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News and Information for BC/BE Neonatologists and Perinatologists

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IN THIS ISSUE

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Neonatology Today (NT) is a monthly newsletter for Neonatologists and Perinatologists that provides timely news and information regarding the care of newborns and the diagnosis and treatment of premature and/or sick infants.

Upcoming Meetings
See wesite for addtional meetings

AAP District VIII Section on Perinatal Pediatrics 35th Annual Evidence-based Neonatology Conference
July 14-17, 2011; Portland, OR USA
http://www.d8neonatalconference.org/

35th Annual Conference- Miami Neonatology 2011 and One Day Workshop, "Advances in Respiratory Care"
October 26-29, 2011; Miami Beach,, FL USA
http://neonatology.med.miami.edu/conference

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A Cold Front is Sweeping Across the Sunshine State: Regionalization of Induced Hypothermia for Neonatal Hypoxia-Ischemia

By Craig B. Sussman, MD; David Auerbach, MD; Hilton Bernstein, MD; Young Byun, MD; Danilo Escoto, MD; Robert Garrison,MD; Mark Hudak, MD; Lewis Otero, MD; Richard Sheridan, MD; Rajan Wadhawan, MD; Lewis P. Rubin, MD, David J. Burchfield, MD; and Michael D. Weiss, MD

Background

Data from four multicenter trials[1-4] indicates that hypothermia is effective in diminishing brain injury in some neonates with moderate to severe hypoxic-ischemic encephalopathy (HIE). Currently, hypothermia is emerging as a standard of care for certain neonates with HIE. Meta-analysis suggests the therapy may prevent long-term neurologic deficits in one neonate for every 8 treated.[5] Since hypothermia does not help every neonate with HIE, the search for therapies to use in combination with hypothermia is currently a robust area of basic science research.[6,7] As these therapies become available in the future, the need for multicenter trials exists because a single center does not have the capacity to enroll an adequate sample size to generate meaningful clinical results. Multicenter trials are slow to initiate because of variations in the hypothermia protocols among centers, as well as the variability in supportive care. These impediments were the driving force for the creation of the Florida Neonatal Neurologic Network.

Backbone for Regionalization: The Florida Neonatal Neurologic Network Model

The Florida Neonatal Neurologic Network (FN^3) is designed to emulate the Children's Oncology Group (COG) model, but utilizes centers in a close geographic proximity with a long-term focus and commitment to improving the outcomes of neonates with HIE. The network is in the final planning phases. It will take advantage of the geographical proximity of the sites such that study meetings and site visits can be done inexpensively with limited travel (Figure 1). The cornerstone of the network will be a centralized patient registry which is a mandatory infrastructure for clinical trials focused on neonatal brain injury. We plan for registry data entry of demographic data, maternal information, birth history and clinical course, including long-term developmental evaluations. This structure is very similar to the multicenter trial design and the work accomplished by the COG. Our State network will also plan to capture neuroimaging and EEG results, by importing and archiving the actual studies into the registry. Serum samples will also be collected and stored forming a biologic repository for biomarker discovery utilizing proteomics, metobolomics and genomics (Figure 2). In addition, the network will serve as an educational hub with the ability to rapidly disseminate new technologies and therapies, either for study or clinical therapy, to the network sites. The dissemination will be accom-

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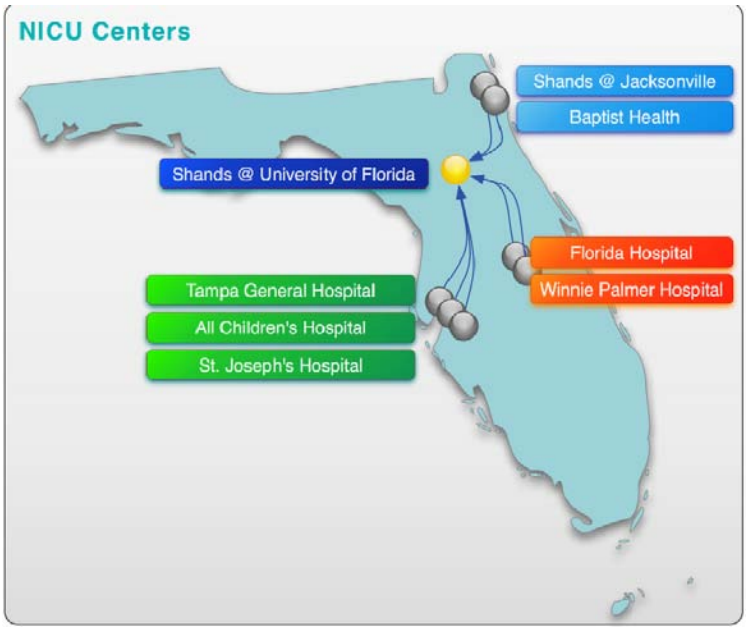

Figure 1. Tentative members of the First Tier of the Florida Neonatal Neurologic Network are shown graphically.

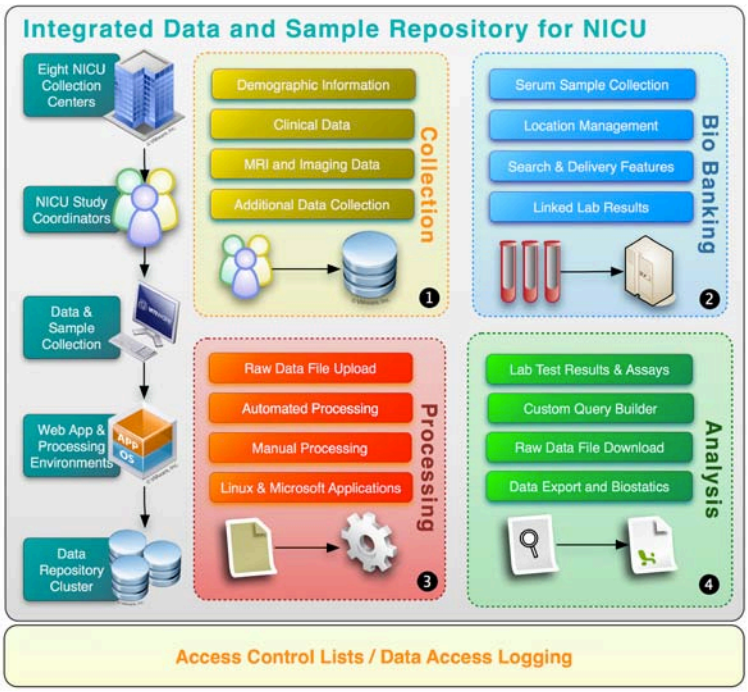

Figure 2. The proposed workflow process for the Florida Neonatal Neurologic Network is shown.

plished via a web-based portal which will feature educational information easily accessible by each of the participating centers. Finally, the network will review the data quarterly and publish a quality improvement newsletter which will be distributed throughout the network. The network is currently in the final planning phase with the inaugural meeting of the first tier sites to occur on June 8th, 2011.

The formation of the network will occur in a tiered design. North-Central Florida institutions will comprise the First Tier (Figure 1) and will tentatively consist of Level III NICUs in North-Central Florida including: Gainesville (Shands-UF), Tampa (Tampa General Hospital-USF, St. Joseph's Hospital), Jacksonville (Shands at Jacksonville and Baptist-Wolfson Children's Hospital), St. Petersburg (All Children's Hospital), and Orlando (Florida Hospital and Winnie Palmer Hospital). We have chosen these centers as First Tier sites due to their geographic proximity and volume of patients. Currently all of the above programs are in the final planning stages of starting a hypothermia program or have programs. Shands-UF will serve as the network hub and is centrally located within 2-3 hours of all the other centers. The initial objective with the First Tier sites is to explore smooth data transmission within the network and validate simplicity of serum shipping between institutions. Once accomplished and identified hurdles overcome, the Second Tier will enroll centers throughout the remainder of Florida.

Regionalization of Hypothermia

A major goal of the network is to ensure that every neonate in the state of Florida with HIE is in close proximity to a center which is capable of induced hypothermia therapy. To accomplish this goal, Shands-UF has been actively assisting major NICUs in North-Central Florida with the creation of their hypothermia programs. These centers are larger Level III facilities which will serve as local hubs for neonates from smaller centers and/or nurseries in each of these centers catchment areas. This model will essentially create cooling zones in each of the regions around the first tier participants.

The successful development of hypothermia programs at all major Level III NICUs in North-Central Florida has enabled infants in these regions access to cooling therapy. However, smaller facilities and nurseries needed to be educated about such therapy before they can be utilized. If a smaller nursery or hospital was unfamiliar with an innovative treatment or unaware of its availability, referrals or transfers for the therapy will not be employed efficiently. To resolve this educational deficit, the "Freeze Warning" program is being created. The Freeze Warning is an educational poster with critical information that will be distributed to smaller centers that provide newborn care. Information included in the Freeze Warning will consist of general guidelines for hypothermia therapy, hypothermia inclusion criteria, initial clinical steps for care of neonates who are hypothermia candidates, and the contact information for their regional hypothermia centers. Using this model, all infants with HIE born at referring centers will be identified as potential cooling candidates rapidly, passive cooling can be initiated, the hypothermia center or centers in their region would be contacted promptly, and transport with consultation can be arranged without detrimental delays.

Within Florida there are smaller Level III NICUs which provide quality care for the high-risk neonate but do not encounter enough infants with HIE to justify the initiation of a hypothermia program. These centers are often remote from larger Level III regional hypothermia programs and, therefore, transport times may be lengthy (3 hours each way). In these circumstances, Shands-UF is testing a more intricate regional approach that will provide state-of-the-art care for these infants that have suffered brain injury at the remote facilities. These centers have been provided with medical outreach programs, given by network members, on the basics of hypothermia and the early management of infants with HIE. These NICUs will obtain a cooling device to initiate active, controlled hypothermia while establishing contact with their regional hypothermia center. The unit selected must be very simple to use since the remote facility will have a low patient volume and staff expertise by experience will not be possible. The Criticool™ (Southampton, PA) is such a device. The device is simple to use and regulates the core temperature very efficiently.[8] If active induced hypothermia is initiated at these remote sites then active induced hypothermia should be maintained during transport (see below).

The above methods are the foundation of providing safe, successful and effective hypothermia to all neonates in North-Central Florida. This design, along with the education provided, will facilitate quality neonatal

care, and serve as the framework for FN[3]'s future endeavors.

Active Hypothermia During Transport

Prompt initiation of hypothermia is critical and must occur within six hours of birth. This six hour window is easily achieved when infants are born in a tertiary care center with all the necessary active cooling equipment and personnel. However, infants born at hospitals not able to provide this level of care require transport to a NICU offering hypothermia therapy.

Passive cooling during neonatal transport involves withholding external heat sources, while active cooling involves using gel packs to achieve target temperatures.[1,9] Neither of these methods provides a continuous feedback temperature loop. As a result, keeping the temperature within a target range is difficult, and babies often arrive at the tertiary NICU with temperatures outside of the target range. Both passive cooling and active cooling with gel packs[8] can cause this overcooling. Overcooling has the potential to increase serious side effects associated with cooling, such as arrhythmias, electrolyte abnormalities, thrombocytopenia, and coagulopathies.[10,11]

The CritiCool™ is a microprocessor-controlled temperature management unit manufactured by MTRE. The system uses a control algorithm which monitors skin and core temperature to make adjustments to the circulating water temperature to maintain the patient's core temperature at a target of 33.5^{0}C. Although not specifically designed for transports, the device is small enough to use on transports.

Shands-UF recently reported the first use of a servo-controlled cooling device during multiple modes of transport- ambulance, fixed wing aircraft, and helicopter (Figure 3).[12] The ability to safely and consistently transport hypothermic infants is a major advancement in the field of neuroprotection for HIE and allows for our above proposed remote center model. With this model, the adverse effects of severe hypothermia may be minimized; neonates falling outside of the critical six-hour window and delays in the initiation of hypothermia may be avoided in instances of lengthy or delayed transports. To illustrate the practical points of transporting with active hypothermia, the following helicopter transport case is presented.

Transport Case

Baby M was a 38-week EGA neonate born with negative serologies, and a birthweight of 3.1 kg to an A+, 23 YO mother. . Rupture of membranes occurred 16 hours prior to delivery. Delivery occurred via emergent C-section for a non-reassuring trace. Apgars were 0^1,3^5,4^{10},5^{15}. The neonate required chest compressions and one dose of epinephrine. Upon

Figure 3. The configuration for transport in helicopter at Shands-UF is shown. The CritiCool™ unit is placed behind the pilot's seat and secured.

arrival to the referring NICU, the neonate was placed on conventional mechanical ventilation with a PIP 20, PEEP 5, rate 40, and 100% oxygen. The initial arterial blood gas was: pH-7.0, pCO2-27, paO2-168, BD (-24). The neonate was placed on Dopamine at 5mcg/kg/min due to hypotension. Upon arrival, the transport team placed the rectal probe for the CritiCool™ and placed the neonate on the cooling wrap. Upon being placed in the helicopter, the neonate was actively cooled. The flight time was approximately 43 minutes from the referring center to Shands-UF. The temperature data for the transport was captured by the CritiCool™ using the Clinilogger™ data capture device (Figure 4). Upon arrival to Shands-UF, the cooling wrap was clamped. Once in the NICU, the cooling wrap was re-hooked to the CritiCool™ and active cooling restarted. The neonate's hospital course was significant for anuria, coagulopathy, and refractory seizures for 24 hours. She was initially started on Phenobarbital with no response. Keppra was added with good control obtained on continuous video EEG monitoring. Her MRI at 7 days of life showed normal appearance of the brain on standard imaging sequences. The MR spectroscopy did, however, demonstrate an elevated lactate peak in the left thalamus. The neonate was discharged on day of life 13 on Keppra with close developmental follow-up.

Lessons Learned

Based on our experience transporting with the CritiCool™, we have learned several practical lessons.[12] First, the device weighs around 70 lbs when completely filled with water.[12] Therefore, it is not practical for the transport team members to move the device from the fixed wing aircraft or helicopter once secured. Second, an alternative temperature monitoring method must be used during long transfers between the facility and fixed wing aircraft or helicopter (if it cannot land close to the referring center) to avoid temperature fluctuations associated with passive cooling.[12] Originally, we placed the neonate on the cooling wrap and placed the rectal and skin probes used by the

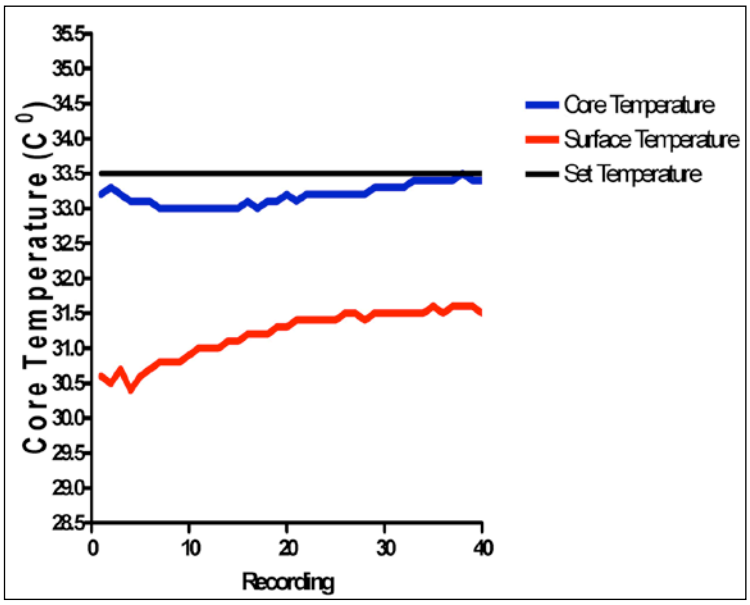

Figure 4. The temperature data for the transport was captured by the CritiCool™ using the Clinilogger™ data capture device which captures core and surface temperature readings once a minute. The set temperature for the CritiCool™ is shown as a solid black line. The core temperature is shown as a blue line and the surface temperature as a red line. The recording times are graphed in minutes.

CritiCool™ before transfer to the transport incubator and this procedure works well for the ambulance and helicopter which involve short transports from the referring NICU to the transport vehicle. Once inside the vehicle, the neonate is ready for active hypothermia using the CritiCool™. However, during fixed wing air and helicopter transports, ground transport times from a referring NICU to the airport can approach 30 minutes. To accurately monitor the patient temperature during these long ground transports back to the aircraft, we place the neonate on the wrap, place a separate continuous rectal probe monitor, and provide passive cooling en route to the transport vehicle. If the neonate's temperature is below 33.5°C, the incubator is turned on to 0.5°C above the neonate's current temperature. Upon arrival to the aircraft the rectal probe is then replaced with the rectal probe for the CritiCool™ and active hypothermia is begun.

The Future….

In an effort to facilitate a research environment with minimal clinical confounding variables, members of the First Tier will meet (June 8th, 2011) and discuss a common hypothermia protocol with standardized entry criteria, lab sampling and monitoring protocols. In addition, the first tier facilities will explore systemic supportive care protocols which include target values for blood pressure, blood gases, fluid therapy, target glucose values and antiepileptic medications. The protocols will serve as a common therapeutic management, establishing a "standard of care" which will allow future therapies to be added to hypothermia while minimizing confounding variables between sites. Further, this will allow the FN^3 to efficiently integrate novel diagnostic tools and therapies into the network for evaluation as they arise. To facilitate such a pipeline, the network will include a basic science component consisting of the major academic research centers in Florida. FN^3's harmonious collaboration between basic and clinical science will allow for straightforward translations to clinical trials with novel future treatments such as stem cell therapy.

After the successful implementation within the Tier 1 sites, Tier 2 will be rolled out to other NICUs in Florida. As FN^3 moves forward in a methodical, stepwise fashion, we envision our collaborative network providing hope and promise for neonates with HIE. The unique conceptual network structure will allow for future grant applications aimed at conducting clinical trials utilizing various neuroprotective treatment regimens combined with hypothermia. In the future, the data obtained from the network registry will be utilized to create an internet-based scoring system to predict outcomes in neonates with HIE in the State of Florida and the serum samples obtained for the biobank will be analyzed using metabolomic and proteomic approaches coupled with specific protein such as phosphorylated axonal neurofilament heavy chain (pNF-H) and ubiquitin C-terminal hydrolase 1 (UCHL1).[13] This information may foster the development of powerful point-of-care biomarkers to predict the pattern of brain injury, prognostic information, and response to therapy. We will also be in a position to one day seek gene-specific risks to add to the prediction model. Combining these clinical and bench-top endeavors, treatment regimens may be refined in the future towards individualized, brain-specific care. Each neonate may be categorized based on their clinical presentation, biomarker results, the pattern of neurologic injury and genotype with a resultant individual, unique regimen designed to improve their outcome.

FN^3 is being developed in a systematic manner, from a variety of scientific contributors, with the ability to have a significant impact in the field of neonatal brain injury. The network's distinctive characteristic of combining state-of-the-art basic science with elite medical institutions within a close geographic proximity is the ideal recipe for success and represents the next evolution of the network design. *Combining hope with excellence*, the mission of FN^3, from regionalization of hypothermia and beyond, to provide the highest level of care for all infants devastated by HIE both within Florida and worldwide. (Note: for more information, please visit www.hopefn3.org).

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River Oaks Hospital: Improving NICU Clinical Workflow Through Perinatal Electronic Documentation System

By Katie Hughes-Crocker, RN

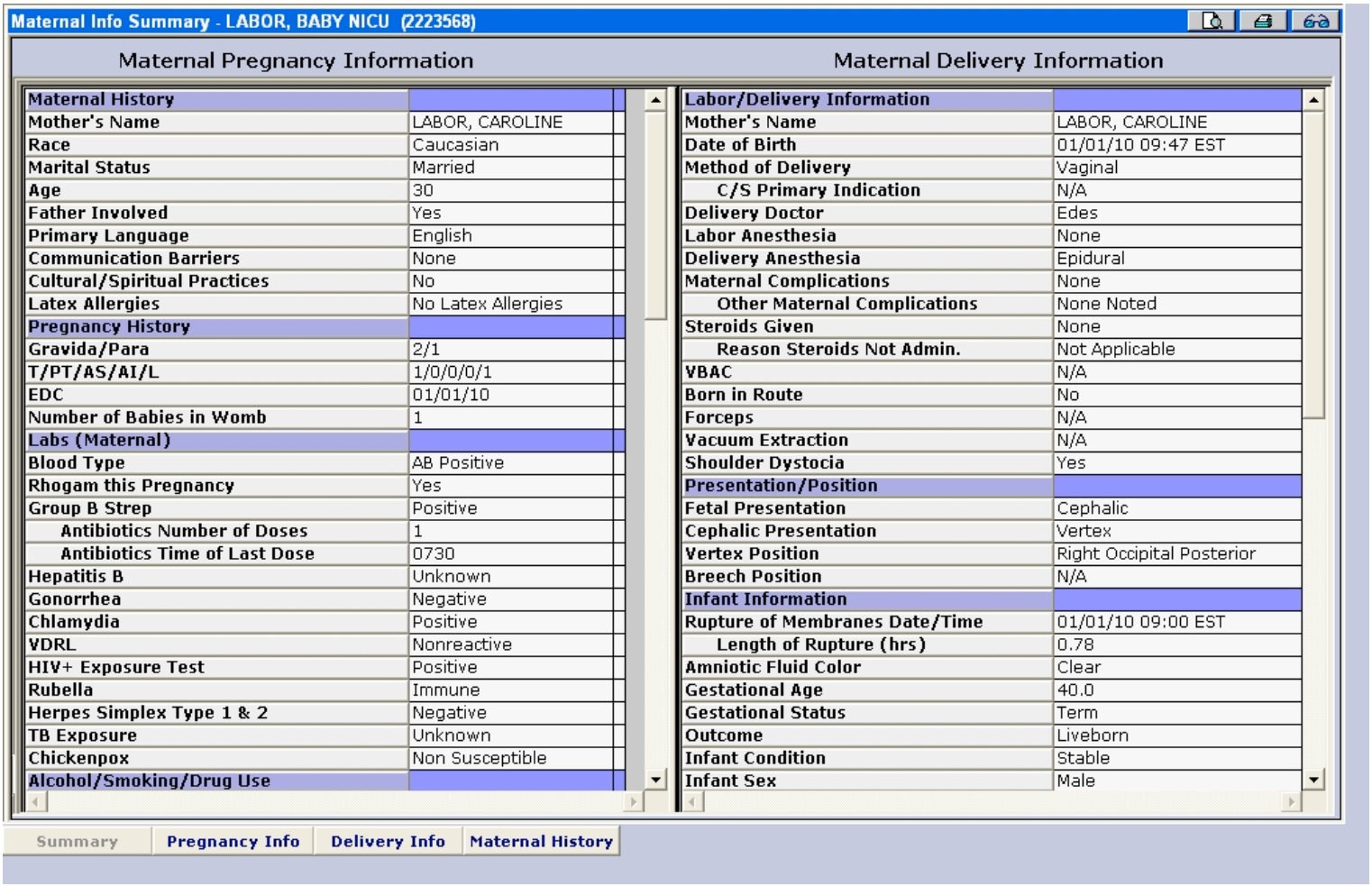
River Oaks Hospital in Flowood, Mississippi handles more than 1,900 deliveries annually in its Labor & Delivery and Post-Partum units. In addition, the Level IIIB Neonatal Intensive Care Unit (NICU) at River Oaks is designated as the area's "Center of Excellence" and referral center for all infants weighing less than 1,000 grams. Given the complexity of care required for this fragile patient population, it was critical for the hospital to implement a robust clinical information system, which would provide clinicians with access to complete, up-to-date records for both mother and baby throughout the continuum of care across multiple units.

Transitioning from Paper Charting to Electronic Documentation

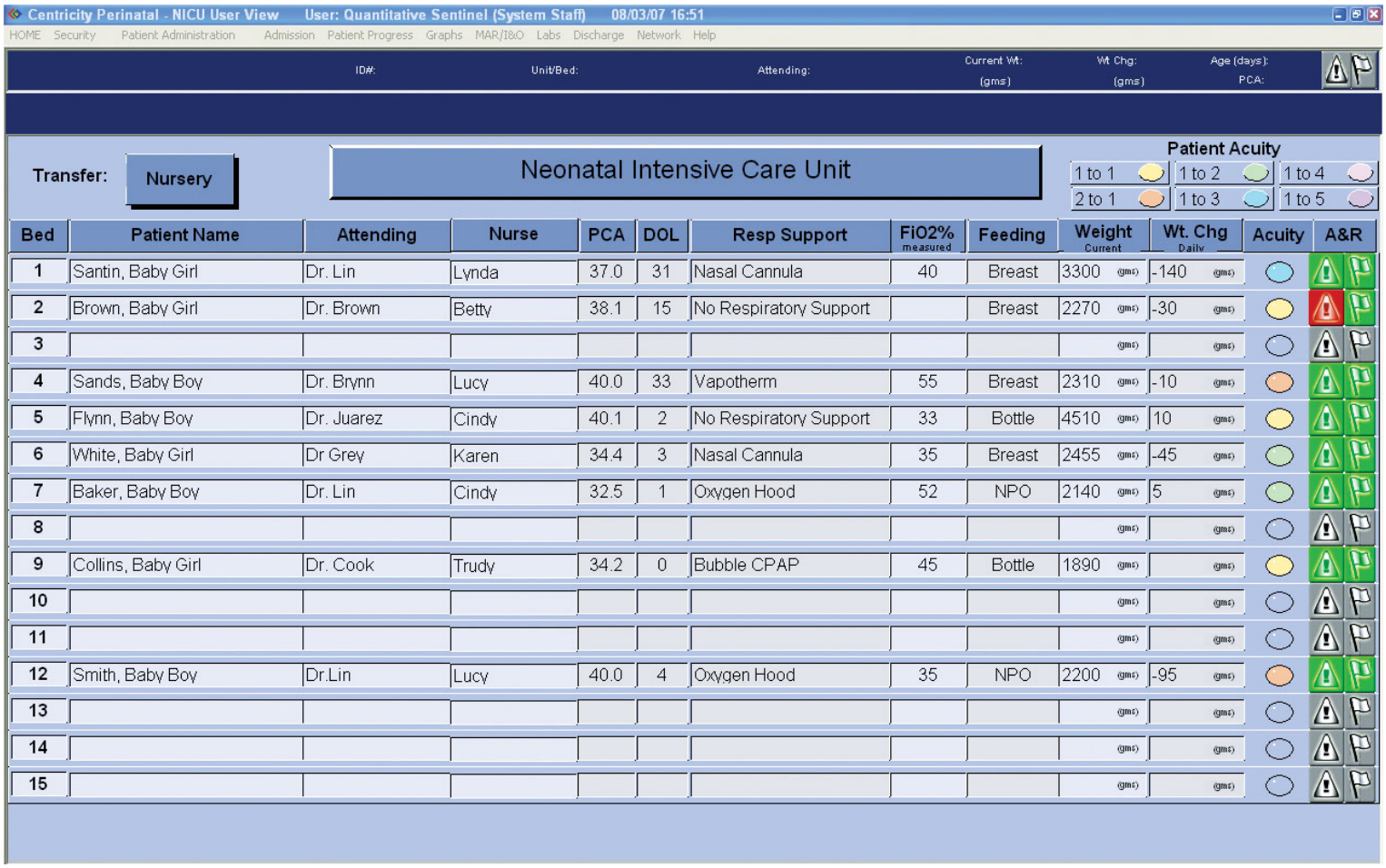
River Oaks transitioned to electronic documentation in the NICU and Post-Partum units in 2010, following a move into a new facility. Previously, our clinicians were doing all their charting the old fashioned way – with pen and paper – which is a cumbersome and inefficient process. Our goal was to eliminate paper charting entirely throughout all our units. GE Healthcare's Centricity Perinatal electronic documentation system had already been in use in our Labor & Delivery unit at Woman's Hospital since 2003, so it was a smooth transition to extend its implementation throughout NICU and Post-Partum. With assistance from GE Healthcare, all the necessary staff training was completed in two weeks for Post-Partum and three weeks for NICU.

Realizing Patient Benefits Throughout the Continuum of Care

Centricity Perinatal helps improve continuity of care by providing doctors, nurse practitioners, and other RNs with an organized picture of an infant's status and mother's record in real-time and at the point of care. When seconds count in a busy, complicated NICU, there is no time to waste in accessing critical information. Our NICU and Post-Partum care teams rely on Centricity Perinatal for an immediate source of patient information, which can help improve the patient's health and safety at every touch point. Providing clinicians with the ability to look up the mother's clinical record when their baby is in the NICU



Screen shot of Mother-Baby link.



Bed	Patient Name	Attending	Nurse	PCA	DOL	Resp Support	FiO2% measured	Feeding	Weight Current	Wt. Chg Daily	Acuity	A&R
1	Santin, Baby Girl	Dr. Lin	Lynda	37.0	31	Nasal Cannula	40	Breast	3300 gms	-140 gms		
2	Brown, Baby Girl	Dr. Brown	Betty	38.1	15	No Respiratory Support		Breast	2270 gms	-30 gms		
3									gms	gms		
4	Sands, Baby Boy	Dr. Brynn	Lucy	40.0	33	Vapotherm	55	Breast	2310 gms	-10 gms		
5	Flynn, Baby Boy	Dr. Juarez	Cindy	40.1	2	No Respiratory Support	33	Bottle	4510 gms	10 gms		
6	White, Baby Girl	Dr Grey	Karen	34.4	3	Nasal Cannula	35	Breast	2455 gms	-45 gms		
7	Baker, Baby Boy	Dr. Lin	Cindy	32.5	1	Oxygen Hood	52	NPO	2140 gms	5 gms		
8									gms	gms		
9	Collins, Baby Girl	Dr. Cook	Trudy	34.2	0	Bubble CPAP	45	Bottle	1890 gms	gms		
10									gms	gms		
11									gms	gms		
12	Smith, Baby Boy	Dr.Lin	Lucy	40.0	4	Oxygen Hood	35	NPO	2200 gms	-95 gms		
13									gms	gms		
14									gms	gms		
15									gms	gms		

Centricity Perinatal - NICU User view

is vital for the infant and especially beneficial during the emergency situations that occur on a daily basis.

Additionally, by streamlining the charting process, Centricity Perinatal relieves the burden of manual documentation, allowing our clinicians to spend more time with patients and families. We have already experienced a significant decrease in charting time since the transition to electronic documentation.

The system also makes the discharge process smoother and more efficient. In the NICU, the average stay can last three months or longer – creating volumes of data which must be rolled into the discharge report. By aggregating patient information on both the baby and the mother from various health IT systems throughout the hospital, Centricity Perinatal can provide detailed discharge summaries at the touch of a button. This detailed report can then be provided for multiple follow-up visits to specialty physicians and pediatricians to assure all information regarding the infant's NICU stay and follow-up care is communicated in a timely manner. We can be confident that appropriate care is maintained even after the patient's discharge from the NICU. In fact, Centricity Perinatal is consider the "legal" OB record.

Next Stage of Electronic Documentation to Benefit Newborn Nursery

Currently, we are working to integrate electronic documentation into our Newborn Nursery, which will fully utilize the functionality of the Centricity Perinatal Mother-Baby Link. The Mother-Baby Link automatically populates the infant's record with relevant maternal and delivery information including vital data from caregivers and records from other units. Neonatologists can document daily physical exams and narrative notes, while viewing relevant reports from nursing, all in a single screen. Data can also be entered manually and updated as necessary. The discharge summaries begin building upon admission, pulling vital data from nursing and combining it with neonatologists' assessments and notes. Having access to the mother's historical patient record is extremely beneficial to our neonatologists and enables them to be more proactive in their care delivery.

Centricity Perinatal remains a central component in River Oaks' continuing endeavor toward excellence in managing the dynamic and complex healthcare needs of our patient population. Our investment in an electronic documentation system has facilitated new levels of connectivity critical to improving patient care and increasing efficiency across the entire perinatal continuum. To that end, we strive to proactively provide the best quality care to the community we serve.

NT

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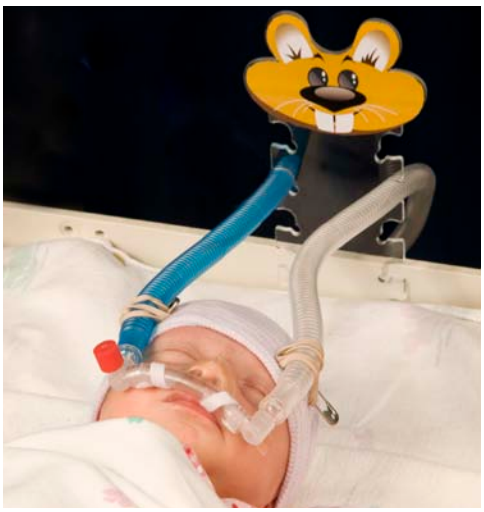
Medical News, Product & Information

New Respiratory Tube Holder for the Smallest Pre-Mature Babies

Through the collaboration of caregivers, hospitals and bedside experts in the Neonatal field; Beevers Manufacturing announces the worldwide product release of the new Gator™ bedside tubing holder. Designed specifically for babies less than 2000g. Gator™ is tailored for the best of care in tube security.



For those NICU's and caregivers who demand only the best care for their little ones; Beevers offers a range of securement products for protection against skin irritations, skin breakdown and "ventilator tubing creep" when NCPAP; oxygen and NG/OG therapies are required.

Kate Beevers reminds our cherished caregivers and customers that "Our [Beevers] mission continues to be developing the simplest of products that enhance the delivery of neonatal therapies. We continue to design into our products the flexibility and usability that enables caregivers to provide the highest quality bedside care."

For further information- www.beevers.net.

Pre-Natal Diagnosis, Timely Treatment Key to Success for Growing Number of Newborns with Clefts

Affecting more than 7,000 US babies each year, cleft lip and/or cleft palate are the second most common birth defect, the cause of which continues to mystify scientists despite growing evidence of a complex interplay of genetic, environmental and lifestyle factors.

Barring ways to prevent these malformations in the first place, timely and appropriate treatment becomes critical, say experts from the Cleft & Craniofacial Clinic at Johns Hopkins Children's Center, which treats more than 650 cleft patients each year.

The key to such success, the experts say, lies in prenatal diagnosis, early surgery and a carefully synchronized treatment by a team of specialists.

"Prompt surgery and treatment by a multidisciplinary team can ensure normal appearance and function for nearly all babies born with cleft lip or palate," says pediatric plastic and reconstructive surgeon Richard Redett, MD, Co-director of the Cleft Clinic at Hopkins Children's.

Prenatal ultrasounds can pick up the majority of cases.

Physicians should counsel parents on what to expect next as soon as the diagnosis is made and before the baby is born, Redett says. This will give parents time to prepare emotionally and allow physicians to devise an optimal treatment plan with the parents. Research has shown that early surgical repair ensures proper speech development. The optimal window for surgery is by 12 months of age, Redett says.

Early surgery provides a much-needed foundation for success, but it is not a silver bullet, he cautions. Post-surgical treatment is critical and should involve ear-nose-throat specialists, speech therapists, pediatric orthodontists and psychologists to best ensure a child's normal development.

Cleft lip and cleft palate occur in the first trimester of pregnancy when the roof of the mouth fails to fuse properly and can be caused by either inherited or new genetic mutations.

A 2010 study led by researchers at Johns Hopkins including Redett identified two genes that may be responsible for the development of oral clefts. Their work in this area continues.

Hopkins experts offer the following tips to help prevent oral clefts:

- Women planning to become pregnant should take 400 micrograms of folic acid each day. The supplement reduces the risk of neural tube defects like spina bifida, and researchers believe it may also help reduce the risk of other birth defects, including oral clefts.
- Pregnant women should not smoke and should avoid secondhand smoke.
- Pregnant women should tell their physicians about any prescription and over-the-counter medications they are taking because certain medicines can cause birth defects or increase the risk of birth defects.
- Discuss with your physician the need for a genetic workup if you have family members with cleft lip/cleft palate as these conditions tend to occur either as stand-alone disorders or as symptoms signaling a complex genetic syndrome that affects several organs and systems.

One in 940 babies is born with cleft lip with or without cleft palate, and one in 1,500 is born with cleft palate, according to the latest estimates from the Centers for Disease Control and Prevention.

Queen's Researchers Pioneer Needle-free Test for Premature Babies

Scientists at Queen's University Belfast have pioneered a new needle-free test to take the sting out of medicine testing in premature babies. The research will not only lead to greater accuracy in prescribing, but will also significantly reduce the trauma of such tests for newborn infants and their families.

In the first published research project worldwide on this new approach to testing medicines in children, the findings were announced in a leading US medical journal, *Pediatrics*.

The study, which involves the use of blood spots obtained from a simple heel-prick, took place in the Belfast Hospital for Sick Children and the School of Pharmacy at Queen's.

The research was carried out by a team from the University's School of Pharmacy in partnership with the Regional Neonatal Unit in the Royal Maternity Hospital. It was funded by the Health and Social Care Research and Devel-

opment Office (HSC R&D) and Action Medical Research.

Principal Investigator, Queen's Professor of Pharmacy Practice James McElnay said: "This type of testing will obviously reduce the discomfort of medicine testing in these vulnerable patients. What is even more important, however, is that it will ensure maximum accuracy in calculating the most appropriate dose of a medicine for a sick child.

"Some 80% of infants in intensive care in hospitals receive medicines which have not been appropriately tested or licensed for use in such young patients, and the dosage is usually calculated based on licensed doses for adults or older children. Sizable blood samples are then required to measure the concentrations of the drug in the infant's bloodstream.

"Our work opens up opportunities for using the same approach to study other medicines which are used in this manner in children, and we are currently studying a number of these."

The Queen's study involved the antibiotic metronidazole. The research team used single drops of blood collected on blotting paper from premature infants who were receiving the medicine as part of their routine care. The 'spots' were dried, analysed in the University's School of Pharmacy, and the results used to develop dosage guidance for doctors.

Dendritic Cells May Have Significant Role in Lung Disease of Preterm Infants

Rates of premature births have increased in recent years, affecting more than 12% of all births and making strategies for managing the associated perinatal complications an important public goal. Preterm infants are particularly at risk for bronchopulmonary dysplasia (BPD), a chronic lung disease. BPD has multiple causes, and uncovering critical interactions within the immune system can lead to new approaches for treatment.

A new study reported in the January issue of the journal *Pediatric and Developmental Pathology* questions the role of dendritic cells in BPD. These are critical immune regulatory cells that can affect formation and development of blood vessels; however, the extent of their role in BPD has not yet been fully explained.

Very low birth-weight infants are at the greatest risk for this lung disease. Thirty percent of those born between 24 and 28 weeks of gestation are affected, and many will require long-term respiratory support. When BPD occurs, it stops alveolar development—the final branches of the respiratory tree where gas and blood are exchanged.

In the current study, postmortem lungs of preterm infants born between 23 and 29 weeks of gestational age were examined to determine the early and late effects of ventilation on both the prevalence and the distribution of dendritic cells. These patients were grouped as: (1) short-term ventilated—infants 23 to 29 weeks at time of death and ventilated for at least four days; (2) long-term ventilated—infants more than 30 weeks in total age, including at least six weeks after birth and dependent on a ventilator at least 75% of that span; (3) early control; and (4) late control. The control groups were age-matched infants who had lived less than 12 hours.

The lungs of early and late control group infants with no evidence of antenatal infection showed scattered dendritic cells in the peripheral lung tissue. In contrast, the lungs of early control infants with a history of antenatal infection and the lungs of short- and long-term ventilated preterm infants displayed a threefold increase in dendritic cells.

This study demonstrates that dendritic cells are a normal presence in the airways and tissue of more developed lungs. However, antenatal infection and ventilation with BPD are associated with excessive accumulation of dendritic cells in the lungs. This massive influx may play a part in the pathogenesis of BPD, and more clearly defining its role may lead to new therapeutic approaches to this disease.

Full text of the article, “Pulmonary Dendritic Cells in Lungs of Preterm Infants: Neglected Participants in Bronchopulmonary Dysplasia?” *Pediatric and Developmental Pathology*, Vol. 14, No. 1, 2011, is available at http://www.pedpath.org/doi/full/10.2350/09-09-0709-OA.1

Prenatal Exposure to Certain Pesticides May Negatively Impact Cognitive Development in Children

Researchers at Mount Sinai School of Medicine have found that exposure during pregnancy to a family of pesticides called organophosphates may impair child cognitive development. The findings are published online in Environmental Health Perspectives.

From 1998 to 2002, the Mount Sinai Children's Environmental Health Study enrolled a multiethnic population of more than 400 women in their third trimester of pregnancy. The research team collected urine samples during pregnancy and analyzed them for the evidence of metabolized pesticides. The women were then invited to participate in follow-up interviews when their children were ages 12 months, 24 months, and six to nine years.

At 12 and 24 months the children were assessed using the Bayley Scales of Infant development, which is a standardized instrument that measures cognitive and psychomotor development in young children. Between the ages of six and nine years, the researchers administered skill and intelligence tests. The researchers found that exposure to organophosphates negatively impacted perceptual reasoning, a measure of nonverbal problem-solving skills.

"Manufacturers withdrew chlorpyrifos and diazinon, two types of organophosphate pesticides, from the residential market. Despite this, general population exposure to organophosphate pesticides is ongoing," said Stephanie Engel, PhD, who led the study while on faculty at Mount Sinai School of Medicine.

"We have previously reported that prenatal exposure to these pesticides was negatively related to measures of neurobehavioral organization and early markers of central nervous system development in newborns. These new findings show that detrimental effects continue to be seen on cognitive development in early childhood, particularly in subgroups of the population that metabolize these compounds less efficiently," Dr. Engel said.

Dr. Engel's team also examined the influence of variants in a key enzyme that metabolizes organophosphates, paraoxonase 1 (PON1). They found that the negative effects of organophosphates were limited to children of mothers who carried a genotype associated with a less efficient version of this enzyme.

"Nearly a third of the mothers in this study carried the PON1 genotype that would put their children at highest risk of negative effects from organophosphate pesticide exposure," said Dr. Engel, who is currently Associate Professor of Epidemiology at the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill. "These highly susceptible individuals may account for the majority of exposure-related cognitive impairment. However, it's not clear how the changing nature of general population exposure following the ban on residential use will impact our understanding of these effects. Exposure source may play an important role, and exposure through diet may now be the predominant source of exposure for the general population rather than indoor pest control."

Dr. Engel added, "Our study will be published along with two independent studies that examined prenatal organophosphate pesticide exposure in relation to childhood IQ using similar research methods. There are definite similarities in our findings that, taken as a whole, warrant careful consideration."

Other Mount Sinai study authors include Mary S. Wolff, PhD, Professor, Preventive Medicine and Oncological Sciences; James Wetmur, PhD, Professor Microbiology and Human Genetics, Jia Chen, ScD, Professor, Preventive Medicine, Pediatrics, and Oncological Sciences; and Chenbo Zhu, Senior Biostatistician, Preventive Medicine.

Global Neonatology Today – Monthly Column: MGDs and the US

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

It is abundantly clear that the success of achieving the UN Millennium Development Goals (MDGs) very much depends on active participation of member states. This underscores the importance of well-established economies of the West as detailed in MDG #8, and the full cooperation of countries receiving the benefits. Over the next few months, I will describe in my column the programs outlined by the most powerful economies of the West in support of achieving MDGs by 2015.

Commitment Made by the United States

The US, in keeping up with its commitment vis a vis global health issues, has developed a strategic plan to support the MDGs. The document developed by the US states, "The Millennium Development Goals (MDGs) are a symbol of our common humanity. They are a declaration of the world's commitment to eradicating extreme poverty and hunger, achieving gender equality, and extending hope and opportunity to millions across the developing world." Unlike other countries, the US proposes to to promote MDGs by investing its resources in four major areas. They are described below:

1. **Leverage innovation:** The US believes that innovation, which is at the heart of the strategy, can be a powerful force multiplier when combined with other investments. The concept of "innovation" includes three things:
   - **a.** The development and application of new technologies, approaches, and methods to address human developmental needs.
   - **b.** The development of new ways to deliver existing solutions to more people, more quickly, and in a cost-effective way.
   - **c.** The introduction of new business models to make aid agencies and the international development architecture more effective. The US proposes to increase access to funding for applied research, increase access to effective technologies, and to encourage partner countries to participate in these programs.
2. **Sustainability:** Progress toward the MDGs will be of little consequence if development gains are not lasting. To help make them sustainable, the US will promote broad-based economic growth by helping countries: formulate and implement pro-growth policies, promote trade, invest in infrastructure, and stimulate entrepreneurship. It also will support partner countries' efforts to nurture well-governed institutions, and will work closely with a broad array of organizations to invest in programs that educate and empower women and girls. Additionally, the US will support efforts to build robust service delivery systems, and help countries mitigate the impact of economic downturns. It believes that these elements are crucial to making development gains sustainable.
3. **Track Development Outcomes, Not Just Dollars:** The US believes that there should be a strong commitment to measuring results in order to progress and also sustain the developments achieved. To this end, the US will upgrade institutional capacity to monitor and measure development outcomes, as well as support and learn from centers of best-practices in evaluation. The US intends to ensure that the presidential initiatives have strong monitoring and evaluation functions, and we will continue to call for the same in the multilateral organizations it supports. Furthermore, the US will help sponsor new methods and data collection initiatives to improve how it measures progress toward the MDGs.
4. **Enhancing Mutual Accountability:** The US proposes to support principles that will strengthen the ability to track, monitor, and report on progress by making donor commitments clearly defined, results-oriented, and time bound. These principles are central to the credibility of multi-organizations involved, just as commitments to good governance are essential for the credibility of partner governments. The G8 (Group of Eight) Accountability Report in 2010 will be the guiding principle.

In summary, the US proposes to employ the above principles to assure reaching the targets of Millennium Developmental Goal around the globe by 2015.

"The Clock is Ticking!"

NT

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