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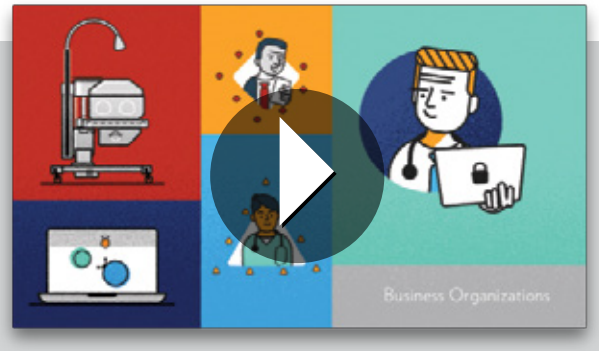

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When, Why, and How to HFJV

J. Bert Bunnell, Sc.D.

HFJV (high-frequency jet ventilation) is the most gentle and effective way to facilitate pulmonary gas exchange. In this paper, I'm going to explain how I can be this audacious, why those of you who work in NICUs and PICUs should consider using HFJV every chance you get, and how you should use it for various types of patients. In the process, I will explain a few of the distinct differences between HFJV and HFOV (high-frequency oscillatory ventilation) and CMV (conventional mechanical ventilation).

When I wandered into the NICU at the Massachusetts General Hospital as a graduate student in chemical engineering from across the river at MIT in 1971, I never expected to spend my career trying to improve the care of neonatal and pediatric patients. I owe the success that I have had there to the mentor I met that day, Dr. Daniel C. Shannon, along with a myriad of other neonatologists, pediatric intensivists, physiologists, and other medical scientists who tutored me in all the subjects many of you learned in medical school. I went to engineering school where I studied fluid mechanics and transport phenomena (energy, heat, and mass transfer). I also learned enough about electronics and microprocessor control to appreciate their importance in medical product development. These are the disciplines that I applied to the problem of how one helps babies breathe.

As an engineer, it seems odd to me that clinicians use machines designed to replicate breathing for babies that can't breathe on their own. I thought we should facilitate their pulmonary gas exchange, but it wasn't obvious how we might do that.

Over the years, I learned that the keys to success for preterm infants are:

1. get the lungs open,
2. keep them open, and
3. gently ventilate, which to me means "facilitate pulmonary gas exchange."

This regimen is ideal for preventing lung injury in preterm infants and rescuing babies born with congenital diaphragmatic hernia and pneumonia. When considering how to most gently facilitate gas exchange, we should include everything you do to support and encourage babies to breathe on their own, such as providing CPAP, artificial surfactant, caffeine, etc. Then the most gentle way to mechanically assist infants would be to use a high-frequency ventilator, because these machines use much smaller tidal volumes compared to conventional ventilators.

Airway pressures used during HFV may appear to exceed those used during CMV, but that observation depends upon where those pressures are measured. Pressure amplitude during HFJV and HFOV attenuates quickly as their tidal volumes move through endotracheal tubes and into lungs such that only a fraction of HFV peak airway pressure makes it down to the alveolar level. (See Figure 1.)

As small as the HFV airway pressures are, they provide the means whereby ventilation is controlled as described by this equation:

$$V_{CO2} = f \times VT^2$$

where V_{CO2} = ventilation or CO_2 elimination,

f = frequency, and

VT = tidal volume.

Since tidal volume is squared in this equation, it is by far the most important determinant of $PaCO_2$. With most HFVs, ΔP (PIP - PEEP) creates VT , and once PEEP is optimized with HFJV, PIP controls PCO_2.

How HFVs can provide adequate ventilation with tidal volumes that are smaller than anatomic deadspace was actually explained long before HFVs were invented. Pulmonary physiologist Yandell Henderson, et al, published a paper in 1915 that explained how animals can maintain normal ventilation while panting and in the process, explained why HFJV is the most efficient form of high-frequency ventilation. Using tobacco smoke and a large glass tube, Henderson demonstrated how inhaled gas penetrates through the anatomic dead space by blowing the smoke into the tube in one quick puff. His colleagues, standing off to one side observed how the smoke streamed into the tube defining a long, thin spike. (See Figure 2.) The paper denotes: "The quicker the puff, the thinner and sharper the spike." Once he finished his puff, Henderson stuck his tongue over the entrance of the tube, stopping the flow, and the effect disappeared as diffusion took over, uniformly filling the tube with smoke. Henderson then inhaled sharply, send a spike of fresh gas back through the smoke towards his mouth, demonstrating that the spike effect could occur in either direction. He labeled the phenomenon "Axial Flow" and noted the opportunity for enhanced diffusive gas exchange produced by the increased surface area of spike. In engineering fluid mechanics textbooks, the phenomenon is called "transitional flow," meaning the fluid is either transitioning from slow-moving laminar to fast-moving turbulent flow or vice versa.

HFJV creates transitional flow with every inspiration, shooting gas into the endotracheal tube (ETT) in quick little bursts.

"HFJV creates transitional flow with every inspiration, shooting gas into the endotracheal tube (ETT) in quick little bursts."

HFOV approaches producing this type of flow when it is set to deliver its tidal volumes most quickly, at 15 Hz where its 0.022 sec inspiratory time is comparable to that of HFJV. However, the pressure waveforms of the two types of HFV are different: HFJV PIP (peak inspiratory pressure) is reached at the end of its inspiration, while HFOV pushes gas in sinusoidally, such that the pressure rises and falls within the inspiratory time. Thus, HFJV inspirations theoretically penetrate deeper into the airways, and at least one animal study demonstrated that HFJV produced the same arterial blood gases as HFOV using significantly lower

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airway pressures. Nonetheless, the fact that both forms of HFV use very small tidal volumes with markedly less airway pressure deep in the lungs infers that both should be preferable to CMV for preventing lung injury, and there are randomized clinical trials that support that contention.

Clinical trials often generate as many questions as they answer. In the case of HFV studies, incidence of severe cerebral injury, including intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) have been worrisome. One HFOV clinical trial found an increased risk of IVH in infants at risk of developing PIE. One HFJV clinical trial found an increased risk of PVL in preterm infants treated with a "low-volume" strategy, which was also associated with hypocarbia in the first 3 days of life, while another multicenter trial found no PVL in comparable patients treated with a "high-volume" strategy. , Conventional wisdom attributes these injuries to hyperventilation, which is easy to generate during HFV. Perhaps it is fear of these adverse side effects as well as normal skepticism of new, disruptive technologies that keeps many clinicians from using HFVs early and often for prevention of lung injury in preemies even though it's now 30 years post-FDA approval of the first HFV (Bunnell LifePulse® HFJV).

The latest Cochrane Review concluded: "This review suggests that there may be benefits of elective HFJV in terms of reduction in risk of CLD at 28 days and 36 weeks PMA and at discharge. Of concern is the significant increase in adverse neurological outcomes in one of the trials which used lower mean airway pressures when ventilating with HFJV."

"The latest Cochrane Review concluded: "This review suggests that there may be benefits of elective HFJV in terms of reduction in risk of CLD at 28 days and 36 weeks PMA and at discharge. "

Treatment of Lung Injury

What happens when preterm babies don't get better? RDS babies develop PIE, PIE babies develop BPD, and some BPD babies just get worse and worse. Since many clinicians restrict their use of HFV to rescue applications, it is prudent to discuss efficacy of HFV use in patients manifesting various pathophysiologies.

The same transitional flow "spike" phenomenon that makes HFJV successful in preventing lung injury also makes it most effective in treating lung disorders associated with airway inflammation. For example, pulmonary interstitial emphysema (PIE) is characterized by disruption of terminal airways and pneumatic dissection of airway and blood vessel walls upstream from the disruption site. Conventional ventilation of patients with PIE and other airleak disorders aggravates such injuries by pushing gas through the disruptions and into damaged areas of the lungs with poor perfusion. A randomized controlled trial published in 1991 revealed better outcomes in babies treated with HFJV compared to rapid-rate CMV with short inspiratory time even though the strategy used with the Jets was sub-optimal. This success with HFJV in treating was attributed to the use of lower PIP and mean airway pressure, which led to some patients randomized to HFJV struggling for adequate oxygenation even though oxygen index (FiO_2 x MAP x 100 / PaO_2) was significantly improved in the HFJV group.

The true key to successfully treating PIE and other airleak disorders is the favorable distribution of ventilation that occurs with HFJV in patients with airways narrowed by inflammation and interstitial gas. Jet inspirations are brief, high-velocity, spurts of gas that automatically avoid narrowed airways with increased airway resistance, enabling better gas delivery to healthier areas of the lungs. Trying to keep mean and end-expiratory pressures low in these patients only compromises gas exchange by allowing airway and alveolar collapse. Hence, getting lungs open and keeping them open is important in rescue as well as lung-injury prevention strategies.

HFOV treatment strategies have always stressed the importance of increasing mean airway pressure (MAP) when switching patients from CMV. This "high lung-volume" strategy counteracts the tendency of active exhalation to cause airway collapse via "choke points" as well as supports surfactant deficient alveoli. However, HFOV has never been shown to be superior to CMV in the treatment of PIE and other lung injuries, perhaps because the slower, longer HFOV inspirations and shorter, active exhalations are less effective in reducing ventilation of inflamed and injured areas of the lungs. (HFOV I:E is only adjustable from 1:1 to 1:2.)

The latest Cochrane Review concluded: "There is insufficient information on the use of rescue HFOV to make recommendations for practice. The small amount of data that exists suggest that harm might outweigh any benefit."

Moving Beyond Treating Air Leaks: BPD

Despite everyone's best efforts, bronchopulmonary dysplasia (BPD) happens. As baby lungs get injured, hyperinflation creeps into the picture, literally, on x-ray. When clinicians see hyperinflation, their first reaction is typically: "we gotta reduce PEEP (or MAP)." That approach usually makes matters worse, because lowering baseline and mean pressures allows airway to become more narrow on exhalation, which makes the lungs even more prone to gas trapping. There is seldom a simple solution to this complex problem, but there is a strategy that we have found to almost always work:

1. Eliminate ventilator settings that are likely to aggravate

hyperinflation, such as big tidal volumes and short exhalation times. Since HFOV is usually limited by an I:E of 1:2, using HFJV where I:E can be stretched to 1:12 is advisable. If you are forced to use low rate CMV with HFJV in order to avoid CMV alarms, use the lowest rate, shortest I-time, and lowest PIP possible.

2. Keep PEEP high enough to facilitate patent airways (at least 8 cm H_2O; possibly much higher).

3. Use the lowest HFJV rate = 240 bpm, where I:E = 1:12.

4. Be patient. You may see improvement in hyperinflation on xray and blood gases within a few hours, but it may take a week to get your patient extubated.

Unlike lowering HFOV rate, lowering HFJV rate does not increase tidal volume unless inadvertent PEEP was alleviated by the consequent increase in exhalation time. Lowering HFOV rate increases inhalation time, which increases tidal volume. Lowering HFJV rate just decreases minute volume, like conventional ventilation.

Managing $PaCO_2$ can be very challenging in BPD babies. While adjusting PIP is the principal route to controlling $PaCO_2$, inflamed and disrupted airways may necessitate additional considerations.

Pressure amplitude (PIP - PEEP) creates tidal volume, but it takes time to deliver it.

The default HJFV I-time of 0.020 seconds may be increased in 0.002 increments up to 0.034. Longer I-times allow more time for tidal volumes to be delivered, so if high $PaCO_2$ is persistent despite adjusting PIP to higher and higher values, try increasing I-time.

It may appear from the displayed I:E that increasing I-time may inhibit complete exhalation, but there is an abundance of time to work with when using HFJV, as illustrated in the following table.

As shown, increasing I-time enables you can increase the time allotted for tidal volume delivery on inhalation by major percentages while decreasing the time allotted for passive exhalation by minor percentages.

Pneumonias, MAS, CDH, PPHN, Congenital Airway Anomalies, and Servo Pressure

The pathophysiology of pneumonia is similar to RDS in many ways, but the presence of excess secretions generates an additional challenge to patient management. The good news is that HFJV facilitates movement of secretions up the airways towards the trachea. The manner in which passive exhalations swirl out along the airway walls during HFJV also helps patients with meconium aspiration syndrome (MAS).

"When a patient is stable with acceptable blood gases, the monitored Servo Pressure value is not only worth charting, it is worth special attention. Every patient has a Servo Pressure value that will become remarkably consistent with their well-being."

The LifePulse jet ventilator monitors "Servo Pressure," the pressure required to generate enough flow to hit the PIP set by its operator. Thus, when secretions accumulate in the airways, Servo Pressure decreases since the increase in airway resistance increases upstream pressure as gas flows into the airways. Automatically set high and low alarm limits alert clinicians to such changes in patients' lung mechanics, and a low Servo-Pressure alarm can be a signal that the patient needs suctioning. A high Servo Pressure alarm indicates that the patient has become easier to ventilate and weaning is probably indicated to avoid hyperventilation.

When a patient is stable with acceptable blood gases, the monitored Servo Pressure value is not only worth charting, it is

Rate	T_I	% Increase over 0.020	T_E	% Decrease from 0.122	I:E
420	0.020		0.122		1:6
420	0.026	30%	0.116	5%	1:5
420	0.034	70%	0.108	11%	1:3
Rate	**T_I**	**% Increase over 0.020**	**T_E**	**% Decrease from 0.180**	**I:E**
300	0.020		0.180		1:6
300	0.026	30%	0.174	3%	1:5
300	0.034	70%	0.166	8%	1:3

Table 1: Relative Effects of Changing HFJV I-Time on Inspiration and Expiration

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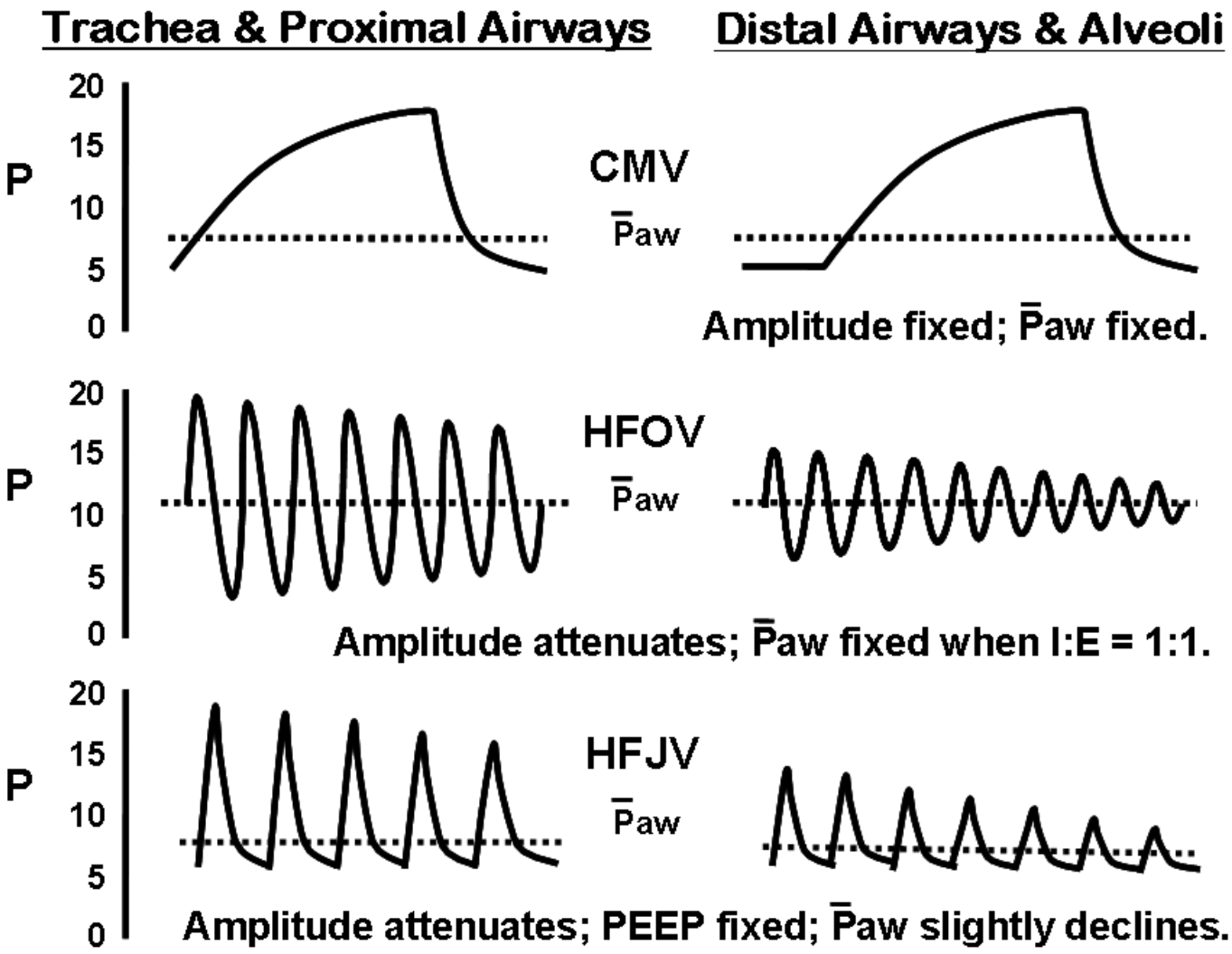

Figure Figure 1: HFV Airway Pressure Waveform Dampening

(Paw = mean airway pressure; used with permission. © 2003, Bunnell Inc.)

worth special attention. Every patient has a Servo Pressure value that will become remarkably consistent with their well-being. As time goes by and the patient's condition becomes better or worse, Servo Pressure will almost always return to the same value when ventilator adjustments are made or procedures such as suctioning and re-recruitment are performed.

Another advantage of HFJV for MAS is its value in dealing with PPHN (persistent pulmonary hypertension): it can ventilate patients using lower mean airway pressure compared to either HFOV or CMV, as noted previously in the Boros publication.[4] This pulmonary vascular resistance-lowering characteristic can also be valuable when treating infants with cardiac surgery patients and newborns with congenital diaphragmatic hernia (CDH), as that condition is commonly complicated by PPHN.

Finally, HFJV's spike effect is life-saving when dealing with airway anomalies such as tracheal-esophageal fistula. Inspirations shoot right past fistula, providing ventilation that is impossible to achieve conventionally.

Summary: Simplified Strategies for NICU and PICU Patients

My motto for the NICU patients is: Rescues are fun, but prevention is more fulfilling. Any baby that can't be managed with nasal CPAP or other non-invasive techniques deserves to receive facilitated pulmonary gas exchange rather than conventional assisted ventilation. HFVs use the smallest effective tidal volumes, and HFJV offers the smallest tidal volumes and lowest effective airway pressures of all.

You can't facilitate gas exchange until and unless alveoli are opened by judicious use of CMV. Then the alveoli must be kept open by adjusting PEEP upwards from the typical 5 cm H_2O starting point until recruitment breaths are no longer needed to maintain oxygenation, hopefully using $FiO_2 < 0.30$. If you have to continue using some CMV to avoid conventional ventilator alarms, pick the lowest CMV rate, PIP, and I-time possible.

Choose a starting HFJV rate that is consistent with the size and condition of the patient. It is important to avoid ventilator-induced gas trapping that can result from using rates that are set too high. Preterm infants with stiff lungs can be ventilated with rates up to the maximum of 660 bpm, but there is no advantage to maximizing rate when you are trying to encourage babies to do their own breathing. The lower the rate, the longer the exhalation time, which is the equivalent of CPAP.

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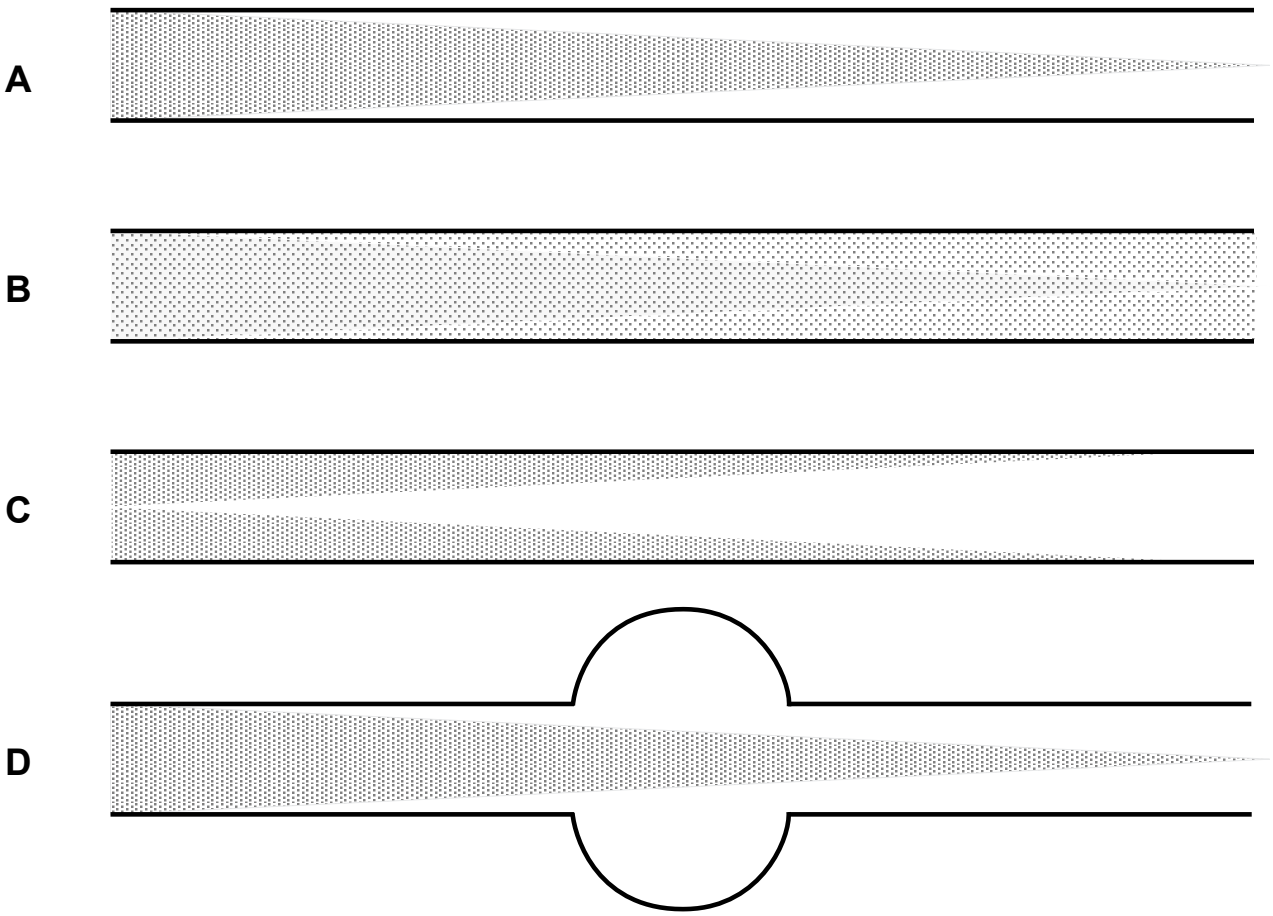

Figure 2: Henderson's smoke experiment. A) A long thin spike or jet stream of smoke shoots downstream when suddenly blown into a glass tube. B) The jet stream disappears when flow stops and diffusion takes place. C) This effect can be duplicated in the opposite direction if fresh gas is drawn back into the smoke filled tube with a sudden inhalation. D) Imperfections in the tube walls (such as a bulb) have little effect on the shape of the jet stream. (Modified with permission from Am. J. Physiol., 38: 5, 1915. © 1915, American Physiology Society.)

Bigger babies and children in the PICU should always be ventilated with lower rates all the way down to the minimum of 240 bpm. If high HFJV PIP is required to achieve a reasonable $PaCO_2$, and there is no evidence of gas trapping, increase rate to blow off more CO_2 . If PEEP monitored by the Jet exceeds that set by the CMV, there may be gas trapping. If the monitored PEEP goes down when you lower HFJV rate, you just alleviated it.

Manage $PaCO_2$ with HFJV PIP, reacting to rising and falling Servo Pressure by adjusting PIP in the opposite direction: if Servo Pressure goes up, reduce PIP; if Servo Pressure goes down, increase PIP, but keep in mind that the baby made need to be suctioned. If Servo Pressure suddenly plummets, there may be a mucus plug, obstructed ETT, or pneumothorax to deal with. Use transcutaneous $PaCO_2$ monitoring, please.

If you are rescuing a patient from some form of lung injury or deadly disorder, start with the same "get the lungs open and keep them open" approach, but consider the effects of the pathophysiology to make your decisions about how to choose HFJV rate and I-time. Acute lung injuries will benefit from the shortest I-time of 0.020 sec, but that may have to be increased in 0.004 sec increments towards the maximum of 0.034 sec if raising PIP fails to alleviate hypercapnia. Thinking that you need CMV breaths to oxygenate may be an indication that your PEEP is set too low. However, if the PEEP is too high, it will impede pulmonary perfusion, so there may be occasions where a few CMV breaths per minute with a bit lower PEEP is a good compromise.

Chronic lung injuries such as severe BPD typically require lower HFJV rates, moderate PEEP, and longer I-times. Such injuries do not occur over-night, so don't expect quick success. Focus on facilitating gas exchange and encourage spontaneous breathing by minimizing sedation.

Weaning directly from HFJV to something non-invasive like nasal

CPAP will reduce the risk of re-injuring the lungs. As oxygenation improves, wean FiO_2 before PEEP (within reason). Always minimize delivery of big tidal volumes, except as necessary for alveolar recruitment after suctioning, etc. As ventilation becomes easier, wean PIP and HFJV rate, the latter of which will encourage more spontaneous breathing. Remember, the ETT presents a significant impediment to spontaneous breathing, so don't think you have to go back to CMV to reduce the patient's work of breathing.

In conclusion, I hope you don't find this paper to be too biased. I came by my bias honestly, from 40 years of study and reflection. We all tend to accept ideas and explanations that confirm our beliefs and reject those ideas and explanations that don't. The proof is in the outcome: can you send your patient home with minimal chronic injury? If you did that, you did it well. My career in this field has ended. I just want to leave behind as much of what I learned as possible. Good luck!

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The author is no longer an employee or owner of Bunnell, Inc.. the employee-owned company that he founded to make and market a high-frequency jet ventilator for infants and children in 1980. His bias stems from helping develop this technology.

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Editor's Note: *The author refers to Bunnell LifePulse® High Frequency Jet Ventilator If you need help or just want to discuss your patient management with an experienced clinician, please call the Bunnell Hotline: 800-800-HFJV (4358). It's available around the clock.*

A New Way Of Monitoring Infants At Home

Gary E. Freed, DO, FAAP, FACOP

Abstract

This paper describes experience with the Owlet Smart Sock (OSS) in physician-verified medical conditions. OSS is currently a consumer product with a wireless sensor (pulse oximeter) powered by a rechargeable battery. All data are stored in a secure cloud-based database available for analysis. The use of the OSS as an early indicator of changing patient status, allowing for timely intervention is discussed.

Background

Since first employed in the 1970's, home monitoring has changed significantly. It has morphed from a simple alarm system, to a sophisticated piece of equipment capable of monitoring the patient's electrocardiogram, respiratory effort, and oxygen saturations1. Recent advances in technology have now led to the development of "wearable" monitoring systems.[2]

Home monitoring was initially used to "prevent" Sudden Infant Death Syndrome (SIDS). Despite data from several researchers finding fewer SIDS cases in areas where monitors were used[3,4,5] the official stance taken by the American Academy of Pediatrics (AAP) is that "home monitoring is not effective in reducing the incidence of SIDS." They refuted the studies showing monitor effectiveness because they were not randomized, double-blinded studies. The use of home monitoring, especially in healthy term newborns, remains a highly controversial topic in the pediatric community. Proponents suggest that home monitoring can provide parents and physicians valuable information about infant health, potentially alerting caregivers when an infant is in crisis, and thus enabling possible life-saving intervention.[6] Monitoring and transmission of physiological parameters in infants are not limited to prevention of untoward events but is an opportunity to identify or predict various pathological conditions. Critics express concern about false alarms, the high cost of monitors, parental anxiety (caused by the need for their infant to be monitored), and the risk of over-diagnosis.[7,8]

In 2001, the final report of the CHIME (Collaborative Home Infant Monitoring Evaluation) Study Group was published.[9] The study was designed to test the hypothesis that "preterm infants, siblings of infants who died of SIDS, and infants who have experienced an idiopathic apparent life-threatening event have a greater risk of cardiorespiratory events than healthy infants."

Findings from the "CHIME study" showed that cardiorespiratory events (apnea, bradycardia, etc.) that met conventional alarm thresholds were quite common, even in healthy term infants. However, more severe events were common only in preterm infants. Timing of these events suggested they were not likely to be immediate precursors to SIDS. Based on this study and other research, the AAP recommended against the use of home monitors to predict or prevent SIDS.

In an editorial published in May, 2001, Dr. Alan Jobe noted the following: "This report disproves the assumption that infants thought to be at increased risk of SIDS have more cardiorespiratory events than healthy infants and is consistent with the conclusion that such events are not precursors to SIDS."10 These comments were made despite the fact that the lead author of the CHIME study, Dr. R. Ramanathan stated, "The CHIME study was not designed to address the important question of whether infants who experience cardiorespiratory events are more likely to die of SIDS." Ramanathan went on to say, "The CHIME study was also not designed to determine whether use of a monitor decreases the rate of SIDS." So, even though the CHIME author specifically stated that this study was not designed to determine if monitoring was useful, the AAP continued similar sentiments to the assumptions like Jobe's and opted to condemn home monitoring by using this study as evidence.

"So, even though the CHIME author specifically stated that this study was not designed to determine if monitoring was useful, the AAP continued similar sentiments to the assumptions like Jobe's and opted to condemn home monitoring by using this study as evidence."

To that point, there are also several important caveats to the CHIME study: 1) the use of the apnea monitor in the CHIME study was on average only 15 days for the term newborns, and 45.5 days (the longest monitored time) for preterm SIDS siblings over the duration of the study (see Figure 1); 2) the use of apnea monitors (not pulse oximeters) that were specially built for the study and never commercialized due to their cumbersome design and functionality, which may have impacted the monitor use in the study; 3) pulse oximeters were used for monitoring but the data derived was not used to define recordings or alarm thresholds9.
Over the last twenty years, there has been an increase in the use of pulse oximeters for many of the applications previously performed by cardiorespiratory monitors. The most recent technology developments made pulse oximetry user-friendly as it was demonstrated in the observation of 47,495 newborns monitored with the Owlet Smart Sock (OSS).[11]

In the past, home monitoring was complicated by the need to have the infant "attached" to the monitor via electrodes and wires; this proved to be cumbersome and limiting to the family. As the child

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got older and more active, the risk of the child becoming wrapped (trapped) in the wires increased and monitor usage decreased. With the advent of wireless communication techniques, and low energy consumption microprocessors with sophisticated algorithms, the development of wearable monitoring systems became possible.[2]

In December, 2017, an article was published in the journal of Global Pediatric Health describing the experience of OSS users.[11] The article, "Initial Experience and Usage Patterns with the Owlet Smart Sock Monitor in 47,495 Newborns" described the sensor-embedded sock that provides the ability to track parameters such as of SpO_2 and HR and is worn while an infant is sleeping in the home setting, as well as shared normative data and usage statistics.

The OSS is designed to fit newborns to children up to 18 months of age (or up to 25 lbs. or 11.3 kg). The wireless sensor (pulse oximeter) is powered by a small rechargeable battery that sends acquired data via Bluetooth Low Energy (BLE) to the Base Station. The WiFi-enabled base station serves as the main notification system via visual and audible signals when changes in SpO_2 occur and/or the HR becomes too high or too low. The OSS smartphone application allows parents to remotely access readings of SpO_2 and heart rate for their infant. All data obtained from the newborn are preserved in the secure cloud-based database. The accuracy of the OSS has been tested against hospital-grade pulse oximeters as well as arterial blood gas samples per standard FDA guidance.

Findings from the OSS article revealed usage statistics among 47,495 newborns, of which about 15% were premature infants. Typical duration of monitor use was on average for 6 months, about 4.5 days per week, and around 9.9 hours per day (for 39,626 full-term and 7,869 premature infants). This contrasts with the average monitor use in healthy term newborns in the CHIME study by an order of magnitude (Table 1).

In addition to providing peace of mind, Owlet demonstrated, in over 200 parent-reported cases, the ability of the OSS to aid in the detection of a clinically-relevant event. This represents only those cases in which the family took the effort to contact Owlet and inform them of the episode. There is no way to know how many other infants benefited from being monitored that didn't notify the company.

Other reports describe the OSS helping diagnose an overlooked condition. The examples presented here have been verified by medical records and/or pediatrician confirmation. Supraventricular tachycardia (SVT), respiratory syncytial virus (RSV) infection, breathing disturbances (laryngomalacia), obstructed airways caused by unsafe sleep practices, congenital heart defects, and apnea have all been detected. Other reports by parents, (but unable to be substantiated with primary health care providers) were the detection of unrecognized seizures and alerts for impending sepsis. The following are examples of reported events by parents. Parental consent was obtained by Owlet for publication of the data and medical experience in this manuscript.

Case 1. Diagnosis of previously unknown abnormality (SVT).

The OSS issued a red notification for this six-week-old infant. The monitor was for a high heart rate (Figure 1). The infant was diagnosed with SVT event and was cardioverted and stabilized with medication. The baby was taken off SVT medications at 12 months of age without recurrence. The infant also had a family history of SVT. SVT is the most common arrhythmia in infants, usually presenting within the first year of life. The presentation of SVT in a neonate is frequently subtle.[12]

Case 2. Onset of monitor alarms prior to clinical illness (RSV).

Due to a RSV diagnosis, a five month-old infant's mother decided to use the OSS on the infant. The OSS issued multiple red notifications for low oxygen saturation levels (Figure 2). The mother of four was reluctant to take the infant to the emergency room (ER) because the infant showed no distress while sleeping; however,

Table 1. Average Monitor Use in CHIME Study and Owlet Observational Series*

	Healthy Term Newborns
Monitor Use in CHIME Study, *(total per infant)*	**N=306**
Mean monitor use, days	15.5
Mean monitor use, hours**	373
Monitor Use in Owlet Data Series*, ** *(total per infant)*	**N=39,626**
Mean monitor use, months	6
Mean monitor use, days	810
Mean monitor use, hours	1,782

** Adopted from the CHIME Study (Table 1), JAMA, 2001, Vol 285: 17, pp 2199-2207*
*** Derived from hours reported in the table by dividing to 24 hours*
**** M. Dangerfield et al. Global Pediatric Health, Vol 4, Dec 4, 2017*

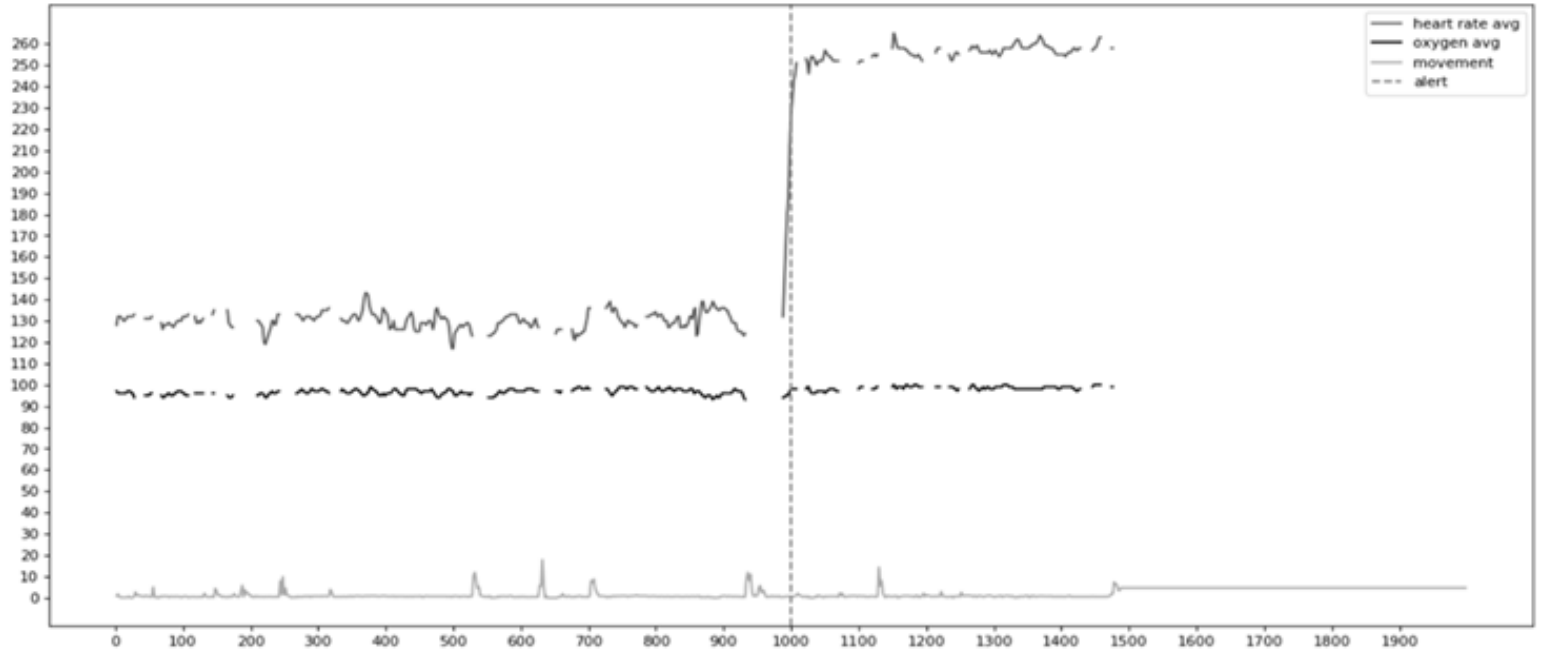

Figure 1

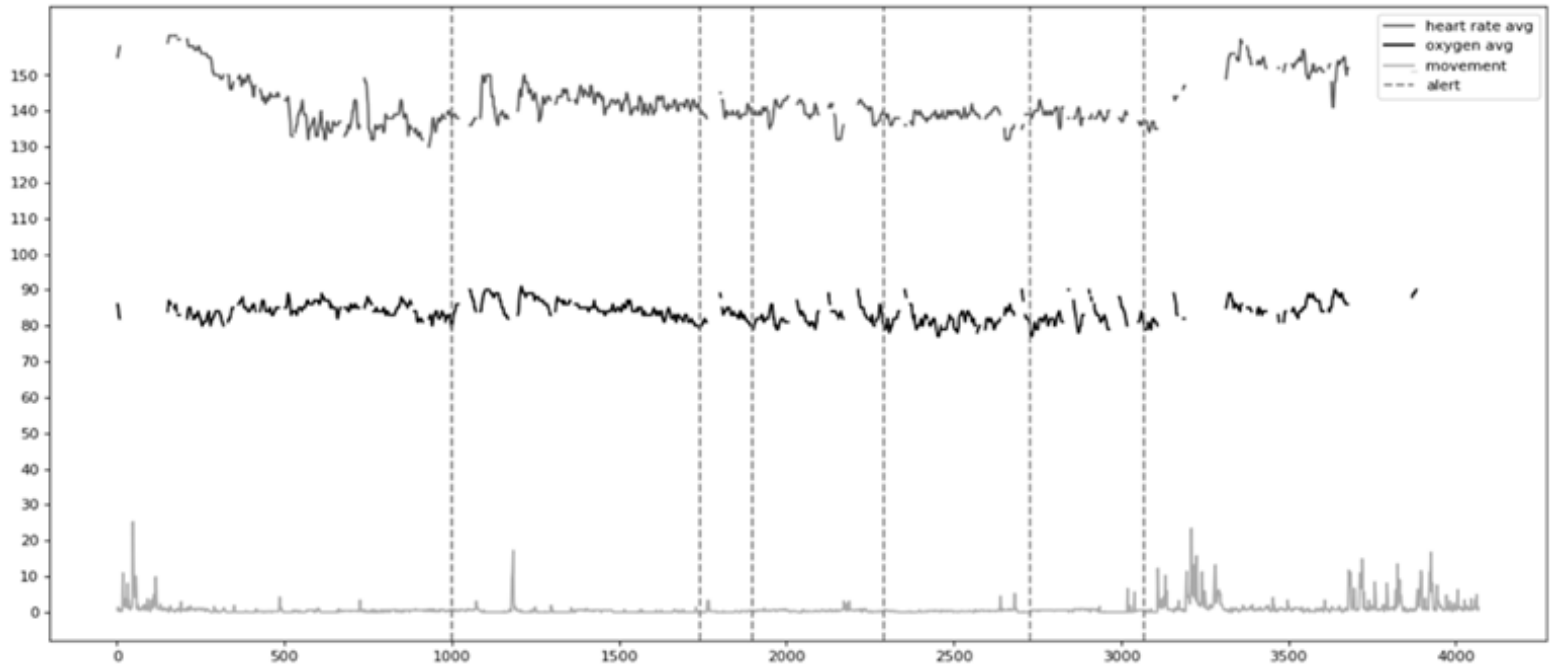

Figure 2

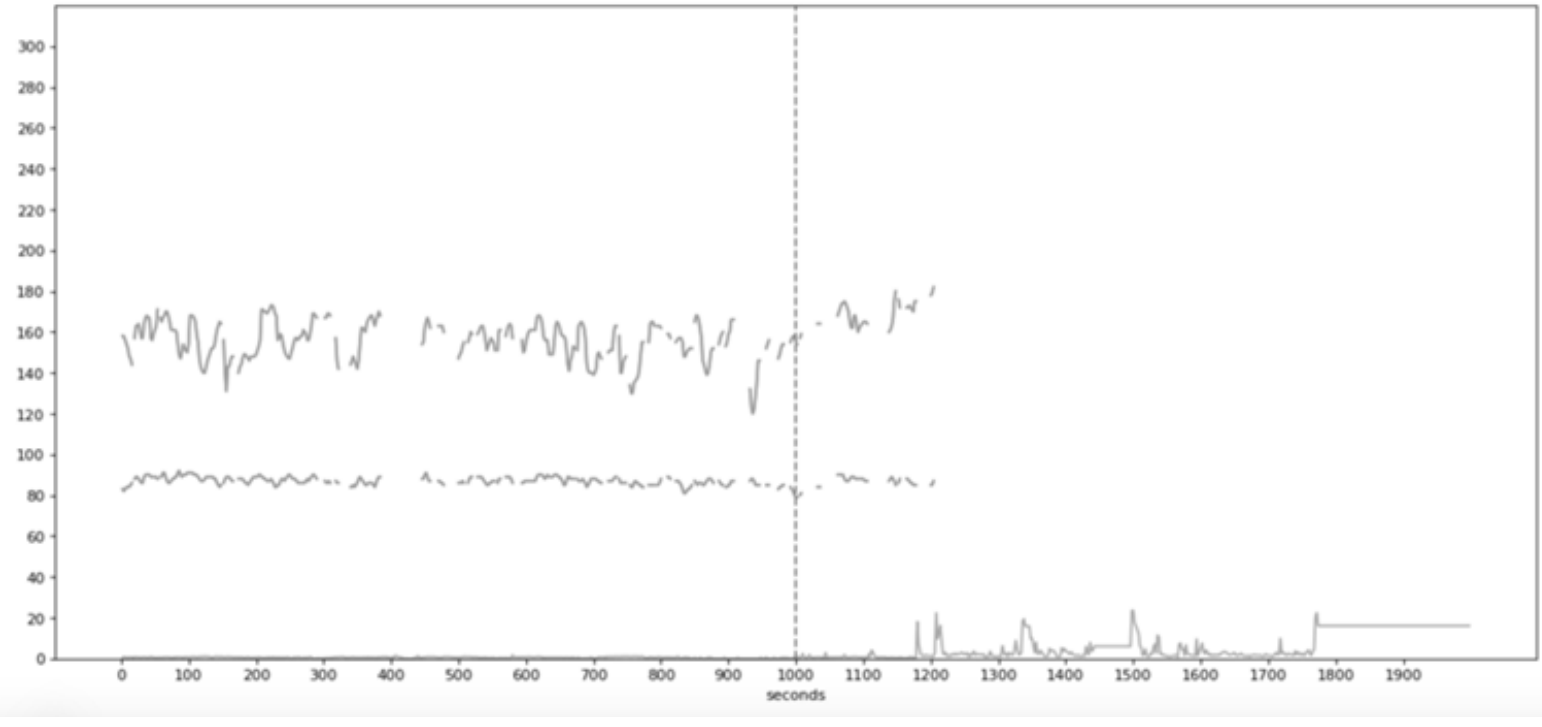

Figure 3

at the ER, the low oxygen readings were confirmed, and the infant was admitted for four days and given supplemental oxygen. Within one week of returning home, the infant's oxygen levels returned to normal baseline of 98-99% SpO_2.

RSV is very contagious, affecting most children younger than two years of age. In younger infants, RSV may manifest only as difficulty feeding, sleeping, or breathing, or irritability. Infants younger than six months of age may be hospitalized if they are experiencing difficulty breathing.[13]

"RSV is very contagious, affecting most children younger than two years of age. In younger infants, RSV may manifest only as difficulty feeding, sleeping, or breathing, or irritability."

Case 3. Early detection of sepsis.

The OSS delivered a red notification for an eight-week-old boy with an oxygen saturation level reading below 80% SpO_2. The infant was reported sleeping with no other symptoms when the OSS sounded a Red Alert (Figure 3). The mother reported the infant appeared pale and dusky. The infant's temperature was 99 0F. The mother contacted her infant's pediatrician office and shared the OSS data along with her observations. The mother was told to take the infant to the ER. Upon arriving to the ER, within a reported 15 minute-timespan, the infant's temperature increased to 102°F and was reported to have clinical sepsis and treated with antibiotic therapy for 10 days.

Early diagnosis and immediate intervention are paramount to prevent serious morbidity and mortality in neonates and infants with sepsis. A young infant is often incapable of demonstrating clinical evidence of illness, and even a "well-appearing" infant may have a bacterial or viral disease.[14]

Discussion

Although the initial reason for monitoring an infant at home was to prevent SIDS, the focus has changed from SIDS prevention to that of saving lives (whether it be due to SIDS or other cause of death) and "saving brain cells." In 2004, Carl Hunt published: "Cardiorespiratory Events Detected by Home Memory Monitoring and One-Year Neurodevelopmental Outcome"15 which concluded that: "Having 5+ conventional events (apnea and/or bradycardia detected on a home cardiorespiratory monitor) is associated with lower adjusted mean differences in MDI (Mental Developmental Index) scores in term and preterm infants." In the same year, an article appeared in the Journal of Perinatology titled: "Apnea Is Associated with Neurodevelopmental Impairment in Very Low Birth Weight Infants"16. That study concluded that "An increasing number of days that apnea was recorded during hospitalization was associated with a worse outcome. Among the potential explanations for this finding is the possibility that multiple recurrent hypoxic (apnea) and bradycardic spells may cause brain injury." The thought is that if we can interrupt prolonged events, we can possibly mitigate the adverse effect of the hypoxia that would ultimately develop in prolonged events. Although the American Academy of Pediatrics has taken the stance that monitors are not an effective way to reduce SIDS, they do note that "There are other groups of infants for whom use of a home cardiorespiratory monitor may be warranted, not because of an increased risk of SIDS, but because of other factors that increase the risk of sudden death. Home cardiorespiratory monitoring may be justified to allow rapid recognition of apnea, airway obstruction, respiratory failure".[17] The Owlet Smart Sock Monitor provides a relatively easy and inexpensive way of infant surveillance for such critical events. And, despite the criticism that home monitoring increases parental stress, 75% of parents who purchased an OSS system did so for "Peace of Mind" knowing that if their infant experienced an event in which SpO_2 dropped below 80% (whatever the initial cause) they would be notified and could respond appropriately.

As noted in that old song "When Everything Old Is New Again" the OSS touts anecdotal reports of monitoring that enabled detection of previously undiagnosed conditions, but with no double-blinded studies to support the claims. This is exactly what existed in 1986 when the NIH held a Consensus Development Conference to determine the effectiveness of home monitoring in reducing the incidence of SIDS. An examination was conducted of the scientific studies, published or unpublished, as they applied to the effectiveness of home monitoring when employed for infants at high risk for SIDS: infants who had an ALTE (Apparent Life-Threatening Event), subsequent siblings of a SIDS victim, and premature infants. This review failed to identify any "reports of scientifically designed studies of the effectiveness of home monitoring"[18] The panel also examined the annual SIDS rate and concluded that "evidence from several communities in which SIDS surveillance has been maintained for a decade or more indicates that annual SIDS rates vary from year to year but have not declined perceptibly since the introduction of home monitoring."[18] However, the panel's report and conclusion did not accurately reflect the status of scientific information available at the time. The data for the annual SIDS rate for the United States were published yearly in Pediatrics.[19-22] Contrary to the impression left in the Consensus Development Conference report, an examination of the annual death rates reveals a slow but progressive decrease in the incidence of SIDS (1.525 deaths per 1,000 live births in 1980 down to 1.405 deaths per 1,000 live births in 1986). There were actually a number of studies that collectively supported the conclusion that home monitoring programs, when employed for infants at risk for SIDS, were associated with a decreased incidence of SIDS,[3,4,23]. Unfortunately, none of the data supporting the use of monitors was obtained from randomized controlled clinical trials and therefore, they were dismissed. Thus, the conclusion of the expert panel and ultimately the position taken by the AAP was that home monitoring was not effective in reducing the incidence of SIDS.

We are now faced with a similar situation. With no support of any double-blinded studies, the manufacturer of the OSS reports a large number of parent-reported cases that lead to parental action

following OSS notification of an abnormality from baseline, and in effect, aided in either prevention of a critical event or helped diagnose an overlooked condition. However, given the number of anecdotal cases reported in the literature, one must remember the words written by David L. Sackett, the "father of evidence-based medicine" in the introduction to his book How to Practice and Teach Evidence-Based Medicine.[24] He stated that, "Evidence-based medicine is not restricted to randomized trials and meta-analyses." stating that "individual clinical expertise" (clinical observations/trials) are important and cannot be ignored.

"Unfortunately, none of the data supporting the use of monitors was obtained from randomized controlled clinical trials and therefore, they were dismissed. "

Conclusion:

Contemporary health monitoring systems represent tools that provide an early indication of changing patient status, thus allowing for quick and timely intervention.[11]. The Owlet Smart Sock has been shown to be an effective home monitor, yet it remains relatively inexpensive. The rapid and continuous rate of adoption of the OSS suggests excellent parental acceptance and extensive testing. It appears that the OSS has made significant advances in the world of home monitoring in that it is wireless and maintains information in the cloud, which can then be obtained immediately or at a later date. Perhaps the manufacturers could develop prospective randomized trials to finally convince the public and the AAP of the usefulness of home monitoring for aiding in the screening or early detection of the potentially preventable catastrophic events.

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FROM THE NATIONAL PERINATAL INFORMATION CENTER

Neonatal Special Care: 2017 Statistics and 5 Year Trends from the NPIC Perinatal Center Data Base

Janet H. Muri, MBA and Marilyn B. Escobedo, MD

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, patient safety organizations, insurers, and researchers to collect and interpret the data that drives better outcomes for mothers and newborns.

National Perinatal Information Center

Babies admitted to neonatal intensive care are costly. Costs to the family are the anxiety of illness, interruptions in family bonding and breastfeeding, travel if the higher level of care is removed from the birth hospital, difficulties in returning to work, and the financial strain of unreimbursed health costs.(In the composite metric, the Adverse Outcome Index (Neonatology Today June, 2018), admission of a term infant to an intensive level bed for more than a day without a specific identified condition, is considered an "adverse" event.) Hospitals, neonatologists, and nurses who provide care in NICUs are aware of these costs both to the family and the larger health care system. Proactive efforts are made to reduce costs, keeping neonates in hospital for a time only as long as necessary for lifesaving treatment.

Over the years of reporting on special care (NICU) utilization, the National Perinatal Information Center has seen the impact of providing peer comparison, benchmarking, as a powerful tool for clinicians to scrutinize their policies and guidelines around special care admissions. No longer is it acceptable to have a standing policy to admit all infants delivered by c-section to a special care bed for a minimum of 24 hours as was the case for one large regional hospital. On the other hand, readmissions due to inappropriate early discharge also must be avoided. Looking at the combined experience of the NPIC data base which includes nearly 10 % of the birth population nationally can be instructive for any NICU service.

In calendar year (CY) 2017, the NPIC data base profiled 343,728 newborns across 94 hospitals. 97.1 % percent of those were born at the reporting hospitals. The remaining 2.9% included babies that were transferred in immediately following delivery (presumably for a higher level of care), readmissions, and a small number of ER admissions or physician referrals.

Key Metrics from the NPIC Perinatal Center Data Base (PCDB)

CY 2017	
Special Care Admissions	**52,658**
Percent of total neonates	14.4%
Percent transferred from an acute care facility	4.0%
Percent ≤ 1500 grams (ALOS)	9.2% (48.6)
Percent 1500-2499 grams (ALOS)	28.3% (15.6)
Percent ≥ 2500 grams (ALOS)	53.7% (7.0)
Percent discharged to home with or without home health	85.2%
Percent died	1.2%
Complication rates:	
MAS for Inborns	1.4%
MAS for Transfers In	2.5%
IVH Grade III	.3%
IVH Grade IV	.4%
Infection (Septicemia/Bacteremia)	6.1%
RDS	18.7%
TTN	18.0%
NEC	.7%
Linked Mother/Infant Discharges	
Rate of infant special care admission for mother with specific condition/delivery type	
Hypertension	22.8%
Diabetes Mellitus	34.8%
Obesity	17.1%
Thyroid dysfunction	16.6%
Primary c-section ≥ 37 weeks	12.9%
Repeat c-section ≥ 37 weeks	8.0%
TRENDS 2013-2017	
Special Care Admissions (% of TTL neonates)	16.2% to 15.8%*
Special Care ALOS	15.5 to 15.0 days
Complications for neonates 500-1499 g	
Proportion of BPD to RDS	20.2% to 13.7%*
NEC	4.4% to 4.6%
IVH Grade III or IV	5.4% to 4.6%

**Significant Change*

In CY 2017, 14.4% percent of total newborns were admitted to a special care nursery area, whether to an intensive care or intermediate care bed. When NPIC isolated just those facilities that participated in the Perinatal Center Data Base for the previous five year period (2013-2017), the 2017 rate was 15.8%, significantly lower than the 16.2% for the same cohort of hospitals in 2013. The 2017 14.4% rate for the full cohort of hospitals suggests that the rate will continue to decline.

Ultimately, the goal is to keep infants out of special care nursery. Greater payor scrutiny is likely to drive some of the change as will the focus on quality of care. The challenge for many hospitals with special care units is to change their budget modeling from one that is revenue dependent on the NICU/NINT days of care to one that provides adequate support to continue providing the range and depth of services necessary to meet the special care demand but removes the incentive to over-utilize subspecialty services.

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Dr. Escobedo received her undergraduate education at Baylor University and her MD at Washington University in St. Louis. She completed her pediatric residency at St. Louis Children's Hospital and her neonatology fellowship at Vanderbilt University under Dr. Millie Stahlman. She started her academic career at Indiana University then moved to University of Texas at San Antonio where she was Division Chief for 23 years. In 2000, she accepted the Reba McEntire Endowed Chair in Neonatology at the University of Oklahoma where she was Division Chief, Director of all Neonatal Services for OU Medical Center until October 2017. She has been named Professor Emeritus University of Oklahoma.

Peer Reviewed

Case Report: Hepatic fibrosis from transient myeloproliferative disorder in a trisomy 21 newborn

Giang Truong, MD, Anita Patel, MD, Aprille Febre, MD

Abstract:

Transient myeloproliferative disorder (TMD), also known as transient abnormal myelopoiesis (TAM), is a condition that occurs perinatally in up to 10-15% of patients with trisomy 21 (T21).[1] Although transient in nature, the acute phase of clinical illness can be severe. While some recover quickly with only mild symptoms, many can develop multiorgan failure. Overall mortality of TMD is about 20%. If myeloproliferation happens antenatally, the fetus may develop hydrops and carry worse outcomes.[4] We are presenting a case of late premature infant with T21 who had evidence of TMD at the time of birth and progressed to end staged liver failure.

Case study:

A 34 week gestation female was born to a healthy 20 year-old prima gravida mother via Cesarean section due to non-reassuring fetal heart rate. She was prenatally diagnosed with T21 with an AV canal defect. Apgars were 2 and 7. Birth weight was 2900 grams.

On physical exam, she had typical Down syndrome facies, grade 3/6 systolic murmur and hepatomegaly. Initial laboratory tests showed severe leukocytosis consistent with transient myeloproliferative disorder and hepatic dysfunction. CBC showed WBC 88,000/μL, Hgb 14.9 g/dL, platetes 294 bil/L. Peripheral smear showed 25% segmented neutrophils, 16% blasts, 7% myelocytes/metamyelocytes and 1% promyelocytes, 36% lymphocytes and 15% monocytes. There were also increased anisopoikilocytosis, schistocytes, burr cells, ovalocytes and nucleated red blood cells. Complete metabolic panel showed total protein 3.4 g/dL, albumin 2 g/dL, AST 290 U/L, ALT 174 U/L, AP 366 U/L, total bilirubin 12.7 mg/dL and direct bilirubin 1.3 mg/dL. Prothrombin time (PT) 52 seconds, partial thromboplastin time (PTT) 80 seconds and INR 5.4.

The leukocytosis normalized after 3 days of life without chemotherapy; however, hepatic dysfunction persisted. Highest value for AST 292 U/L, ALT 415 U/L, total bilirubin 28.2 mg/dL and direct bilirubin 23.4 mg/dL at 4 weeks of life. She received multiple transfusions of fresh frozen plasma, cryoprecipitate and platelets and Vitamin K throughout her hospital course without resolution of coagulopathy. INR remained between 1.9-3.7, PT 19-36 seconds and PTT 32-119 seconds. Evaluation of hepatic dysfunction included hepatitis panel, TORCH infection, metabolic disorders, thyroid function, Progressive Familial Intrahepatic Cholestasis (PFIC) and Alagille Syndrome Sequencing Panel which all returned negative. Abdominal ultrasound showed coarse echotexture of liver with prominence of biliary radicles. She also had a hepatic vein thrombus which resolved without intervention.

At 1 month of life she developed necrotizing appendicitis and necrotizing enterocolitis. She underwent a laparotomy with appendectomy and Jackson-Pratt drain placement. Cultures grew Pseudomonas aeruginosa. She slowly developed worsening liver dysfunction leading to severe anasarca and respiratory failure. Infant was transitioned to comfort care and expired on day of life 67.

Autopsy report showed diffuse lobular and pericellular fibrosis of liver. Congestive hepatosplenomegaly without evidence of thrombus in main portal vein branches.

Discussion:

The case vignette represents a severe case of TMD. Management of severe TMD can be challenging. The overall survival at age 3 years in the 2011 COG study of postnatal TMD was 77% .[2] Mortality risk is increased in patients with severe liver dysfunction, severe hyperleukocytosis (white blood cell count >100,000/uL), early age at presentation, renal dysfunction, and of African American heritage.[1]

Liver fibrosis from TMD is less common. Miyauchi reported four unusual diffuse liver fibrosis without myelofibrosis. The authors suggested that unlike leukemia, TMD originates from the fetal liver.[3] It has been suggested that the first step in the development of TMD is disturbance of fetal hematopoiesis by trisomy 21 itself, starting as early as first trimester. Altered hepatic hematopoiesis leads to acquisition of mutations in transcription factor gene GATA1, a regulator of normal megakaryocyte and erythroid differentiation.[2] Since this process initiates during early embryonic development, it is not surprising that hepatic dysfunction is frequently observed in TMD. If hepatic dysfunction does not improve with remission of TMD, patients should be evaluated for hepatic fibrosis as it has an important prognostic role.

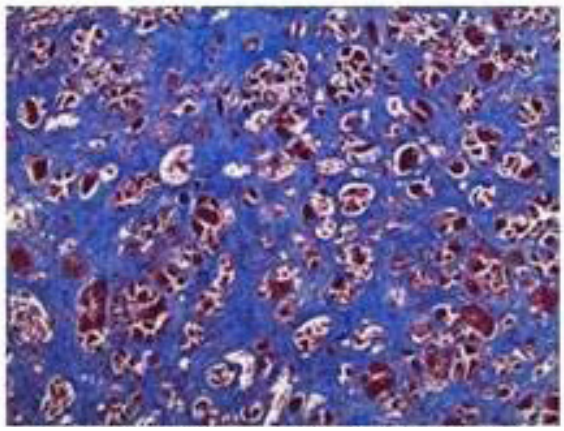

Figure 1: Autopsy image. Blue areas represent fibrous tissues.

The reported patient had evidence of possible fibrosis on abdominal ultrasound obtained on first day of life, reported as heterogeneous and coarse echotexture. Interestingly, multiple follow up ultrasound and Doppler studies showed normal liver size and echogenicity yet autopsy showed diffuse hepatic fibrosis, suggesting limitations of liver ultrasound in studying liver fibrosis in neonates. Autopsy did not show evidence of myelofibrosis, supporting the hypothesis that TMD is of liver origin.

Most patients with TMD (80%) need supportive care until TMD spontaneously resolves. The remaining 20% develop severe disease. They typically have white blood cell count greater than 100,000/uL with associated life threatening heart failure, respiratory failure and coagulopathy which might benefit from additional treatment with exchange transfusion, leukopheresis or cytarabine. Mortality is about 50% in these patients.[4]

Approximately 25% of those who survive TMD initially will develop acute MKL during the subsequent 4-5 years.[4]

Conclusion:

TMD affects up to 10% of patients with Down syndrome. The disease occurs during the perinatal period, with an overall mortality

rate of 20%. Patients who present with prenatal hydrops have very high mortality rate of up to 90%. Hepatic fibrosis is a rare complication and should be considered in the presence of persistent hepatic dysfunction.

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The authors have no conflicts to identify.

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Peer Reviewed

"A person's a person, no matter how small."[1]

Andrea Werner Insoft, LICSW, Perinatal Social Worker

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

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

National Perinatal Association
Educate. Advocate. Integrate.

There is no word in the English language to describe a person whose child has died. If your wife dies, you are a widower. If your husband dies, you are a widow. If your parents die, you are an orphan. All of these are tragic losses. But there is no word for a person whose child has died. That kind of death defies spoken language.

Our western society does not do a particularly good job of supporting people through death, grief and mourning. It seems that mourners are allowed 1-2 months and then it is back to the usual routine. Any mention of the deceased is done in whispers and behind closed doors. Nobody wants to upset the bereaved by mentioning his/her loved one. If this is how we handle the death of an adult, imagine how much more complicated it is to support someone after the death of a child.

When a child dies during pregnancy or shortly thereafter, it is hard to know how to mourn. If this is your experience, you may be wondering, "How do you grieve someone you have never met, or met only briefly?" And yet, the connection with that child started months earlier – at conception or even before. You have an image of what your child might look like. How you want to raise him or her. Piano lessons, baseball, chess. The options are endless, your future feels so bright and sure; and then, in a flash he or she is taken from you. You have to grieve your child and your dreams. Molly Fumia wrote, "Grief is a journey, often perilous and without clear direction, that must be taken. The experience of grieving cannot be ordered or categorized, hurried or controlled, pushed aside or ignored indefinitely. It is inevitable as breathing, as change, as love."

> ***"If your parents die, you are an orphan. All of these are tragic losses. But there is no word for a person whose child has died. "***

The choice of words in these situations can be important. People who have experienced the death of a fetus, infant or child have not "lost" a child. The child was not "lost" or left in the supermarket. Choosing the right words includes what to call someone who has lost a baby who was never born. As a Perinatal Social Worker, I consider every person who walks into my office, while grieving the sudden end of a pregnancy, to be a parent. It does not matter that they do not have a child living at home, tucked nicely into a bassinet with hand knitted blankets. They have loved a child just the same. They have wished for and dreamed of this child. They are a parent in every sense of the word. Each person's journey through this grief is unique. Some people may bristle at being called a parent after their pregnancy ended unexpectedly. When a client tells me that he or she is not a parent, I respect that feeling. I truly do. But, I don't believe it. A person becomes a parent the moment they become aware they have created a child who is growing in the womb.

As I write this article, it is a warm, somewhat muggy July evening. When I finish writing, I will turn on the television to "veg out" a bit. And what will I see? Commercials. Many, many commercials for back-to-school items. You know the ones; "It's the most wonderful time of the year." But for a couple who has suffered childbirth loss, the death of an older child, or infertility, this is far from the most wonderful time of the year. All the reminders of back-to-school shopping, sales and school necessities only reinforce the fact that there will be no shopping for the child who died, no new school year, no excitement about meeting new friends. If this is your experience or the experience of someone you know, some of the questions that may come up include, "How can I cope with the isolation of such grief? How can I put one foot in front of the other and take the steps necessary to get through my day? Here are some strategies many have found helpful.

- Turn off the television/radio. It is too much and can be overwhelming. You may have been on the road to recovery and hearing or seeing a particular commercial can send you right back. And that is the nature of grief. Healing is not a linear process. It is more a meandering path. Allow yourself to wander the path and look at everything you encounter. Also, please allow yourself to get off the path from time to time and take a break.
- Surround yourself with people who understand. Or, if they don't actually understand, at least they try. They are able to say things like, "Tell me what's up for you today." Or "Do you want to talk, walk, see a movie, get some coffee?"
- Realize that the goal is not to let go. I believe that the goal is to hold on. It is

only in the holding on and the belief that this child will always be a part of you that you can heal.

- Talk about your child. Use his or her name. He is real. She lived, if only for the briefest of moments. Your child touched you and has changed you.

- Embrace the ways in which you have been changed. Many clients tell me that they are so much softer around the edges. They are more compassionate. They are more comfortable reaching out to others. Those whose pregnancy ended often say that, had they known their pregnancy would end the way it did, they would still choose to have the experience. Mothers say they are grateful that they had the opportunity to experience carrying their child within their womb. Look for the changes you see in yourself and hold fast to them, for they exist because of your son or daughter.

- Find ways to honor your child and yourself as a parent. Plant a garden, name a star, send balloons up with messages for others to find, or volunteer for an organization that has meaning for you. I have found that many people find solace at the Children's Memorial Lighthouse in Edgartown, MA.

- Take comfort in others who have walked your path. Harold Kushner wrote beautifully about the importance of living after the death of a child. "We cannot choose. We can only try to cope. That is what one does with sorrow, tragedy, or with any misfortune. We do not try to explain it. We do not justify it by telling ourselves that we somehow deserve it. We do not even accept it. We survive it. We recognize its unfairness and defiantly choose to go on living. I now tell bereaved parents: you have inherited from your child all the years he or she never got to live… you inherited their unlived years. Those years are a precious legacy from them to you; use them well. Don't be afraid to enjoy life just because your loved one isn't there to enjoy it with you. Live their years along with your own and feel their presence as you do so."[2]

For those who work with or interact with grieving parents, please try to remember that it is not a wonderful time of the year for parents whose child has died and will not be going to school this year or whose infant (unborn or born) has died and will never go to school. Be as gentle and understanding as you can be.

In this season, as in all, I wish all grieving parents, peace, healing and hope.

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The author has no conflicts of interests to disclose.

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Alliance for Patient Access / About AfPA

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.

Founded in 2006, the Alliance for Patient Access 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.

To promote a better understanding of the benefits of patient access to approved therapies and appropriate clinical care, the Alliance for Patient Access sponsors physician working groups, health policy initiatives, workshops, conferences, stakeholder coalitions and the production of educational materials.

AfPA Physician Working Groups serve as a means to bring together physicians who share a common therapeutic interest or access challenge so that they might work collaboratively in the development of education resources that are used to promote informed policymaking.

Through Health Policy Workshops and Policy Dinners, AfPA provides physicians health policy briefings and advocacy training. The objective of these sessions is to equip policy-minded physicians with the knowledge, skills and advocacy tools necessary to successfully challenge restrictive health policies that serve to deny patient access to approved therapies and/or appropriate clinical care.

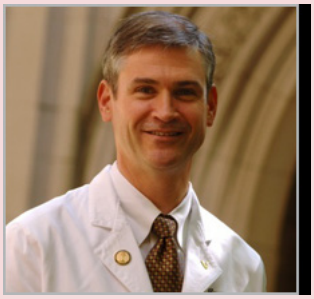
In keeping with its above stated mission, AfPA continues to offer the physician's perspective on global health policy issues implicating patient access and physician clinical decision making. To that end, AfPA sponsors the following programming:

- Conducting health policy and advocacy training workshops
- Sponsoring therapy specific physician working groups
- Providing media outlets with op-eds and comment
- Hosting physician advocate social media networks
- Organizing physician meetings with health policymakers
- Participating in policy conferences and stakeholder coalitions
- Producing on-line resources and video testimonials
- Offering comment and/or testimony on proposed regulations

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.

David Charles, M.D.

Nashville, Tennessee



The AfPA is led by David Charles, M.D., who is the Chief Medical Officer of the Vanderbilt University Clinical Neurosciences Institute. Dr. Charles is a national leader in Movement Disorders research. He took leave from his practice in 1998 and spent a year on the staff of U.S. Senator Bill Frist, where he served as a health policy advisor. Following this experience in Washington, Dr. Charles conducted Parkinson's disease research in France as a Fulbright Senior Scholar.

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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.

Graham's FOUNDATION
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Visit **www.GrahamsFoundation.org** to learn more.

Compiled and Reviewed by Mitchell Goldstein, MD Editor in Chief

Exclusive human milk-based diet for extremely premature infants

The benefit of an exclusively human milk diet.

sjacobs

August 8th, 2018 Focus On Family, Lafayette

LAFAYETTE, La. – Women's & Children's Hospital is the first facility in Acadiana to provide an exclusive human milk-based nutritional diet for the most critically ill, premature infants in the neonatal intensive care unit (NICU).

Premature infants require more protein, calcium and other minerals than what breast milk alone can supply. As a result, the American Academy of Pediatrics (AAP) recommends fortifying mother's milk or pasteurized donor milk with protein, minerals and vitamins to ensure optimal nutrient intake for preemies weighing less than 3 pounds 4 ounces (1,500g)1.

Women's & Children's Hospital, Acadiana's premier source for critically ill and premature infant care, for years has provided donor breast milk to premature babies whose mothers were unable to provide breast milk.

"The benefits of breast milk are so great. Human milk has important antibodies in addition to vitamins and fats that are important for premature infants," said Dr. Amy Zeringue, MEDNAX-affiliated neonatologist at Women's & Children's Hospital and the hospital's NICU medical director.

The NICU at Women's & Children's previously used cow's milk-based fortifier with breast milk to improve nutrition for premature infants. Since March, the NICU team has been able to take that one step further and fortify either mom's own milk or donor breast milk with human-milk based fortifier rather than the cow's milk-based fortifier. Prolacta Bioscience provides the human milk-based fortifier for Women's & Children's Hospital.

"Allowing us to provide an exclusive human milk diet to the most at risk and premature infants means that all of the carbohydrates, proteins and fats of our premature infants' diet are derived only from human milk," Dr. Zeringue added. "An exclusive human milk diet has many benefits, including decreasing sepsis and necrotizing enterocolitis, which can be a devastating disease of the intestines. Exclusive human milk diet also enables our tiniest babies to reach full feeds sooner, meaning these babies are requiring fewer days of intravenous nutrition."

NT

CDH (Congenital Diaphragmatic Hernia) International is looking for: Grant Writer / Fundraisers ((Originally posted in NT July, 2018)

An international search is under way..

Wake Forest, NC – 21 Jun

JOB OPPORTUNITY: Grant Writer / Fundraiser

23 year old international medical non-profit based locally in Wake Forest, NC is looking for a part-time grant writer / fundraiser.

Job duties would include; finding and applying for operating and research grants, follow up on all grant applications, networking with potential donors and grantors, planning and executing large annual gala, assisting with annual on-line telethon, overseeing fundraising committees, assisting volunteers planning smaller fundraisers through information and guidance and social media posts of fundraisers.

Office located in beautiful downtown Wake Forest. Required 3 days a week on a flexible schedule. Preferably in house but telecommunication considered for the right applicant. Base salary. Bonus compensation for goals met. No benefits at start. Quarterly goals set and expected to be met.

We have a great working environment and our goal is to make this position full-time by the end of the year (dependent upon success of employee to achieve funding goals).

CDH International works with children born with Congenital Diaphragmatic Hernia (CDH). CDH occurs when a baby's diaphragm fails to fully form, allowing organs to enter into the chest cavity and prevent lung growth. 50% of babies diagnosed with CDH do not survive. The cause is unknown. CDHi works with over 6400 families in 70 countries, provides research, support services and raises global awareness. Learn more at http://www.cdhi.org

This is an incredible opportunity to work with the largest CDH charity in the world and to directly help save the lives of 1000's of children.

No recruiters please.

Please send cover letter, CV and 2 references to dawn.ireland@cdhi.org

NT

American Academy of Pediatrics, Section on Advances in Therapeutics and Technology Membership Drive (Originally posted in NT June, 2018)

American Academy of Pediatrics (AAP), Section on Advances in Therapeutics and Technology (SOATT) announces a membership drive

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

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

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

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

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

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

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

NT

The 'secret sauce' for high-performing NICUs

Children's National Health System - Public Release: 23-Jul-2018 (from EurekALert!)

Leaders of neonatal intensive care units (NICUs) across the nation share the same play books as they strive to provide safe, high-quality medical and surgical care for vulnerable newborns. A growing number of quality collaborations share best practices and evidence-based guidelines across the nation in the hopes of replicating quality and safety success stories while minimizing harms.

Still, NICUs that use similar interventions in similar fashions often do not achieve identical results.

"This unexplained variability in outcomes between NICUs begs the question: What is the secret sauce? Why do some NICUs consistently outshine others in spite of the application of the same 'potentially best practices,' " the leaders of Children's award-winning NICU ask in an editorial published online July 12, 2018, by Archives of Disease in Childhood (ADC) - Fetal & Neonatal edition.

Quoting the literature, Lamia Soghier, M.D., Children's NICU medical director, and Billie Lou Short, M.D., chief of Children's Division of Neonatology, write that hospitals with strong performance-improvement programs share eight critical factors in common:

- Strong performance-improvement leadership at the administrative and executive levels
- Boards of Trustees who are actively involved and provide continuity in vision regardless of changes in senior hospital leadership

- An effective oversight structure that avoids duplicating efforts
- Expert performance-improvement staff who are trained in quality and safety and able to carry out projects successfully
- Physicians who are involved and held accountable
- Staff who are actively involved
- Effective use of data in decision-making
- Effective communication strategies for all stakeholders

The " 'secret sauce' may lie in establishing systems that promote the culture of quality and safety rather than waiting for a reduction in morbidity," write Drs. Soghier and Short.

For the second year running, Children's neonatology division ranked No. 1 among NICUs ranked by U.S. News & World Report. Despite challenges inherent in being a "busy level IV NICU in a free-standing children's hospital with a rapidly growing capacity, higher levels of complex patients, [the] presence of trainees on rounds and routine 3:1 and 2:1 staffing models," Children's NICU has continued to have the lowest rates of such objective quality measures as central line-associated bloodstream infections and unintended extubations, they write.

"We attribute our success to direct involvement of all levels of leadership in our unit in [performance improvement] PI initiatives, a dedicated local PI team, quality trained medical unit director, engagement of front-line staff in PI, the presence of local subject-matter experts, multidisciplinary diverse team both within the NICU and with other departments that bring an array of experiences and opinions and a supportive data infrastructure through local information technology, and use of the Children's Hospital Neonatal Database that allows benchmarking to other non-delivery NICUs, Drs. Soghier and Short write. "Our team finds motivation in solving local issues routine in our work, and leadership prioritises these issues and promotes engagement of front-line staff."

The commentary was a companion to "Using a Composite Morbidity Score and Cultural Survey to Explore Characteristics of High Proficiency Neonatal Intensive Care Units," also published by ADC Fetal & Neonatal.

NT

Fetal gene therapy prevents fatal neurodegenerative disease

A fatal neurodegenerative condition known as Gaucher disease can be prevented in mice following fetal gene therapy, finds a new study led by UCL, the KK Women's and Children's Hospital and National University Health System in Singapore. Public Release: 16-Jul-2018.

Fetal gene therapy prevents fatal neurodegenerative disease.

A fatal neurodegenerative condition known as Gaucher disease can be prevented in mice following fetal gene therapy, finds a new study led by UCL, the KK Women's and Children's Hospital and National University Health System in Singapore.

The study, published today in Nature Medicine, highlights the potential of fetal gene therapy to prevent and cure neonatal lethal neurodegenerative diseases in humans in utero.

Gaucher disease is an irreversible, inherited genetic metabolic disorder that results from not having enough glucocerebrosidase (GCase) - an enzyme that breaks down fatty chemicals called glucocerebrosides (GBA). Because the body cannot break down this chemical, the fat-laden Gaucher cells build up in the spleen, liver, bone marrow, and nervous system, causing bone disease, anaemia, fatigue, eye problems, seizures, and brain damage.

Mutations in the GBA gene, which encodes the GCase enzyme that is deficient in Gaucher disease, are also a risk factor for Parkinson's disease."Although the symptoms of some mild forms of Gaucher disease can be treated postnatally, more severe forms that cause early-onset, irreversible neurodegeneration are currently untreatable and are often fatal in infants. Being able to provide therapy at the earliest possible opportunity is vital in treating the brain which has a limited capacity to regenerate," explained senior author, Dr Ahad Rahim (UCL School of Pharmacy).

Scientists used a viral vector to deliver genetic material into the brains of fetal mice carrying neuropathic Gaucher disease, caused by mutations in GBA. Mice who received the gene therapy exhibited less brain degeneration and survived considerably longer than untreated mice.

"We found that the mice who received an injection of adeno-associated virus (AAV) vector were more able to break down fatty chemicals and re-express the gene encoding an enzyme that is deficient in Gaucher disease," said corresponding author, Dr Simon Waddingdon (UCL Institute for Women's Health).

"The mice who received the injection in utero, lived for up to at least 18 weeks after birth compared to 15 days in untreated mice and had no signs of neurodegeneration and were fertile and fully mobile. Neonatal intervention also rescued mice but less effectively."

Given the promising results shown in mice, the team from Singapore performed the test in non-human primates (NHP) at the early stages of pregnancy. This is the gestation when a clinical diagnosis of genetic conditions can be made, and when the immune system is more responsive to gene therapy. The research involved the use of NHPs due to their similarity to

humans in the development of the central nervous system, and other organs, allowing for an accurate model to be achieved in fetal gene transfer.

The team showed that the delivery of viral vectors to the developing brain is feasible using an established clinical approach that resulted in the distribution of the transgene to the developing brain.

"Macaques and humans share a very similar neurological, immunological and physiological developmental time-line in the womb, making them accurate models for pre-clinical investigations before clinical trials can proceed. We have used a clinically relevant method to deliver the GBA gene using AAV vectors to the brain efficiently.

"This new approach will bring hope, not only for Gaucher disease, but also for other inborn errors of metabolism that can potentially be treated using fetal gene therapy," said Associate Professor Jerry Chan, Senior Consultant, Department of Reproductive Medicine, KK Women's and Children's Hospital.

The team, which also involved scientists from King's College London, Imperial College London, the University of Oxford and an international team of researchers, are now engaged with Apollo Therapeutics in developing gene therapy for Gaucher disease.

Dan Brown, Chairman of the Gauchers Association added, "The Association has been involved as part of this project from a very early stage providing the initial grant to which allowed them to begin their research and are delighted to hear of the promising results published today."

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NT

Researchers find differences in infant morbidity-mortality rates in NYC hospitals

Blacks and Hispanic preterm infants more likely born at hospitals with higher morbidity-mortality rates

The Mount Sinai Hospital / Mount Sinai School of Medicine. Public Release: 2-Jan-2018 from EurekAlert!

Topic: Do differences in where very preterm infants are born contribute to racial and ethnic disparities in morbidity and mortality among blacks, whites, and Hispanics?

Corresponding Author: Elizabeth Howell, MD, Director of the Women's Health Institute, Icahn School of Medicine at Mount Sinai, New York, and other coauthors.

To watch a media release of Dr. Howell discussing her important research watch this youtube video: https://www.youtube.com/watch?v=afwxMJW9H5U&feature=youtu.be

Bottom Line: Poor performances at New York City hospitals where non-Hispanic black and Hispanic mothers deliver are an important and modifiable cause of racial disparities in neonatal deaths and severe complications.

Results: The risk-standardized morbidity-mortality rate was twice as high for preterm infants born in hospitals in the highest morbidity-mortality tertile versus those born in hospitals with the lowest morbidity-mortality.

Why the Research Is Interesting: Neonatal care has improved substantially over the past decade, yet racial and ethnic disparities in morbidity and mortality continue.

Who: Thirty-nine New York City hospitals were included in the study; participants included 7,177 "very preterm" infants born between 24 and 31 weeks.

When: The study examined data from 2010-2014.

What: The study measured the composite of mortality (neonatal or in-hospital up to a year) or severe morbidity.

How: A population-based retrospective study linked hospital discharge abstract and birth-certificate data sets. A risk-adjusted neonatal morbidity-mortality rate was generated for very preterm infants in each hospital. Hospitals were ranked using this measure, and differences in the distribution of black, Hispanic, and white very preterm births were assessed among the hospitals.

Study Conclusions: Blacks and Hispanic very preterm infants are more likely to be born at hospitals with higher risk-adjusted neonatal morbidity-mortality rates, and these differences contribute to excess morbidity and mortality among black and Hispanic infants. These differences in hospital of birth explained 39.9% of the black-white disparity and 29.5% of the Hispanic-white disparity in outcomes.

Paper Title: Differences in Morbidity and Mortality Rates in Black, White, and Hispanic Very Preterm Infants Among New York City Hospitals

Said Mount Sinai's Dr. Elizabeth Howell of the research:

It is very important to seriously think about the cause for the severe preterm babies' morbidities and how it will affect these children later on in life. When a baby is born prematurely, many complications can occur--they can have problems with their lungs, eyes, intestines, and brain, which will affect them later on in life. The real focus here is to try to reduce morbidity in preterm babies and give these kids a chance at a healthier life. This study shines light on the idea that we really need to focus on narrowing disparities when we think about quality improvement. Additionally, these disparities are not just local to New York City. We know that there are infant and neonatal racial and ethnic dis-

parities that have been longstanding in this country.

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To request a copy of the paper or to schedule an interview with Dr. Elizabeth Howell, please contact Mount Sinai's Director of Media and Public Affairs, Renatt Brodsky, at Renatt.Brodsky@mountsinai.org or at 212 241-9200.

NT

Vaginal progesterone reduces preterm birth and neonatal complications in women with a mid-trimester short cervix

"Results of a major international study released today in the American Journal of Obstetrics & Gynecology, coinciding with World Prematurity Day"

(Public Release: 17-Nov-2017 from ErekAlert!)

Philadelphia, November 17, 2017 - Prematurity is the main complication of pregnancy, and 15 million babies are born preterm worldwide each year.

Progesterone is a natural hormone produced by the ovaries in early pregnancy, and then later by the placenta. A decline in progesterone action is implicated as one of the causes of spontaneous preterm labor and delivery. Physicians worldwide have investigated in many studies whether vaginal progesterone administration to women with a mid-trimester sonographic short cervix reduces the rate of preterm birth.

Most major studies have been positive, until the publication of a study in February 2016. Now physicians and researchers have summarized the results of all studies in an article published today in the American Journal of Obstetrics & Gynecology, and found that when all available information is considered in an individual patient data meta-analysis -- the gold standard for summarizing clinical evidence -- the results are clear.

Vaginal progesterone reduces the rate of preterm birth at <28, <30, <32, <34, <35, and <36 weeks. Moreover, it reduces the frequency of complications of prematurity and the number of babies weighing less than 1500 grams (also called very low birth weight).

The authors also reviewed cost-effectiveness studies, which showed that measuring the uterine cervix with ultrasound in the mid-trimester of pregnancy and giving vaginal progesterone to those with a short cervix is cost-effective (this strategy has been estimated to save the U.S. healthcare system approximately $500 million dollars per year). The researchers also reviewed the evidence of studies, which showed that when this approach is implemented in clinical practice, it reduces the rate of preterm birth in the "real world."

"The findings of our meta-analysis of individual patient data, which includes all available trials, should reassure clinicians and professional/scientific organizations that vaginal progesterone is efficacious and safe for reducing preterm birth and neonatal morbidity and mortality in women with a sonographic short cervix," commented Roberto Romero, MD, DMedSci, Chief of the Perinatology Research Branch, NICHD/ NIH/ DHHS, and Kypros Nicolaides, MD, professor and head of Obstetrics and Gynecology, Kings College, London, and head of the Fetal Medicine Foundation. "In addition, recent evidence assessing the implementation of universal cervical length screening in women with a singleton gestation and treatment with vaginal progesterone to those with a short cervix suggests that this intervention could contribute to a reduction in the rate of preterm birth and associated neonatal morbidity and mortality in the United States."

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NT

Length of stay in neonatal ICU can affect behavior of premature babies

Research by Brazilian scientists shows that emotional development of children born preterm should be evaluated as much as physical growth and motor skills.

A study conducted by researchers at the University of São Paulo's Ribeirão Preto School of Medicine (FMRP-USP) in Brazil, with support from the Sao Paulo Research Foundation - FAPESP , indicates that length of stay in the ICU is the factor that best explains some preterm babies' behavioral problems relating to emotional regulation, regardless of the degree of prematurity and the presence of bronchopulmonary dysplasia and retinopathy of prematurity (ROP).

According to the research, whose results were published in the journal Early Human Development, neonatal pain and stressful experiences can impair both early and later child development.

"Moreover, the neonatal ICU environment includes other factors that impair child development, such as high levels of noise and luminosity, repetitive tactile stimuli, and maternal separation", the authors write.

The sample population consisted of 100 preterm babies aged 18-36 months with differing levels of prematurity. The aim of the study was to find out how neonatal and socio-demographic factors influence early-childhood temperament and behavior. All the infants were born in

FMRP-USP's hospital and enrolled in a multidisciplinary intervention program in its neonatal ICU. A number of tests were applied to evaluate temperament, stress and behavior, leading to scores for the relevant indicators.

Predictors of behavioural patterns in adulthood

The researchers' study of 100 preterm babies showed that longer stays in the neonatal ICU were a risk factor for behavioral problems.

According to Maria Beatriz Martins Linhares, an associate professor at FMRP-USP and principal investigator for the study, early childhood is a window of opportunity for regulation of the individual's lifelong development.

"Initial physiological and emotional regulation lays a foundation for several behavioral regulation processes," she said. "For this reason, it is important to recall that neonatal and childhood behavioral problems can point to the risk of behavioral problems in adulthood. These can potentially be prevented in the window between birth and about six years of age."

The self-regulation process is completed by the age of five, starting with emotional regulation up to the age of approximately 18 months and followed by behavioral regulation.

"Self-control emerges at around three or four years of age, with development of the executive attention system, which is relevant to effortful control, enhancing the potential for behavior regulation," the authors write.

Temperament changes during the course of development. With typical child development, therefore, "systems that are initially more reactive become increasingly regulated to the extent that the inhibition control systems directed toward fear and attention control become more mature", according to the authors.

Linhares sublinha que o desenvolvimento cognitivo envolve não só o crescimento físico e as habilidades - nas áreas de linguagem, locomoção, motora -, mas também os aspectos afetivos, sociais e comportamentais. "Portanto, da mesma forma que o desenvolvimento motor precisa ser acompanhado, os indicadores do comportamento e traços do temperamento também devem ser", disse Linhares.

Linhares stresses that cognitive development involves not only physical growth and language and motor skills; it also has affective, social and behavioral aspects. "Not only motor development but also behavioral indicators and temperamental traits should be monitored."

Recommendations of the study

According to the World Health Organization (WHO), Brazil has the world's tenth-highest rate of premature births.

However stressful a neonatal ICU may be for babies - considering some painful procedures which ensure weight gain and proper oxygenation for the infant (a premature baby's lungs are not yet fully formed) - they simply cannot survive without the support of the equipment and the multiprofessional team of specialists found there.

The researchers say this finding confirms the need for developmental care programs in ICUs to reduce stressful and painful experiences for newborn infants and also to enhance protective strategies during their early development.

Methodology

Mothers of these babies who met the criteria for inclusion, which included understanding the instrument used to report their infant's behavior, participated in interviews and responded to questionnaires.

Babies with grade 3 or 4 intracranial hemorrhage, limited mobility or cognitively impaired mothers were excluded. Thirty-six had bronchopulmonary dysplasia, and 63 had ROP, the most common diseases among preterm babies.

"Previous studies compared preterm and term babies, given that preterm babies

are more likely to display behavioral problems. Our study advances knowledge of development in preterm babies. There are risks, but if we identify the risks, we can plan strategies for protection, prevention and intervention to improve the development of these children," said Rafaela Guilherme Monte Cassiano, a psychologist and PhD researcher in FMRP-USP's Department of Neurosciences & Behavioral Sciences and one of the authors of the study.

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About São Paulo Research Foundation (FAPESP)

The São Paulo Research Foundation (FAPESP) is a public institution with the mission of supporting scientific research in all fields of knowledge by awarding scholarships, fellowships and grants to investigators linked with higher education and research institutions in the State of São Paulo, Brazil. FAPESP is aware that the very best research can only be done by working with the best researchers internationally. Therefore, it has established partnerships with funding agencies, higher education, private companies, and research organizations in other countries known for the quality of their research and has been encouraging scientists funded by its grants to further develop their international collaboration. For more information: http://www.fapesp.br/en.

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36th Annual Conference - Advances in Therapeutics and Technology

March 26-30, 2019

The Cliff Lodge and Spa in Snowbird, UT USA

Registration:

http://paclac.org/advances-in-care-conference/

Conference Description:

Educational and networking opportunities for healthcare professionals who provide care for pediatric patients including those in critical care environments with a focus on advances in therapeutics and technologies. Includes featured speakers, workshops and abstract presentations on research on advances in these areas.

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Special Panel Discussion:

Avoiding the Conflict, Working to Develop Better Relations with Industry. Colleen Kraft, MD, President, AAP with Don Null, MD and Mitchell Goldstein, MD

Agenda:

1. Rashmin Savant MD BPD New Concepts in Pathogenesis and Prevention
2. Cynthia Blanco MD Metabolic Disturbances of Prematurity When How and Who to Treat
3. Sinjo Hirose MD Fetal Surgery
4. Arun Pramanick, MD. Game Changers in Neonatal-Perinatal Medicine- A View Through a Retroscope
5. Don Null Persistent Pulmonary Hypertension in the Preterm Newborn Etiologies and Cardiopulmonary Management
6. Marty Keszler, MD New Modalities in High Frequency Ventilation
7. Mitchell Goldstein, MD. Rediscovering the Denominator
9. Steve Derdak, DO. Pediatric Origins of Adult Disease

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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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Peer Reviewed

The Challenge of Resuscitating Bilateral Congenital Diaphragmatic Hernias at Birth

Dr Sean Armstrong MB, BCh, BAO, MRCPI, Professor Adrienne Foran MSc, MD, MRCPI, Dr Ailbhe Tarrant MB, MSc, FFR RCSI, Dr Emma Doyle MRCOG, FRCPath

Case History:

A male infant was delivered by Elective Caesarian Section at 37 weeks gestation due to placenta previa and bilateral CDH. Two fetal MRIs had confirmed poor lung volume – at 25 weeks gestation; the Total Lung Volume (TLV) was 2.5 ml (expected TLV 26.15ml ± 9.15 ml); and at 33 weeks gestation, the TLV was 5.62 ml (expected TLV 72.29 ml ± 17.18 ml). Fetal Lung-to-Head Circumference Ratios (LHR) were not performed. Antenatal counselling warned of an extremely poor prognosis. (4.7, 2.2-10.2 95th CI).

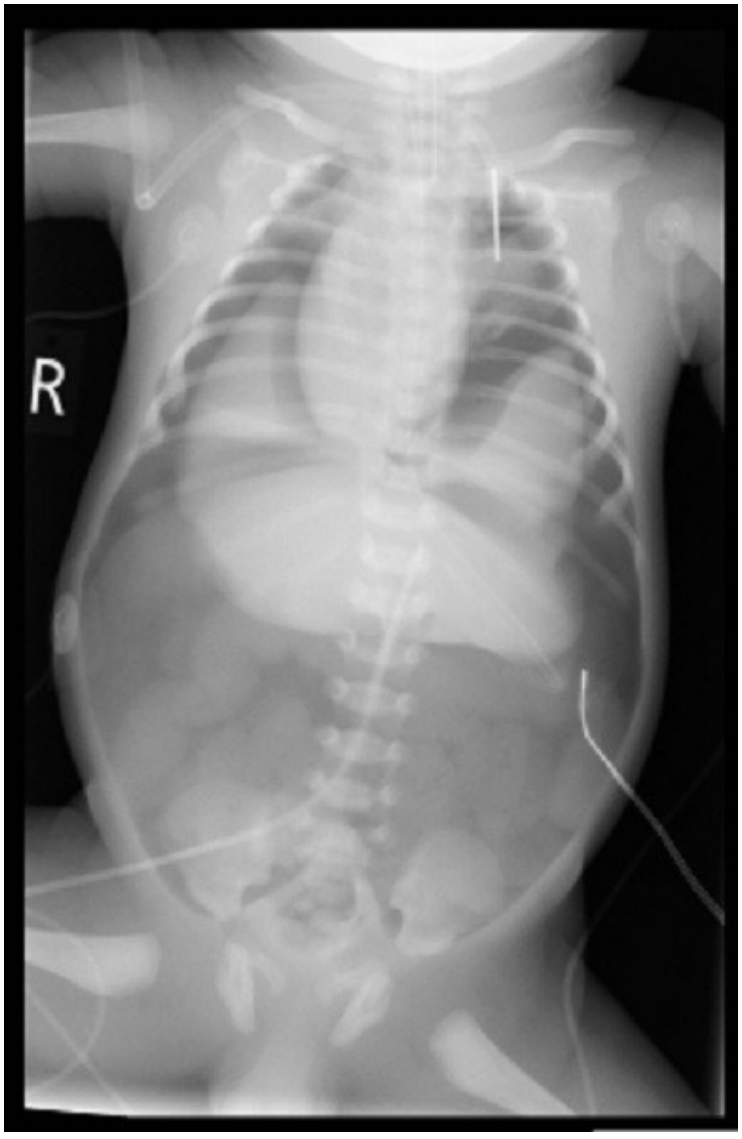

Figure 1: Plain Film imaging of the infant's chest and abdomen.

Here we present a radiological image displaying the herniation of bowel, liver and spleen into the thoracic cavity, and pneumoperitoneum and bilateral pneumothoraces from resuscitation attempts.

A full post-mortem revealed bilateral large posterolateral diaphragmatic hernias with ambiguous genitalia, an accessory spleen, a stenotic length of large bowel and a small muscular VSD. The lung volumes were 2.71g (right) and 1.66g (left) – both markedly hypoplastic (expected weight at 37 weeks gestation 38.7g ± 22.9g). Karyotype and CGH Microarray were normal.

Discussion:

Bilateral Congenital Diaphragmatic Hernia is a rare condition occurring in 1-2% of CDH cases. The mortality rate is estimated to be as high as 74%.[1] Associated anomalies occur in up to 95% of cases with bilateral CHD, often in midline structures as evidenced here.[2] A fetal TLV of <15% of expected gestational values correlates with poor outcomes.[3] A higher LHR expressed as a percentage of expected LHR for gestational age correlates with an increase in survival.[4]

Learning Outcomes:

- This case demonstrates the difficulty in surviving severe pulmonary hypoplasia as shown by the lung volumes – which were less than 10% of the expected volume for gestational age
- In attempting resuscitation, we may create more difficulties as evidenced by the large pneumothoraces – which hamper ventilation efforts.
- It is important to explain to expectant parents that subsequent anomalies may be discovered via post-mortem examination.
- Fetal Lung-to-Head Ratios should be performed on all CDH diagnoses to better predict survival.

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The authors have no conflicts to identify.

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23rd Annual PAC/LAC Conference
Quality of Life for Families

June 13, 2019

The California Endowment
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The Genetics Corner: A Genetics Consultation for Omphalocele

Robin Clark, MD

Case History:

This 36 week 6 day gestation SGA male was prenatally diagnosed with gastroschisis and symmetric IUGR. He was born at a local community hospital to a 27-year old primigravida mother by C-section for late decelerations after spontaneous rupture of membranes. The father was 42 years of age. The mother, who denied alcohol use, had prenatal care from 6 weeks. She had formerly smoked tobacco and reportedly used marijuana daily during the pregnancy. Her midgestation HgA1c was normal at 4.6%. Apgar scores were 8 and 9. BW was 2070 grams and HC was 31 cm, both <10th%ile.

When examined by the geneticist at 12 days of age, the baby had a low set, small, covered omphalocele, imperforate anus, bladder exstrophy and diastasis of the symphysis pubis. He passed feces through a prolapsed ileum. He had a duplicated phallus. He was alert and responsive, nondysmorphic with normal limbs. He had a normal neuro exam and no discernable anomalies of the spine.

Chromosome microarray was normal. Head US, abdominal US and spine US were normal without evidence of a tethered cord. A bladder was not visualized on the MRI of the pelvis and abdomen. Vertebrae were normal on AP and lateral views of the spine. The echocardiogram showed only a small PDA and possible PFO, shunting L>R.

Consultant's report:

This infant has cloacal exstrophy, also known as OEIS complex (Carey, et al., 1978), a rare condition that occurs in 1/35,000-50,000 with a near equal male to female ratio. This infant lacked only the spinal defects that would complete the acronym: Omphalocele, Exstrophy of the bladder, Imperforate anus and Spinal defects. The cause is unknown and no gene testing is available.

The cloaca is a temporary U-shaped cavity into which the genitourinary and gastrointestinal systems open early in embryonic life. It is present at about the 3rd- 7th weeks of gestation. The urorectal septum normally divides the cloaca and fuses with the cloacal membrane, separating the ventral urogenital sinus (the bladder) and the dorsal anorectal canal. Later, the anal membrane creates the lower third of the rectum. The cloacal membrane, which separates the cloaca from the outside, normally ruptures creating the orifices for the urinary and GI tracts. In OEIS complex, the urorectal septum and the cloacal membrane fail to form resulting in an open common orifice for both urinary and GI systems. The last third of the rectum does not form and the anus is imperforate. In this patient, the divided pegenital tissue formed a complete dupli-

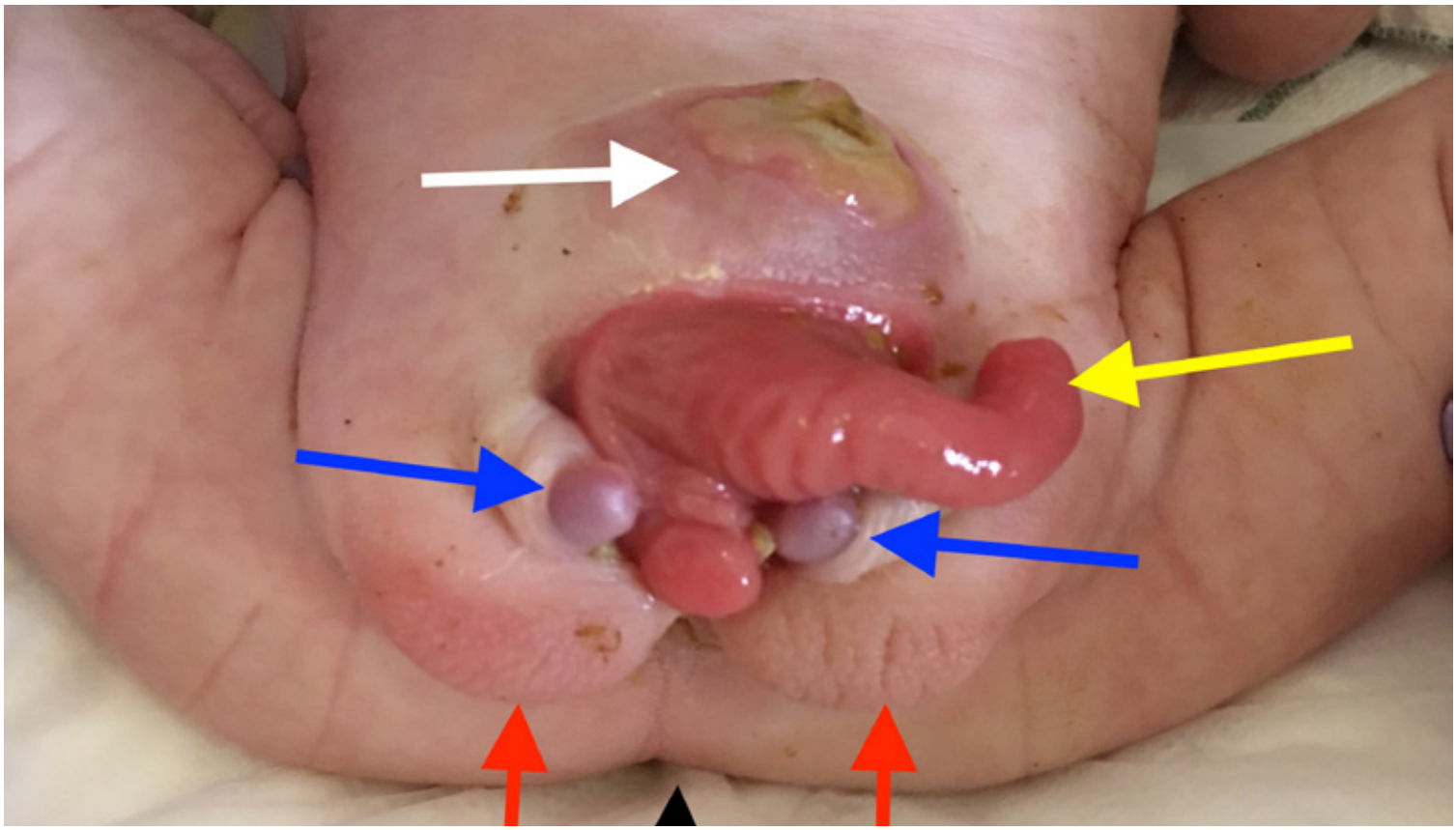

Figure 1: Caption for photo:

The anatomy of OEIS complex is illustrated in this male infant with almost all
White arrow – low lying omphalocele, closed
Blue arrows – duplicated phalluses, foreskin is absent, glans penis are exposed
Yellow arrow – terminal ileum prolapsed through the cecum (so-called "elephant trunk")
Red arrows – duplicated rugated scrotal sacs; each sac contains one palpable testis
Black arrow – imperforate anus

cated phallus, or diphallus.

Persistent cloaca is a related but distinct entity. It refers to a persistent, common cloacal cavity without exstrophy, usually with imperforate anus. In this condition, there is an excess of females. Most patients with persistent cloaca have additional structural anomalies. Renal anomalies occur in one half of cases. In some patients with OEIS, VATER association may be suspected based on the shared features of imperforate anus and spinal anomalies. In this case, the low lying ventral defect was misidentified on fetal ultrasound exam as a gastroschisis, which is also associated with low birth weight and preterm delivery.

OEIS complex is associated with low birth weight and preterm delivery. The most frequent associated anomaly is a congenital heart defect. Other associated anomalies of the GI, skeletal, spinal and GU systems are common.

The etiology for OEIS is unknown. Most cases occur sporadically with a low empiric recurrence risk. A single gene etiology has not been identified. Chromosome anomalies have been reported in individual cases of cloacal exstrophy, including Trisomy 18 and deletions of 1p36.13, 3q12.2-q13.2 and 9q24.1-qter. OEIS has been associated with monozygotic twins, conjoined twins, conception using clomiphene citrate and other fertility medications, in-vitro fertilization, intracytoplasmic sperm injection and other types of assisted reproductive technology (ART). Keppler-Noreuil and colleagues (2017) reviewed data from the National Birth Defects Prevention Study on 47 infants with cloacal exstrophy and found statistically significant associations with ART (cOR 3.7, 1.6-8.3, 95th CI), any reported x-ray (cOR 4.7, 2.2-10.2 95th CI), any reported maternal progesterone use (cOR 1.7, 0.2-6.4 95th CI) and maternal weight: underweight (BMI <18.5 kg/m^2; cOR 2.0, 0.5-6.1 95th CI) and obese (BMI>30 kg/m^2; cOR 1.5, 0.6-3.3 95th CI). There was a positive association with folate antagonist medications (cOR 2.3, 0.1-13.8 95th CI) but no association with cigarette smoking or recreational drug use.

Practical applications:

1. When a fetal ultrasound reveals a low lying abdominal wall defect and genital anatomy is unclear, consider OEIS, especially in twins or a conception with ART.
2. Because complications cannot always be anticipated, delivering at a community hospital followed by infant transport should be avoided because it can delay treatment for abdominal wall defects. All infants with prenatally diagnosed abdominal wall defects, regardless of type, should be delivered at an appropriate medical facility with subspecialists who can treat their anomalies.
3. The “elephant’s trunk” or prolapsed terminal ileum is a characteristic sign of OEIS anomaly.
4. When OEIS is suspected, test for chromosome anomalies, and examine the infant for spine defects, cardiac and renal anomalies.

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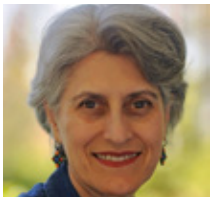

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NCfIH National Coalition for Infant Health

Protecting Access for Premature Infants through Age Two

A collaborative of professional, clinical, community health, and family support organizations improving the lives of premature infants and their families through education and advocacy.

The National Coalition for Infant Health advocates for:

- **Access to an exclusive human milk diet** for premature infants
- **Increased emotional support resources** for parents and caregivers suffering from PTSD/PPD
- **Access to RSV preventive treatment** for all premature infants as indicated on the FDA label
- **Clear, science-based nutrition guidelines** for pregnant and breastfeeding mothers
- **Safe, accurate medical devices** and products designed for the special needs of NICU patients

www.infanthealth.org

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

Understanding the Lack of Clinical Trials

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.

Dear Colleagues,

Newborns face an innovation desert when it comes to medical therapies. It's been nearly 20 years since a currently available drug was tested and approved specifically for the newborn population. The Coalition for Clinical Trials Awareness and the National Coalition for Infant Health co-hosted a Washington, DC policy panel discussion on May 1, 2018 to explore the issue. Conducted at the United States Capitol, the event invited participants to consider why newborns don't have more options – and what advocates, parents and policymakers can do about it.

CLINICAL TRIALS AWARENESS WEEK 2018

About 4 million babies are born each year in the United States, David Charles, MD, noted, yet 90 percent of the medications they take have never been tested for children and neonates. Calling the enrollment of children and infants in clinical trials "woefully inadequate," Dr. Charles emphasized that the body metabolizes and responds to medications differently at different ages. Dr. Charles conducts clinical research for Parkinson's patients at Vanderbilt University.

Andrew Rosenberg of the Newborn Health Initiative brought an economic perspective to the issue. About 200,000 newborns require admission to NICU for prematurity treatments, Rosenberg explained, costing about $26 billion each year. Prematurity is the leading cause of newborn mortality; the second leading cause of infant mortality.

There are also some conditions for which drugs are needed in neonates that don't occur in older children and adults, Rosenberg

Picture: Panelists discuss the need for improved access to pediatric clinical trials.

Coalition for Clinical Trial Awareness

noted, heightening the need for clinical trials conducted specifically for infants.

"Kids get hand-me-down clinical trials," explained Jaszianne Tolbert, MD, who specializes in pediatric hematology-oncology. Dr. Tolbert added, "We see kids as little adults." The reality is far different.

"Kids get hand-me-down clinical trials," explained Jaszianne Tolbert, MD, who specializes in pediatric hematology-oncology. Dr. Tolbert added, "We see kids as little adults." The reality is far different."

Dr. Tolbert illustrated the importance of clinical trials for newborns and children by telling the story of Bailey. Doctors said, "Love your daughter as much as you can," Dr. Tolbert explained. But after one month in a clinical trial, Bailey was in disease remission. Her mom thought the doctor was lying, Dr. Tolbert recalled, explaining, "She had never heard the words, 'Your daughter is cancer free.'"

Joe Murray of debra of America conveyed the experiences of his daughter, Ella, who was born with a rare genetic skin disorder known as epidermolysis bullosa. "We were told there was no hope," Murray recalled of his daughter's first month of life. Murray depended upon patient advocacy groups, online research and webinars to learn about the disease and to find clinical trial opportunities for his daughter.

Steps Forward

The panel's discussion arrived at three key components for changing the landscape for neonates and clinical trials.

1. Congressional Action

The Promoting Lifesaving New Therapies for Neonates Act (H.R. 2641) would provide incentives for industry to invest in the development of neonate-specific drugs.

1. Patient Narratives.

Joe Murray and Dr. Tolbert emphasized the power of storytelling in conveying the importance of clinical trials for neonates. "It doesn't have to be a magic wand," Murray explained, "It can start with one child, one story."

3. Public-Private Partnerships.

Industry-government collaborations can produce valuable research, panelists agreed. They can also play a critical role in heightening public awareness about the critical need for more treatments and clinical trials geared toward neonates.

Learn more about Clinical Trials Awareness Week 2018 at www.cctawareness.org.

Mitchell Goldstein, MD
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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.

TOP 10

RECOMMENDATIONS FOR THE PSYCHOSOCIAL SUPPORT OF NICU PARENTS

SUPPORT 4 NICU PARENTS

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

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

1 PROMOTE PARTICIPATION

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

Welcome!

2 LEAD IN DEVELOPMENTAL CARE

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

3 FACILITATE PEER SUPPORT

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

4 ADDRESS MENTAL HEALTH

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

5 SCREEN EARLY AND OFTEN

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

6 OFFER PALLIATIVE & BEREAVEMENT CARE

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

7 PLAN FOR THE TRANSITION HOME

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

8 FOLLOW UP

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

9 SUPPORT NICU CARE GIVERS

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

10 HELP US HEAL

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

SUPPORT4NICUPARENTS.ORG

New Moms Need Access to Screening & Treatment for POSTPARTUM DEPRESSION

1 IN **7** MOMS FACE POSTPARTUM DEPRESSION, *experiencing*

- Uncontrollable crying
- Disrupted sleep
- Anxiety
- Shifts in eating patterns
- Thoughts of harming self or baby
- Withdrawal from friends and family

15%

Yet only 15% receive treatment[1]

UNTREATED POSTPARTUM DEPRESSION CAN IMPACT:

- *Mother's health*
- *Baby's sleeping, eating, and behavior as he or she grows*[2]
- *Ability to care for a baby and siblings*

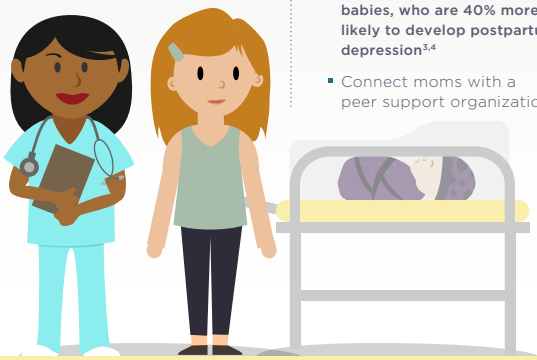
TO HELP **MOTHERS FACING POSTPARTUM DEPRESSION**

POLICYMAKERS CAN:

- Fund Screening Efforts
- Protect Access to Treatment

HOSPITALS CAN:

- Train health care professionals to provide psychosocial support to families... **especially those with preterm babies, who are 40% more likely to develop postpartum depression**[3,4]
- Connect moms with a peer support organization



NCfIH National Coalition for Infant Health

Protecting Access for Premature Infants through Age Two

www.infanthealth.org

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

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

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

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

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

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

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

15%

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

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

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

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

LOS ENCARGADOS DE FORMULAR POLÍTICAS PUEDEN:

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

LOS HOSPITALES PUEDEN:

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

NCfIH National Coalition for Infant Health

Protecting Access for Premature Infants through Age Two

www.infanthealth.org

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

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

Peer Reviewed

Please Don't Present Another Newborn with Non immune Hydrops Fetalis!

Joseph R. Hageman, MD

Our pediatric chairman was Dr. Jim Stockman in 1986 and as you may know, he is an incredibly gifted teacher. He would travel from Children's Memorial Hospital to do morning report at Evanston Hospital each week where the residents would present interesting cases. It just so happened that when I was on service in the NICU, we had a "run" on fetuses and newborns with Non-Immune Hydrops Fetalis (NIHF). As anyone who cares for these babies in the delivery room knows, they can be a real challenge to resuscitate after they are disconnected from the placenta that had provided gas exchange and maintained fetal stability. After delivery, those with severe hydrops require vigorous attention to the ABC's and frequently require bilateral chest tubes to drain significant pleural effusions, sometimes a pericardial catheter to drain a pericardial effusion to relieve cardiac tamponade and allow venous return and possibly some drainage of peritoneal fluid accumulation to allow the chest to expand more effectively (1).

A few days prior to one of Dr. Stockman's visit, I recall managing one of these babies in the delivery room. When I went to perform the endotracheal intubation, I had to press on the baby's face to spread the edema out so I could open his mouth to insert the laryngoscope blade. Dr. Jeff Sroka, who is now a general pediatrician, was my senior resident and placed most of the other tubes and the umbilical line with help from our excellent neonatal intensive care unit nurses. We were able to stabilize the baby and admit him to our Infant Special Care Unit at Evanston Hospital. I believe that this was our 6th infant with NIHF in a short period and in a few cases we had an etiology (one infection with parvovirus, 2 babies with fetal arrhythmia) but the remaining were unknown or Idiopathic Non Immune Hydrops.

As our discussions at morning report had not been too enlightening about these babies, I thought this would be an ideal case for Dr. Stockman. A few days prior to his arrival, I let him know about the case so he could prepare a discussion. He informed me, in a polite way, that he was not very excited about this particular case of yet another NIHF. I was also very fortunate that Dr. Stockman, as editor of the Yearbook of Pediatrics, asked me to write a review of a recent article by Holzgreve and colleagues describing the antenatal evaluation and management of 50 infants with NIHF (1). With the assistance of my Chairman, Dr. David Ingall, I completed this review and felt so honored. In this review, we had had 15 infants with NIHF since 1980. The etiology of the NIHF included: "idiopathic 27%, fetal-fetal and fetal-maternal transfusion 25%, and cardiac, infectious, pulmonary and metabolic 25% each (1)". Our mortality rate in this group of infants was 87% (1).

I tell this story to link this blog presentation to a number of recent, clinically relevant articles in NeoReviews which include the discussion of NIHF secondary to fetal arrhythmia, pulmonary malformation, cardiac mass and hemoglobinopathies (3-6). I highly recommend these articles to you as you will be consulted by your maternal fetal medicine colleagues to help with the discussion of these fetuses for management and discussion with their families. The article by Shainker et al. describes a fetus with an intracardiac rhabdomyoma which was discovered after concern for a fetal arrhythmia. This paper is particularly relevant as both of these mechanisms may result in the development of NIHF (5). I also recommend a comprehensive article in NeoReviews by Murphy (1). Although it was published in 2004, I think you will find it helpful clinically for preparation for resuscitation at the time of their delivery of infants with NIHF. Interestingly, 30 years later, after reading each of these articles, the good news is we are better prepared as the diagnosis of NIHF is being made earlier and the etiologies are being better characterized compared to what was presented in 1986.

Addendum from Dr. Stockman:

On reading a draft of this blog on NIHF, I was taken back to the mid 1980's and the reason why, as co-editor with Dr Frank Oski of the Year Book of Pediatrics, I had asked Dr Joe Hageman if he would prepare a commentary for the Year Book based on the report of Holgreve et al who in 1984 summarized experiences with 50 cases of NIHF. Evanston Hospital, where Joe was an attending at the time, had had a run on newborns with NIHF and I thought that hospital's experience with the disorder would provide additional understandings on this complex entity. Interestingly, the Holgreve report contained a table listing 14 categories of 92 different disorders that were known to be associated with NIHF. If one fast forwards more than three decades, that list of etiologies has not changed very much at all.

As all roads, it is said, once lead to Rome, its likely that NIHF is not a discrete disorder, rather, merely a final common pathophysiologic pathway for scores upon scores of disease entities that find a weak point in the way the fetus normally maintains proper fluid balance. Identify that weak point and part of the problem will be solved. In the meantime, Dr Hageman is correct in this blog when he notes that we need to continue to identify NIHF as early as possible and then manage the underlying disorders associated with it…which, by the way, is exactly what he wrote in his Year Book of Pediatrics commentary in 1986! Meanwhile, our understanding of NIHF remains fuzzy, which is a reminder of the story of the Hubbell telescope that was initially sending images of space that were fuzzy… until it was determined that the universe is, in fact, quite a bit fuzzy.

-JAS III

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1. *Murphy JH. Non Immune Hydrops Fetalis. NeoReviews. 2004; 5(1):e5-e14.*
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May begin with a brief case summary or example.

Summarize the pearl for emphasis.

No more than 7 references.

Please send your submissions to:

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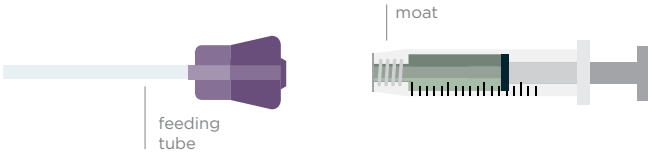
A new tubing design meant to eliminate tubing misconnections has introduced new challenges for the NICU population. Pediatric providers must deliver medication in small volumes to tiny patients with high levels of accuracy. The new tubing design, known as ENFit®, could present dosing accuracy and workflow challenges.



DOSING ACCURACY

- The moat, or area around the syringe barrel, is difficult to clear. Medication can hide there, inadvertently increasing the delivered dose when the syringe and feeding tube are connected; patients may receive extra medication.

INFECTION RISK

- The moat design can increase risk for infection if residual breast milk or formula remains in the moat and transfers to the feeding tube.

WORKFLOW ISSUES

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Letters to the Editor

To the Editor (via email),

From: Philip Spiller <pspiller@verizon.net>

Subject: Letter to the Editor

Date: Sunday 8/12/2018 0752

Letter to the Editor,

Dr. Goldstein,

Dr. Mitchell Goldstein's letter to colleagues ("Fish Consumption for Pregnant Women," July 2018) performed an important service for medical professionals who advise pregnant women and mothers by accurately summarizing the state of the science relating to fish consumption during pregnancy. Dr. Goldstein clearly described how, in addition to health benefits to the mother, fish intake has been repeatedly associated with improved child development scores. As Dr. Goldstein pointed out, fish are a unique source of omega-3 fatty acids that promote a baby's brain development plus they contain other important vitamins and minerals.

Dr. Goldstein's letter is both necessary and urgent. As he pointed out, advice to pregnant women issued by FDA and EPA in 2017 may perpetuate rather than clear up confusion on both the safety and nutritional importance of fish consumption during pregnancy, with the unintended consequence of increasing the number of pregnant women who err on the side of eating too little fish rather than too much. This possibility has raised concerns in the medical, scientific, and public health communities. In certain key respects, the FDA/EPA advice does not match either FDA's own 9 year study on the effects of fish consumption on fetal neurodevelopment that Dr. Goldstein cited [in the spirit of full disclosure I was senior manager and a co-author of that study], or a similar study conducted by the Food and Agriculture Organization of the United Nations together with the World Health Organization (FAO/WHO), or the Dietary Guidelines for Americans 2015, or the science as Dr. Goldstein summarized in his letter. Key discrepancies include:

- There is no mention in the FDA/EPA advice (actually an implied rejection) that fish consumption during pregnancy can benefit brain development -- the critical and unique benefit that fish have to offer as Dr. Goldstein's letter pointed out. A "viewpoint" published in the July issue of JAMA Pediatrics ("Fish Consumption During Pregnancy An Opportunity, Not a Risk") stressed this same point [again, full disclosure: I was one of three authors].

- There is a strong inference in the FDA/EPA advice that 2-3 servings per week of most fish represents a dividing line between safe and unsafe. By contrast, FDA's study found that 2-3 servings is within an optimum range of consumption at which benefits to brain development are at their peak. The FAO/WHO study made a similar finding. The results of those two studies closely align.

- There is an implication in the FDA/EPA advice that two of the fish consumption categories in the advice represent significant differences in risk, e.g, that "good" fish are 2-3x riskier than "best" fish. Neither the FDA nor the FAO/WHO study, nor any empirical data support this inference. The risk for all these fish from methylmercury is low at and beyond normal levels of consumption. As Dr. Goldstein alluded, the most meaningful differences between and among fish in these categories is the size of the benefit to brain development when eaten optimally. Had the categories focused on size of benefit, a number of fish in the "good" category would have been in the "best" category and a number of fish in the "best" category would have been in the "good" category.

- There is no mention in the FDA/EPA advice of the recommendation in the Dietary Guidelines for Americans (actually, an implied rejection of that recommendation) that pregnant women should eat at least some fish that are higher in omega-3 fatty acids. This is a critically important recommendation for reasons Dr. Goldstein addressed.

It is imperative that Dr. Goldstein's letter receive wide distribution among medical practitioners who counsel their pregnant patients. It should form the basis of advice that they provide.

Philip Spiller
Retired
Former Director
Office of Seafood
Food and Drug Administration

Dear Mr. Spiller

Thank you for your comments. The National Coalition for Infant Health has made a serious commitment to improve communica-

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

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

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tion regarding health challenges faced by mothers during pregnancy. Perhaps one of the most important is for these moms to received correct information regarding seafood consumption during pregnancy. The positive effects on brain development must be emphasized to ensure optimal potential especially for those at high risk for disparity.

In so far as distribution, by design, Neonatology Today is free to all, and open access extends to all of our submissions. The July, 2018 issue was accessed on-line over 100,000 times to date. We welcome links to our website and redistribution of our monthly PDF.

Sincerely,

Mitchell Goldstein, MD
Editor in Chief

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Erratum (Neonatology Today July, 2018)

Neonatology Today regrets that the initial title for "The Morgan Leary Vaughan Fund and NEC Unplugged: Meeting Overview" was incorrect. Early PDF's downloaded from the website are affected by this erratum. A corrected copy of the manuscript may be downloaded from www.neonatologytoday.net.

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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.

This month's selection (see the next page) features a drawing (3 of 3 in a series) that Dr. Vasquez produced for the cover of the 2008 National Perinatal Association Annual Meeting brochure. The meeting focused on the topic of "The Spectrum of Violence in Perinatal & Neonatal Care: Reducing the Risks." In this graphic,the "violence of neonatal care" is highlighted. For neonatologists, this is routine, but for parents, even appropriate care has violent aspects as we apply invasive techniques to improve a baby's chance of survival.

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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, email 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 JAMA 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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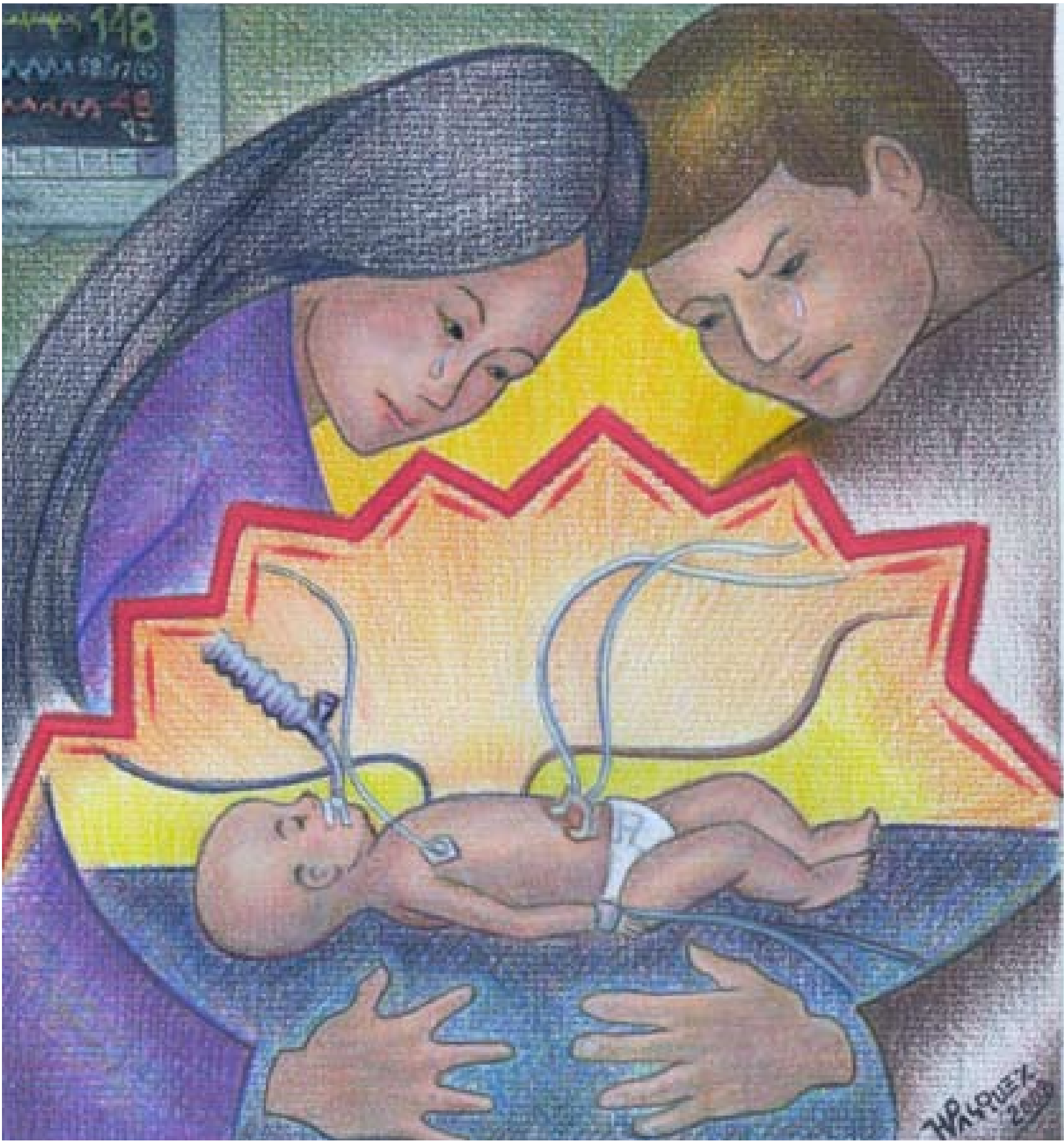
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