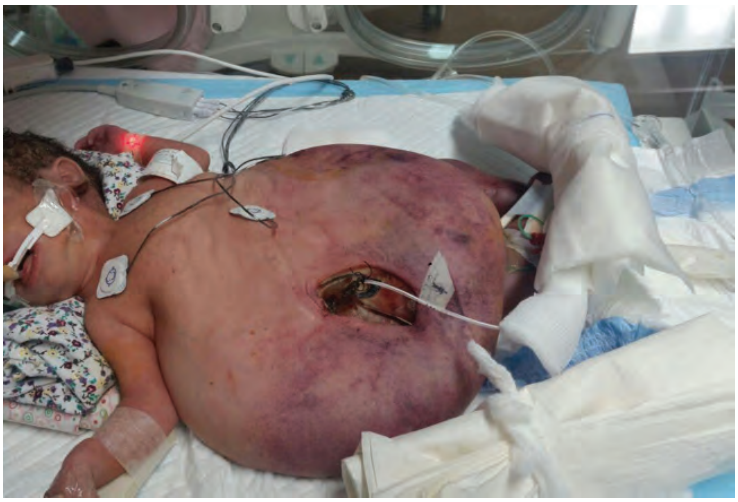
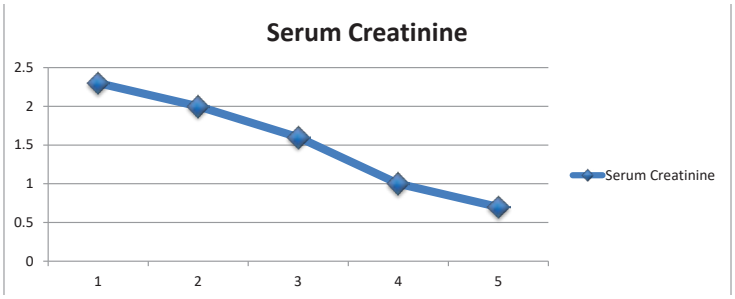


Fig 3 –Severely distended abdomen on admission

through the vesicostomy every 8 hours to empty the residual urine which is continued by the caregiver at home.

His cardiac evaluation, including echocardiography, was normal. He has a normal 46XY karyotype.



Graph 1 - Decreasing serum creatinine

His initial creatinine level was high (maximum of 2.3 then gradually decreased to a normal level, graph 1). He is on prophylactic antibiotics.

After discharge baby had a multidisciplinary follow-up and further investigation in the outpatient clinic:

- DMSA Scan – showed normal left kidney with good and uniform uptake while the right kidney shows no evidence of functioning renal tissue.
- MCUG scan done shows grossly enlarged urinary bladder, dilated ureters with evidence of grade 3 vesicoureteric reflux (VUR) on the right side.
- He had recurrent Urinary tract infection requiring admission and IV antibiotics. His prophylactic antibiotics were continued.

Discussion:

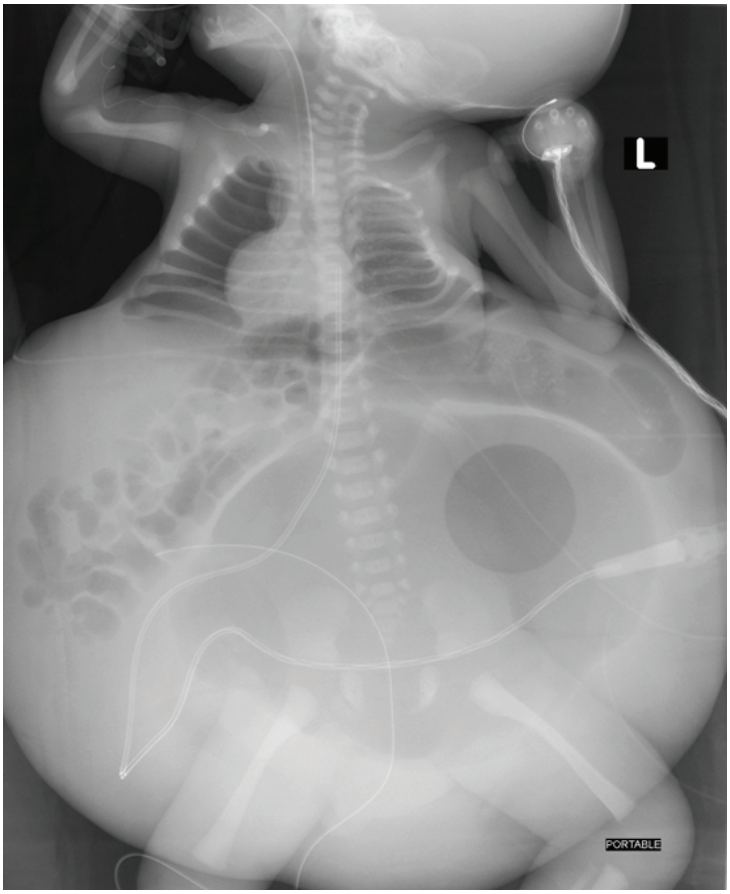


Fig 4- X ray showing severely distended abdomen with narrow thorax.

Our case had an unusual presentation with a hugely distended abdomen with shiny skin due to the presence of massive urinary ascites. Few cases with similar presentation have been reported in the past. (5) He had megaureters and megacystis. He required paracentesis to relieve the abdominal distension on admission. The megaureters were deflated by ureteral drains and vesicostomy performed to drain the urine. Once the abdominal distension was relieved, wrinkling of the skin, a feature of Prune Belly syndrome was evident. Ultrasound abdomen also showed resolution of the megaureters and megacystis. This indicates the probable presence of an obstruction to the urine outflow antenatally resulting in megaureters and a huge bladder leading to a leak of urine into the peritoneal cavity, causing the massive ascites. The huge distension of the bladder has most probably led to vesicoenteric fistula formation.

"In unstable patients who cannot tolerate an operation, Cystostomy and pyelostomy are undertaken to shunt the urine temporarily. There is evidence that prenatal vesicoamniotic shunting results in a good outcome with preservation of renal and pulmonary function in a patient with severe lower urinary tract obstruction."

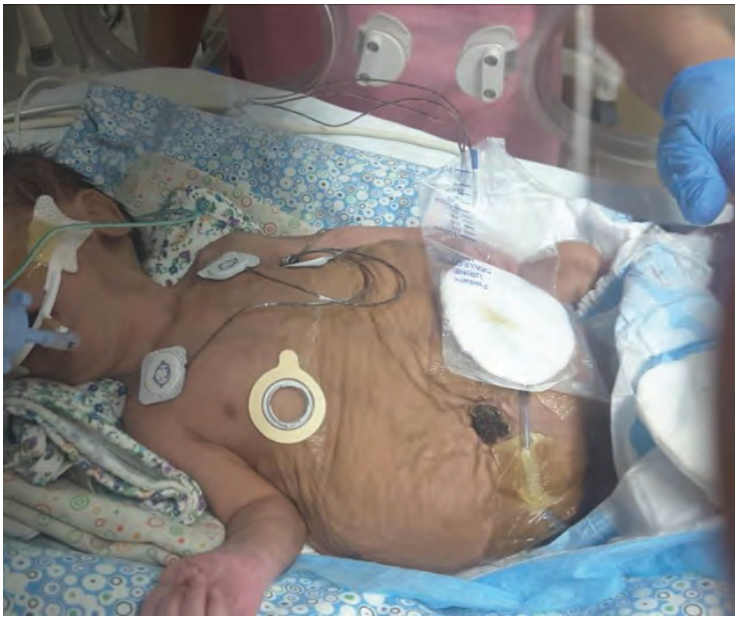


Fig 5 – Baby with vesicostomy drain and showing decreased abdominal distension showing the wrinkles

In unstable patients who cannot tolerate an operation, Cystostomy and pyelostomy are undertaken to shunt the urine temporarily. There is evidence that prenatal vesicoamniotic shunting results in a good outcome with preservation of renal and pulmonary function in a patient with severe lower urinary tract obstruction. (2)

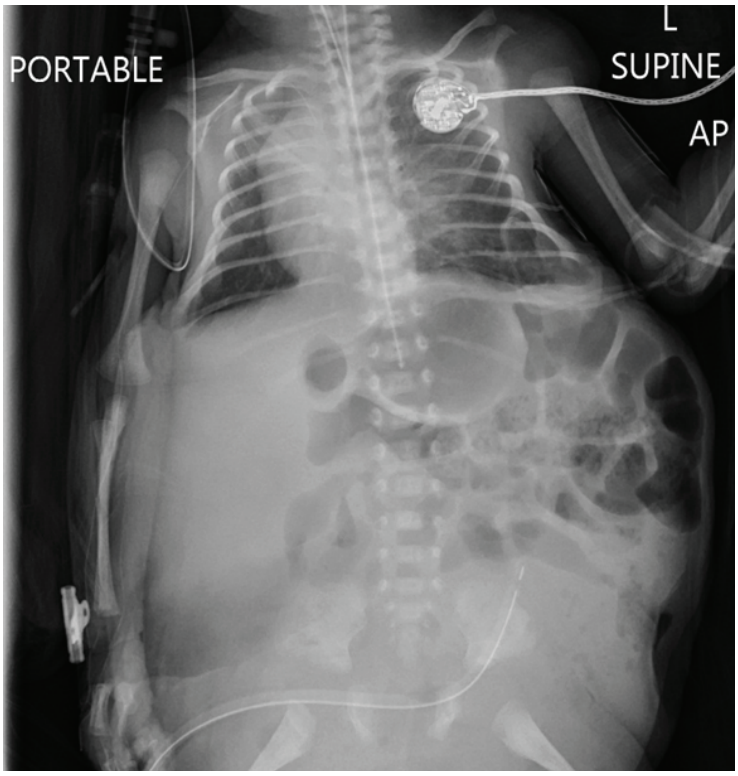


Fig 6 – X ray abdomen showing vesicostomy tube and less distended abdomen.

55% of patients with PBS show significant clinical pulmonary manifestations. Hypoplasia of the lungs and cystic adenomatoid malformation are some of the common respiratory manifestations of PBS. (2). Pulmonary hypoplasia is the main cause of mortality in the neonatal period. (2)

Our baby had respiratory distress and lung hypoplasia, requiring prolonged ventilation. In addition, he had an imperforate anus, which was addressed surgically, and a colostomy was performed. 30% of patients with PBS have evidence of gastrointestinal manifestation which includes midgut malrotation and hindgut abnormality leading to anorectal malformation (e.g., the persistence of embryonic cloaca, agenesis of rectum and anus). (3)

Also, the baby had bilateral talipes equinovarus deformity, which is being managed by physiotherapy. 45% of babies with PBS can have skeletal abnormality Skeletal abnormalities. (e.g., clubfeet, limb deficiencies, teratologic hip dysplasia) (4) and 10% of patients can have cardiac anomalies including atrial septal defect, ventricular septal defect, patent ductus arteriosus, and Tetralogy of Fallot. (2)

Long term outcome in a patient with PBS is determined by the severity of urinary tract abnormality and renal function. (2)

Our patient is being managed with a multidisciplinary team approach including neonatologist, pediatric surgeon, pediatric nephrologist, orthopedics and physiotherapist. In the outpatient follow up baby was having recurrent UTI, which was treated by IV antibiotics by the pediatric nephrologist. Baby is on prophylactic antibiotics as MCUG shows grade 3 VUR. DMSA scan showed normal functioning left kidney while the right kidney is non-functioning.

Parents have been taught intermittent catheterization through the vesicostomy. The plan is to refer the patient to plastic surgery for reconstruction of the abdominal wall.

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Respiratory Report: Between Rocks and Hard Places (And Things They Didn't Teach You in School)

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.

I had the pleasure of speaking to Dr. Alison Froese, an anesthesiologist from Kingston, Ontario, following a conference. I asked her what she thought of the Glidescope® video laryngoscopy device. "Don't get me started," she replied. "I now spend my time teaching basic laryngoscopy because no one knows how to do it anymore!". (1) I laughed and replied that I tease anesthetists all the time, telling them "when I learned to do this, you actually had to do it." While Dr. Froese's practice is in the adult world, with the introduction of pediatric and neonatal video laryngoscopes combined with the transition to non-invasive respiratory support, it is only a matter of time before her experience is visited upon the world of neonatology.

"While technology has given us many tools to make our clinical lives easier, sometimes the cost of that technology is the loss of clinical skill sets that can be lifesaving in dire situations. I present this month an assortment of "tricks" that may help clinicians in similar circumstances."

I have been practicing as a respiratory therapist for 30 years, 22 of those being exclusively in the NICU. In that time, I have encountered many situations where the standard practice simply wasn't working. As staff approach retirement age, there is a wealth of experience and practical bedside knowledge poised to leave with them. While technology has given us many tools to make our clinical lives easier, sometimes the cost of that technology is the loss of clinical skill sets that can be lifesaving in dire situations. I pres-

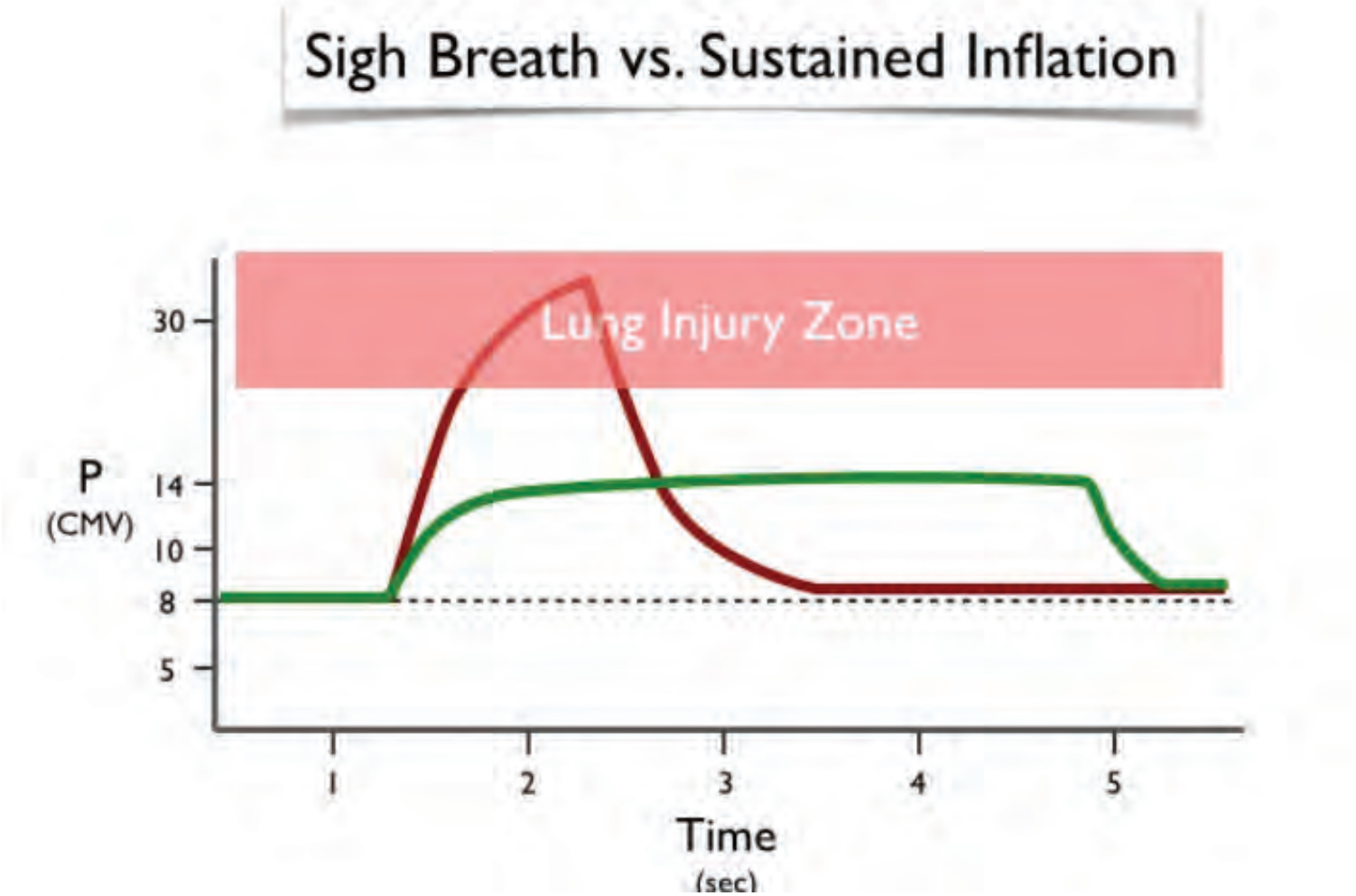

Figure 1 courtesy Bunnell Inc

Figure 2: Traditional grip

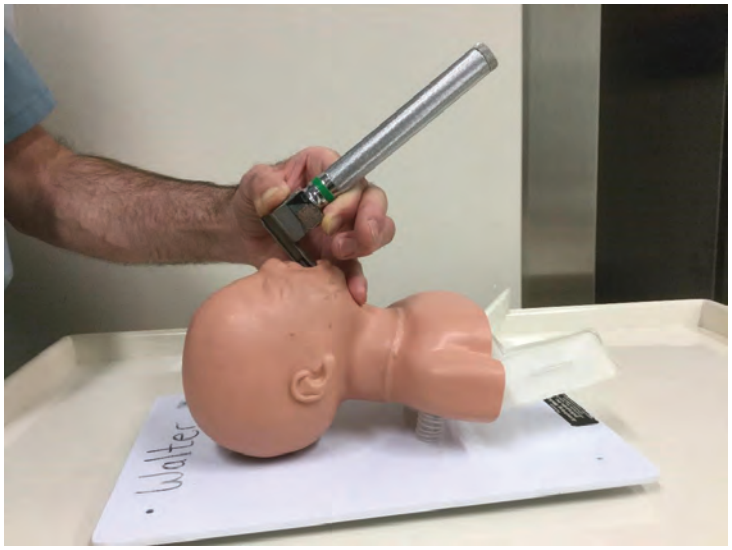

Figure 3 preferred grip: note position of pinkie

ent this month an assortment of "tricks" that may help clinicians in similar circumstances.

When the Lungs Say "Yes" and the Heart (or Brain) Says "No."

There are times when the balance between perfusion and ventilation is almost impossible to achieve. While an under-recruited lung will impair venous return as much as an over-inflated one, there are times when the immature heart cannot pump effectively against the pressure required to maintain optimal pulmonary recruitment. Normal pulmonary arterial pressure (PAP) outside the neonatal period is 19 cmH_2O +/- 4 cmH_2O, and this value is independent of age. This pressure is higher in the newborn, and higher still in the premature infant. (2) It stands to reason that the closer mean airway pressure (MAP) is to PA pressure, the less perfusion pressure is available. Further, infants with chronic lung disease (CLD) often exhibit a degree of pulmonary hypertension, although structural in nature rather than reactive.

A normal, functioning, premature heart should not have difficulty pumping against a MAP of 10 cmH_2O. Unfortunately, pressures much higher than this are often required to maintain lung patency and provide adequate oxygenation without potentially damaging high oxygen concentrations, and occasionally this results in hypotension.

I rarely advocate for lower MAP, but when faced with this scenario will sometimes reduce PEEP/MAP while introducing recruitment maneuvers. This may seem counter-intuitive since recruitment maneuvers are best used sparingly and for short duration in concert with increasing PEEP/MAP. In this case, the maneuvers are meant to maintain alveolar stability, while the lower PEEP/MAP gives "windows" of lower pressure to lessen cardiovascular load: think of it as "biphasic PEEP."

Traditionally we have been taught as clinicians to use "standard" intermittent mandatory ventilation (IMV) breaths for recruitment, typically with an inspiratory time (Ti) of 0.5 seconds and peak inspiratory pressure (PIP) of 20 cmH_2O or more. We now know that large volume breaths are damaging to the developing lung, and a study by Pillow et al. showed increased inflammatory markers using IMV breaths with PIP of 25 cmH_2O at rates of 2 and 5 respectively, and with Ti of either 0.5 or 2 seconds. Markers were more prevalent with the increased Ti. (3) In addition, the low Ti does not provide sufficient time for proper pendelluft to occur, but provides enough time to over-inflate areas with high compliance. A more recent approach to recruitment maneuvers is to lower the PIP (typically to 5-6 cmH_2O above PEEP in high-frequency jet ventilation (HVJV)) and increase the Ti to 2-3 seconds. This approach provides a degree of lung protection for compliant areas while giving more time for pendelluft to occur and for less compliant areas to begin filling. (see figure 1) It should be noted that research by Drs. Jane Pillow and Gabrielle Musk (Australia) have shown inflammatory markers in tracheal aspirates using IMV pressures as low as 12 cmH_2O. Hence any recruitment strategy should be used judiciously and as briefly as possible.

Similarly, a high MAP can impair cerebral blood drainage. Very small babies with attending fragile cerebral vasculature are most prone to this, and cerebral blood congestion may cause blood vessels to leak with dire consequences. A case in my unit comes to mind. This was a baby who required very high pressures to ventilate and oxygenate, and we were happy to oblige. Unfortunately, a head ultrasound done prior to discharge revealed severe periventricular leukomalacia not present in previous scans and appearing much later in the infant's course than would be expected. The pri-

mary suspect was prolonged high MAP with cerebral congestion. While no treatment strategy offers 100% efficacy, lowering PEEP (the baby was on HFJV) and using recruitment maneuvers may have saved this patient's brain.

"Similarly, a high MAP can impair cerebral blood drainage. Very small babies with attending fragile cerebral vasculature are most prone to this, and cerebral blood congestion may cause blood vessels to leak with dire consequences."

While these maneuvers are typically used with HFJV, once 3rd generation ventilators are approved for use in the U.S. this option will be available in high-frequency oscillation mode (HFO) as these machines offer integrated and customizable sigh breaths with HFO and I have no doubt would provide the same effect. Also, these maneuvers should not be confused with sustained inflations as the duration of the breath is shorter than is typical of sustained inflations, and the PIP is also much lower. The SAIL trial, for example, used a PIP of 25 cmH_2O for 15 seconds.5 I do not recommend this strategy.

HFJV Maxed Out

There have been occasions when ventilating a baby with HFJV where even with maximum PIP of 50 and jet Ti 0.34 the CO_2 doesn't budge. The Bunnell Life Pulse® high-frequency jet ventilator measures and servo-adjusts pressure via the patient box. Since the diameter and length of the pressure line attached to the LifePort ® are of known length and diameter, the resistance associated with it is factored into the algorithm used to very accurately estimate tracheal pressure.

This procedure is off-label and not endorsed by Bunnell. Increasing the length of this pressure line increases the associated resistance and thus makes the machine "see" lower pressure than there actually is. In response, servo pressure is increased to provide set pressure. When using maximum settings, increasing the pressure line length will increase pressure delivered to the patient, this will not be reflected by measured pressure, and the actual pressure delivered will not be known. However, it will provide more ventilation, and the large attenuation of jet pressure still applies. I have seen this work very well and quite quickly; in one case, it was required for only a few minutes to achieve the desired reduction in CO_2 before being discontinued. In this case, the length of the pressure line was doubled by cutting the line off another LifePort® adaptor and joining the two with a blunt needle (further increasing resistance). When between a rock and a hard place, this off-label use of the ventilator can be a lifesaver. Proceed with caution and discontinue as quickly as possible.

Difficult Intubations

I have yet to meet a clinician who has not been unsuccessful in placing an endotracheal tube (ETT) in a baby at one time or another. One might say a healthy serving of humble pie should be on everyone's menu on occasion as it keeps us aware that even the best of us will inevitably fail sooner or later. Keeping in mind a few tools and tricks can help delay that meal.

Tools

The standard intubation kit is fine most of the time, but there are situations where having a few add-ons can make the task at hand much easier. To that end, I recommend having available an assortment of ETT's kept in a freezer, lubricant, and an assortment of suction catheters. The reason for frozen ETT's is that they are stiffer and less prone to bending, and the cold tube may mitigate inflammation.

Technique

At times, despite a clear view of vocal cords, the ETT simply will not pass through the vocal cords, other times it will not advance sufficiently below the vocal cords for one reason or another. If the ETT does not pass through the vocal cords, applying constant, gentle pressure while rotating the ETT may help. Dr. Andrew Shennan, my mentor, explained to us that the ETT bevel is designed such that it will slip between the vocal cords and open them while being rotated, a technique we refer to as "corkscrewing." Care must be taken to avoid too much pressure being applied, but the vocal cords themselves are relatively robust.

"Finally, the way in which the laryngoscope is held can provide better control and visualization. Most clinicians learn to intubate adults or children first. "

If despite using the corkscrew maneuver, the ETT bends on itself rather than passing through the cords, there are two options. One is the use of a frozen ETT to prevent bending. The other is to use a suction catheter as an introducer. This is done by feeding the largest suction catheter that will pass through the ETT and then advancing the catheter through the vocal cords. It should be advanced far enough to ensure it does not become dislodged, and some lubricant may be used to aid in its removal once the ETT is properly positioned. This technique can help guide an ETT past a sub-glottic obstruction such as a granuloma, and it has saved my hide on more than one occasion. Another trick I have used and seen used is attaching a resuscitation bag to the end of the ETT and bagging when the tube is at the cords. This sometimes helps open the cords to allow the ETT to pass through, but it can be awkward and is best done with a second set of hands.

Sometimes vocal cords can be very difficult to visualize. I often will leave a feeding tube in situ while intubating as it serves as an easy landmark. Even if the glottis cannot be seen, its location can be estimated as about 1 cm due north of the feeding tube's location, and the ETT can often be placed simply aiming in that location using Magill forceps to direct it.

Finally, the way in which the laryngoscope is held can provide better control and visualization. Most clinicians learn to intubate adults or children first. This involves holding the laryngoscope by the handle. (See figure 2) With neonates and micro-prems, this grip does not work as well and increases the risk of damaging the gum and tooth buds and may increase the likelihood of hyperextending the neck and "levering" against the gum. I was taught to hold the blade, as shown in figure 3. Doing so gives finer control of the blade and reduces the risk of levering and hyperextension since the laryngoscope is held at the pivot point. This technique also frees the pinkie or ring finger to provide cricoid pressure dur-

ing visualization. Pressing down brings the trachea in line with the ETT, and since it is the intubating person themselves providing pressure, proper alignment is easier to obtain. This is particularly useful when intubating nasally, the preferred and usual placement in my unit for developmental reasons. Dr. Shennan would apply a significant amount of pressure this way, and his intubation skills were so good we nicknamed him "Slick." I am unaware of any sequelae as a result of using tracheal pressure this way, and it is the way I teach learners to hold a laryngoscope. It is particularly useful with very small babies.

I welcome input from other clinicians wishing to share their own "tricks" as well as suggestions for future articles. The purpose of this publication is, after all, the sharing of knowledge and practice.

References:
1 *Personal communication*
2 *Dhillon, R, Archives of Disease Child Fetal Neonatal Ed 2012 97: F223-F228*
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4 *https://link.springer.com/article/10.1007/s00134-011-2237-x*
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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

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Happy Father's Day

On a lukewarm evening, wind gently caress on my face.

Chirping birds silenced by their tired sleep,

Geese take turns honking to keep themselves safe from predators.

Calm surface of pond, waves good bye to passing breeze.

As dark night chases left over evening,

A star twinkles inviting planets,

shines on me trying to brighten my mood.

Fireflies light flickers on the trees aimlessly,

Grown up trees look up to the age-old ones.

Restful night tries to sleep expecting sweet dream but dreading sun rise.

Curious full moon hiding its dark side awakens sleeping giant hogs.

In the rhythm of whistling wind,

trees dance branching out musical notes.

My meditative breaths listen to heart beats echoing all over.

I look up to the endless dark sky and see,

memories of my father ending my Father' Day.

My Fatherhood joins Fatherless Children of our Motherland.

What's life got to do with it?

FRESENIUS KABI

caring for life

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.

REFERENCES:

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

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Lake Zurich, IL 60047
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www.fresenius-kabi.com/us

Featured Conference: Fragile Infant Feeding Institute (FIFI) August 22–25, 2019 Ray Conference Center, Butler Hospital Campus, Providence, RI

Bobbi Rose

Course Description:

The purpose of the Fragile Infant Feeding Institute is to assist professionals in understanding the story of the infant, both in the hospital and beyond. Everyone involved in the care of the infant and family should understand the factors influencing successful, enjoyable feedings, across time and across disciplines. Feeding is supported both by the development and functioning of the infant and the experiences (history) during feedings. The parents are the lifelong partners in this story. Collaborating with the family, emphasizing their intrinsic strengths and knowledge, optimizes infant outcomes. NICU and Early Intervention professionals must work together integrally to improve feedings and feeding outcomes. We emphasize the complex interplay between nutrition, lactation, therapy, medical/nursing, mental health, and family desires and choices. We welcome professionals to come, study, and interact with us, and reflect upon their current practice within their system.

"Everyone involved in the care of the infant and family should understand the factors influencing successful, enjoyable feedings, across time and across disciplines."

The Fragile Infant Feeding Institute is a four day intensive study of feeding and nutrition for infants with special needs. FIFI 2019 is held in an environment that allows for close interaction between faculty and participants. Participating faculty represent a variety of perspectives from both research and clinical backgrounds, and provide evidence-based research with a focus on practical application. This course expands the knowledge base of professionals caring for infants with feeding and nutrition challenges. The development of feeding skills and the impact of early nutrition and feeding experiences is discussed in the context of developmentally appropriate and family centered care. Based on concepts adapted from the Synactive theory, the Newborn Individualized Developmental Care & Assessment Program (NIDCAP) and the Family Infant Relationship Support Training (FIRST) program, the Institute provides a sound foundation for observation and assessment of developing feeding skills. Supportive interventions for infants while in the hospital, as well as during the transition to home are addressed. The Institute places a special emphasis on feeding and nutritional issues through the transition to supplementary (baby) foods. The nutritional needs of premature infants and those with special medical needs, as well as the interaction between feeding skills and nutritional needs are discussed. Presenters represent the disciplines of nursing, nutrition, therapy, parenting, and psychology. Each day successively builds on the knowledge and information from the previous day. An interactive process with the faculty results in the participant applying the information during the four day Institute.

Disclosure: Conference and CME are supported by the University of South Florida Health (USF Health).

NT

Needs Assessment:

A common challenge in the NICU, especially with very premature infants, is feeding. Typically the focus is on quantity, and subsequent growth of the infant. However, an argument can be made that focus should be on the quality of the feeding skills over quantity of food consumed. "...Many studies show that infants who develop feeding problems are averse to food and feeding...repeated experiences solidify over time into behavioral repertoires, and therefore the quality of the feeding experience should also be measured...". This course seeks to close the gap on feeding challenges by focusing on the neurodevelopmental aspects of infant feeding, supporting the infant-parent relationship, and the development of systems to enhance practice behaviors.

Who should attend?

NICU / PICU Nurses
Physicians
Nutritionists / Dieticians
Speech / Language Pathologists
Parents / Family Members
Early Interventionists
Community / Public Health Nurses
Occupational Therapists

Program # AE 2020 141 1183

FIFI | Fragile Infant Feeding Institute

Thursday—Sunday, August 22-25, 2019

Ray Conference Center

(on Butler Hospital campus)

345 Blackstone Blvd.

Providence, RI

Conference registration includes light breakfast & lunch.

Revision date: 05-08-19

Provided by:

USF HEALTH

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Occupational Therapists

FIFI Fragile Infant Feeding Institute

Learner Objectives:

As a result of participation in this activity, *participants should be able to*:

- Describe neurodevelopmental issues that impact appropriate nutrition and feeding for infants with special needs;
- Utilize assessment and intervention techniques to support optimal growth of infants with special needs;
- Identify nutritional requirements for at-risk infants in the NICU and after hospital discharge;
- Demonstrate both individual and collaborative expertise with other professionals and families in support of better growth for infants;
- Develop an individual and/or team action plan;
- List three new professional and / or parent contacts that have the potential to collaborate on current or future projects, or to assist with problem-solving.

Learner Objectives apply to all members of the target audience.

Accreditation

Certificates of Attendance or Certificates of Continuing Education Credit are obtained online after the event.

PHYSICIANS:
USF Health is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

USF Health designates this live activity for a maximum of **27.00** *AMA PRA Category 1 Credits™.* Physicians should claim only the credit commensurate with the extent of their participation in the activity.

NURSES FBN (Florida Board of Nursing):
USF Health is an approved provider of continuing education for nurses through FBN 50-2970. This program has been approved for **27.00** contact hours.

FLORIDA LICENSED OCCUPATIONAL THERAPISTS:
USF Health is an approved provider of continuing education for Occupational Therapy Licensees by the Florida Board of Occupational Therapists. This program has been reviewed and approved for up to **32.50**, 50-minute contact hours. Licensee numbers are required prior to the issuance of certificates.

REGISTERED DIETICIANS:
USF Health, CO001, is a Continuing Professional Education Accredited Provider with the Commission on Dietetic Registration (CDR) from 2/22/19 to 2/21/2021**.** Registered dietitians (RDs) and dietetic technicians, registered (DTRs) will receive 27.00 Level 2 continuing professional education units (CPEUs) for completion of this program. Continuing Professional Education Provider Accreditation does not constitute endorsement by CDR of a provider, program or materials. Licensee numbers are required prior to the issuance of certificates.

The University of South Florida is approved by the Continuing Education Board of the American Speech-Language-Hearing Association (ASHA) to provide continuing education activities in speech-language pathology and audiology. **See course information for number of ASHA CEUs, instructional level and content area.** ASHA CE Provider approval does not imply endorsement of course content, specific products or clinical procedures.

SPEECH LANGUAGE PATHOLOGISTS:

This course is offered for up to 2.7 ASHA CEUs (Advanced level, Professional area).

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Program Disclosures:

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Relevant financial and non-financial relationships exist between the following individuals and commercial interests

Person	Disclosures & Relationships
Joy Browne, PhD, MSN, MS, BSN, PCNS, IMH-E (IV)	Dr. Browne is employed as a Clinical Professor of Pediatrics and Psychology at the University of Colorado, Denver Anshutz Medical Campus, JFK Partners in Aurora, CO. She is on the faculty of Fielding Graduate University, and the Irving Harris Program for Child Development and Infant Mental Health at the University of Colorado Denver School of Medicine. . Dr. Browne is a Newborn Individualized Developmental Care and Assessment Program (NIDCAP) Master Trainer,. She is the Director of the Family Infant Relationship Support Training (FIRST) program, the BABIES model Learning Collaboratives, as well as the Fragile Infant Feeding Institute. Dr. Browne is the Executive Director of WONDERBabies, LLC. She receives consulting fees from Stollery Foundation in Edmonton, Canada, Developmental Pathways in Colorado, University of Alaska, Hospital Erasme in Toulouse, France, and Grace Nursery in Sydney, Australia. She is on the Medical Advisory Board for the non-profit organization, Feeding Matters, and the Board of Directors for the Alliance for the Advancement of Infant Mental Health. These two positions are non-financial relationships. Dr. Browne has no other relevant financial or non-financial relationships to disclose.
Theresa Crocker, PhD, RD	Dr. Crocker is the Director of the Nutrition and Dietetics Program, and Assistant Professor, at the College of Public Health, University of South Florida, in Tampa, FL. She has no other relevant financial or non-financial relationships to disclose.
Lisbeth Gabrielski, MS, RN, IBCLC	Lisbeth Gabrielski is employed as a NICU and Lactation Clinical Manager, NICU and Lactation Support Services at Children's Hospital Colorado Aurora. She has no other relevant financial or non-financial relationships to disclose.

Person	Disclosures & Relationships Continued
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Erin Ross, PhD, CCC-SLP	Erin Ross is a consultant Speech Language Pathologist. She is the owner of Feeding Fundamentals, LLC. She is also a Clinical Instructor in the School of Medicine, Dept of Pediatrics, at the University of Colorado Denver within the Center for Family and Infant Interaction. She also is Faculty at the Rocky Mountain University of Health Professions. She has a non-financial relationship with Feeding Matters, where she is on the professional advisory committee.
Bobbi Rose, BSW, MA, MPH	Bobbi Rose is employed by the University of South Florida. She has no other relevant financial or non-financial relationships to disclose.
Vincent C. Smith, MD, MPH	Dr. Smith is employed as Division Chief of Neonatology at Boston Medical Center, and Associate Professor of Pediatrics at Boston University School of Medicine, in Boston, MA. He has no other relevant financial or non-financial relationships to disclose.
Kay Toomey, PhD	Kay Toomey is President of Toomey & Associates, Inc. She has a financial relationship with Gerber, for whom she is a paid consultant. She is on the paid Speaker's Bureau for Educations Resources, Inc. and acts as a Clinical Consultant to the Feeding Clinic at the STAR Institute. She has a non-financial relationship with Feeding Matters as a non-paid board member.
Joan Zerzan, MS	Joan Zerzan is recently retired from the Washington State Dept. of Health, Healthy Starts, and Transitions/CSHCN. She consults for the WA State Dept. of Health as requested.. Ms. Zerzan has no other relevant financial or non-financial relationships to disclose.

Conference Agenda: (subject to modification)

THURSDAY, AUGUST 22, 2019	
	SESSION / EVENT
7:00 – 8:00 AM	BREAKFAST (COFFEE SERVICE + PASTRIES)
8:00 – 8:15 AM	Welcome: Introduction to the Institute and Institute Faculty (*Joy Browne*)
8:15 - 9:30 AM	Perspectives in Providing Support for the Development of Feeding Skills in Infants (*Debra Paul*) Case Study with video (*Joy Browne*)
9:30 – 10:00 AM	Liquid Gold: Why Breast is Best (*Beth Gabrielski)*
10:00 – 10:15 AM	BREAK
10:15 – 11:00 AM	Neurobehavioral and Neurosensory Development – Essential Foundations for Successful Feeding (*Joy Browne*)
11:00 –12:00 PM	Relationships, Regulation and Reflection (R^3) (*Joy Browne)*
12:00 – 1:15 PM	LUNCH (PROVIDED)
1:15 –1:45 PM	Foundations of Growth and Growth Assessment (*Joan Zerzan*)
1:45 – 3:00 PM	Developmental Neurophysiology of Eating (*Erin Ross*)
3:00 – 3:15 PM	BREAK
3:15 – 4:00 PM	Foundations of Breastfeeding (*Beth Gabrielski)*
4:00 – 4:30 PM	What and How Do Infants in the NICU Learn About Eating (*Kay Toomey*)
4:30 – 5:00 PM	A Mother's Story (*TBD*)

FRIDAY, AUGUST 23, 2019	
TIME	SESSION / EVENT
7:00 – 8:00 AM	BREAKFAST (COFFEE SERVICE + PASTRIES)
7:55 – 8:00 AM	Welcome (*TBD*)
8:00 – 9:15 AM	Observational Approaches and Guidelines for Feeding Interventions (*Joy Browne*)
9:15 – 9:40 AM	Case Study: Normal Development of Eating (*Erin Ross*)
9:40 – 10:00 AM	Write it up: Basics of a Feeding / Eating Assessment Report (*Debra Paul*)
10:00 – 10:30 AM	BREAK
10:30 – 11:30 AM	"In the Trenches": Supportive Interventions for the Caregiver and Infant (*Erin Ross)*
11:30 – 12:15 PM	The Influences and Impact on Mental Health Related to Having a Fragile Infant (*Kay Toomey* OR *Joy Browne*)
12:15 – 1:30 PM	LUNCH (PROVIDED)
1:30– 3:00 PM	Breastfeeding Issues: Mothers and Infants (*Beth Gabrielski*)
3:00– 3: 15 PM	BREAK
3:15 – 4:00PM	Assessment for Children with Special Health Care Needs Part 1: The Nutrition Care Process (*Joan Zerzan*)
4:00 – 4:30 PM	Assessment Part 2: Evaluating Breast Milk Substitutes and Nutrition Supplements (*Joan Zerzan*)
4:30 – 5:00 PM	BREAK
5:00 – 6:15 PM	It's Not Rocket Science: Nipples / Bottles (*Debra Paul & Erin Ross)*

Conference Agenda: (subject to modification)

Saturday, August 24, 2019	
Time	**Session / Event**
7:00 – 8:00 AM	Breakfast (Coffee Service + Pastries)
8:00 – 8:05 AM	Welcome
8:05 – 8:30 AM	ABCs of Attachment and Influence on Feeding (*Kay Toomey*)
8:30 – 9:15 AM	Nutrition Support in the NICU: A Systems Approach (*Joan Zerzan*)
9:15 – 10:00 AM	Supplemental Tube Feedings Before and After Discharge: Supporting Oral-Feeding Development (*Kay Toomey & Joy Browne*)
10:00 – 10:15 AM	Break
10:15 – 11:15AM	Supportive Interventions for Breastfeeding (*Beth Gabrielski*)
11:15 – 12:00 PM	Gastro-Esophageal Reflux (*Joan Zerzan)*
12:00 – 1:15 PM	Lunch (Provided)
1:15 – 1:30 AM	Introduce Action Plans
1:45 -2:30 PM	Growing after Going Home: Supporting Nutrition in the Preterm Infant after Discharge from the NICU (*Joan Zerzan)*
2:30 – 3:30 PM	Partnering with Parents (*Kay Toomey*)
3:30 – 4:00 PM	Break
4:00 – 5:00 PM	Listen to Their Stories: Parent Panel *(Joy Browne & parents)*

Sunday, August 25, 2019	
Time	**Session / Event**
7:00 – 8:00 AM	Breakfast (Coffee Service + pastries)
8:00 – 8:05 AM	Welcome (*TBD*)
8:05 –8:50 AM	Early Connections: Supporting Feeding through Discharge to the Community (*Debra Paul)*
8:50 – 10:00 AM	Supporting the Breastfed Infant after Discharge from the NICU (*Beth Gabrielski)*
10:00 – 10:15 AM	That Amazing First Year: Transitions in Oral Feeding (*Erin Ross)*
10:15 – 10:30 AM	Break
10:30 – 11:15 AM	Active Group Practice with Video (*Erin Ross, support of Full Faculty*)
11:15– 12:15 AM	Action Plans (*Full Faculty*)
12:15 – 1:30 PM	Lunch (Provided)
1:30 – 2:30 PM	Rocking the Boat: Using Reflective Practice in Your Own Unit(*Joy Browne)*
2:30 – 3:00 PM	Wrap-Up: Feedback, Remaining Q & A, and Evaluation

Disclaimer:

The information provided at this CME/CE activity is for continuing education purposes only and is not meant to substitute for the independent medical/clinical judgment of a healthcare provider relative to diagnostic and treatment options of a specific patient's medical condition.

Meeting Venue: Ray Conference Center @ Butler Hospital

- The meeting will be held at the Ray Conference Center, which is on the campus of Butler Hospital, in Providence, RI. The meeting room is the “Main Hall”. A map will be emailed to registrants.
- Driving: Parking is free. Use Lot B and D.
- Bus: RIPTA bus # 40 goes between Kennedy Plaza (downtown hotels) and Butler Hospital on Aug. 22—23. This route does not run on the weekend. https://www.ripta.com/40
- Shuttle service to/from downtown hotel and Butler is being researched.

The distance between the hotel, Graduate Providence, and Butler Hospital is just under 3 miles.

Ray Conference Center @ Butler Hospital: 345 Blackstone Blvd, Providence, RI www.butler.org

A special Thank You to Rose Bigsby and colleagues at the Women and Infants Hospital of Rhode Island NICU for obtaining the venue for this event.

Lodging Options: Two hotels were contracted for rooms. Neither is tied to the meeting venue. Choose any lodging that works for your budget, and transportation options.

Graduate Providence (formerly Providence Biltmore) https://www.graduatehotels.com/providence/

11 Dorrance St., Providence, RI 02903 (401) 421-0700

- King Deluxe Room: $179 + taxes = $202.27 per night, or
- 2 King Beds Junior Suite: $199 + taxes = 224.87 per night
- To reserve a room ONLINE, click on the reservation link: **http://bit.ly/GraduateProvidence**
  Group reservation code: 1908FIFIRB
- PHONE: Guests can call a Hotel Reservations Agent directly at 401-421-0700 and choose Option 1, open seven days a week, twenty-four hours a day, and use your group code when speaking with the reservations agent.
- Group rate deadline is July 21, 2019
- Cancellation within 48 hours of arrival will result in one night's room + taxes.
- Parking is at a municipal garage, and can be as high as $35 a day.

This hotel is within an easy walk to Kennedy Plaza, the bus stop for Bus #40, which goes to Butler Hospital. Butler is approximately 3 miles away. Shuttle service to/from Ray Conference Center is being researched at the time of this writing. Shuttle service to event venue will only be from the Graduate Providence.

This hotel does not have an airport shuttle. Buses run from the airport to downtown Providence; Kennedy Plaza is an easy walk, i.e., about 1/10 of a mile. There are shuttles for hire at the airport that take you into downtown.

Crowne Plaza @ Providence Warwick Airport: https://www.ihg.com/crowneplaza/hotels/us/en/warwick/wrwri/hoteldetail?cm_mmc=GoogleMaps-_-CP-_-US-_-WRWRI

801 Greenwich Ave., Warwick, RI 02886 (401) 732-0261

- Single / Double rooms are $139 + taxes = $157.07 per night
- To reserve room, call 401-732-6000. You must reference the Fragile Infant Feeding Institute to get the group rate.
- Can also reserve room at www.crownehotelwarwick.com, using the three letter group code of FIF.
- Cancellations within 24 hours prior to arrival will result in one night's room + taxes.
- Free parking

This hotel has an airport shuttle. It is 12 miles from Butler Hospital. NO transportation between the hotel and event venue is offered. It is suggested you have a car, or are willing to use a service like Uber, Lyft or taxi.

IF you are interested in sharing a room, email brose@health.usf.edu and I will share your information with others that are interested in sharing.

Airport & Ground Transportation: The Providence Airport "PVD" is T. F. Green airport, and is located in Warwick, not Providence proper.

National Perinatal Foundation / FIFI Affordability Scholarship

To help broaden participation at the Fragile Infant Feeding Institute, the Chiles Center at the University of South Florida is offering a limited number of ***affordability scholarships*** to clinicians and allied healthcare workers who have a compelling need and lack adequate funding or sufficient employer support to otherwise attend. The scholarships are funded by the generous institutional support from the National Perinatal Foundation. The overarching goal of the donation is to improve the health outcomes of mothers and babies.

The scholarship will cover registration, valued at $800.

Applicant Information: You may print this page and fill in the information, or include the information on a WORD document, along with your reply to the 4 open-ended questions listed below. Submit to Bobbi Rose at brose@health.usf.edu or fax to 813-974-5172 by the end of the day on June 30, 2019

A FIFI committee will review all completed applications and provide feedback to all by July 14, 2019.

Event Name: The Fragile Infant Feeding Institute
Event Date: August 22—25, 2019 (Thursday—Sunday)
Venue: Ray Conference Center at Butler Hospital in Providence, RI.

Name:	Degree(s):
Email:	Phone:
Job Title:	
Organization:	City, State:

Open ended questions (put into a WORD document):

1. Why do you want to attend?
2. How will training be used specifically in your hospital or organization?
3. What is your justification for the need for funding?
4. Why should you be selected?

Evaluations & Post-Event Survey:

The evaluation process is a critical component in our strategy to offer excellence in our future conferences, and to ensure we are addressing the education needs of our audience. Your comments and feedback make a difference! Please complete the evaluation forms, which will be distributed on-site, (or possibly as an electronic survey), and return them to either the Session Facilitator or the registration desk.

In accordance with the guidelines for medical continuing education credits, we will measure outcomes of this educational event. You will receive an electronic post-event survey via email approximately 6-8 weeks after the conference ends. The results of this survey are equally important as the aforementioned evaluations in assisting us with building future programs. We ask that you take the time to complete the post-event survey when you receive it.

Cancellation & Refund Policy:

Cancellation notification must be made in writing (email is preferred and fax is also acceptable) and received by **July 30th** . A cancellation fee of $100 will be assessed. Cancellations made later will not be refunded. Substitutions are welcome without penalty. Please allow up to 3 weeks after the conference for any refunds. The Office of Continuing Professional Development at the University of South Florida reserves the right to cancel this activity due to unforeseen circumstances. In the event of such cancellation, only the registration fee will be returned to the registrant.

Cancellation notification should be sent to:

brose@health.usf.edu and cpdsupport@health.usf.edu

Registration Information:

Fees: "Regular" Registration is $800, and goes through July 22nd. "Late" registration, beginning July 23rd is $875 There are no partial day registrations allowed. Your fees must be paid before the event begins.

Registration Fee includes (per participant): Attendance at the Institute, continuing education credit, exhibits (as applicable), **light breakfast (coffee service & pastries), lunch**, daily refreshment breaks, and the conference syllabus, which will be electronic. You will receive the electronic files in advance so that you have time to print the slides if you prefer to have paper copies with you during the sessions.

Registration & Payment Policy:

Payment is collected in USD. Confirmation will be sent after receipt of check, and after online registration is paid with a credit card (Visa, MasterCard, American Express or Discover).

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Accommodations for Disabilities:

Please notify the USF Health CPD Office, 12901 Bruce B. Downs Blvd., MDC 60, Tampa, Florida, 33612, or call (813) 224-7860, or email cpdsupport@health.usf.edu a minimum of ten working days in advance of the event if a reasonable accommodation for a disability is needed.

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Information needed to register online:

Dear Administrative Assistant,
I recognize that hospitals send teams, and often it is the administrative assistant of the unit that is responsible for registrations. Below is a check list of items that you will need to obtain from the attendees in order to complete the online registrations. If payment is by check, rather than the corporate credit card, be sure to untick the default setting for credit cards.

- ❑ First Name and Last Name
- ❑ Academic degree(s), Gender, Birthday (mm/dd)
- ❑ License Number (if applicable)
- ❑ Email address
- ❑ Organization
- ❑ Home address (including city, state and zip).
- ❑ Professional Profile, for example: Physician, Nurse, SLP, OT, Dietician etc.
- ❑ Any special needs that would require a reasonable accommodation of a disability? (If so, email me details within 10 working days of event to: brose@health.usf.edu or cpdsupport@health.usf.edu)
- ❑ Any allergies that would require me to notify the hotel kitchen? Examples include nut allergies, Celiac disease etc.
- ❑ And finally, if they already exist in the USF's Continuing Professional Development's registration system, they have a password. You would need to know it. If you are creating a profile for the first time, let the person know what password you've created. They can change it later.

Registration Fees in USD	
Regular Registration Fee (received on or before July 22, 2019)	$800
Late Registration Fee (July 23, 2019 onward)	$875

IF PAYING BY CHECK:

Registration must occur online. An email requesting payment will be sent to you. Include it with the check. (This page will NOT be accepted for manual entry of registration.)

Mail check to the address below.

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If requesting group rate, who are the attendees that comprise the group?
Online registration link: https://bit.ly/2H8k3ZS

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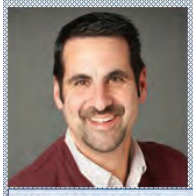

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Peer Reviewed

From the National Perinatal Association: NICU Discharge Preparation and Transition Planning

Vincent C. Smith, MD, MPH

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.

The American Academy of Pediatrics (AAP) recommends the transition to home occur when the infant achieves physiologic maturity, and there is an active program for parental involvement and preparation for care of the infant at home. The timing of a Newborn Intensive Care Unit (NICU) discharge is mostly based on the physiologic maturity of the infant. Secondary factors are discharge planning and include the assurance that arrangements for outpatient follow-up have been completed and that the family has received the necessary teaching and demonstrated mastery of the essential knowledge and skills. The importance of discharge planning has been captured in a recent article:

https://pediatrics.aappublications.org/content/143/6/e20182915.abstract

There are two related concepts involved in this transition process:

1) The discharge readiness of the families

2) The discharge preparation program.

NICU discharge readiness is the attainment of technical skills and knowledge, emotional comfort, and confidence with infant care by the primary caregivers at the time of discharge. NICU discharge preparation is the process of facilitating discharge readiness to successfully make the transition from the NICU to home. Discharge readiness is the desired outcome, and discharge preparation is the process.

"NICU discharge readiness is the attainment of technical skills and knowledge, emotional comfort, and confidence with infant care by the primary caregivers at the time of discharge."

Discharge Readiness

Discharge readiness is an important milestone achievement. Studies in adult, pediatric, and neonatal populations have demonstrated that adverse outcomes are associated with not being prepared at hospital discharge. These adverse outcomes range from tangibles such as increased health care utilization and costs to less tangible, but equally important, factors such as greater difficulties with stress, recovery, self-care, confidence with self-care management abilities, coping with challenging family-related issues, obtaining necessary help and emotional support, and overall adjustment.

Discharge readiness assessment should be a standard part of the discharge process. Each NICU should make every effort to ensure that parents are prepared for the discharge of their infant(s) in order to prevent subsequent untoward events. Additionally, NICUs should conduct regular evaluations of their existing discharge program to allow improvement over time.

Discharge Preparation

NICU discharge preparation is the process of facilitating comfort and confidence as well as the acquisition of knowledge and proficiencies to make the transition from the NICU to home successfully. Suggested content for a NICU discharge preparation program would include all of the following:

1) Well-defined discharge teaching philosophy

2) Structured education program

3) Defined curriculum

4) Family assessment of discharge readiness

5) Process for the transition of care to a medical home.

A well-defined discharge teaching philosophy refers to the approach that a NICU takes to all discharge preparation including identifying the discharge planning team, understanding the importance of partnering with the family, and having a willingness to accommodate different types of families. The discharge planning team typically consists of a combination of clinical nurses, physicians, neonatal advanced practice nurses, physician assistants, case managers, and social workers. It is also imperative to remember that the infant's parents or primary caregivers are also an integral part of the discharge planning team. Families are able to build on their strengths if given the opportunity to participate in the care early and be active

participants in the discharge process. To embrace the concept of parents as part of the team, a NICU can follow the four central tenets of family-centered care (i.e., dignity and respect, information sharing, family participation in care, and family collaboration). It is also important for a NICU to recognize that some families may have limited English proficiency and/or functional health literacy, and may have varied developmental needs (as in teen parents or parents with mental limitations) and will need support and special accommodation during their discharge preparation. All these are factors to consider when developing a discharge teaching philosophy.

"It is also important for a NICU to recognize that some families may have limited English proficiency and/or functional health literacy, and may have varied developmental needs (as in teen parents or parents with mental limitations) and will need support and special accommodation during their discharge preparation."

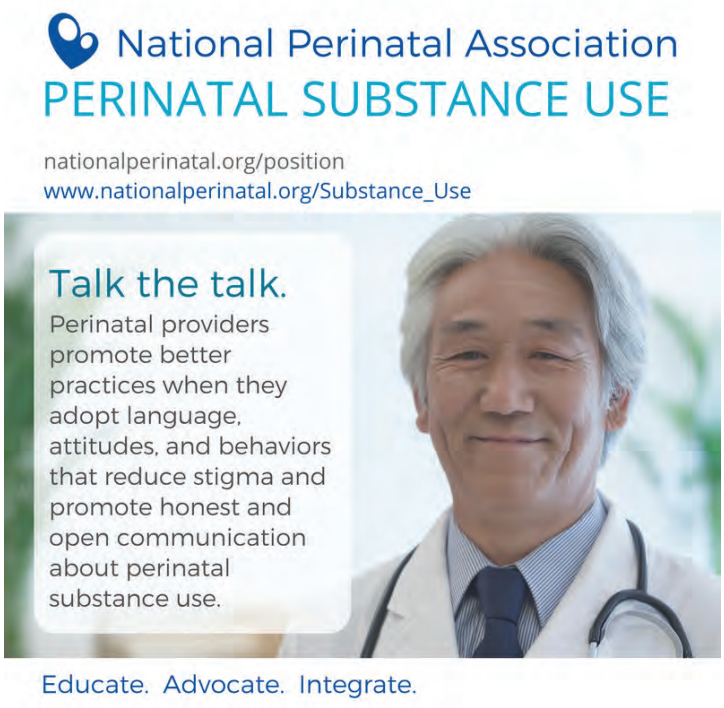
After a NICU family has completed the structured education program with its well-defined curriculum, it can be considered to be progressing towards discharge. This is a potentially optimal time to have a family assessment (a key component of a successful discharge process). The goal of a family assessment would be to understand a family's specific needs and circumstance better. A family assessment could include some of the following questions: what is family structure and social support systems; what does the family think of its social support systems; are they adequate; what potential barriers to learning does the family have; what is their home environment like; are there financial considerations to take into account; are there transportation challenges: how much previous experience does the family have; what are their coping habits and styles; and how equipped are they to handle their infant at home. These questions will complement the discharge readiness assessment and should be a standard part of the discharge process.

Each NICU should make every effort to make sure that parents are prepared for discharge to prevent untoward events after discharge. Each NICU should also conduct regular evaluations of their discharge program to allow improvement over time. With discharge planning beginning shortly after admission, structured education, and attention to the family's needs, circumstances, and resources, the transition to home can be smooth, even in the most complex cases.

NPA Guidelines for Discharge Preparation and Transition Planning

The NPA is coordinating an interdisciplinary workgroup to develop guidelines and recommendations for the discharge preparation and transition planning from the NICU to home for infants admitted to the NICU and their families. These guidelines will cover the following topic areas:

- Family/Home assessments: Family assessments, caregiver mental health, infant mental health, and anticipatory guidance
- Special circumstances: understanding the needs of military families, supporting families with limited English proficiency and/or cultural differences, supporting families with unique cultural and philosophical expectations, supporting LGBT families, supporting families with disabilities, supporting families with complex medical needs
- Support Systems: Mentoring programs (peer-to-peer support), social work involvement, community providers/programs, mental health support, communication with families who have left the NICU, safe technologies discussion with parents
- Transfer and/or Coordination of Care: primary care providers and the medical home, care coordination or navigators, communication among providers, more integration of the NICU and community provider, subspecialty care needs, routine nursing home visits, early intervention, and discharge summary



NPA's Vision for Change

- Every family being discharged from a NICU will have a quality discharge preparation and transition planning program that is tailored to the specific needs of the family.
- The goal is to facilitate the creation of national guidelines for NICU discharge preparation and to encourage neonatal clinicians to prioritize discharge teaching so that families are better prepared for the transition to home from the NICU.
- The work will be coordinating an interdisciplinary workgroup to develop guidelines and recommendations for the discharge readiness and preparation, and thus the transition from the NICU to home for infants admitted to the NICU and their families.

TAKE HOME POINTS

1. Making the transition from the NICU to home involves both discharge readiness and discharge preparation
2. NICU discharge preparation and transition planning should begin shortly after admission and continue until families are prepared to take their infants home.
3. A NICU discharge preparation and transition planning program should include all of the following: 1) well-defined discharge teaching philosophy; 2) structured education program; 3) defined curriculum; 4) family assessment of discharge readiness; and 5) process for the transition of care to a medical home
4. The family should be included as team members in the discharge preparation and transition planning process by following the tenets of family-centered care as much as possible
5. The structured family education program should be tailored to the family's specific needs and circumstances.

References:

1. *American Academy of Pediatrics Committee on Fetus and Newborn. Pediatrics. 2008;122(5):1119-26*
2. *Gupta M, Pursley DM, Smith VC. Preparing for Discharge From the Neonatal Intensive Care Unit. Pediatrics. 2019;143(6):e20182915*
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5. *Smith VC, Hwang SS, Dukhovny D, Young S, Pursley DM. Neonatal intensive care unit discharge preparation, family readiness, and infant outcomes: connecting the dots. J Perinatol 2013 Jun;33(6):415-21.*
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7. *Sheikh L, O'Brien M, McCluskey-Fawcett K. Parent preparation for the NICU-to-home transition: staff and parent perceptions. Child Health Care. Summer 1993;22(3):227-239*
8. *Sneath N. Discharge teaching in the NICU: are parents prepared? An integrative review of parents' perceptions. Neonatal Netw 2009;28:237-246.*

The author has no relevant disclosures.

NT

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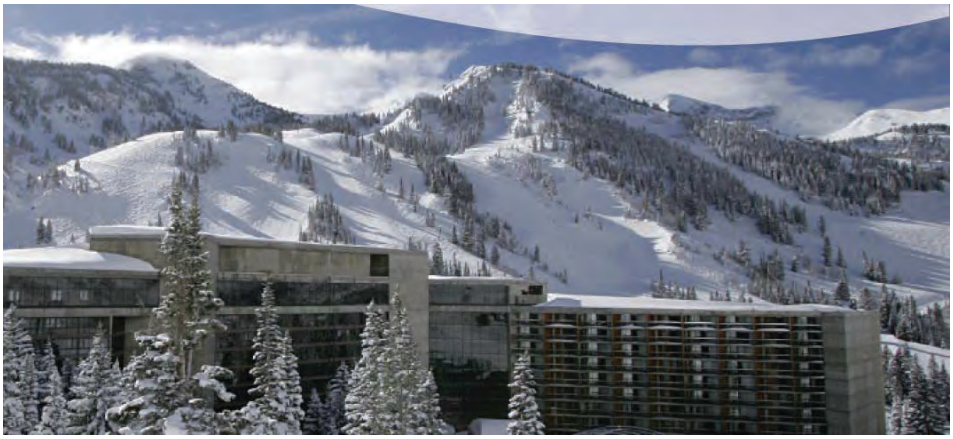

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If you would like to pay by credit card, please complete the credit card authorization form and email it along with the Exhibitor & Sponsorship Registration Form to asimonian@paclac.org.

Fellow's Column: A Case of Hypoplastic Left Heart Missed on Congenital Heart Defect Screening

Matthew Wood, MD, Rachel Davidge, DO

Introduction:

In September 2010, the US Health and Human Services Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) recommended that screening for critical congenital cyanotic heart defects be added to the uniform newborn screening panel. The goal was to identify infants with structural heart disease that develop morbidity and mortality due to normal physiologic changes in infancy, such as the closure of the ductus arteriosus. They initially recommended a list of seven cardiac lesions to be primary targets of such screening: hypoplastic left heart syndrome, pulmonary atresia, tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia, and truncus arteriousus. All of these lesions are traditionally associated with hypoxia. (1)

The SACHDNC assembled a workgroup composed of the AAP, pediatric generalists, pediatric specialists, and other relevant parties in 2011 and developed the screening recommendations for congenital heart defects, which were published in Pediatrics in November 2011. In that article, an additional list of secondary screening targets were added: coarctation of the aorta, interrupted aortic arch, double outlet right ventricle, Ebstein anomaly, and single ventricle complex. (1)

Since that time, congenital heart defect screening has become mandated and has undergone implementation across the nation. The CDC has tracked outcomes since these recommendations have been published. According to CDC data, pulse oximetry screening has reduced early infant death related to critical congenital heart defects by 120 instances per year (a 33% reduction). Additional research has postulated that there is a cost of $12,000 for every year of life gained for babies detected by congenital heart defect screening. This would indicate that pulse oximetry screening for congenital heart disease is, in fact, quite effective. (2)

We will discuss the case of an infant impacted by congenital cardiac defect screening.

"According to CDC data, pulse oximetry screening has reduced early infant death related to critical congenital heart defects by 120 instances per year (a 33% reduction). Additional research has postulated that there is a cost of $12,000 for every year of life gained for babies detected by congenital heart defect screening."

Case Presentation:

Our patient is a full term Caucasian male born via SVD to a 32-year old G3P3 woman. Pregnancy was uncomplicated with normal prenatal labs and normal prenatal ultrasound anatomy scan. Delivery was uncomplicated, and baby remained with mother throughout the nursery course. Baby breastfed well and did not have excessive weight loss or hyperbilirubinemia. He was discharged home with mother on day of life two after normal congenital heart defect screening.

After discharge, the baby was noted to develop rhinorrhea on day of life three with subsequent development of left eye discharge. Siblings were noted to have viral URI symptoms as well. PCP prescribed a seven-day course of ocular erythromycin for presumed lacrimal duct obstruction. On day of life 12, mother noted that the baby developed increased work of breathing with subcostal retractions but continued to feed well with normal elimination habits.

On day of life 19, the mother again took the baby to PCP's office. In PCP's office, the baby was noted to have retractions with SpO_2 as low as 86% and so was directed to ED. While in the ED, the baby was noted to have tachycardia, tachypnea, nasal flaring, and retractions. He was started on high-flow nasal cannula (HFNC) 10L with noted improvement. The patient was admitted to NICU for further management.

At time of admission to the NICU, the initial exam was notable for yellow discharge from the left eye, bilateral subcostal retractions, upper airway sounds transmitted throughout all lung fields, and mildly diminished breath sounds in the right lung fields. Labs on admission were notable for a metabolic acidosis thought to be secondary to dehydration and were otherwise unremarkable, including normal lactate. Initial CXR showed pulmonary vascular congestion with the suggestion of bilateral

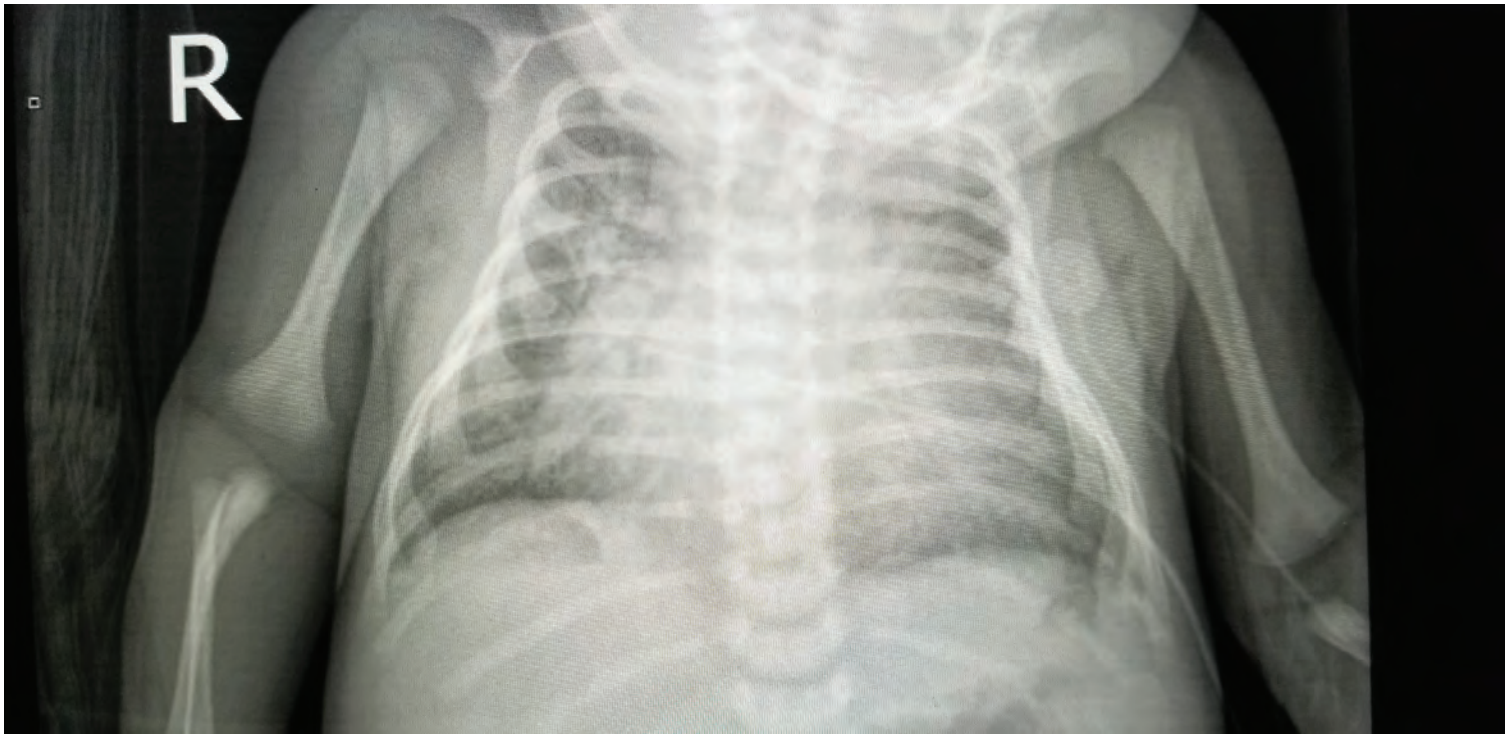

Fig 1. Initial CXR showed pulmonary vascular congestion with the suggestion of bilateral perihilar airspace disease, which obscured the cardiothymic silhouette.

perihilar airspace disease, which obscured the cardiothymic silhouette. Baby was diagnosed with acute respiratory failure likely secondary to viral vs bacterial infectious etiology and was started on ampicillin and gentamicin.

During the first few days of treatment, only minimal improvement in clinical status was noted. By day five of admission, the baby had been unable to wean fully from HFNC support and had frequent episodic tachypnea and desaturations requiring tactile stimulation. Additionally, a new mid systolic murmur was heard.

Echocardiogram was subsequently performed and demonstrated hypoplastic left heart syndrome, long-segment coarctation, moderate PDA with bidirectional shunting and signs of impaired RV function. The patient was started on milrinone and alprostadil. The baby underwent Norwood procedure on day of life 32. After recovery from surgery, the patient was noted to be improved clinically and was discharged to home to await further palliative surgery and probable eventual cardiac transplant.

Discussion:

While current data may indicate the cost-effective nature of pulse oximetry for congenital heart defect screening at the population level, cases like the one above may call into question the sensitivity of the screen at the patient level.

A study published in Pediatrics in 2015 evaluated the number of infants detected and missed on neonatal congenital heart defect screening. Data analyzed from metropolitan Atlanta, GA from 2000 to 2005 was used to create a simulation model of detection rates of both primary and secondary screening targets. (3)

"While the above case is one in which significant morbidity and mortality appear to have been avoided, it does serve as a reminder to always have a high index of suspicion for congenital heart defects when it matches the patient's symptoms, even if the newborn congenital heart defect screening was normal."

It was determined that ~25% of all congenital heart defects would fall under the critical disease heading, which constitutes the primary and secondary screening targets for congenital heart defect screening. Using data previously gathered by the National Birth Defects Prevention Study, it was determined that

30% of critical congenital heart defects were detected prenatally on ultrasound. An additional 40% were detected within the first three days of life due to neonatal symptoms. These two categories were labeled "timely detection," in that they would lead to initial echocardiogram by the third day of life and prior to birth hospital discharge. The remaining 30% of congenital heart defect cases would, therefore, fall into the "late detection" category and represent the infants that we would hope to detect on neonatal cardiac screening. (3)

The simulation model predicted that over the course of a year, half of the infants who would fall into the "late detection" category would be caught by newborn congenital heart defect screening; ~800-1100 cases per year. However, the remaining half of late detection cases were predicted to be false negatives on the congenital heart defect screen and therefore remain undetected. This represents ~800-1000 cases per year of critical congenital heart defects that remain undetected past the third day of life in spite of congenital heart defect screening. (3)

It is worth noting that the rates of detection vary based upon which critical congenital heart defect is being screened. For example, pulmonary atresia is highly likely to present clinically while still admitted to the birth hospital, and essentially zero cases are predicted to be missed on congenital cardiac defect screening. In contrast, 16% of cases of tetralogy of Fallot and 38% of cases of coarctation of the aorta are predicted to slip past screening. Looking at the data, we see that an anticipated two percent of hypoplastic left heart syndrome cases are predicted to be missed through initial discharge, similar to the patient discussed above. (3)

These infants are at substantial risk of morbidity and mortality related to their critical congenital heart defects, which are often exacerbated by normal newborn physiologic changes such as PDA closure. The above case likely represents one such infant whose condition was potentially exacerbated by physiologic alterations of blood flow across the PDA. It is conceivable that other missed cases of congenital heart defects may present similarly.

While the above case is one in which significant morbidity and mortality appear to have been avoided, it does serve as a reminder to always have a high index of suspicion for congenital heart defects when it matches the patient's symptoms, even if the newborn congenital heart defect screening was normal.

We would like to discuss one possible method for improved detection of congenital heart defects that has been proposed, called peripheral perfusion index (PPI). PPI is calculated by taking the ratio of pulsatile to non-pulsatile blood flow through tissue and is measurable by certain types of pulse oximeters. PPI is affected by stroke volume and therefore, may be an indicator of circulatory or cardiac disease.

A case-control study was conducted in Sweden, where data from 10,000 newborns without CHD were tested to define a normal PPI range. During data collection, nine infants were diagnosed with ductal-dependent systemic circulation related to congenital heart disease; four cases of coarctation of the aorta, two of interrupted aortic arch, two of hypoplastic left heart syndrome, and one of critical aortic stenosis. All nine of these infants were noted to have measurement of PPI below the interquartile ranges of the normal controls and five of the nine tested had a PPI below the fifth percentile of the calculated normal range. Additionally, it was noted that three of these nine infants were not detected on standard pulse oximetry screening. This data may suggest that PPI merits further evaluation as a congenital heart defect screening tool. (4)

While this study does not provide definitive data on rates of detection for various cardiac defects or delve into important population health topics like rates of false positive screening and cost-effectiveness, it does open the door to further discussion on new or adjunctive congenital heart defect screening practices.

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Fellow's Column is published monthly.

- Submission guidelines for “Fellow's Column”:
- 1250 word limit not including references or title page.
- 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:

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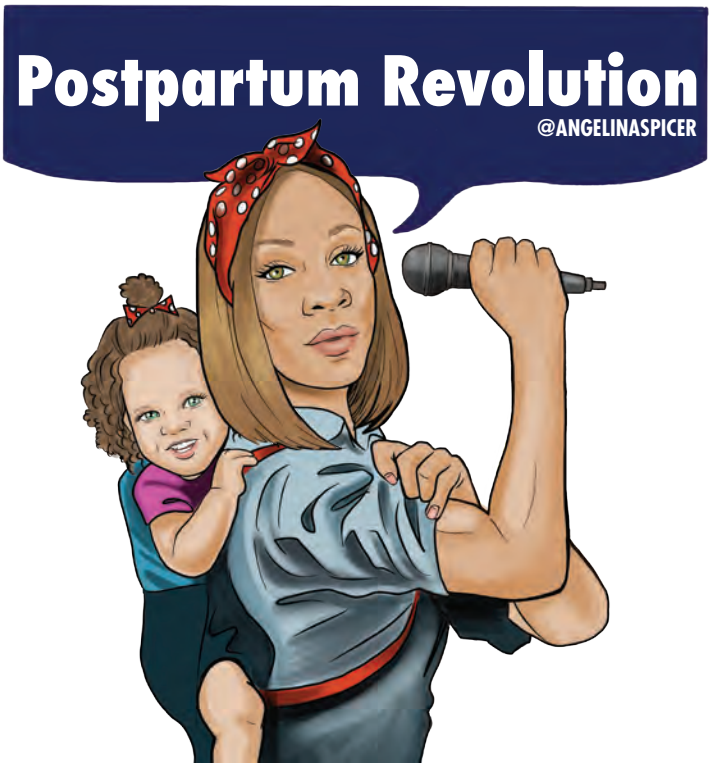
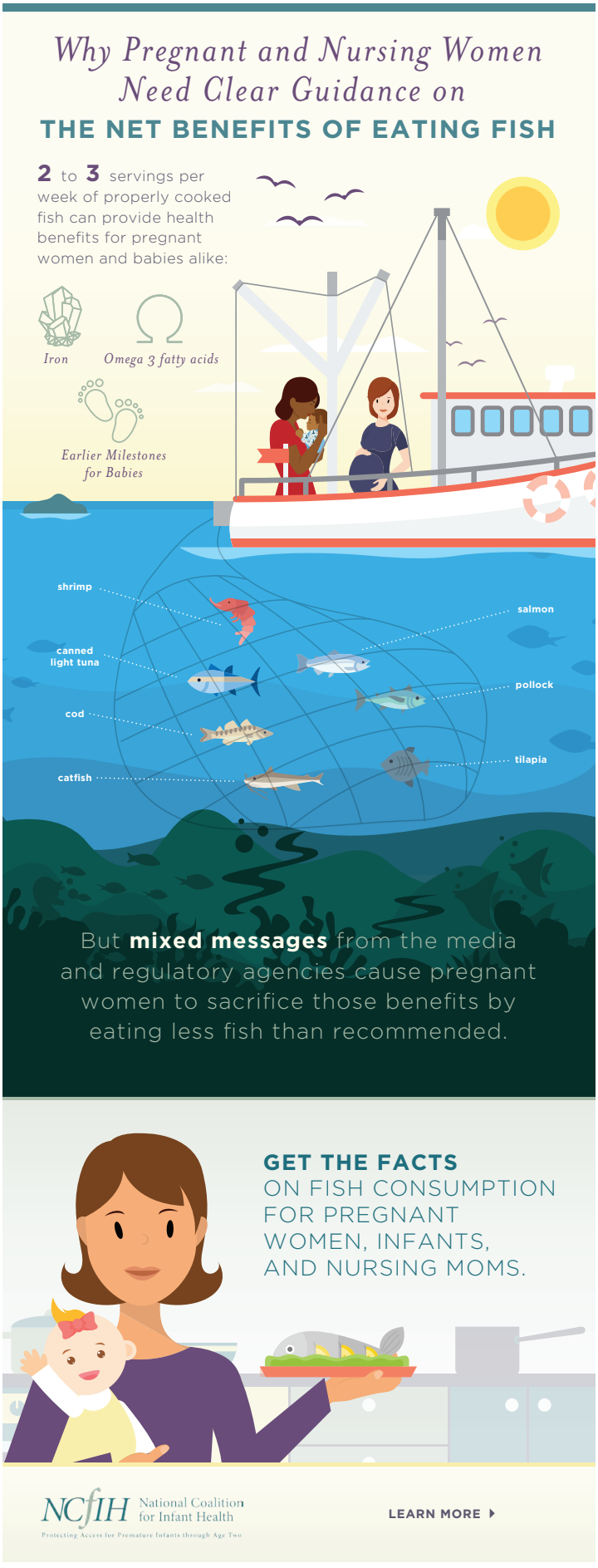
Interim Fellowship Column Editor
efayard@llu.edu





Efforts to Reduce Infant Mortality Rates in the United States Championed by House Democrats

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.

Over 23,000 infants died in the United States in 2016. Members of Congress are paying attention.

In August 2018, Congressman Steve Cohen (D-TN) hosted a symposium on infant and maternal mortality at Mississippi Boulevard Christian Church in Memphis, TN, in his home district. According to a press release, "The event focused on the needs of mothers in Memphis, the barriers to improving maternal health care, and reducing infant mortality and resources available in Shelby County, including free car seats for those who need them."

The meeting lead Congressman Cohen to introduce the NEWBORN (*Nationally Enhancing the Wellbeing of Babies through Outreach and Research Now*) Act (H.R. 117) on January 3, 2019. (1)

The legislation focuses on targeting areas of the country with high rates of infant mortality and providing federal support through pilot programs to those high-risk areas.

In a "Dear Colleague" asking Members of Congress to consider cosponsorship of the bill, Congressman Cohen writes, "A child is 76 percent more likely to die before their first birthday in America than in 19 other wealthy nations, including Australia, Canada, France, Sweden, Switzerland, and the United Kingdom."

The NEWBORN Act would help address the problem of infant mortality through the awarding of grants to infant mortality pilot programs that seek to address one or more of the top five reasons for infant mortality: birth defects, preterm birth and low birth weight, sudden infant death syndrome, maternal pregnancy complications, and/or injuries to the infant.

"The NEWBORN Act would help address the problem of infant mortality through the awarding of grants to infant mortality pilot programs that seek to address one or more of the top five reasons for infant mortality: birth defects, preterm birth and low birth weight, sudden infant death syndrome, maternal pregnancy complications, and/or injuries to the infant."

Programs may use such funds for counseling on infant care, feeding, and parenting. Also, the funds are eligible for delivery of services to aid in postpartum care and prevention of premature delivery. Smoking cessation, drug treatment programs, nutrition, and physical activity, domestic violence programs, and other social and psychological services are listed as eligible uses of the federal funding too.

After one year, each program is required to submit a report to delineate methodology of the program and outcomes associated with the program.

Currently, the bill has 46 cosponsors.

Outside of Congress, MomsRising is an organization that endorses the legislation. The background of the organization is listed on their website as: "unified by a mission of increasing family economic security, decreasing discrimination, and building a nation where both businesses and families can thrive." The MomsRising team covers all 50 states. (2)

"We must do more to make sure that women have the resources they need to deliver healthy babies – and that starts by improving access to health clinics and recruiting the best and brightest medical students to be inner city doctors. At the same time, we need a much more expanded outreach, education, and research program, and the NEWBORN Act will lay the foundation for that effort."

This is not the first time Congressman Cohen has introduced similar legislation to address infant mortality. Over the last decade in Congress, Steve Cohen has introduced multiple measures to decrease infant mortality rates and to focus on prenatal care for at-risk mothers. Nearly a decade ago, the Congressman remarked:

"We must do more to make sure that women have the resources they need to deliver healthy babies – and that starts by improving access to health clinics and recruiting the best and brightest medical students to be inner city doctors. At the same time, we need a much more expanded outreach, education, and research program, and the NEWBORN Act will lay the foundation for that effort."

The bill, H.R. 117, was referred to the House Energy and Commerce Subcommittee on Health where it now rests.

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1. https://www.govtrack.us/congress/bills/116/hr117/text
2. https://www.momsrising.org/

The author has not indicated any disclosures.

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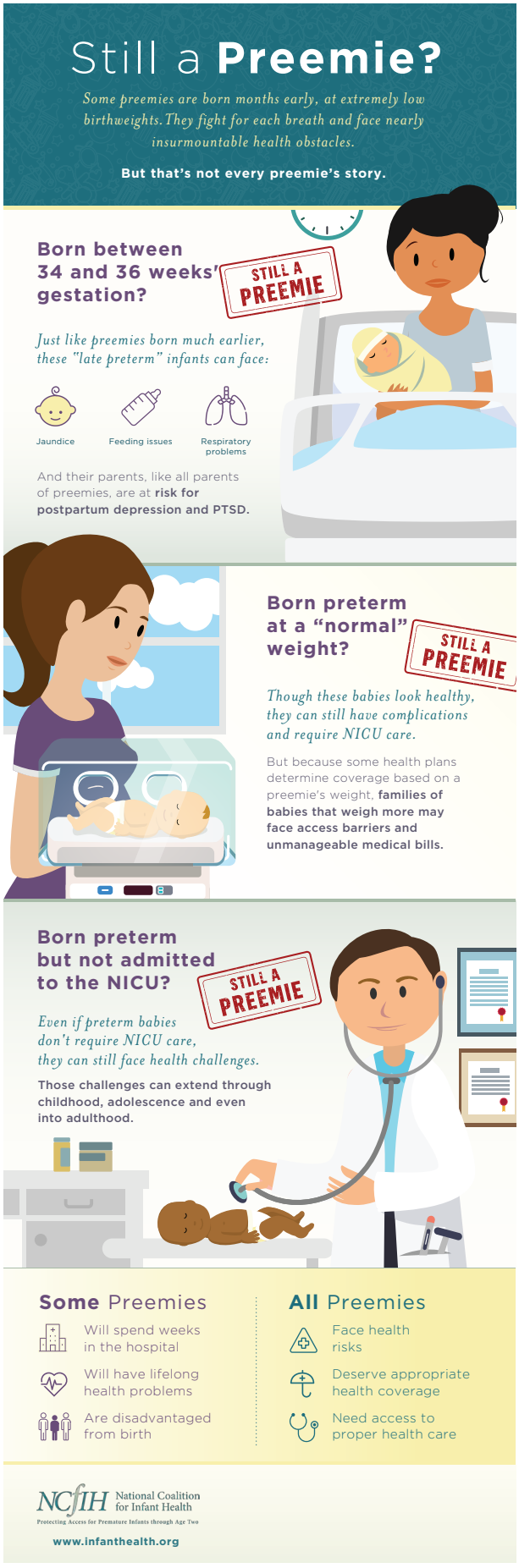

Helping Parents Chart Their Path Through Their NICU Journey: The Peekaboo ICU Parent App Hitting Its Mark

Deb Discenza

In just two and a half years since its official debut at the October 2018 National Neonatal Nurses Conference (NANN) in Palm Springs, CA, the Peekaboo ICU free parent app has become an essential "go-to" for preemie parents faced with navigating the uncharted journey of the Neonatal Intensive Care Unit (NICU). Available on apple and android devices, its goal is to reduce anxiety for parents by equipping them to understand, document, record, and celebrate their preemie's story. And indeed, this comprehensive resource is working.

"The app is exceeding our expectations of growth and utility," said Mark Dolezel, co-founder, producer, and husband of the app's clinical author, Jodi Dolezel. With over 13,500 downloads and 9,600-page views per month, Jodi's dream of providing a credible one-stop resource for NICU has become a reality, primarily in the US, but is also in Canada, the United Kingdom, Australia, and South America. No Wi-Fi needed and conveniently accessed at the bedside. A tutorial is available at https://m.youtube.com/watch?v=2H5WsjxCjIw.

Jodi was determined to find a way to support and prepare parents to feel comfortable and confident while caring for their child as essential partners with the NICU healthcare team. In her many years of NICU bedside practice as a nurse, she has seen this is not always the case. "Parents feel alienated," she said, "out of control and vulnerable at a time when they themselves are physically and emotionally drained. We decided to try to change this."

So, the app's first feature was a tool for parents to customize and track their individual preemie's growth and development, and to journal their preemie's unique experience. However, because so many parents are having multiples, that additional capacity was soon added.

Next, the Dolezels researched each critical area of knowledge for preemie parents, and organized them into sequential sections.

Navigating the NICU is the essential first step in helping parents understand unfamiliar medical terminology, staff roles, medical equipment, and the intense clinical environment. The **Weekly Developmental Guide** provides what every parent wants to know what to expect week to week. They want to know what is considered "normal" and how is my baby progressing towards those norms? **Anatomy** presents a system-by-system look at each body function relevant to pre-term infants with the option of diving deeper into content regarding complications if they should arise. **Growth Tracker** allows parents to record and graph ongoing progress of their baby's head circumference, weight, and length. This area also promotes strong interaction and discussion points between parents and the healthcare team. With **Milestones**, parents can capture the moments and achievements they experience with their baby throughout their journey together, all of which can be downloaded and saved as a lifelong keepsake. **Steps to Discharge** offers a thorough explanation of the achievements required for taking your baby home, which is always a priority for preemie parents. **Feeding & Nutrition** has tips for successful breastfeeding, a feeding tracker, and pumping logs are essential resources and very helpful for encouraging collaboration with staff. There is a thorough education about the options available to parents, including pasteurized human donor milk and human milk-based fortifiers to ensure optimal nutrition, according to gestational weight. **Journaling** allows parents to import photos and document their thoughts, experiences, and feelings as often as they'd like. If desired, they can share these with friends and family through e-mail and social media, setting up a "caring network" while decreasing the burden of endless phone calls. And finally, the Support section provides a guide to parent support organizations all over the country that moms and dads can tap into both before and after discharge.

But Peekaboo ICU is not resting on its laurels. With the success of the app comes "an obligation to continue to find new ways of making it even better and more accessible," said Jodi.

This will include an After the NICU Section for parents to document appointments, medications, nutrition, procedures, a daily schedule, and notes with HIPPA-compliant server integration for capturing real-time data. Server integration will also afford synchronization between multiple apps and provide safety backups. Lastly, there will be an option to create a lasting "baby book" with the ability to download the entire content recorded in the app.
"We estimate the app is now available in at least 40 hospitals and the number is growing every day," said Mark. "The number is very likely much higher as individuals using the app are not required to register their location."

Jodi feels gratified. She says, "We are receiving amazing feedback from nurses, lactations specialists, hospitals and, of course, parents. Nurses tell us the app makes their job easier. Lactation specialists say it encourages moms to track pumping, which often leads to better outcomes. Hospitals call it an invaluable tool they can use because it is non-branded, without advertisement. And parents simply say, 'thank you.'

"That's all we need!"

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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

Compiled and Reviewed by Mitchell Goldstein, MD Editor in Chief

Statement on Warning for Women of Childbearing Age about Possible Safety Risks of Dietary Supplements Containing Vinpocetine

Vinpocetine, a dietary supplement may cause miscarriages or harm fetal development.

For Immediate Release: June 03, 2019
Statement From:

Principal Deputy Commissioner - Office of the Commissioner
Amy Abernethy MD PhD.
Deputy Commissioner for Food Policy and Response - Food and Drug Administration
Frank Yiannas

Today, the U.S. Food and Drug Administration is warning consumers about safety concerns regarding an ingredient called vinpocetine that is found in dietary supplements, specifically concerns about the use of this ingredient by women of childbearing age. According to data reviewed by the FDA, including a recent report by the National Institute of Health's (NIH) National Toxicology Program (NTP), consumption of vinpocetine is associated with adverse reproductive effects – in other words, vinpocetine may cause a miscarriage or harm fetal development.

These findings are particularly concerning since products containing vinpocetine are widely available for use by women of childbearing age. That's why today we're advising pregnant women and women who could become pregnant not to take vinpocetine. We are also advising firms marketing dietary supplements containing vinpocetine to evaluate their product labeling to ensure that it provides safety warnings against use by pregnant women and women who could become pregnant.

Vinpocetine is a synthetically produced compound that is used in some products marketed as dietary supplements, either by itself or combined with other ingredients. Vinpocetine may be referred to on product labels as Vinca minor extract, lesser periwinkle extract, or common periwinkle extract. Dietary supplements containing vinpocetine are often marketed for uses that include enhanced memory, focus, or mental acuity; increased energy; and weight loss. Scientists who have studied the effects of vinpocetine on pregnant animals concluded that vinpocetine decreased fetal weight and increased the chances of a miscarriage. The blood levels of vinpocetine measured in the pregnant animals were similar to those reported in people after taking a single dose of vinpocetine, indicating that pregnant women may experience adverse effects from vinpocetine similar to those seen in the pregnant animals.

In some countries outside of the U.S., vinpocetine is regulated as a prescription drug. When products like vinpocetine are sold as dietary supplements in the U.S., they have not been reviewed by the FDA under the safety and effectiveness standards that apply to drug products. This means that the FDA has not reviewed each vinpocetine product, or its labeling, before those products become available to consumers.

COLUMBIA | MAILMAN SCHOOL OF PUBLIC HEALTH

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Next-Level Perinatal/Neonatal Comfort Care Training

Creating an Interdisciplinary Palliative Care Plan for Each Baby and Their Family

A 3-day intensive training of seminars and hands-on activity sessions to provide an overview of the methods, elements, and strategies needed to create a comprehensive neonatal comfort care plan for the entire perinatal team.

Perinatal detection of congenital anomalies leads to the identification of infants who are affected by life-limiting conditions with a short life expectancy. Moreover, a significant number of newborns admitted to the neonatal ICU in critical condition face potentially adverse prognoses. Perinatal palliative care offers a plan for improving quality of life of the infant and the family, when extending the baby's life is no longer the goal of care or the complexity of the medical condition is associated with uncertain prognosis. The evidence base for perinatal palliative care continues to grow. However, there is no consensus about best clinical practice in promoting support for the family or comfort for the neonate. Support for the family is achieved through appropriate pre- and postnatal consults, shared-decision making, and advance care planning. A state of comfort for the neonate is achieved when relational basic needs such as bonding, maintenance of body temperature, relief of hunger/thirst, and alleviation of pain/discomfort are met.

This three-day training will cover virtually all aspects of perinatal palliative care, including information about the successful experiences of the Neonatal Comfort Care Program in providing perinatal palliative care for over a decade at Columbia University Irving Medical Center (CUIMC). Faculty will discuss evidence-based rationale, practical aspects and strategies for implementing and applying aspects of the CUIMC to provide support for families and achieve a state of comfort for newborns with limiting or life-threatening conditions. Health professionals at all career stages are welcome to attend. Registration is required.

Elvira Parravicini, MD, Columbia University and New York Presbyterian/Morgan Stanley Children's Hospital, Director of Columbia University's Neonatal Comfort Care Program

Brian Carter, MD, University of Missouri-Kansas City and Children's Mercy Hospital

Charlotte Wool, PhD, RN, York College of Pennsylvania; Perinatal Palliative Care Consultant

See site for full instructor list.

Continuing Medical Education (CME) and Continuing Nursing Education (CNE): This course has been approved for CME credits. CNE credits pending.

Accreditation Statement: The Columbia University Vagelos College of Physicians and Surgeons is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. **AMA Credit Designation Statement:** The Columbia University Vagelos College of Physicians and Surgeons designates this live activity for a maximum of 18.75 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

More details and registration: mailman.columbia.edu/comfort-care

In the 1990s, the FDA received several premarket safety submissions (known as new dietary ingredient notifications) for vinpocetine as an ingredient in dietary supplements. In 2016, we requested comment from stakeholders as part of an administrative proceeding to evaluate whether vinpocetine is legal for sale as a dietary supplement. With the results in NTP's report, it was important to issue today's warning because the availability of dietary supplement products containing vinpocetine has grown and the labels of vinpocetine products often have no warnings about the dangers of miscarriage and harm to fetal development. For the same reasons, the FDA will expedite completion of the administrative proceeding that we began in September 2016.

The dietary supplement market is a growing industry, with sales multiplying ten-fold over the past 25 years and more than half of all Americans taking at least one dietary supplement on a regular basis. This expansion is one reason why earlier this year, the FDA announced new efforts to strengthen the regulation of dietary supplements by modernizing our regulatory framework.

Today's safety warning is just one of many steps the FDA is taking to adapt to the realities of the evolving dietary supplement industry. Protecting the public from unsafe dietary supplements remains a top priority for the FDA. We've also created a public-private partnership, the Botanical Safety Consortium, to promote scientific advances in evaluating the safety of botanical ingredients and mixtures in dietary supplements. In April, we introduced a new tool, the Dietary Supplement Ingredient Advisory List, to more quickly alert the public when we become aware of ingredients that appear to be unlawfully marketed in dietary supplements. And finally, just last month, we held a public meeting with our stakeholders to discuss responsible innovation in the dietary supplements industry.

These efforts, along with today's announcement regarding vinpocetine, underscore how the FDA will continue to preserve access to safe, well-manufactured, and accurately labeled dietary supplements, while we protect the American public from potentially unsafe or otherwise unlawful products.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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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:

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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/

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FDA Approves Innovative Gene Therapy to treat Pediatric Patients with Spinal Muscular Atrophy, a Rare Disease and Leading Genetic Cause of Infant Mortality

The approval of an innovative gene therapy offers hope for infants born with SMA.

For Immediate Release: May 24, 2019

The U.S. Food and Drug Administration today approved Zolgensma (onasemnogene abeparvovec-xioi), the first gene therapy approved to treat children less than two years of age with spinal muscular atrophy (SMA), the most severe form of SMA and a leading genetic cause of infant mortality.

"Today's approval marks another milestone in the transformational power of gene and cell therapies to treat a wide range of diseases," said Acting FDA Commissioner Ned Sharpless, M.D. "With each new approval, we see this exciting area of science continue to move beyond the concept phase into reality. The potential for gene therapy products to change the lives of those patients who may have faced a terminal condition, or worse, death, provides hope for the future. The FDA will continue to support the progress in this field by helping to expedite the development of products for unmet medical needs through the use of review pathways designed to advance innovative, safe and effective treatment options."

SMA is a rare genetic disease caused by a mutation in the survival motor neuron 1 (SMN1) gene. The gene encodes the survival motor neuron (SMN) protein – a protein found throughout the body, which is critical for the maintenance and function of specialized nerve cells, called motor neurons. Motor neurons in the brain and spinal cord control muscle movement throughout the body. If there is not enough functional SMN protein, then the motor neurons die, leading to debilitating and often fatal muscle weakness. SMA caused by mutations in the SMN1 gene is generally classified into several subtypes, based on the age of onset and severity; infantile-onset SMA is the most severe and most common subtype. Children with this condition have problems holding their head up, swallowing and breathing. These symptoms may be present at birth or may present by the age of 6 months.

"Children with SMA experience difficulty performing essential functions of life. Most children with this disease do not survive past early childhood due to respiratory failure" said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "Patients with SMA now have another treatment option to minimize the progression of SMA and improve survival. This approval demonstrates the continued momentum of this promising new area of medicine and the FDA's commitment to supporting and helping expedite the development of these products."

Zolgensma is indicated for the treatment of children less than two years of age with SMA. The product is an adeno-associated virus vector-based gene therapy that targets the cause of SMA. The vector delivers a fully functional copy of human SMN gene into the target motor neuron cells. A one-time intravenous administration of Zolgensma results in expression of the SMN protein in a child's motor neurons, which improves muscle movement and function, and survival of a child with SMA. Dosing is determined based on the weight of the patient.

The safety and effectiveness of Zolgensma is based on an ongoing clinical trial and a completed clinical trial involving a total of 36 pediatric patients with infantile-onset SMA between the ages of

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July 13, 2019
Sierra Lakes Golf Club
Fontana, California

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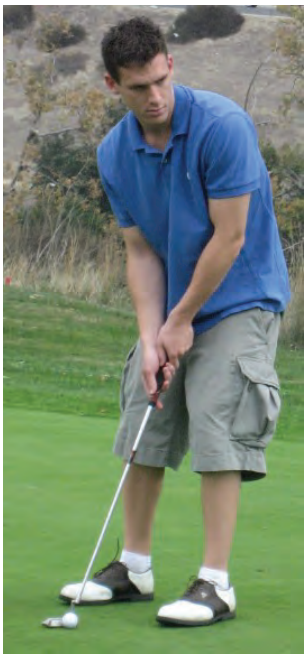

The Tournament will take place Saturday, July 13, 2019 at Sierra Lakes Golf Club in Fontana, California, beginning promptly with a shotgun start at 8:00 am. Great on-course contests are included! Banquet luncheon and silent auction to follow, beginning at 1:00 pm. If you are not a golfer, please join us by participating in our luncheon, raffles, live and silent auctions with great items such as numerous hotel stays including Four Seasons at Beverly Hills, Disneyland, sports memorabilia, and many more. Also there will be a goody bag with wonderful gifts from donors for each registered guest.

All proceeds support The Brett Tashman Foundation's efforts in funding research to find a cure for Desmoplastic Small Round Cell Tumor (DSRCT), a deadly cancer. Funding will assist doctors in discovering a cure to other childhood cancers and sarcomas that may be similar in certain aspects, such as Ewing Sarcoma. Unfortunately, less than 4% of federal cancer research funding is dedicated to childhood and young adult cancer research. We look forward to your partnership, as we strive to surpass last year's commitment of more than $45,000 to this cause.

We look forward to seeing you there!

With Gratitude,

The Brett Tashman Foundation

approximately 2 weeks and 8 months at study entry. The primary evidence of effectiveness is based on results from the 21 patients treated with Zolgensma in the ongoing clinical trial. In this trial, there are 19 remaining patients, who range in age from 9.4 to 18.5 months; 13 of these 19 patients are at least 14 months of age. Compared to the natural history of patients with infantile-onset SMA, patients treated with Zolgensma also demonstrated significant improvement in their ability to reach developmental motor milestones (e.g., head control and the ability to sit without support).

The most common side effects of Zolgensma are elevated liver enzymes and vomiting. Zolgensma has a boxed warning that acute serious liver injury can occur. Patients with pre existing liver impairment may be at higher risk of experiencing serious liver injury. Clinical examination and laboratory tests to assess liver function should be completed prior to treatment with Zolgensma, and patients' liver function should be monitored for at least three months after Zolgensma administration.

Certain vaccines are contraindicated for patients on a substantially immunosuppressive steroid dose. Therefore, caregivers should consult with their healthcare professional to determine if adjustments to the patient's vaccination schedule are necessary to accommodate concomitant corticosteroid administration.

The FDA granted this application Fast Track, Breakthrough Therapy, and Priority Review designations. Zolgensma also received Orphan Drug designation, which provides incentives to encourage the development of drugs for rare diseases.

The FDA also awarded the manufacturer a rare pediatric disease priority review voucher, under a program intended to encourage the development of new drugs and biological products for the prevention and treatment of certain rare pediatric diseases.

The FDA granted the approval of Zolgensma to AveXis Inc.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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NT

FDA Clears First Diagnostic Tests for Extragenital Testing for Chlamydia and Gonorrhea

FDA clears first diagnostic tests for extragenital testing for chlamydia and gonorrhea

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For Immediate Release:
May 23, 2019

Today, the U.S. Food and Drug Administration cleared for marketing two tests that can detect the presence of the bacteria Chlamydia trachomatis and Neisseria gonorrhoeae, which cause the sexually-transmitted infections, respectively, chlamydia and gonorrhea, through diagnostic testing of extragenital specimens. The Aptima Combo 2 Assay and the Xpert CT/NG are the first devices cleared for extragenital diagnostic testing of these infections via the throat and rectum. These tests were previously only cleared for testing urine, vaginal and endocervical samples.

"Prior to today, there were no chlamydia or gonorrhea tests cleared for use on samples

Perinatal Advisory Council:
Leadership, Advocacy and Consultation

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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.

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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.

from the throat and rectum. The availability of these two tests will fill an unmet public health need, by allowing for more screening," said Tim Stenzel, M.D., Ph.D., director of the Office of In Vitro Diagnostics and Radiological Health in the FDA's Center for Devices and Radiological Health. "It is best for patients if both of these sexually transmitted infections are caught and treated right away, as significant complications can occur if left untreated. Today's clearances provide a mechanism for more easily diagnosing these infections."

According to the Centers for Disease Control and Prevention's Sexually Transmitted Infections Surveillance Report, the rate of sexually transmitted infections is steadily increasing, with an estimated 1.7 million cases of chlamydia and more than 500,000 cases of gonorrhea in the U.S. in 2017 alone. Both infections can be contracted through vaginal, anal or oral intercourse. Typically, both infections can be easily treated, but if left untreated, both infections can cause serious complications for patients, including infertility.

The Aptima Combo 2 Assay and Xpert CT/NG were reviewed through the premarket notification (510(k)) pathway. A 510(k) is a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device.

In its evaluation of the devices, the FDA reviewed clinical data collected through a cross-sectional study coordinated by the Antibacterial Resistance Leadership Group, which is funded and supported by the National Institute of Allergy and Infectious Diseases. The study was a collaborative, multisite clinical study of more than 2,500 patients that evaluated the diagnostic accuracy of multiple commercially available nucleic acid amplification tests for detection of Neisseria gonorrhoeae and Chlamydia trachomatis from throat and rectal sites. The results of this study, along with other information reviewed by the FDA, demonstrated that the Aptima Combo 2 Assay and the Xpert CT/NG for extragenital specimens are safe and effective for extragenital testing for chlamydia and gonorrhea.

The FDA granted clearance of Aptima Combo 2 Assay to Hologic, Inc.

The FDA granted clearance of the Xpert CT/NG to Cepheid.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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American Academy of Pediatrics Names Dr. Beena Kamath-Rayne as Vice President, Global Newborn and Child Health

AAP selects VP for Global Newborn and Child Health

5/23/2019

ITASCA, IL – Beena Kamath-Rayne, MD, MPH, FAAP has been hired by the American Academy of Pediatrics (AAP) to support and provide leadership for global newborn and child health initiatives.

Dr. Kamath-Rayne comes to the AAP from the Cincinnati Children's Hospital Medical Center and the Department of Pediatrics at the University of Cincinnati College of Medicine, with an affiliation with the Global Child Health Center, where she serves as an Associate Professor of Pediatrics and a neonatologist.

Dr. Kamath-Rayne has expertise in clinical research and quality improvement which has earned her funding from NIH, Cerebral Palsy Alliance, and AAMC, among others. Her more than 50 publications address a variety of topics affecting neonatal and pediatric outcomes. She has successfully built teams of collaborators from a variety of disciplines including obstetrics, pediatrics, infection control, biostatistics, simulation, and medical education. Recently, her research has focused on the educational and clinical outcomes after implementation of Helping Babies Breathe. Dr. Kamath-Rayne currently serves as a member of the AAP Helping Babies Survive Planning Group. She was Associate Editor for the 2nd Edition of Helping Babies Breathe, and had editorial roles for other Helping Babies Survive Programs, including Essential Care for Small Babies and Improving Care for Mother and Babies Quality Improvement Workbook. She has also served as a member of the International Liaison Committee on Resuscitation Neonatal Delegation since 2016.

"The AAP is dedicated to optimizing the health and well being of all children. Our global health initiatives are essential to our mission, and the addition of Dr. Kamath-Rayne to the organization will position the AAP to strengthen existing programs and expand this important work. We are delighted to have a leader like Dr. Kamath-Rayne join Dr. Janna Patterson and our strong global health team," said Mark Del Monte, JD, CEO\Executive Vice

President (Interim).

"I am thrilled to welcome Dr. Kamath-Rayne to the AAP! She brings deep clinical and training expertise as well as a proven track record in implementation research to our growing global portfolio. She has the experience and skills the AAP needs to sustain current programs and offer fresh ideas for the future," said Janna Patterson, MD, MPH, FAAP, SVP of global child health and life support.

"I am very excited to join the Global Child Health and Life Support team at the AAP and to collaborate with Dr. Patterson and others in expanding its already successful global health initiatives and venturing out to build new ones. With interest in global health at an all-time high, I feel privileged to be given this opportunity to work on behalf of the AAP and its members to provide evidence-based, high-quality care to newborns and children around the world," said Dr. Kamath-Rayne.

Dr. Kamath-Rayne received B.A. degrees in biological anthropology/anatomy and history at Duke University and her medical degree at Georgetown University. She completed her pediatrics residency and neonatal-perinatal fellowship training at University of Colorado Health Sciences/ Children's Hospital of Colorado. In between residency and fellowship training, she spent two years living and working abroad as a general practitioner at a clinic in rural Ecuador and as a neonatal registrar/fellow at the Children's Hospital of Westmead in Sydney, Australia. She earned an MPH from the Colorado School of Public Health and is currently board certified in general pediatrics and neonatal-perinatal medicine. She has spent the last 10 years at Cincinnati Children's Hospital Medical Center.

As VP of Global Newborn and Child Health, Dr. Kamath-Rayne will be responsible for advancing AAP training programs and technical assistance in newborn and child health, including Neonatal Resuscitation Program (NRP), Advanced Pediatric Life Support (APLS), Helping Babies Survive (HBS), and Pediatric Education for Pre-hospital Professionals (PEPP).

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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.

NT

Early Life Exposure to Nicotine Alters Neurons, Predisposes Brain to Addiction Later in Life

In mouse study, neonatal exposure changed biochemistry of reward circuitry; researchers suggest same mechanism may be at work in humans

Released: 21-May-2019 3:05 PM EDT-Source Newsroom: University of California San Diego Health

Newswise — Neonatal exposure to nicotine alters the reward circuity in the brains of newborn mice, increasing their preference for the drug in later adulthood, report researchers at University of California San Diego School of Medicine in a study published "in press" April 24, 2019 in Biological Psychiatry.

A UC San Diego School of Medicine team of scientists, headed by senior author Davide Dulcis, PhD, associate professor in the Department of Psychiatry, with colleagues at Veterans Affairs San Diego Healthcare System and Michigan State University, found that exposure to nicotine in the first few weeks of life (through maternal lactation) induced a variety of long-term neurological changes in young mice.

Specifically, it caused a form of neuroplasticity that resulted in increased numbers of modified neurons in the ventral tagmental area (VTA) of the brain following nicotine re-exposure as adults. These neurons displayed a different biochemistry than other neurons, including greater receptivity to nicotine and a greater likelihood of subsequent addictive behavior.

"Previous studies have already shown that maternal smoking and early postnatal exposure to nicotine are associated with altered children's behaviors and an increased propensity for drug abuse in humans," said Dulcis. "This new research in mice helps elucidate the mechanisms of how and why. Neonatal nicotine exposure primes VTA neurons for a fate they normally would not have taken, making them more susceptible to the effects of nicotine when the animals are again exposed to nicotine later in life."

When young neurons are exposed to a foreign drug, such as nicotine, they create a molecular "memory," said first author Ben Romoli, PhD, a postdoctoral fellow in the Dulcis' lab. By increasing the expression of nicotine receptors and the molecular marker Nurr1, a protein that is normally found only in dopaminergic neurons, these GABA- and Glutamate-expressing neurons acquire the "readiness" to switch to a dopaminergic program when properly motivated by nicotine in the adult.

"We found that when the same animals are exposed to nicotine in adulthood, a fraction of these 'primed' glutamatergic neurons in the reward center begins to express genes required to produce dopamine. More dopamine in the system generates enhanced reward responses that lead to increased nicotine preference."

Dulcis said uncovering the molecular mechanism and the identity of the neuronal network involved is an important step toward a fuller comprehension of how a complex condition like addiction may work.

"Our pre-clinical work identified new cellular and molecular targets that may guide future clinical studies to refine treatment strategies," Dulcis said. "Because we found that this form of nicotine-induced neuroplasticity facilitates addiction to other addictive substances, such as ethanol in adults, uncovering the mechanism contributing to increased addiction susceptibility offers the rare opportunity to discover new ways to interfere with the mechanism of drug-mediated plasticity and prevent the negative consequences on reward-seeking behavior in the adult."

Researchers said the results are highly relevant to tobacco control programs because the neonatal nicotine effect observed in the study were induced by exposure through maternal lactation and current state and local policies do not regulate this particular type of nicotine intake.

"We are planning to investigate whether early exposure to other commonly used drugs, such as alcohol or recently legalized marijuana or opioids, can induce similar adaptations of the reward center that affects drug preferences in adulthood," said Dulcis. "It would be also interesting to determine whether this form of neurotransmitter plasticity is inducible or reversible at different stages of life when the brain is still extremely plastic and prone to drug addiction, like in adolescence."

The scientists are also investigating applications aimed at improving the behavioral performance of animal models for diseases associated with a loss of dopaminergic neurons, such as Parkinson's disease.

Co-authors of the study include: Adrian F. Lozada and Darwin K. Berg, UC San Diego; Ivette M. Sandoval and Frederic P. Manfredsson, Michigan State University; and Thomas S. Hnasko, UC San Diego and Veterans Affairs San Diego Healthcare System.

Funding for this research came, in part, from the National Institutes of Health, the Kavli Institute for Brain and Mind (grant 2012-18), the Tobacco-Related Disease Research Program (271R-0020) and the National Institute of Neurological Disorders and Stroke (5R21NS098079).

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NT

Family Centered Care is trendy, but are providers really meeting parents needs in the NICU?

Consider the following:

Surveys show hospital support groups are being widely underutilized by parents.

And only 10% of NICUs surveyed connect parents with non-hospital support.

Graham's Foundation, the global support organization for parents going through the journey of prematurity, set out to find the missing piece that would ensure all parents have real access to the support they need.

See what they found by emailing info@grahamsfoundation.org to request a free copy of the 2017 whitepaper, "Reaching Preemie Parents Today" (*Heather McKinnis, Director, Preemie Parent Mentor Program, Graham's Foundation*).

You may be surprised to see what NICUs are doing right and where their efforts are clearly falling short.

Graham's Foundation empowers parents of premature babies through support, advocacy and research to improve outcomes for their preemies and themselves.

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Fighting for Premature Babies

Visit www.GrahamsFoundation.org to learn more.

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37th Annual Conference

The Cliff Lodge
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This conference provides education and networking opportunities to healthcare professionals who provide care for pediatric patients with a focus on advances in therapeutics and technologies including telemedicine and information technologies. Along with featured speakers, the conference includes abstract presentations on research on advances in these areas. Registration open mid June, 2019!
http://paclac.org/advances-in-care-conference/

Physician, Nursing, and Respiratory Care Continuing education hours will be provided.

Call for Abstracts – Deadline December 15, 2019

Abstract submission: As are currently being accepted. Download the Abstract Guidelines from the website.

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#99nicuMeetup lectures online. See you on 99nicu.org!

Stefan Johansson, MD, PhD and Francesco Cardona, MD, MSc

Our previous column in the May Issue was all about the Future of Neonatal Care conference in Copenhagen last April, a.k.a. the #99nicuMeetup. If you regrettably were not able to attend, we now proudly present the lecture videos online! Find them on https://99nicu.org/meetup2019/ or view the lectures on our dedicated Youtube channel on https://www.youtube.com/99nicu/videos.

Plans are currently shaping up for the 4th conference in 2020. It is still too early to disclose dates and venue but to give you a hint, our banner will have a "Welcome back" theme :) Besides support by a university, we are also engaged in discussions with a first conference partner - an internationally awarded barista and his espresso bar. And that is not a joke! We regard coffee as a key component of great meetups!

After all positive feedback from delegates, speakers and conference partners, we are committed and feel privileged to work for an IRL meeting spot for a global group of neonatology professionals. The interactivity between lecturing experts and dedicated delegates, results in a co-created learning experience that few other conferences can offer.

Naturally, we strive to further improve and develop our #99nicuMeetup concept. We are currently inspired by two super-cool conference projects that also work outside-the-box, SMACC for critical care professionals (https://smacc.net.au/) and dotMD that "..aims to reawaken a sense of wonder and curiosity… and… find deeper meaning and satisfaction…" (http://www.dotmd.ie/)

There is also plenty of online activity going on at the 99nicu web site. One question posed is on the risk of using phototherapy – is there any? How do you feel about the available evidence connecting phototherapy and epilepsy? https://99nicu.org/forums/topic/2195-neonatal-hyperbiliphototherapy-and-long-term-risks/

There has been quite a discussion going on about extrauterine growth retardation. How can we measure it? When should we be concerned, and what can we do? https://99nicu.org/forums/topic/2197-what-really-constitutes-extrauterine-growth-restrictioneugr/

What is your experience with placement of a UAC line in patients with a single umbilical artery? All the same or more challenging? https://99nicu.org/forums/topic/2198-uac-insertion-in-2-vessel-cord/

> ***"If you regrettably were not able to attend, we now proudly present the lecture videos online! Find them on https://99nicu.org/meetup2019/ or view the lectures on our dedicated Youtube channel on https://www.youtube.com/99nicu/videos."***

Further topics worth mentioning are on early intervention after neurological injury (https://99nicu.org/forums/topic/2190-early-intervention/), balloon atrial septostomy (https://99nicu.org/forums/topic/2192-post-balloon-atrioseptostomy-collapsehy-potension), persistent neonatal hypoglycemia (https://99nicu.org/forums/topic/2187-persistent-neonatal-hypoglycemia-insulin-glucose-ratio), and ethical decisions at end-of-life (https://99nicu.org/forums/topic/2180-newborn-in-terminal-stage-which-are-the-bioethical-specialist-decisions).

We also share interesting links on the 99nicu website. One very popular link is from the NY Times who have published a guide for parents on the NICU. Definitely worthwhile to pass it on here as well: https://parenting.nytimes.com/health/nicu-care

With this column, we will pause our writing as we need to focus on the development of the #99nicuMeetup and the online presence of 99nicu.org. We would like to thank Neonatology Today and especially Mitchell Goldstein, editor-in-chief, for sharing space for our reflections related to the 99nicu project.

See you online on 99nicu.org, and maybe meet you in person at the 2020 Meetup!

2019-06-09

Stefan Johansson

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The authors indicate that they have no disclosures

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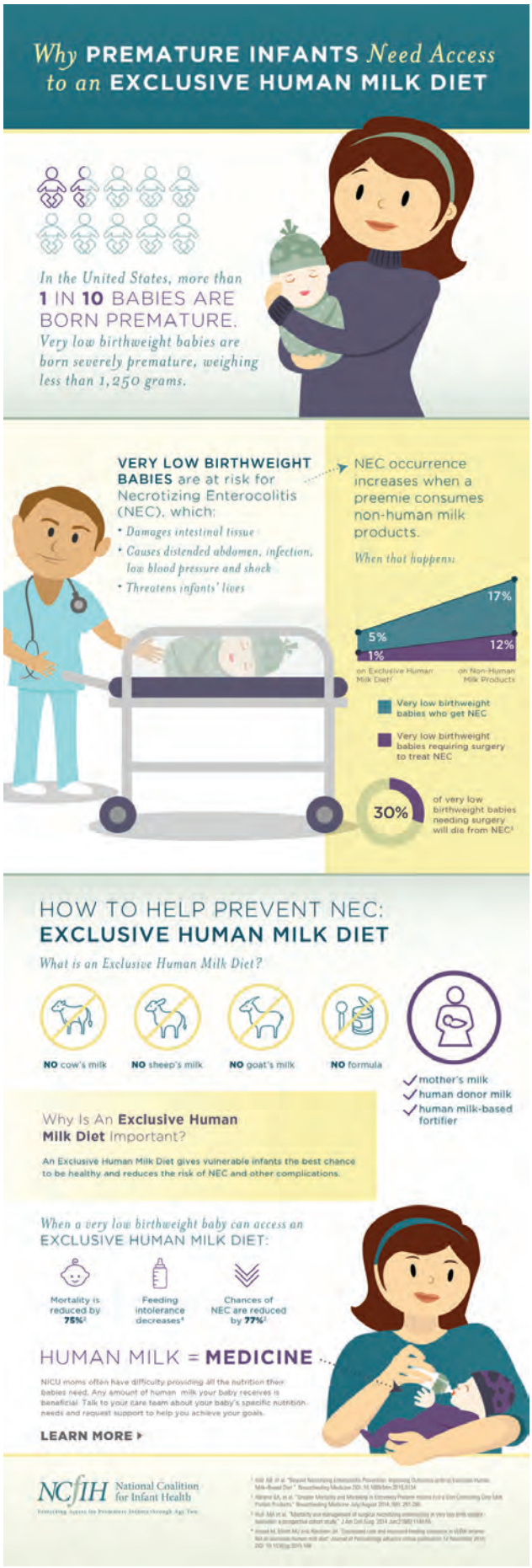
Survey Says: RSV
RESPIRATORY SYNCYTIAL VIRUS, or RSV, is a dangerous virus that can lead to:
Hospitalization
Lifelong health complications
Death
for infants and young children.
ACCORDING TO A NATIONAL SURVEY,
Specialty Health Care Providers say:
80%
They treat RSV as a priority, "often" or "always" evaluating their patients
77%
RSV is the "most serious and dangerous" illness for children under four
77%
Barriers to access and denials from insurance companies limit patients' ability to get preventive RSV treatment
But Parents are Unprepared.
18%
Only 18% know "a lot" about RSV
22%
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
Protecting Access for Premature Infants through Age Two
Learn More about RSV at www.InfantHealth.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%
5%
12%
1%
on Exclusive Human Milk Diet
on Non-Human Milk Products
Very low birthweight babies who get NEC
Very low birthweight babies requiring surgery to treat NEC
30%
of very low birthweight babies needing surgery will die from NEC
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?
An Exclusive Human Milk Diet gives vulnerable infants the best chance to be healthy and reduces the risk of NEC and other complications.
When a very low birthweight baby can access an EXCLUSIVE HUMAN MILK DIET:
Mortality is reduced by 75%
Feeding intolerance decreases
Chances of NEC are reduced by 77%
HUMAN MILK = MEDICINE
NICU moms often have difficulty providing all the nutrition their babies need. Any amount of human milk your baby receives is beneficial! Talk to your care team about your baby's specific nutrition needs and request support to help you achieve your goals.
LEARN MORE
NCfIH National Coalition for Infant Health

The Genetics Corner: A Genetics consultation for a Family History of Permanent Neonatal-Onset Diabetes Mellitus

Robin Clark, MD

Case History:

A genetics consultation was requested for a 2 day old term AGA male infant of a poorly controlled diabetic mother, whose gestation was complicated by two admissions for uncontrolled diabetes mellitus (DM) with ketoacidosis treated with insulin. Mother's HbA1c was elevated x3 (8.8 at 14 weeks, 8 at 22 weeks 5 days and 7.2 at 27 weeks 4 days). She told her OB providers that she had "monogenic diabetes", but she did not provide any other information about her diagnosis. Birth weight was 3260 grams (43rd%ile.) The infant's glucose was closely monitored after delivery with a maximum level of 135 mg/dL on day 2 of life. His physical examination was normal. Echocardiogram revealed moderate right ventricular hypertrophy.

The family history was pertinent for early onset diabetes mellitus in the patient's mother, who was diagnosed at 4 months, and in all three siblings: a 9-year old maternal half-sister diagnosed at 7 days, an 8-year old maternal half-sister diagnosed at 30 days and a 4-year old maternal half-brother diagnosed at birth. The maternal grandfather and paternal grandmother had DM type II.

Consultant's report:

Permanent neonatal diabetes mellitus (PNDM, MIM 606176) is a monogenic form of diabetes mellitus characterized by persistent hyperglycemia in infants younger than 6 months. It is distinct from the typical childhood-onset autoimmune diabetes mellitus type I. Both autosomal recessive and autosomal dominant types of PNDM exist and five responsible genes have been identified: ABCC8, GCK, INS, KCNJ11, PDX1. Pathogenic variants in KCNJ11 are the most common cause of PNDM, accounting for 30% of affected patients. Syndromic PNDM also occurs: pancreatic agenesis can accompany cardiac defects (MIM 600001) or cerebellar agenesis (MIM 607194).

We suspected autosomal dominant PNDM in this child based on the early onset and vertical transmission of diabetes mellitus in his family. When we reviewed the medical records of the oldest affected child, we found that the molecular diagnosis had been established in 2009 when a heterozygous pathogenic variant had been identified in KCNJ11: c.602G>A.

KCNJ11 encodes the Kir6.2 subunit of the octameric ATP-sensitive potassium channel (KATP), which normally closes in response to glucose. This closure precipitates a cascade of events that leads to insulin secretion by pancreatic beta cells. Gloyn, et al. (2004) demonstrated that heterozygous activating mutations in KCNJ11 cause PNDM. Intrauterine growth retardation, polyuria, and dehydration, although not present in this case, are common. This channelopathy can also affect the central nervous system. When there are developmental delay and epilepsy, the condition is called DEND syndrome: developmental delay, epilepsy, and neonatal diabetes.

"This case illustrates the challenges of effective medical communication and documentation and offers many missed opportunities for genetic education and counseling. Although the diagnosis of PNDM had been made ten years prior, it did not "stick" and important information pertinent to the pregnant mother's diagnosis and management was not available to her providers. "

PNDM caused by KCNJ11 variants can be effectively treated with (often high dose) oral sulfonylurea (glibenclamide), which binds to the receptor, SUR1, and closes the KATP channel. Oral agents can be started as soon as the genetic disorder is confirmed.

Over the next several days, this infant's glucose levels rose, he was diagnosed with PNDM and treated with glyburide. Targeted variant testing for this familial change was ordered for the new baby, rather than the larger and more expensive gene panel. The mother's physicians were also made aware of the diagnosis. They ordered targeted variant analysis for the familial variant in her and transitioned her therapy from insulin to oral sulfonylurea.

This case illustrates the challenges of effective medical communication and documentation and offers many missed opportunities for genetic education and counseling. Although the diagnosis of PNDM had been made ten years prior, it did not "stick" and important information pertinent to the pregnant mother's diagnosis and management was not available to her providers. The mother was informed about her daughter's and her own diagnosis of PNDM, shortly after the birth of her first child, when she was a 17-year old primigravida. Her first affected daughter was in the NICU for five weeks. After discharge, she was referred for genetic outpatient follow up, but she was never seen (insurance authorization was requested but never received).

Although two more affected children were subsequently born, genetic testing had only been performed on her first affected daughter. No other family members had gene testing, including the mother. Ten years later, the mother remembered that she and

her children had "monogenic diabetes," but she did not recall the details, and nothing about this diagnosis was documented in her own medical record. The mother's obstetric providers presumed that she had DM type 1 and treated her as such, with insulin, with poor results.

"The mother's obstetric providers presumed that she had DM type 1 and treated her as such, with insulin, with poor results."

Practical applications:

1. All patients diagnosed with diabetes before the age of 6 months should undergo genetic testing for PNDM.

2. PNDM caused by KCNJ11 can be effectively treated with high dose oral sulfonylurea.

3. Genetic consultation is warranted in pregnant women and infants with "monogenic diabetes" because establishing the genetic diagnosis can change treatment

4. Be curious. When a genetic disorder is segregating in the family, search for test results in near relatives. With permission from the parent, health care providers can access medical records on older affected siblings.

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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

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

7 Steps to Assess Every aEEG

Kathi Salley Randall, MSN, RNC, CNS, NNP-BC

INTRODUCTION

Over the last decade, amplitude-integrated EEG, aEEG has gained in popularity, but many Neonatologists state that they feel uncomfortable reading aEEG patterns and most say they have never received any training on aEEG (1,2).

As a brief review, aEEG is derived from the EEG signal collected from surface or needle electrodes placed over the central and parietal regions. The EEG signal is filtered, rectified, and compressed and then plotted every 15 seconds on a semi-logarithmic scale at a rate of 6 centimeters per hour. Normative voltage for the five most common aEEG patterns has been published for both term and preterm infants. (3,4)

There are currently three common ways that aEEG is utilized at the bedside:

- Assess background pattern to look for severity of brain injury
- Assess for the presence of sub-clinical seizures
- Assess for changes in background patterns over time that might indicate the effectiveness of medications and other neuroprotective interventions, like therapeutic hypothermia.

Although aEEG was historically used to select infants for some of the randomized control trials for hypothermia, this is no longer deemed necessary for determining eligibility for cooling in the era of clinical cooling for HIE. However, there may be a role for the use of aEEG to assess infants with "mild" encephalopathy who may benefit from cooling, or enrollment in future trials, who do not initially qualify for cooling based on the clinical exam score alone.

Since aEEG monitors have switched from paper to digital devices, there have been many enhancements that have increased their reliability but also their complexity. Due to its popularity, aEEG is now available as an optional display for most continuous video-EEG monitors. This integration allows for bedside care providers to assess the real-time brain function of infants in the NICU while still recording a comprehensive array of EEG. This dual set-up offers the advantage of easy bedside review of aEEG and full reporting and remote access by the neurodiagnostic and neurophysiology team.

Other monitors offer what is known as multi-modal monitoring which integrates several streams of monitoring data (i.e., aEEG, NIRS, HR, Sats, and BP) on to one screen for easier interpretation of changes in both neurologic and physiologic vital signs. These devices are especially useful for big data analysis for neonatal research projects as well as for clinical use.

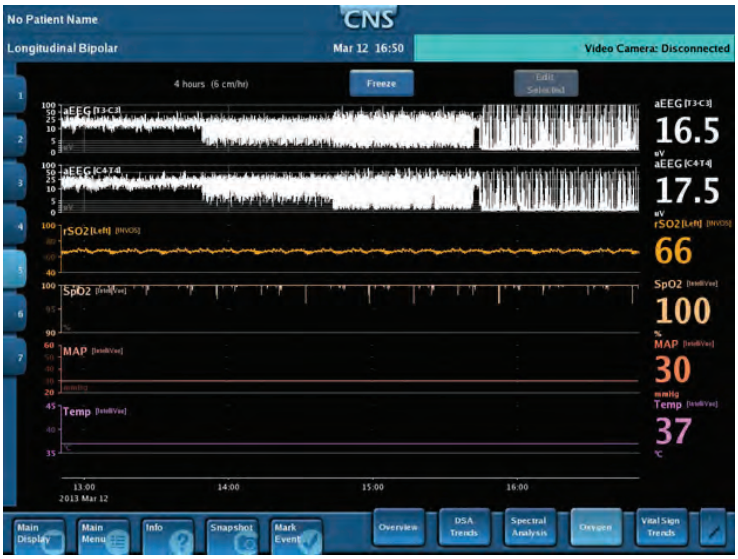


Fig 1 -Multi-Modal CNS Monitor - Image Source: Moberg Research.

7 STEP METHOD

It is easy to be overwhelmed with the task of interpreting aEEG if you do not have a systematic way to approach your assessment.

In the sections that follow I will outline a comprehensive yet simple system that I developed after years of training NICU providers around the world, I call it my "7 Step Method" and coincidentally, each step begins with the letter S:

- Story
- Signal Quality
- Strength of Background
- Sleep-Wake Cycles
- Symmetry
- Seizures
- Stability

Step 1: Story (Infant History)

Before you assess the aEEG tracing itself, stop and think about why aEEG was ordered for this baby in the first place, and what information you are seeking from the aEEG.

- Is the baby encephalopathic?
- Are you considering cooling the baby?
- Are you hoping to identify electrographic-only (i.e., sub-clinical) seizures?
- Are you using the aEEG to manage anti-epileptic medication dosage?

- Are you using the aEEG to trend the baby's background brain activity over a few days to determine the severity of injury or watch the recovery of injury?

After you have determined why the baby is being monitored and what information you are seeking, then it is important to consider the factors that might complicate your interpretation and findings.

History: Consider the infant's labor, birth, and even prenatal history and determine if any risk-factors exist for brain injury or dysfunction.

Exam: Take both the physical and neurological exam into account. Always assess the condition of the scalp. Edema will give you a dampened aEEG and a high impedance signal, which we will cover in the next step.

Medications: Some medications can have a dramatic effect on the aEEG background pattern and may falsely alarm you. A quick review of all ordered and recently administered medications is always a good idea.

Age: Gestational age and corrected age both impact EEG and aEEG waveforms so be sure you know the baby's age before you review the aEEG.

"After you have determined why the baby is being monitored and what information you are seeking, then it is important to consider the factors that might complicate your interpretation and findings. "

Step 2: Signal Quality

Before you go any further with your assessment, you must ensure that the electrode impedance is acceptable. In the EEG world, the lower and more balanced the impedance values, the better. The international standard for quality EEG tracings is impedance less than or equal to 10 Kilo-Ohms (kOhms). (5)

Each EEG and aEEG machine you encounter will have a different way to display and trend the impedance value, but the most important thing is that your entire team knows how to find these values and that you have a protocol in place that requires a review of impedance at least every few hours to ensure a quality recording. There are typically no audible alarms on EEG or aEEG monitors, but many of the stand-alone aEEG devices do offer visual indicators of high impedance that can alert staff to attend to an elevated value quickly.

The impedance values you see on the monitor will vary based on the type of electrodes used. Needle electrodes have been used widely throughout the world for decades and have the advantage of quick application and stable, low impedance values (0 to 2 kOhms). They are used for up to 5 days in most centers without risk to the site or systemic infection. The biggest risk to consider when using needles is the risk to staff as needle-sticks are not uncommon if the electrodes become dislodged.

As an alternative to needles, there are many skin or surface electrodes available. They range from peel-and-stick hydrogel electrodes (similar to those used for ECG) to disposable plastic, or reusable metal, cups or disks electrodes that are attached to the scalp using a conductive paste. EEG departments commonly use these cup and disk electrodes for full EEG monitoring.

"Each EEG and aEEG machine you encounter will have a different way to display and trend the impedance value, but the most important thing is that your entire team knows how to find these values and that you have a protocol in place that requires a review of impedance at least every few hours to ensure a quality recording"

New pre-measured electrode systems and caps are entering the neonatal market to simplify and standardize the electrode application procedure. One such device, the Incereb neon was developed by an EEG tech in Ireland and is showing promise for those who use aEEG infrequently or who have limited access to techs on nights and weekends.

The disadvantage of using any of the non-invasive electrodes is that the skin must be prepped before the electrodes are applied. A water-based exfoliant product is typically used to cleanse the application sites gently. While this technique is not difficult, it does take patience and practice to be able to perform quickly and without injuring fragile neonatal skin.

As EEG and aEEG amplifiers have improved over the years, they can typically compensate for higher impedance values, but as a

general rule, try to keep your impedance balanced and below 10

kOhms.

Step 3: Shape and Strength of the aEEG band

The good news is that there are only 5 neonatal aEEG patterns.

The first, most mature aEEG pattern is named Continuous Normal Voltage (CNV). This pattern is expected in term newborns starting around 35-36 weeks and is considered normal until approximately 44 weeks post-conceptual age normal. (3)

The next pattern, Discontinuous Normal Voltage (DNV), is expected and considered to be normal for premature infants. This pattern is also seen in term infants with HIE and who are undergoing therapeutic hypothermia. Most experts consider this pattern to be strongly predictive of a favorable outcome in the HIE/Cooling population; especially after 48 hours of life. (6, 7)

The remaining three patterns, Burst Suppression (BS), Continuous Low Voltage (CLV), and Inactive/Flat tracings (FT), are not considered to be normal regardless of gestational age; however, they may be expected patterns based on the infant's history. (3)

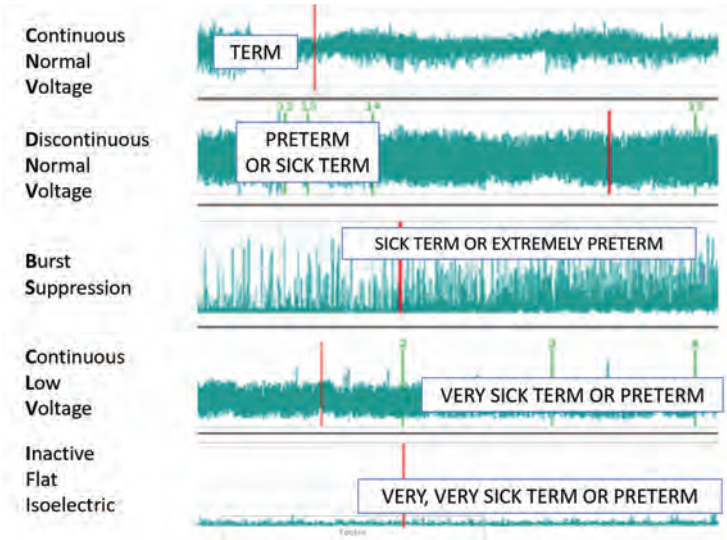
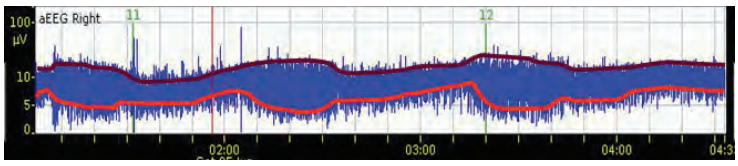


Fig 2 -Image Courtesy of Karl Florian, Munich

Each of the five patterns has a distinct visual appearance which can be learned over time, but an alternative to this subjective method of classification is to compare patterns to published voltage limits. I have provided a summary of the voltage limits and pattern classifications for the five basic aEEG patterns in the table on the next page.

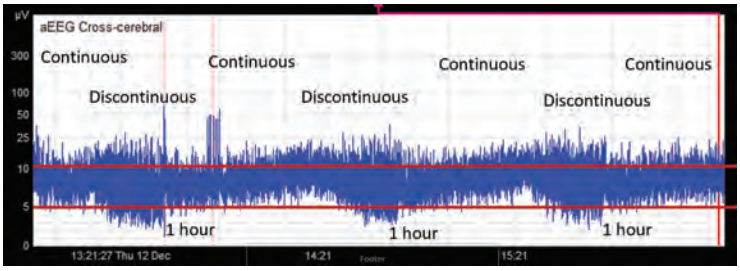
When using voltage to describe the aEEG band, you must assess the upper edge and the lower edge of the band, which correspond to the minimum and maximum voltages recorded and integrated into a single "pen-stroke" every 15-second epoch.



Step 4: Sleep-Wake Cycles

While we can look at an infant and determine if they are asleep or awake, we know very little about the quality of their sleep just by looking at them.

A mature sleep-wake pattern is seen on aEEG as an alternation from continuous normal voltage to discontinuous normal voltage. The continuous normal voltage is seen during wakeful periods and active sleep periods, and the discontinuous pattern is seen during quiet sleep periods.



Cyclicity can be seen on the aEEG of extremely premature infants (as young as 28-30 weeks) and becomes more organized and well defined as the infant matures.

A mature sleep-wake pattern emerges by 32 to 34 weeks gestation, and each cycle lasts for approximately 20-40 minutes (if not interrupted) and has a smooth entry and exit.

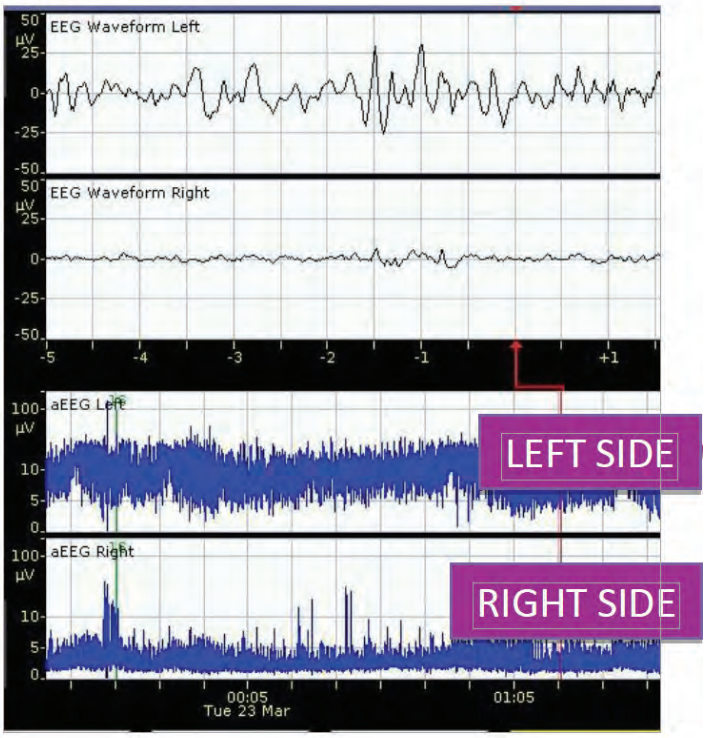
Due to rapid brain development and changes in sleep patterns in the first weeks of life, the typical alternating pattern seen in the term infant (also known in the literature as trace alternant) is no longer apparent after 44 weeks post-conceptual age.

For infants with HIE, the presence and onset of sleep-wake patterns on aEEG during the first three days of life has been shown to be very highly predictive of long-term neurodevelopmental outcome. (6, 7)

Step 5: Symmetry

Modern, digital, aEEG monitors give you the ability to apply more than one pair of sensors to the baby's head (this is a blessing and a curse). The downside is you have to apply more sensors to the baby, but the blessing is that the extra sensors allow you to compare the electrical signal from each hemisphere of the brain.

Each electrode pair will collect and display one channel of EEG signal. Each channel of EEG will then become its own separate aEEG waveform. Assess each aEEG pattern, right and left, separately. Evaluate the shape and voltage of each of the aEEG patterns (just like in STEP 3) and then compare them. You may also be able to see that seizures arise from one hemisphere more than the other. We will cover seizures in more detail in the next section.



.
Are the patterns similar or different?

If asymmetries are present, then investigate.

- Verify that the electrodes are applied symmetrically across the head. Electrodes that are too close together will give a falsely low voltage pattern, and electrodes that are further apart will give you a wider aEEG band.
- Localized edema can cause a dampening of the electrical signal and give the impression that one hemisphere of the brain is suppressed.
- If everything looks good with the head and the electrodes, then you may want to consider imaging the infant to determine if there may be a unilateral or focal ischemic injury.

Step 6: Seizures

Although beyond the scope of this paper, we would likely agree that neonatal seizures are a complex problem for the neonate. Subclinical seizures are more common than ever imagined, medications are only modestly effective, and our ability to identify seizures clinically is depressing. (8)

Seizures have been observed on EEG as repetitive, rhythmic electrical discharges from the brain that last for more than 10 seconds. (9) On aEEG, seizure patterns are often described as a rapid increase in both the upper and lower margins of the aEEG.

Although aEEG is not a perfect tool for seizure detection, it is far better than relying solely on our clinical assessment skills.

The most common pitfalls when it comes to using aEEG for identification of seizures include:

1. One or two channels of EEG may miss a focal seizure occurring in an area away from the recording electrodes
2. Short seizures (less than 1 or 2 minutes) will likely be missed on aEEG due to the dense time compression that occurs to create the aEEG band

Pattern Classification	Minimum Voltage	Maximum Voltage	Other features
1. Continuous Normal Voltage	> 5	> 10	A thin band with sinusoidal alterations every hour
2. Discontinuous Normal Voltage	< 5	> 10	Wide band, with good variability
3. Burst Suppression	0-3	> 25	Wide band, with no baseline variability
4. Continuous Low Voltage	< 5	< 10	Dense pattern that
5. Inactive/Flat	< 5	< 5	Often contaminated with artifacts due to the lack of cerebral activity

Table 1: Adapted from Amplitude-integrated EEG classification and interpretation in preterm and term infants. Hellstrom -Westas, L., Rosen, I., de Vries, L. S., & Greisen, G. (2007). Neoreviews, 7(2), 76-86

3. Low voltage seizures might not cause a change in the appearance of the aEEG

4. Seizure detection algorithms are not widely available in all markets, and those that are available have limited reliability (about 80%)

As with any assessment tool, if you understand its limitations, then you can determine how and when to incorporate it into your practice. The important point to keep in mind is that aEEG is significantly better than clinical assessment alone. All aEEG monitors in use today simultaneously display both the raw EEG and the aEEG tracings, which significantly improves the accuracy and reliability of seizure detection. (10)

Video-EEG continues to be the gold standard for seizure diagnosis; however, in times of limited resource, expertise, and staff, aEEG is a valuable complementary tool, especially for bedside care providers.

Step 7: Stability of the aEEG Background Pattern

In order to harness the power of aEEG, you really should be monitoring infants over long periods of time (days, not hours) and then looking at the aEEG trend every few hours.

It can also be fascinating to observe changes in the aEEG trend from hour to hour, shift to shift, and day to day. Especially in combination with other changes in the infant's clinical picture.

Special Note -- For infants with HIE: The background aEEG pattern within the first three days of life, especially after 48 hours, has been well-document as strongly predictive of long-term outcomes even in the era of therapeutic hypothermia (6). Also, the onset of sleep-wake cycling in this population has also been shown to have strong positive predictive of outcome (with or without therapeutic hypothermia). (7) As we saw in Step 4, sleep-wake cycling is much easier to assess using aEEG than traditional EEG recordings.

CONCLUSION

Assessment of aEEG may seem overwhelming at first glance but using a systematic approach like the "7 Steps" outlined in this article can provide a template to follow both in bedside review and documentation in the patient record.

As a quick recap of the 7 steps in a comprehensive aEEG recording review, your assessment should include:

- A review of the infant's story (why the infant is being monitored with aEEG)
- The signal quality (impedance)
- The background (by pattern recognition or voltage limits)
- The presence or absence of sleep-wake cycling
- Inter-hemispheric symmetry and areas with possible seizures
- Finally how the background aEEG pattern compares to previous periods in time.

Research programs around the globe continue to investigate aEEG, expand our understanding of its benefit in novel populations and continue to confirm that in dedicated hands, aEEG is a powerful tool for the NICU. If you have not yet become a fan of aEEG technology, it is my hope that this article has piqued interest and that you will feel more confident in using aEEG the next time you see it being used in your NICU.

It appears that aEEG is here to stay in the NICU (for now) and although it is not a perfect tool it does offer the opportunity to trend an infant's brain activity right at the bedside at any time. We can use aEEG to identify subclinical seizures, assess the effectiveness of prescribed therapies and even to counsel parents; especially at times when other resources and expertise are not available.

MORE RESOURCES:

To learn more about aEEG Interpretation there are several online and in-person educational opportunities.

A great video with an overview of aEEG by Dr. Courtney Wusthoff, Neonatal Neurologist, Stanford University -

https://www.vido.wiki/video/gGHjkrQCB6g/evidence-based-neonatology.html

Brigham & Women's Hospital in Boston is offering their bi-annual Neonatal Brain Monitoring & Imaging Workshop in October of this year at www.newbornbrainworkshop.org. The next International Brain Monitoring & Neuroprotection meeting will be held in Ireland in October 2020 and traditionally has offered a half-day workshops for those with both the beginner and advanced aEEG skills.

You can also visit the author's website - www.synapsecare.com - for a listing of free and paid resources. I have recently revised my 7 Step E-Book which is available as a free download at courses.synapsecare.com and now includes 8 short training videos that accompany the E-Book. The Online aEEG Mastery course by Synapse Care Solutions is a comprehensive training for individuals and teams.

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Discslosure: The author is the owner of Synapse Care Solutions and creator of several online education programs for individuals and groups related to aEEG, Brain Cooling and Neuro-Protective Care. Kathi is a paid consultant to Aspect Imaging, Neotech Products and Moberg Resarch.

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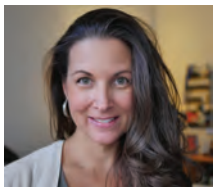

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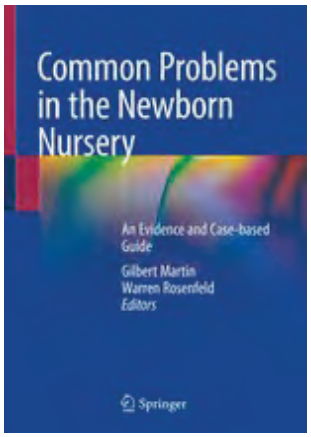

Common Problems in the Newborn Nursery
An Evidence and Case-based Guide

- **Provides practical, state of the art management guidance for common clinical problems in the newborn nursery**
- **Written by experts in the field in a clear, easy-to-use format**
- **Utilizes a case-based approach**

This comprehensive book thoroughly addresses common clinical challenges in newborns, providing an evidence-based, step-by-step approach for their diagnosis and management. *Common Problems in the Newborn Nursery* is an easy-to-use, practical guide, covering a full range of clinical dilemmas: bacterial and viral infections, jaundice, hypoglycemia, hypotonia, nursery arrhythmia, developmental dysplasia of the hips, newborn feeding, cardiac problems, late preterm infants, dermatology, anemia, birth injuries, ocular issues, and hearing assessments in the newborn.

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Human Milk Based Human Milk Fortification: At Legislative RIsk

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.

Pennsylvania's HB 1001 PN 1126, the Keystone Mothers' Milk Bank Act, will worsen disparity for premature infants. If the bill passes, extremely premature infants being cared for in neonatal intensive care units (NICUs) in Pennsylvania would no longer have access to nutritional fortifiers made from 100% donor breast milk. There is no net gain; babies would be placed at risk for necrotizing enterocolitis needlessly, mortality would increase, and NICU costs would rise exponentially.

"Pennsylvania's HB 1001 PN 1126, the Keystone Mothers' Milk Bank Act, will worsen disparity for premature infants. If the bill passes, extremely premature infants being cared for in neonatal intensive care units (NICUs) in Pennsylvania would no longer have access to nutritional fortifiers made from 100% donor breast milk. "

The language of the bill is clear. Access would be restricted. There is no question as to the extent of those patients who would be affected. Extremely premature infants have different and more critical nutritional needs that are not easy to meet. The American Academy of Pediatrics (AAP) has provided direction on the use of an added fortifier to mother's own milk or pasteurized donor human milk to provide the requisite protein, calories, and minerals to support growth and development in preemies born weighing less than 1,500g. (1)

Bovine fortifiers are available, but they are potentially life-threatening. There are increased complications in premature babies fed a bovine fortifier. Neonatologists often delay giving cow milk fortifier, resulting in growth and developmental delays. A metanalysis of two randomized clinical studies demonstrated that for every 10% increase in the volume of fluid containing cow milk given to premature infants weighing less than 1,250 grams, the risk of necrotizing enterocolitis (NEC) increases by 11.8%; surgical NEC, by 20.6%; and sepsis, by 17.9%. (2)

An exclusively human milk fortifier does exist. The availability of this fortifier has changed clinical practice and substantially reduced the risk. Development of this product required extensive research and development. The manufacturer of this product is the only manufacturer of a fortifier made exclusively from donor breastmilk. Providing extremely premature infants an exclusively human milk diet during the early postnatal period is associated with a lower risk of death, NEC, NEC requiring surgery, and sepsis in these most at-risk infants. (2, 3, 4) It decreases hospital costs, since a single case of NEC or sepsis can cost upwards of $250,000 to treat. (5, 6, 7)

A fortifier made from human milk has been associated with lower risks. Importantly, extremely premature infants will have a decreased risk of immediate, life-threatening complications and can be given fortifier sooner, thus providing better nutritional support during a period where they are most at risk.

The Keystone Mothers' Milk Bank Act threatens access to these life-saving donor breast milk-based fortifiers in Pennsylvania NICUs by prohibiting remuneration of mothers who donate their surplus milk to produce this fortifier, mothers who provide this life-saving milk from their own bodies. Pumping milk is time intensive and expensive. The process requires electricity to operate the pump and freezer, constant attention to sterility and hygiene, and effort to ship the expressed milk. Remuneration is not unreasonable for the excess breast milk these women provide.

The Keystone Mothers' Milk Bank Act, as drafted, prohibits, "remuneration of value provided to a milk donor by an entity." Effectively, this could mean that the one company that produces a human milk-based human milk fortifier would not be able to provide this product in Pennsylvania. Many fragile premature infants in Pennsylvania's NICUs depend on this product. Implementation of this act would be an unmitigated disaster for Pennsylvania NICUs most fragile premature infants, many who are already at increased risk from disparity.

Moreover, NICUs depend on donor breastmilk to feed preemies when mothers' milk is unavailable, but the Keystone Mothers' Milk Bank Act could allow adulterated, contaminated, and improperly handled breastmilk to reach NICU babies. The standards for screening, processing, and storing breastmilk in the current iteration of the bill are not stringent enough to meet the need and fail to reference the comprehensive safety standards published by the US Food and Drug Administration (FDA) for all other foods.

Further, there is no requirement to screen breastmilk for opiates,

nicotine, or certain other drugs of abuse. As the AAP endorses, regulations regarding the handling of breastmilk by milk banks should be in the hands of the FDA and the Centers for Disease Control and Prevention (CDC), which have the resources and integrity to implement and enforce these essential regulations. Regulations must be neither propriety nor left to individual, unregulated entities. Regardless of the source, the protection of the public is at stake.

Legislators must listen to the concerns of experts in neonatology regarding this bill. These most fragile preterm infants must be protected. The intent may be good, but the ramifications are clear. "A good intention, with a bad approach, often leads to a poor result." (8) Please give our most at risk, most fragile premature babies what they need in the safest way possible. The bill, in its present form, will make this goal more challenging to achieve.

"The intent may be good, but the ramifications are clear. 'A good intention, with a bad approach, often leads to a poor result.'"

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NT

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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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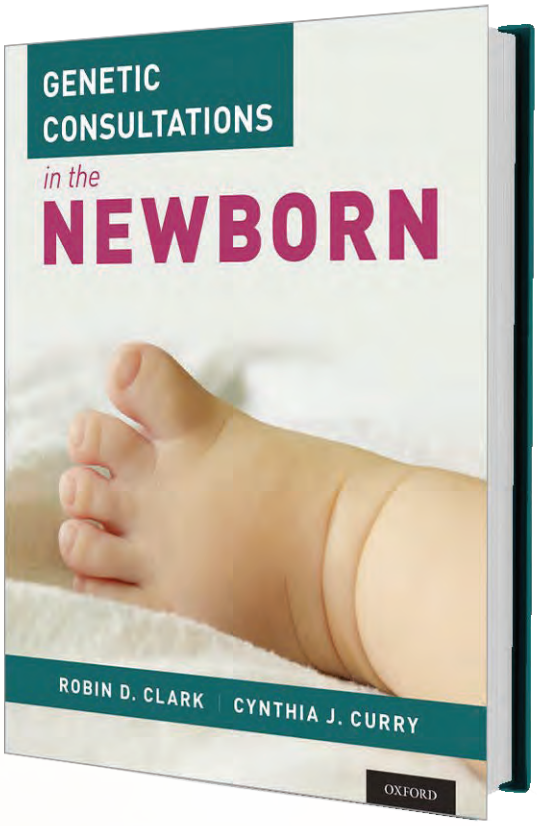

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RSV AWARENESS:
A National Poll of Parents & Health Care Providers

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

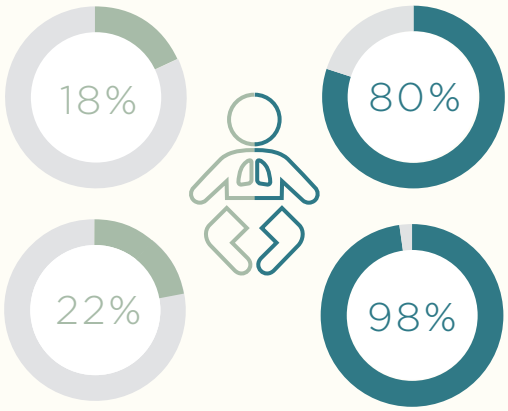
Parents of children age four and under report that understanding of RSV is lacking. That leaves them less than fully prepared to prevent their young children from catching the virus.

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%).

Monthly Clinical Pearl: Being in Middle Management is A Challenge! Who was William Henry Wills?

Joseph R. Hageman, MD.

I have a long history of being in middle management…almost 40 years in medicine. It was a conscious choice on my part, for the most part. Being in middle management in medicine is challenging and interesting. In certain parts of your job, you are in a leadership role, like being the head of inpatient pediatrics, the pediatric intensive care service, the apnea service, and having a lung injury research lab…the fun stuff. Then there is the administrative stuff, which was the only part of my job that I considered work. My favorite parts of my career are clinical care, teaching, research, and lastly, administrative responsibilities. Nowadays, I consider Quality improvement (QI) in the research category…although, I have to say, I am not the most popular person in the NICU (1). This is another middle management position. Why am I talking about middle management? Because recognition for your efforts is limited. Please don't get me wrong, I have enjoyed everything and feel fulfilled in my career. I am enjoying my present role as well and have figured out ways to accomplish small steps in neonatal QI, help young trainees publish their first and early career papers, and help with clinical, educational and QI research projects. Being pleasantly persistent is a necessity in all of these efforts and I have received a "thank you" from my more senior colleagues and friends. You work in the background to help and continuously re-evaluate your positive vs. negative balance in your professional life. For those of you who are in a middle management position, you know what am I referring to in this discussion. Work with yourself as the satisfaction balance is dynamic.

"You work in the background to help and continuously re-evaluate your positive vs. negative balance in your professional life. For those of you who are in a middle management position, you know what am I referring to in this discussion. Work with yourself as the satisfaction balance is dynamic. "

William Henry Wills was Charles Dickens' subeditor for his journals, including Household Words and All the Year Round. Has anyone ever heard of him? He was in a middle management position. He was in charge while Dickens traveled, while he was writing some of his novels, while he went through domestic changes in his complicated life. Wills was very productive in his professional life as the "go to" editor where almost all submissions went to be reviewed. If the papers came to Dickens first, he forwarded them to Wills. He also published some articles, books and collections of poems and stories as the primary author or editor while he was Dickens' sub-editor. We know how incredibly productive Charles Dickens was and what a brilliant author and editor he was during his professional life. From the brief biographies presented in Wikipedia, Spartacus Educational, William Henry Wills was a trusted, consistent, detail oriented, and thoughtful editor, author and friend of Dickens (2,3,4).

So, as you progress in your careers, think about how you enjoy spending your time, both professionally and personally. Sometimes you can make choices and sometimes, the choices are made for you, depending on what the needs of your group, section, department, hospital, university and community are. If you do get the chance to spend time doing things that help you and the organization and get a chance to work with a mentor, like Charles Dickens, and you are in "middle management," it might be worth your while!

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From The National Perinatal Information Center

Neonatal Special Care Statistics: CY 2018 Update with CY 2017 and Five-Year Trend Comparisons

Janet H. Muri, MBA

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.

NPIC
National Perinatal Information Center

In the calendar year (CY) 2018, the NPIC Perinatal Center Data Base (PCDB) profiled 309,497 newborns across 80 hospitals. 91.5 % percent of those were born at the reporting hospitals, and 4.0 % were transferred in following delivery, presumably for a higher level of care. The 2018 rate of infants transferred in is unchanged from the CY 2017 rate.

In CY 2018, 15.5 % percent of total neonates were admitted to a special care nursery, whether to an intensive care or intermediate care bed. When NPIC isolated just those facilities that participated in the Trend Data Base for the previous five year period (2014-2018), the 2018 admission rate was 16.7%, reflecting a stable trend from the 16.1% for the same cohort of hospitals in 2014.

Below is a table that profiles key metrics from the NPIC Calendar Year 2018 Perinatal Center Data Base (PCDB) in comparison to CY 2017 and the NPIC Trend Data Bases for years 2013-2017 and 2014-2018.

Key Metrics from the NPIC Perinatal Center Database (PCDB)

	2017	2018
Special Care Admissions	**52,658**	**50,999**
Percent of Total neonates	14.4%	15.5%
Percent of special care admissions transferred from an acute care facility	4.0%	4.0%
Special Care Admission Trends	16.2 to 15.8 % * (CY 2013-2017)	16.1 to 16.7% (CY2014-2018)
Special Care ALOS Trends	15.5 days to 15.0 days	14.3 days to 14.3 days
Percent ≤ 1500 grams (ALOS)	9.2 % (48.6)	10.4% (50.0)
Percent 1500-2499 grams (ALOS)	28.3% (15.6)	26.9% (16.5)
Percent ≥ 2500 grams (ALOS)	53.7% (7.0)	54.9% (6.8)
Percent discharge to home with or without home health	85.2%	85.0%
Percent died	1.2%	1.2%
Complication rates:		
MAS for Inborns	1.4%	1.3%
MAS for Transfers In	2.5%	1.1%
IVH Grade III	.3%	.4%
IVH Grade IV	.4%	.4%
Infection Septicemia/Bacteremia	6.1%	5.1%
RDS TTN	18.7% 18.0%	19.2% 17.7%
NEC	.7%	.7%
PDA without repair	5.9%	6.1%
PDA with repair	.3%	.4%
IE/pneumothorax	3.1%	3.2%
ROP with eye procedure	2.7%	1.9%
Complications for neonates 500-1499 grams : Trends	**2013-2017**	**2014-2018**
Proportion of BPD to RDS	20.2% to 13.7% *	17.4%-16.3%*
NEC	4.4% to 4.6%	4.3%-3.8%
IVH Grade III or IV	5.4% to 4.6%	4.4%-4.9%
Linked mother/infant records: Rate of infant special care admission for infant linked to a mother with a specific condition		
Hypertension	22.8%	23.1%
Diabetes Mellitus	34.8%	36.4%
Obesity	17.1%	18.2%
Thyroid dysfunction	16.6%	17.7%
Primary C-section ≥ 37 weeks	12.9%	14.1%
Repeat C-section ≥ 37 weeks	8.0%	9.4%

*Significant change

Increased Attention on Special Care Admissions

As we stated in our review of CY 2017 Special Care statistics from the Perinatal Center Data Base (Neonatology Today, August 2018), the ultimate goal is to keep infants out of the special care nursery. While there will always be a need for neonatal special care services, greater payer scrutiny is likely to drive some decreases in admissions as well as external attention on unnecessary special care admissions as a quality of care issue.

The Joint Commission's newest measure for the Perinatal Care Measure set is PC-06: Unexpected Complications in Term Newborns. (1) This measure must be reported by almost all hospitals with more than 300 deliveries annually and includes analysis of 100% of all newborn discharges starting with 1/1/2019 discharges. (This is a departure from other PC measures that permit sampling). The PC-06 denominator is all live-born single term newborns 2500 grams or over in birth weight, excluding those that have congenital anomalies, (1) pre-existing fetal conditions or indications of maternal substance abuse. Numerator cases reflect severe and moderate complications as defined by the TJC algorithm in consultation with the measure developer, the California Maternal Quality Care Collaborative.
PC-06 is divided into an overall rate (PC-06.0), a severe rate (PC-06.1) and moderate rate (PC -06.2). The severe category includes infants transferred out to another acute care facility (for a higher level of care). Since not all transfers are for a higher level of care, TJC abstraction guidelines include the following language:

"For PC-06 Only: If a newborn is transferred to another acute care facility for purposes other than medical treatment or the need for a higher level of care, abstract allowable value 8 (not documented or unable to determine). Examples include: Newborn is transferred to another facility covered by their healthcare plan or for disaster evacuation."

This qualifier will require hospitals to review their transferred out cases carefully to ensure only those meeting the measure definition are included in their numerator. On the positive side, the measure may also incentivize greater antepartum referral/transfer of high-risk pregnancies to the appropriate level of care.

References

1 *Source: Specification Manual for Joint Commission National Quality Measures v2018B1, www.jointcommission.org.*

The author has no relevant disclosures.

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- Discuss ways to optimize nutrition in the extremely premature infant

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Letters to the Editor

Vitamin K Dosing Problem and Proposed Solution for Extremely Low Birth Weight Infants. Letter to the Editor
Tuesday, May 30th, 2019

Shabih Manzar, MD
Assistant Professor
Department of Pediatrics
College of Medicine
Louisiana State University Health Sciences Shreveport

Dear Dr. Goldstein,

Vitamin K dosing and administration for infants weighing less than 1000 grams is a problem in the NICU. We proposed a potential solution to this problem. This report would act as a resource for pharmaceutical company to act on the need to add one more calibration to the pre-filled vial/injector Vitamin K.

American Academy of Pediatrics (AAP) recommends Vitamin K prophylaxis to all newborn infants, irrespective of their gestational age. (1) The dose of Vitamin K for infants less than 1000 grams is 0.3-0.5 mg/kg. The problem encountered with this dose is that the volume generated is too low and would be in two decimal points. The current "solution" is to draw the dose from a pre-filled vial to a 1 mL syringe. This involves the risk of medication errors. We proposed (personal communication sent the pharmaceutical company; Phytonadione, International Medication System, Inc. and Amphastar Pharmaceuticals, Inc.) to add another marking on the pre-filled vial/injector. Figure 1-4 explains the process in detail.

There is no available evidence that vitamin K is harmful, or at potential risk of over dosing with these constraints. When comparing vitamin K levels at day five, vitamin K levels were significantly lower in the 0.2 mg IM group as compared to the 0.5 mg IM group; while on day 25, vitamin K levels in the 0.2 mg IM group and the 0.5 mg IM groups were not significantly different. (2)

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Figure 1

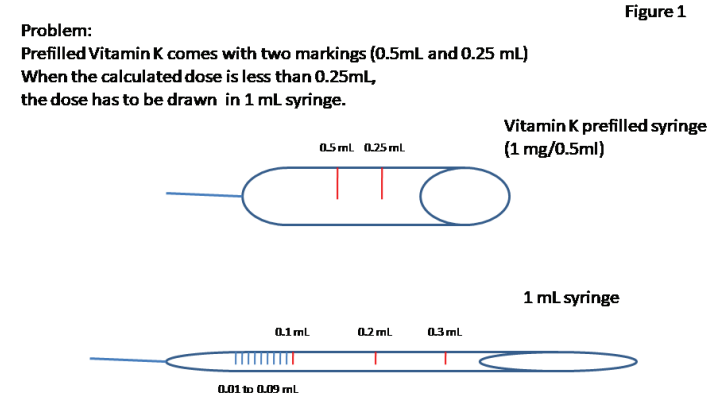


Figure 2

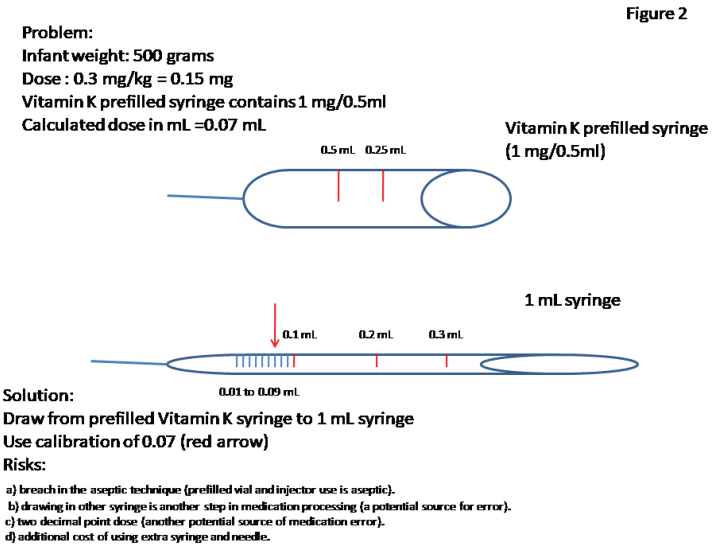


Figure 3

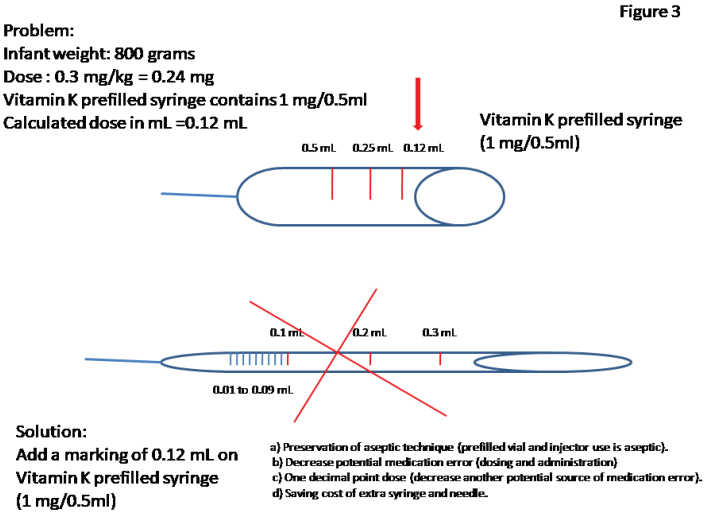
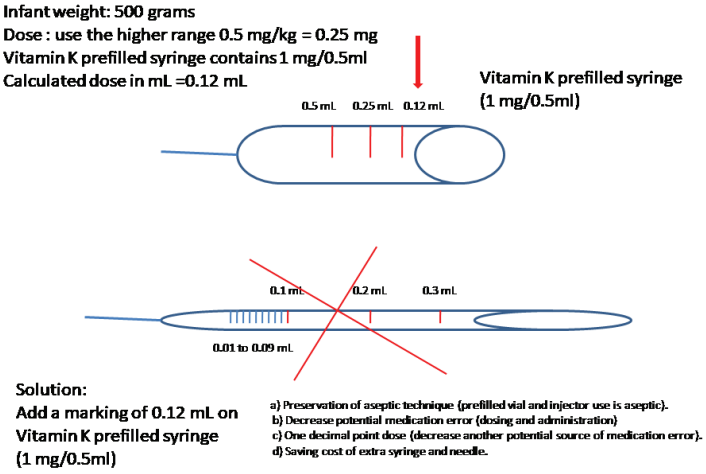


Figure 4



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Dear Dr. Manzar,

These issues are very important. With increased parental questioning of standard vaccines and other therapies, hemorrhagic disease of the newborn has become a real concern. It would be public relations disaster if a baby were to receive appropriate prophylaxis, but in fact an under dose, and then go on to have a significant bleeding episode.
Standardized solutions have produced significant improvements in the accuracy of dosing for adults but have imperiled our most at risk neonates for the same reasons that you indicate here. The improbability of dosing to two digits past the decimal mark is a constant challenge.

The solution proposed here is thoughtful and appears to address the limitations of dosing even the smallest premature neonates. I applaud your efforts and encourage manufacturers to fully evaluate this novel concept.

Sincerely,
Mitchell Goldstein, MD
Editor in Chief

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Erratum (Neonatology Today May, 2019)

Neonatology Today has not identified an erratum affecting the May, 2019 edition. 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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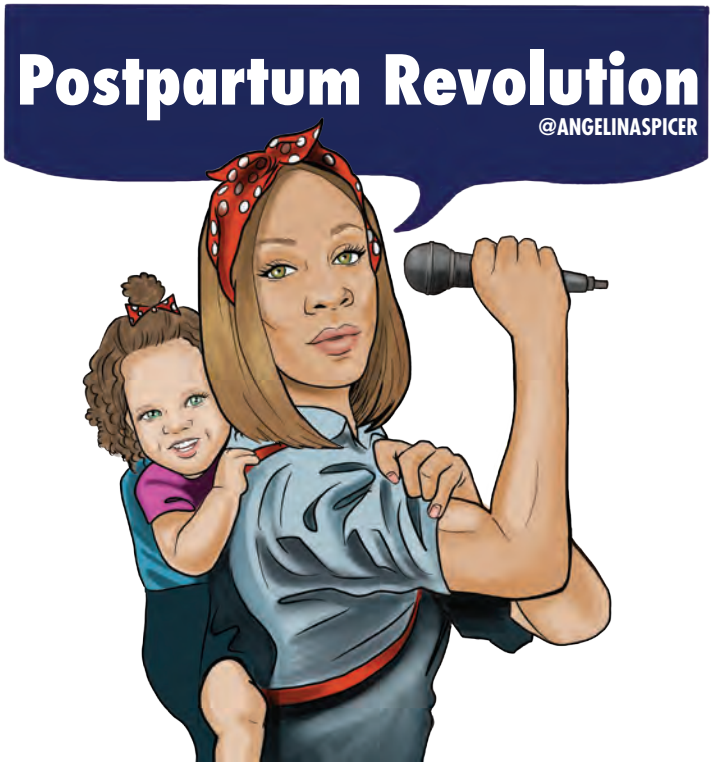

INA International Neonatology Association

Neonatology from a Global Perspective

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The 5th International Neonatology Association Conference (INAC) will be held in the beautiful, city of Tijuana, Mexico on July 12-16, 2019.
For the 2019 edition, a wide spectrum of topics will be covered by highly esteemed international speakers. Participants will have the opportunity to enjoy both expert keynote lectures on main topics as well as more focused discussions on specific aspects of neonatal care during concurrent sessions. Emphasis will lie on the neonatal brain and various facets of neonatal neurology.

Abstract Submission now open

Abstract Topics Include:

★ Birth Defects ★ Neonatal Cardiology ★ Neonatal Jaundice
★ Resuscitation Best Practices ★ Respiratory Support: New Approaches
★ Neurology of the Newborn ★ Neonatal Radiology



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Next-Level Perinatal/Neonatal Comfort Care Training
June 19–21, 2019 | 9am – 5pm
Columbia University | New York City
http://mailman.columbia.edu/comfort-care

The 5th annual 2019 iCAN Research & Advocacy Summit
June 23-28, 2019
Kansas City, Missouri
https://www.icanresearch.org/2019-summit

5th Conference of the International Neonatology Association
July 12-14, 2019
Tijuana, Mexico
http://worldneonatology.com/2019/welcome-letter-2

Innovations in Neonatal Care: Celebrating 10 Years. The Future is Now!
August 11-13, 2019
Austin, Tx
http://innovationsconference.com

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

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

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/

For Additional Meeting Information, visit NeonatologyToday.net and click on the events tab.

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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.

LOMA LINDA UNIVERSITY
Faculty Medical Group

For more information please contact:

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efayard@llu.edu

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Physician Recruitment Coordinator
kswensen@llu.edu

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- Care of high acuity NICU patients
- State of the art technology
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Who We Are

With over 900 beds in four hospitals, we operate some of the largest clinical programs in the nation. We also offer the only Level I Regional Trauma Center and Children's Hospital in the Inland Empire servicing the largest county in the US. We lead in many areas of excellence; pediatrics, cardiac services, cancer treatment and research, mental health, chemical dependency, and other essential clinical disciplines. All this adds up to endless possibilities for our patients and for you.

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

Please visit our website **http://careers.llu.edu** or contact Jeannine Sharkey, Director of Advanced Practice Services at jsharkey@llu.edu or (909) 558-4486.

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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.

The topic is yet again "birds" for this month. Elmar P. Sakala, MD, MA, MPH, Professor of Gynecology & Obstetrics, Section of Maternal Fetal Medicine, Loma Linda University School of Medicine shares a photograph of an introspective parrot. The birds continue to rule.

Herbert Vasquez, MD

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NT

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.

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