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Upcoming Meetings

Hot Topics in Neonatology

Dec. 5-7, 2010; Washington, DC USA
www.hottopics.org

The 24th Annual Gravens Conference on the Physical and Developmental Environments of the High Risk Infant

Jan. 26-27, 2011; Clearwater Beach, FL USA
www.cme.hsc.usf.edu/events.html

Recruitment Ads

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Real-Time Visual Monitoring of Cerebral Autoregulation In Premature Infants: A "Voyage of Discovery"

By Willa H. Drummond, MD, MS (Informatics); Rosanne D. Conliffe, RN; T. Chris Carnes, PhD; Michael D. Weiss, MD; Julie S. Baines, MD; Cindy K. Miller, RN; George J. Magee, RN, MSN; David W. Kays, MD; and David J. Burchfield, MD

Abstract

We studied 20 premature babies of 28-34 weeks gestation. They had cardiac and surgical conditions, plus many problems of prematurity of all types. We found many sequential, previously unappreciated internal cerebral destabilization events. Many were associated with routine care practices, in an "older" premature infant population.

Suctioning is usually a very large, discrete stress. Medications, in the combinations used, may have unpredictable effects. Blood is nearly always helpful in improving cerebral mixed venous saturations. Saline infusions have not been observed to be helpful. Care sometimes helps (holding), and more often doesn't (e.g. IVs, procedures, exams). A premature baby can autoregulate cerebral blood flow for (presumably) days, then lose that ability within 60 minutes of sepsis/cytokine storm onset, or after a "Code."

Introduction

The concept of "Cerebral Autoregulation" is based on many animal and human research studies showing that healthy brains will adjust vascular resistance using many different cellular and neurologic reflexes, to maintain constant cerebral tissue oxygenation over wide ranges of perfusion pres-

sure, blood oxygen and carbon dioxide concentrations^{1, 2}. Interacting pathophysiologic factors that alter brain blood flow in adults include: cardiac output, blood oxygenation and carbon dioxide; intrathoracic and intracerebral pressure; local hormonal and biochemical modulation of cerebral vasomotor tone; plus external influences like gravity and medications. Local cerebral blood vessel resistance control systems operate independently of changes in peripheral oxygenation and blood pressure. Mixed venous oxygenation is determined by blood flow, arterial oxygen carrying capacity and tissue oxygen extraction.

Developmentally immature human infants' ability to appropriately "autoregulate" brain blood flow is an unresolved issue^{2, 3}. Neuroregulatory responses are genetically programmed to change as fetuses develop over gestation. Ex-utero preterm babies have immature autoregulatory cardio-vascular mechanisms that are genetically tuned for in utero conditions. Premature infants may also have serious prematurity-related diseases and poor tolerance of many environmental stresses associated with preterm birth.

Dynamic data from unstable preterm infants is needed to facilitate treatment decisions by clinicians. Non-invasive tools to monitor local flow, oxygenation and peripheral vascular responses, over time, have been unavailable for use in very small infants. Now new technology automatically integrates physiologic parameters from cardio-vascular, ventilator, and oxygen monitors with cerebral mixed venous saturation measurements and visually integrates the bedside results on real-time trend graphs. The immediate visual access to "all the data" in zooming real-time trends at the bedside is remarkably educational.

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Project Description

We embarked on a 'voyage of discovery' with each premature infant subject, because it immediately became obvious that ordinary and customary care sometimes had acutely destabilizing effects on infants' cerebral mixed venous/tissue oxygenation. Many destabilizing cerebral oxygenation events were unassociated with alerting-level changes in other monitored parameters, indicating that problems may exist with detecting and alerting caregivers of failure of cerebral autoregulation.

The Clinical Environment

Sick premature infants are cared for in Neonatal Intensive Care Units (NICU) that are staffed for round-the-clock critical care by specialist nurse and physician caregivers. Many simultaneous processes feed information into the clinical decision-making that facilitates appropriate care delivery to unstable NICU patients. A prime goal for brain salvage is quickly detecting failure of cerebral autoregulation which may help caregivers discover and immediately correct contributing problems. For example, anemia needing treatment contributed to cerebral oxygenation problems in two study babies (Case 2 and Case 10), where team problem solving evolved the care plan change.

Critical care bedside clinicians are "hands on" providers whose care decisions must often be made in real-time seconds. Neonatal Intensive Care Units are crowded with people and devices. Caregivers are often summoned from one task, to respond to a more urgent one, in seconds. Business-style computer use, access and log-off are unsupportive of interruptive, multitasking workflows where seconds matter⁴.

Clinical data integration in ICUs to date has depended on pen and long paper "flowsheet" charting methods. This practice creates a hard to read, chaotic, "information overload" situation that can lead to oversights and potentially avoidable errors. However, clinician experts learn to grasp the essence and status of a given baby's multi-system problems in a few seconds of flowsheet review. The immediately available, shared bedside paper flowsheet document tracks individual patient changes while informing the "situational awareness" needed by managerial physicians and nurses (i.e. attending neonatologists, charge nurses and unit managers) for optimizing overall unit workflow management, especially in crisis moments.

Clinical Computerization: A Current National Priority

Computerization of all ICU care data is an emerging paradigm, driven by national mandates to computerize healthcare. Previous attempts often were associated with difficult workflow process problems⁵. Most electronic hospital information systems present data entry challenges for meaningfully archiving patients' clinical data into a storage system. Clinical data entry is an unresolved challenge. The usual solution is to ask nurses and physicians to retype clinical observations and streaming, multi-source, alpha-numeric data back into the archival computer. Keyboard data entry methods add typographical errors, caregiver distractions and nosocomial infection risks to the overall environmental situation. Data entry solutions involving keyboard data entry are very often impossible for hands-on caregivers to accomplish in real-time. Retyping previously computerized data is a very poor operational solution that distracts and slows time-pressured critical caregivers.

Bedside Caregiver Critical Information Communication

Poorly designed reports on many small screens, each containing different "departmental" subsets (i.e. respiratory therapy, care interventions, pharmacy medication dosing), fragment the patient-centric, streaming time-sensitive clinical overview. Real-time integration of automated machine data and lab results with time-matched observation, treatment, and medication data to support expert critical care clinical decision-making in real-time, is, to-date an unmet dream⁶.

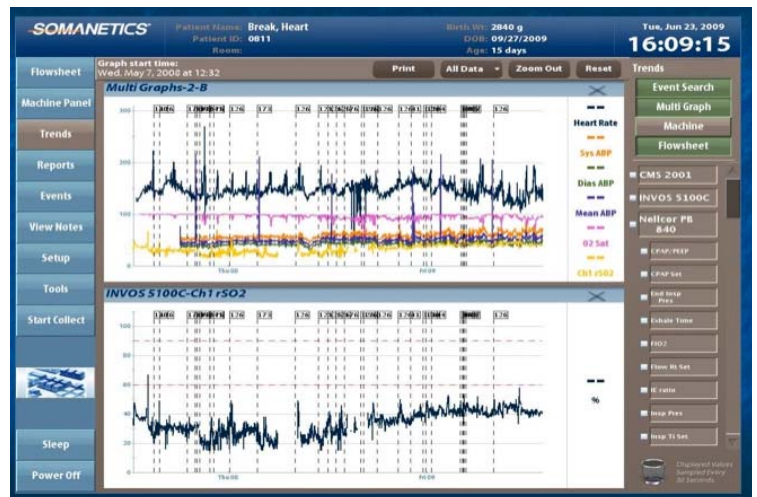


Figure 1 - Case 11: 48 hour study overview; 34 week infant with congenital cardiomyopathy. The infant was in severe pulmonary edema, and had very low, fixed cerebral blood flow due to very low cardiac output. This overview figure shows improved cerebral oxygenation after transfusing blood, giving extra lasix, increasing ventilator CPAP, and discontinuing all suctioning. Event markers: 126-Suction ET Tube; 173-nothing charted; 176-Family Visit.



Figure 2 - Case 11: Congenital cardiomyopathy. Close-up of this baby's pattern associated with endotracheal suctioning. Findings are tachycardia, acute peripheral desaturation, and no consistent associated change in the preexisting low, fixed cerebral oxygenation. The single identified discrete improvement occurred during a family visit, with chest to chest semi-upright holding. Event markers: 41-Miscellaneous; 176-Family Visit.

History

Attempts to computerize ICU bedside clinical data management led to development of free-standing, computerized bedside physiologic monitoring and treatment systems (physiologic monitors, ventilators, pumps, flowmeters). Each device type monitors and/or manages a sub-set of the patient's overall problems. An alternative way to rapidly integrate all machine-managed and/or generated data is needed to fully utilize recent advances in NIRS technology that has

Table 1: Patient condition and control of Cerebral Autoregulation, defined as independence of (good) or concordance with (poor) cerebral oxygenation vs. peripheral oxygenation and/or blood pressure, sorted by independent patient clinical condition assessments.

Control of Autoregulation: Patient Condition	Patient # Condition	Patient # Condition	Patient # Condition	Patient # Condition	Patient # Condition	Patient # Condition	Patient # Condition
Excellent/Good	3	8	12	14	15	17	19
	well	well	well	well	well	well	borderline
Fair/Intermittent	1	2	6	9	10	16	18
	sick	sick	borderline	sick	well>>sick good>>none	borderline	borderline
No Autoregulation	4	5	7	11	13	20	
	well	sick	sick	sick	sick	sick	

improved near-infrared sensors designed for very small premature infants. The marked destabilization the sensors show in real time compels most doctors and many critical care nurses to seek more data to clarify causative and contributing risk factors. Case histories are a cognitive starting point.

Our project combined INVOS® measurements along an accurate timeline with automated data entry from other bedside devices. We used the Vital Sync™ device to acquire real-time physiologic and treatment data from many different vendors' bedside machines, each minute. Then Vital Sync™ created a highly accurate, visually trended bedside electronic flowsheet, reporting dozens of machine-measured patient parameters. Parameters are selected for a particular patient or situation at the bedside, by users. Caregivers usually display automated trends on a zooming touchscreen that can be expanded, or changed, without affecting the underlying database or ongoing data collection, when they need to explore treatment changes, as dynamic situations evolve [Figures 1 and 2].

Validation Project Goals

Our project was a structured usability trial of the pre-release prematurity NIRSensor probes for the INVOS® 5100C monitor. NIRS cerebral monitoring is currently used in high-risk cardiovascular surgery, extracorporeal membrane oxygenation (ECMO), shock/trauma and hypoxic/ischemic brain injury situations in older patients. Our usability data from premature infants guided pre-marketing sensor adaptation and supported FDA-required documentation. Those data were independently collected and reported, as federally required.

Our ancillary clinical research goal was to gather care-related, non-invasive INVOS® 5100C near-infrared spectroscopy (NIRS) oximeter measurements of brain and renal oxygenation simultaneously with physiologic parameters from monitors, ventilators and oximeters, using the Vital Sync™ device. We hypothesized that early detection of complications affecting internal organ blood flow could facilitate early correction, leading to prevention of secondary brain and other organ injury. We also hypothesized that improved information integration, visual presentation and real-time speed could help caregivers see and correct developing "physiological systems" problems early. Early detection of internal organ perfusion complications could help prevent secondary organ injury, shorten hospital stays, and improve long-term outcomes.

Materials and Methods

Subjects & Study Procedures

Premature infant patients between 28 and 34 weeks gestation were enrolled after IRB approved informed consent. The study population included 20 high risk infants, some who had onset of new problems during their 48-hour study. Problems included apnea and bradycardia (A&Bs) necrotizing enterocolitis (NEC), sepsis, cardiac failure due to congenital cardiomyopathy and patent ductus arteriosus (PDA), complicated by anemia. INVOS® sensors were placed on the infants' heads

and flanks, and the INVOS® and infants' physiologic monitors and ventilators connected into the Vital Sync™ system. Usual care continued while circulatory responses to care situations were automatically collected each minute in the background. At 24 hours, the probes were removed, the skin rested for an hour, and the probes were replaced for 24 more hours. Caregivers were not expected to interact with the study devices. Bedside nurses were clinically trained in proper hands-on nursing management of the NIRSensor® skin probes.

Analysis

Before data analysis, the infants were clinically scored as "sick" (n=8), "well" (n=8), or "borderline" (n=4) based on a clinical chart review [Table 1]. Many "sick" infants were clinically judged to be "critically ill" by caregivers. "Borderline" infants were defined as those having single known problems such as apnea of prematurity or a suspect PDA. "Well" infants had no recognized medical problems when they were enrolled in the 48-hour study. Physiological parameters, cerebral and renal mixed venous oxygen content (a blood flow indicator), and ventilator-generated respiratory data were automatically collected by the Vital Sync™ system.

We "data-mined" paper flowsheets and chart notes for ancillary information regarding instabilities and discontinuities seen in the infants' time-stamped INVOS® + Vital Sync™ traces. Event markers were back-posted into the research database from flowsheet/chart information using the Vital Sync™ event time marking utility that stores the temporal data into an object relational, time-sensitive, open-standards database, then processes and returns time-stamped trend and/or tabular data to bedside clinicians, as minute-by-minute in visual trends, grid box reports, or both. The Vital Sync™ automated data entry timestamp was accurate to the nearest minute. Paper flowsheet time was usually approximate, due to the limitations to charting of changes within the hour on the very small boxes intended for hourly point observations.

Results

Population Overview

Visual overview judgment estimated the status of autoregulation before in-depth case analysis. Visible matching of an infant's cerebral versus peripheral oxygen traces were classified into "excellent/good," "fair or intermittent," or "none" by viewing time-matched trend graphics. Excellent autoregulation was defined as cerebral oxygenation remaining stable in the normal range in the face of acute alterations of blood pressure and/or peripheral blood oxygen saturation. Table 1 shows the study population's well, sick or borderline categorical subdivisions. Observations of poor autoregulation clearly cluster in the "sick" population in this 28 to 34 week gestation cohort.

Case Observations

In several patients, very important new findings developed during the study. Case analyses of 5 study situations that were particularly informative for clinical learning are reported in scenarios and color graphs.

Observations suggest there is much room for improvement in many neonatal critical care situations, patient status assessments and management of common care procedures.

Scenario - Infant with Congestive Cardiomyopathy

Case 11; Synopsis

The patient was a two week old 34-week infant who had hydrops caused by a severe congenital cardiomyopathy, in Class 5 heart failure, unstable on a ventilator and pressors, and a transplant candidate. The very low INVOS-measured, mixed venous cerebral oxygenation saturations were real (Figure 1, top panel, yellow trace, and simultaneously isolated as a blue trace, lower panel). Nearly all acutely unstable events were associated with suctioning for pulmonary edema related "crackles"; many uncharted suctioning events were occurring. Caregivers noticed the extreme instability, and when a chest x-ray confirmed severe pulmonary edema, the care plan was changed. Suctioning was stopped, CPAP was increased, and a slow, packed red cell transfusion with extra lasix started, because the baby's hematocrit had dropped well below the target range of mid-40s%.

Cerebral oxygenation improved and stabilized over several hours. Figure 2 shows a close-up of this baby's characteristic cardiovascular destabilization patterns related to suctioning. His responses were profound tachycardia, systemic hypoxemia, and very little change in his preexisting, extremely low cerebral mixed venous oxygenation. The stable period with improved cerebral oxygenation (Event #175) was associated with a family visit that included chest to chest holding in a semi-upright position, while the baby was on a ventilator.

Case Comment: Baby 11 could not autoregulate his brain blood flow within normal ranges because he had a fixed, very low, cardiac output caused by severe congenital cardiomyopathy. His brain was able to extract sufficient oxygen to sustain its' viability, as shown by his subsequent good neuro-developmental outcome, despite the apparently severe and prolonged mixed venous hypoxemia noted during the study. His brain desaturations continued intermittently for several monitored weeks of pre-discharge stabilization attempts, before discharge for home hospice care. Pathophysiologically, fetal brains in utero tolerate as "normal" similar levels of "hypoxemia" at this baby's developmental age (36 weeks); fetal forms of cardiac and other enzymes and adaptive fetal hemoglobin contribute to normal growth in a low oxygen environment.

This baby's brain appeared to be maximally extracting oxygen from the low cardiac output flow it was receiving. The baby ultimately survived with good neurologic function to age >1 year and counting, without cardiac transplantation. He remains a potential transplant candidate.

Scenario - Twenty-nine Week Twin Boys with "Apnea & Bradycardia"

Case 4; Twin A; Synopsis: Infant was 29 weeks, 1134 grams; born by C-section for breech position of Twin B. APGARS 9/9, mild transient tachypnea of the newborn (TTN); he had no patent ductus arteriosus. Apnea and bradycardia (A&Bs) started on Day 2; caffeine was started @ age 40 hours then reloaded and continuous positive airway pressure (CPAP) started @ 64 hours because symptoms continued. Study age was 96 -144 hours, while the baby was on CPAP. Feeds were 4 ml q3 hours, withheld @ study hour 7 to 15, then restarted for rest of study. No billight was present. MRI at discharge was normal, except for "interstitial edema".

Figure 3a shows an overview of the entire study that is remarkable for many "apnea and bradycardia" episodes, most associated with close coupling of peripheral and cerebral desaturations, indicating poor cerebral autoregulation; **Figure 3b** shows a zoomed-in close-up of a major "A&B" episode, with normal blood pressure and marked simultaneous decrease of cerebral mixed venous oxygenation. These findings indicate



Figure 3a - Case 4; Twin A: Overview of study. Twin A, born by C-section, 9/9 Apgars. Infant was having many episodes of bradycardia, some of which were associated with acute decline in cerebral oxygenation, indicating instability of cerebral autoregulation. Ultimately both twins were diagnosed with gastroesophageal reflux.



Figure 3b - Case 4, Twin A: "A & Bs" with unstable cerebral autoregulation. Zoomed-in view of a few desaturation episodes associated with several events: 126, Suction ET tube; 136, A&B; and, 133, Bag/mask ventilation.

the baby at 30 weeks post-conceptual age had poor cerebral autoregulation, even at "normal" blood pressure, despite having no PDA on echocardiography, or any known systemic illness. These findings may simply represent developmental immaturity; or may relate to some interaction with caffeine, coupled with the premature response to gastroesophageal reflux, an autosomal dominant genetic condition that was later confirmed in both twins.

Case 3, Twin B; Synopsis: Baby was 29 weeks gestation, 1148 grams; C-section for breech position & nuchal cord; APGARS 8/9. Apnea, bra-



Figure 4a - Case 3: Twin B: Overview of entire study, initially showing reasonable cerebral oxygenation stability. The step change in cerebral oxygenation occurred with a care episode, and may reflect either an artifact, or readjustment of CPAP apparatus that may have changed cerebral vascular dynamics, perhaps by relieving cavernous sinus pressure. Events: 166-Caffeine load; 167-PIV insertion.



Figure 4b - Case 3: Twin B: Close-up of poor autoregulation associated with some, but not all bradycardiac spells, without apnea. The baby's ability to autoregulate cerebral oxygenation during bradycardia-induced fall in peripheral oxygenation was poor. Events: 136-Apnea & Bradycardia; 167-PIV Insertion.

“The concept of ‘Cerebral Autoregulation’ is based on many animal and human research studies showing that healthy brains will adjust vascular resistance using many different cellular and neurologic reflexes, to maintain constant tissue oxygenation over wide ranges of perfusion pressure, blood oxygen and carbon dioxide concentrations^{1, 2}.”

dyscardia and caffeine were started age 2 days. Feeds were started on Study Day 1, but were poorly tolerated, so were stopped at 0200 on Study Day 2. A clinical PDA developed during the NIRsensor study at age 56 to 82.5 hours. Bilirubin was on the baby from study start to ~6 hours from end. Figures 4a and 4b show a 48 hour overview and a two hour close-up of the baby's circulatory and cerebral blood flow response to "life". Since these desaturation episodes showed no association with apnea, they may have reflected immature neurohormonal reflex responses to gastro-esophageal reflux. Subsequently, Twin B developed medical necrotizing enterocolitis (NEC) at age 4 weeks, and recovered uneventfully. Six week MRI was normal except for mildly delayed myelination. The twin babies came off apnea monitors at 48 weeks post-conceptual age, and at one year were in community follow-up.

Case Comment: Both 29-30 week twins were considered 'well' prior to analysis. The cerebral oxygenation instability was surprising, especially in Twin A, who was believed by caregivers to be doing very well. Baby A's persistent, unexpected cerebral dysregulation may relate to developmental immaturity, perhaps of fetal central respiratory & circulatory control systems, immature myocardium, and/or an intermittently shunting PDA coupled with gastroesophageal reflux that was diagnosed later (Figure 4a and b). Note that the respiratory rate trace (Figure 4b, lower panel) shows very little apnea. Retrospectively, both twins should have been scored as "borderline" despite superficially appearing well; both had "late" problems, prior to discharge.

Case 10: "Lightning NEC"

Baby 4 (Case 10) was a 15 day old, 27 week gestation, 775 gram, small-for-gestational-age (SGA) premature born to a mother who had severe preeclampsia. Apgars were 5 and 8; the baby did well after one dose of surfactant and was successfully extubated on Day 2 of life. He had been slowly advanced to full feeds, and was on caffeine and low flow nasal cannula oxygen when he was enrolled in the study, at a weight of 875 grams.

A routine hematocrit check on the morning of Study Day 1 was 19%, so an elective packed red blood cell transfusion was given at 0225-0500 (study hours - 14-17.5), about 18 hours after the anemia was diagnosed. The baby began vomiting at 0300; by 0400 abdominal x-ray showed extensive pneumatosis intestinalis. Figure 5a shows the infant's Vital

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Figure 5a - Case 10: "Lightning NEC:" 24 hour overview of a 27 week, SGA baby developing "Lightning NEC" over about 90 minutes, 10 hours after graphic trend review suggested that a PDA reopened near Event 173-Nothing Charted. The trend view of the cuff blood pressures shows the systolic, diastolic and mean blood pressure dropped about 40% while the baby had a HCT of 19%. A routine packed red cell transfusion was given for the anemia, starting at 0220, near the beginning of an acute destabilization episode diagnosed as severe NEC by a 0400 abdominal x-ray. Events: 43-enteral feeding; 136-A & Bs, 163-KCl infusion; 173-nothing charted; 182-Suction + X-ray.

Sync trends with INVOS running in real-time. Figure 5a, is a 24-hour study overview and includes the acute destabilization period, starting 0300 with tachycardia. The tachycardia was followed by worsening peripheral arterial desaturations, progressive increase in regional cerebral oximetry starting at about 0600. Right panel (Figure 5b) "zooms in" on the final 5 hours of the study, to show acute loss of previously good cerebral autoregulation over about 70 minutes. The baby's capillary PaCO₂ changed from 40mmHg at 0530 to >130 mmHg by capillary gas, on a ventilator, by 1155. The large PaCO₂ change would have had profound effect on cerebral circulatory control.

Case Comment: Acute loss of cerebral autoregulation was associated with rapid onset of extensive necrotizing enterocolitis (NEC), presumed sepsis, disseminated intravascular coagulopathy (DIC), and acute respiratory failure. The study documented events as Case 10 changed from "well" to "very sick" (acutely critically ill) during the last five hours of the 24-hour study. Complete cardio-respiratory collapse over about 60 minutes was associated with starting pressors, mechanical ventilation, antibiotics, platelet and fresh frozen plasma transfusions. By dawn, the baby was critically ill.

The persistent cuff blood pressure drop earlier in the day, with widening of pulse pressure between the times "Monday 1800 to mid-night" is visible in the retrospective trended overview (Figure 5a). The change may have represented reopening of a ductus arteriosus, possibly cytokine-induced. A reopened ductus would increase left-to-right pulmonary shunting, with an associated decline in intestinal blood flow, especially in an infant with normal lungs and pulmonary circulation. The actual cuff blood pressure values were charted on the paper flowsheet, but the retrospective diagnosis of new ductal shunting was not appreciated in real-time; feeding continued, and the ensuing events show the pathophysiology of evolving NEC-related sepsis in a premature infant.



Fig 5b - Case 10: Lightning NEC with acute loss of cerebral autoregulation; the final five hours of Case 10's twenty-four hour study, expanded on the timeline. Good cerebral autoregulation is seen on the left side of the tracing. Acute loss of cerebral autoregulation is indicated by new onset of 'pressure-passive' cerebral oxygen saturation on the right side of the tracing. Prior to that, the baby tolerated peripheral desaturation episodes with no associated cerebral deoxygenation. Loss of cerebral autoregulatory capability occurred over 75 minutes, while the baby "crashed" with hypotension, acute respiratory deterioration and disseminated coagulopathy. The timeline is artificially offset by several hours, as a pictorial deidentifying adjustment. Event 163-KCl infusion.

The baby's mother requested study discontinuation at 0900 when the sensor was changed, due to the seriousness of the baby's clinical condition. Despite maximal medical and surgical management, the baby died about 24 hours later. All but 12 cm of bowel had necrosed; the blood culture drawn on Study Day 1 at 0400 showed no growth, final.

Case 2: Spontaneous Perforation with Mild Necrotizing Enterocolitis (NEC)

Baby 2 was a 27 week gestation, 1136 gm baby, age 21 days, born to Group B strep positive, multi-substance using mother. The baby had recovered from hyaline membrane disease (HMD) and was started on medication for suspect seizures. The baby was supported on CPAP, doing well until Day 13, when E. Coli sepsis developed and was successfully treated. An associated PDA and an atrial septal defect (ASD) were diagnosed prior to the onset of the acute, focal intestinal perforation at age 21 days, associated with possible necrotizing enterocolitis. At surgery, minimal pneumatosis was found, and only about 5 cm of bowel were resected and reanastomosed. At age six weeks, cranial ultrasound showed a right grade 3 intraventricular hemorrhage, with an intraparenchymal hematoma and possibly an evolving porencephalic cyst.

Surgical Events: The baby was enrolled in the study on the evening of Day 20, but by morning had acutely developed an intestinal perforation with minimal radiologic evidence of necrotizing enterocolitis. The radiographic diagnosis was reported just as the scheduled study was starting at ~0900. The NIRsensor probe was used for monitoring during the emergency trip to the operating room, with the surgeon's caveat that Dr. Drummond accompany and manage the INVOS monitor during surgery.

Figure 6 shows cerebral mixed venous oxygenation data from the free-standing INVOS monitor. Many events occurred in the operating room

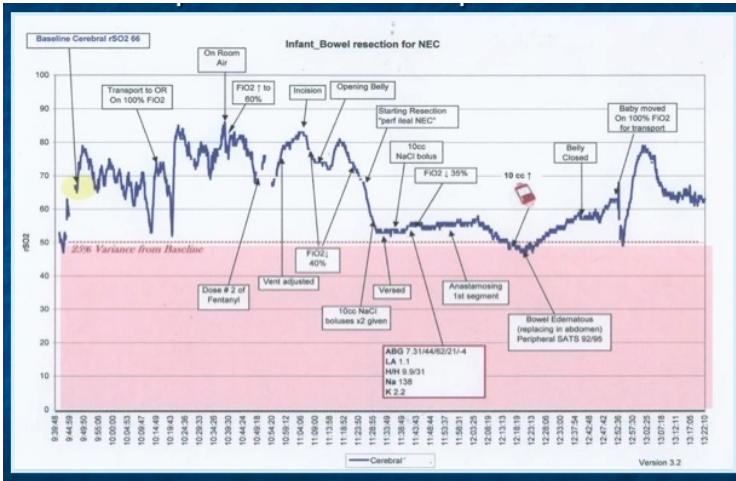


Figure 6: Case 2: Perforated "NEC": NIRS monitoring during surgery for a spontaneous bowel perforation in a baby who had minimal NEC. Surgery, and the immediate post-operative period were complicated by severe fentanyl intolerance and situational instabilities. The annotated INVOS NIRS Sensor trace shows events during the baby's emergency exploratory laparotomy in the operating room. The NIRS view shows the internal instability of baby's blood oxygenation in response to a variety of stressors, indicating poor cerebral autoregulation.

that affected cerebral oxygenation, including respiratory problems associated with fentanyl dosing that required pre-operative hand ventilation for several minutes before restabilization on the ventilator. The baby had multiple episodes of peripheral hyper-oxygenation and hypoxemia, bowel manipulation, normal saline boluses, blood administration, and an acute endotracheal tube obstruction due to kinking during the patient transfer from the operating table to the transport warmer bed.



Figure 7 - Case 2: Perforated NEC: Overview of the 48 hour post-operative study, after the baby was returned to the NICU and Vital Sync monitoring of multiple parameters was started. The 35 minute "code" episode is the blurred vertical bar on the far left side. Note that cerebral autoregulation (yellow line) was unstable for about 18 hours (see Figure 8) after the code episode. Subsequently the baby regained cerebral autoregulation, which was stable over the final 24 hours of the study.

Figure 7 shows a post-operative 48 hour overview of the Vital Sync/NIRS traces integrated with blood pressures and heart rate from the physio-monitor (upper panel), and ventilator pressure, respiratory rate and FiO₂ (lower panel), that begins upon the infant's return from the operating room. The marked destabilization episode at the beginning of the trace began suddenly, just after the baby had been settled in the NICU warmer bed, and rapidly evolved into a full CPR episode of unclear etiology.

Figure 8 shows a zoomed-in close-up of the post-operative "code" showing the acute physiologic changes associated with the 35 minute resuscitation. Progressive resuscitative efforts were: endotracheal tube suctioning, intermittent bag/mask hand ventilation, chest transillumination to diagnose a pneumothorax, endotracheal tube change out, ventilator change out, and finally, CPR (cardiopulmonary resuscitation) with several minutes of chest compressions.

The attending was stat paged by the senior fellow to the difficult code scene. Remembering the poor tolerance to fentanyl in the OR, the key question became, "Did anybody just give this baby a dose of fentanyl?" A quick check with nursing and pharmacy confirmed that the baby was given a routine post-operative fentanyl dose as part of a pathway order-set for post-operative pain control, just before the episode began. An emergency dose of narcan was administered (Event 161), and the baby recovered and stabilized within 2-3 minutes.



Figure 8 - Case 2: Perforated NEC: Close up of the fentanyl-induced post-operative "Code" episode. The drastic destabilizations of all physiologic parameters during this 35 minute long resuscitative attempt are very obvious. Equally marked is the nearly immediate normalization of the baby's condition after the Narcan administration (Event 161). Also note the probable acute cerebral over-circulation (yellow trace) after the code episode ended. By the second post-operative day, the baby had recovered cerebral autoregulatory control. Events: 78-Sedation with fentanyl; 126-Suction ET tube; 129-Intubated/Extubated; 138-Cardiac Arrest/CPR.

Discussion

NICUs are high-cost, complex, real-time environments. Current record-keeping methods often fall far behind real events impacting NICU infants. The smallest and sickest babies have very immature and vulnerable brains. Our study population was relatively mature premature infants born at 28 to 34 weeks gestation. We used non-invasive, near-infrared reflectance spectroscopic (NIRS) technology, coupled with tiny premature infant sensors for non-invasive, continuous, real-time measurement of mixed-venous oxygen saturation in the small and sick pre-

mature infant brains. Mixed venous oxygen saturation of any regional tissue is a good indicator organ flow coupled with oxygen consumption and uptake.

This clinical study added a new type of computerized data-integrating system, a Vital Sync device, that automatically acquires and integrates real-time clinical data from many different bedside monitors and treatment machines. That integrated real-time trend data gave a clear picture of how interacting variables changed acutely, within seconds or minutes. The computer-assisted, physiologically-integrated vision that the plug and play data delivered from several different bedside monitoring and treatment devices as an accurate, visual timeline, clearly shows remarkable internal instability of many premature infants' brain blood flow responses to many stressors.

Our study population of moderately premature infants had a variety of different condition and care events; some were very sick (Cases 2 & 10), or very physiologically stressed (Case 11). The mystery of the twins who appeared well, but had an undiagnosed, neuroregulatory destabilizing, "preexisting condition" (i.e. GE reflux), Cases 4 & 3, was solved in retrospect. The twins' problem set was quite diagnostic of a situation other than ordinary "apnea and bradycardia of prematurity," since the trends clearly showed that neither twin was having confirmed apnea associated with the bradycardia. It is possible that the caffeine and CPAP that both twins were treated with may have aggravated the twins' problem with congenital, genetically-based gastroesophageal reflux. Reflux was ultimately a clinical diagnosis of exclusion, and was confirmed with later pH probe studies.

In the moderately premature population, autoregulatory control of brain oxygenation was inconsistently present over time. Intercurrent treatment events, sepsis, medications, and care procedures all influenced "autoregulation" of cerebral perfusion. Well babies are more likely to autoregulate their cerebral oxygenation appropriately than sick ones. The transition between well and sick states can happen very quickly (Case 10). External ability for caregivers to judge the stability of cerebral oxygenation can be poor (i.e. Case 4, Twin A). Human clinical judgments of "well" may underestimate the actual internal, currently invisible, tissue oxygenation instability situations that some babies are experiencing, over time.

Acknowledgements

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NMTB policies/positions and no official endorsement is inferred. A research grant from Somanetics funded a research nurse and equipment. Dr. Drummond has a potential conflict of interest because she is consultant to Somanetics, Inc., and lead developer of the patent on the Vital Sync Device, held by UF.

The Summary of the Exploratory Voyage

- We studied 20 total babies: Cardiac, Surgical, Renal agenesis, Premies of all types
- Findings:
 - Suctioning – a very large stress
 - Medications – unpredictable
 - Blood – nearly always helpful
 - Saline – not so good, and that may be the most important first finding
- Care sometimes helps (holding),
 - Sometimes doesn't ... (IVs, Procedures, Exams).
- A premie baby can autoregulate brain oxygenation for (presumably) days, then lose that ability within 60 minutes of sepsis/cytokine storm onset, or after a "Code."

References

1. Kaiser JR, Gauss, CH, Williams DK. The effects of hypercapnia on cerebral autoregulation in ventilated very low birth weight infants. *Pediatr Res.* 2005 November; 58(5): 931–935.
2. du Plessis AJ, Cerebrovascular injury in premature infants: current understanding and challenges for future prevention. *Clin Perinatol.* 2008; 35(4):609-41 (review).
3. O'Leary H, Gregas MC, Limperopoulos C, Zaretskaya, I, Bassan H, Soul JS, DiSalvo, DN, duPlessis. Elevated cerebral pressure passivity is associated with prematurity-related intracranial hemorrhage. *Pediatrics* 2009; 124(1):302-309.
4. Brixey JJ, Tang Z, Robinson DJ, Johnson TR, Turley JP, Patel VL, Zhang J. Interruptions in a level one trauma center: A case study. *Int J Med Inform.* 2008; 77(4): 235-41.
5. Patel VL, Zhang J, Nicole A. Yoskowitz NA, Green RA,. Sayan OR: Translational cognition for decision support in critical care environments: A review. *Journal of Biomedical Informatics* 2008; 41(3): 413-431.
6. Whitehead SF, Goldman JM. Connectivity to improve patient safety: making medical device "plug-and-play" interoperability a reality. *Patient Safety and Quality Healthcare.* 2010 January/February 2010; 7(1):26-30.

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Global Neonatology Today: A Monthly Column

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

UNITED NATIONS MILLENNIUM DEVELOPMENT GOAL #6 - (MDG 6) - Target 6C

THE TARGETS:

- Target A: To halt HIV/AIDS by 2015, and begin to reverse the spread of HIV/AIDS.
- Target B: To achieve universal access to treatment of HIV/AIDS by 2010 for all those who need it.
- Target C: To halt by 2015 and begin to reverse the incidence of malaria and other major diseases.

We discussed MDG 6, Targets A & B with the Goal to combat HIV/AIDS. In this review we will address the status of the Goal of combating malaria and tuberculosis. Target 6C is to halt and reverse the incidence of malaria and other major diseases by 2015.

“In summary, work to achieve the MDG 6C goals of preventing and treating tuberculosis and other major diseases, such as malaria, is moving in the right direction, but much more needs to be done to meet the target of reaching the goals by 2015.”

CURRENT STATUS OF TARGET 6C

MALARIA

One million deaths are attributed to malaria, mostly in African children under five years of age. In fact, on the average, one child dies every 30 seconds from malaria in Africa!

Three strategies recommended for prevention:

1. Use of insecticidal nets.
2. Prevention of indoor residual spraying with effective malarial medicines.
3. Focusing on preventing malarial infection in pregnant women and young children.

The target is to cut malaria in half by 2010; and meet MDG 6 target by 2015.

THE PROGRESS

Although the production and use in the community of insecticide-treated mosquito nets is increasing, poverty continues to hinder progress toward

achieving Goal 6C. Global procurement of more effective anti-malarial drugs continues to rise rapidly. Generally speaking, children from the poorest households are least likely to receive treatment for malaria. However, funding from various NGOs (non-governmental organizations) is helping to make both the nets and drugs available, thereby reducing the incidence of malaria. There is a need for greater support to make these programs even more effective.

TUBERCULOSIS

Tuberculosis continues to be a major infection worldwide. Of the estimated 9.4 million new cases of TB in 2008, an estimated 1.8 million deaths (including 500,000 people with HIV) occurred. It is good to know that the global incidence rate is slowly falling. All regions of the world are on track to meet the MDG target of halving TB prevalence and deaths by 2015. The six point Stop TB strategies consists of the following principles:

1. Pursue high-quality DOTS (directly observed treatment, short-course) program expansion;
2. Focus on TB/HIV, multi drug-resistant TB, and the needs of poor and vulnerable populations;
3. Contribute to health system strengthening based on primary health care;
4. Engage all care providers;
5. Empower people with TB, and communities through partnership; and
6. Enable and promote research.

THE PROGRESS OF TB CONTROL

- Progress on tuberculosis inches forward.
- Tuberculosis prevalence is falling in most regions.
- Tuberculosis remains the second leading killer after HIV.

In summary, work to achieve the MDG 6C goals of preventing and treating tuberculosis and other major diseases, such as malaria, is moving in the right direction, but much more needs to be done to meet the target of reaching the goals by 2015.

For more information:

www.who.int/topics/millennium_development_goals/diseases/en/index.html

The Clock is Ticking!

NT



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Medical News, Products and Information

Stanford/Packard Researchers Design More Accurate Method of Determining Premature Infants' Risk of Illness

Stanford University researchers have developed a revolutionary, non-invasive way of quickly predicting the future health of premature infants, an innovation that could better target specialized medical intervention and reduce health-care costs.

"What the PhysiScore does is open a new frontier," said Anna Penn, MD, PhD, an assistant professor of pediatrics at the School of Medicine and a neonatologist at Lucile Packard Children's Hospital. "The national push toward electronic medical records helped us create a tool to detect patterns not readily seen by the naked eye or by conventional monitoring. We're now able to identify potential health problems before they become clinically obvious."

Penn is a co-senior author of the research, which was published Sept. 8 in *Science Translational Medicine*. The other senior author is Daphne Koller, PhD, Professor of Computer science in the School of Engineering.

The paper's authors likened their PhysiScore to a more reliable, electronic version of an Apgar score. The Apgar, a simple, repeatable check done shortly after birth, has for more than half a century been the standard method of assessing a baby's physical well-being and predicting whether future medical treatment might be needed.

But by taking into account gestational age and birth weight and using a stream of real-time data routinely collected in neonatal intensive care units — such as heart rate, respiratory rate and oxygen saturation — the Stanford researchers developed a probability scoring system for the health of prematurely born infants that outperformed not only the Apgar but three other systems that require invasive laboratory measurements.

Koller noted that sophisticated computational methods are critical to identifying the subtle patterns in the complex data about these young patients, as well as helping clinicians and researchers accurately discriminate between the different outcomes.

"Our method is similar to fetal heart-rate monitoring, a tool that has profoundly changed

management of labor," added Suchi Saria, the graduate student who led the research as part of her doctoral thesis in computer science. "Rather than observing a single physiological variable, however, we automatically integrate multiple physiological responses to improve accuracy."

"And the beauty is, we don't have to stick anybody with a needle or do more expensive tests," said Penn. "Now we have the possibility of using the power of data already available in the intensive care unit to greatly improve care for premature infants."

The researchers relied on data recorded during the first three hours after an infant's birth as part of a computer algorithm that predicted the baby's likelihood of developing serious illnesses with an accuracy of between 91 and 98 percent. By comparison, the success of Apgar score predictions for the same conditions ranged from 69 to 74%.

In developing the PhysiScore system, the researchers studied 138 infants cared for in the neonatal intensive care unit of Packard Children's Hospital from March 2008 to March 2009. All the babies were born at 34 or fewer weeks of gestation and weighed less than 2,000 grams, or 4 lbs, 6.5 oz. None had major congenital malformations but all suffered complications that ranged from long-term disorders affecting multiple organ systems to relatively mild problems such as slight respiratory distress.

The PhysiScore proved particularly accurate in predicting the overall risk of life-threatening events in subgroups of infants who had intestinal infections and cardiopulmonary complications, even when these were not diagnosed until days or weeks later. The researchers said that adding lab tests, such as blood-gas measurements required for other scoring methods, was not needed to make PhysiScore highly accurate.

The study authors envision infants' PhysiScores being displayed on bedside monitors along with other vital measurements that would help guide care. "This could be done cheaply," Saria said. "The hardware, the bedside monitor, already exists. It would just be a matter of layering in new software that would display the PhysiScore."

The study said better neonatal risk assessment could have the practical effect of keeping more premature infants at their local birth centers, avoiding higher costs of specialized care and transportation and "thus potentially reducing the estimated \$26 billion per year in U.S. health-care costs resulting from preterm birth."

Penn said many preterm babies have relatively good Apgar scores, even those infants who go on to develop serious health complications. "So now, with a PhysiScore, I could have two 25-week-gestation, 700-gram babies and know that they each have a very different individual risk profile," she said. "This really gives us another tool."

Saria added that although the initial research focused on assessing the health of preterm infants, "the state-of-the-art techniques we used produced a flexible framework that can be optimized for other patient populations. This should make these results of interest to a wide range of physicians and researchers."

The PhysiScore system must still go through additional testing before it could be considered for commercial use. Penn said the researchers hope to validate the new tool on a larger group of preterm babies, and study how it influences medical decision-making. "At the same time, we can try applying our methods to other groups of patients, such as children returning from surgery, to determine if there are similar early signals that can be integrated to predict complications during recovery," she said.

Koller emphasized the broader long-term potential of the new approach. "To achieve truly personalized medicine, we have to integrate an enormous amount of data: clinical symptoms, diagnostic test results, physiological data streams and, soon, genetic and genomic data," she said. "Computational methods derived from real patient records can deliver on the promise of personalized, evidence-based medicine."

Other co-authors include Jeffrey Gould, MD, MPH, Professor of Neonatology; and Anand Rajani, MD, a senior fellow in neonatology.

Babies Born Past Term Associated With Increased Risk of Cerebral Palsy

While preterm birth is a known risk factor for cerebral palsy, an examination of data for in-



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FEBRUARY MEETING FOCUS

The 24th Annual Gravens Conference on the Physical and Developmental Environment of the High Risk Infant
In collaboration with the March of Dimes
Jan. 26-29, 2011; Clearwater Beach, FL
www.cme.hsc.usf.edu

Objectives:

Identify current research that contributes to the understanding of the role of touch in development of infants.

- Relate the impact of early NICU experiences on child physical, psychological, and socio-emotional health outcomes.
- Interpret the impact of NICU related stress on parents, infants, and staff.
- Compare and contrast several 'best practices' for improving family support policies.
- Relate the impact of the NICU environment on physical, psychological and emotional health in infants, families, and staff.
- Develop strategies for applying current information to clinical practice in the NICU environment.
- Integrate strategies for cultural change in the NICU, including intrapersonal, interpersonal, clinical, environmental, and system change.
- Improve decision-making when designing physical changes (renovation or new construction) to NICUs a la 'lessons learned' in the Design Track.

Conference Chairs: Stanley N. Graven, MD; Joy Browne, PhD, RN, CNS-BC; George A Little, MD; Robert White, MD; John Hartline, MD, FAAP; George A Little, MD

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fants born at term or later finds that compared with delivery at 40 weeks, birth at 37 or 38 weeks or at 42 weeks or later was associated with an increased risk of cerebral palsy, according to a study in the September 1 issue of *JAMA*.

Cerebral palsy (CP), the most common cause of physical disability in childhood, with limitations that persist throughout life, is characterized by nonprogressive disorders of movement and posture. "One of the strongest predictors of CP is preterm birth, with the risk of CP increasing steadily with earlier delivery. Although risk is lower among term births, about three-fourths of all infants with CP are born after 36 weeks. Within this range of term births, there are few data on the possible association of CP with gestational age," the authors write.

Dag Moster, MD, PhD, of the University of Bergen, Norway, and colleagues examined the relation of CP risk with gestational age among term and postterm births using the Medical Birth Registry of Norway, which identified 1,682,441 children born in the years 1967-2001 with a gestational age of 37 through 44 weeks and no congenital anomalies. The group was followed up through 2005 by linkage to other national registries.

Of the group of term and postterm children, 1,938 were identified as having cerebral palsy. The researchers found that infants born at 40 weeks had the lowest risk of CP, with a prevalence of 0.99/1,000 births. Risk for CP was higher with earlier or later delivery, with a prevalence at 37 weeks of 1.91/1,000 (90% increased risk), a prevalence at 38 weeks of 1.25/1,000 (30% higher risk), a prevalence at 42 weeks of 1.36/1,000 (40% increased risk), and a prevalence after 42 weeks of 1.44/1,000 (40% higher risk).

The authors add that these associations were stronger in a subset with gestational age based on ultrasound measurements, with a gestational age of 37 weeks associated with a 3.7 times higher risk of CP; and 42 weeks, a 2.4 times higher risk. Adjustment for infant sex, maternal age, and various socioeconomic measures had little effect.

"Clinicians typically regard term births (37-41 weeks) as low risk, with the possibility of increased risk with post-term delivery. This standard definition of term does not correspond well with the period of lowest risk for CP in this study or with the weeks when most infants are

born. Weeks 37 and 38 seem more to resemble weeks 42 and 43, both in CP risk and in the general likelihood of delivery, leaving 39 to 41 weeks as the optimum time for delivery. If the time of delivery affects CP risk, then intervention at 40 weeks might reduce CP risk, while elective delivery at 37 or 38 weeks might increase it. If infants prone to CP are disrupted in their delivery times, the prevalence of CP would be unchanged regardless of time of delivery," the researchers write.

"Until the biological mechanisms for these patterns of risk in term and postterm births are better understood, it would be hasty to assume that interventions on gestational age at delivery could reduce the occurrence of CP."

Experts Recommend Universal Screening of Newborns for Congenital Adrenal Hyperplasia

The Endocrine Society released a new clinical practice guideline on the diagnosis and treatment of congenital adrenal hyperplasia (CAH). The guideline features a series of evidence-based clinical recommendations developed by an expert task force.

The guideline, published in the September 2010 issue of the *Journal of Clinical Endocrinology & Metabolism (JCEM)*, a publication of The Endocrine Society, is endorsed by the American Academy of Pediatrics, Pediatric Endocrine Society, the European Society for Paediatric Endocrinology, the European Society of Endocrinology, the Society for Pediatric Urology, the Androgen Excess and PCOS Society, and the CARES Foundation.

CAH is a genetic disorder of the adrenal glands that affects about one in 10,000 to 20,000 newborns, both male and female. The adrenal glands make the steroid hormones cortisol, aldosterone and androgens. In individuals with CAH, the adrenal glands produce an imbalance of these hormones which can result in ambiguous genitalia in newborn females, infertility and the development of masculine features such as development of pubic hair, rapid growth in both girls and boys before the expected age of puberty.

"If CAH is not recognized and treated, both girls and boys undergo rapid postnatal growth and early sexual development or, in more severe cases, neonatal salt loss and death," said Phyllis Speiser, MD, of Cohen Children's Medi-

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cal Center of New York and Hofstra University School of Medicine, and chair of the task force that developed the guideline. "We recommend that every newborn be screened for CAH and that positive results be followed up with confirmatory tests."

Other recommendations from the guideline - prenatal treatment of CAH should continue to be regarded as experimental. Such therapies should be pursued through protocols approved by Institutional Review Boards at centers capable of collecting outcomes data on a large number of patients so that risks and benefits of this treatment can be defined more precisely:

- Diagnosis should rest on clinical and hormone data while genotyping should be reserved for equivocal cases and genetic counseling;
- Regarding treatment, glucocorticoid dosage should be minimized to avoid iatrogenic Cushing's Syndrome. Mineralocorticoids and, in infants, supplemental sodium are recommended in classic CAH patients;
- Clinicians should avoid the routine use of experimental therapies to promote growth and delay puberty, and patients should avoid adrenalectomy;
- Early single-stage genital repair should be considered for severely virilized girls and should be performed only by surgeons experienced in this type of procedure;
- Clinicians should consider patients' quality of life, consulting mental health professionals as appropriate;
- At the transition to adulthood, clinicians should monitor for potential complications of CAH; and
- Clinicians should exercise judicious use of medication during pregnancy and in symptomatic patients with nonclassic CAH.
- "People with classic CAH should have a team of health care providers, including specialists in pediatric endocrinology, pediatric urologic surgery (for girls), psychology and genetics," said Speiser. "Other than having to take daily medication, people with classic CAH can have a normal life."

The Hormone Foundation, the patient education affiliate of The Endocrine Society, has published a new bilingual fact sheet about congenital adrenal hyperplasia for patients. It defines CAH and explains how the condition is diagnosed and treated. The fact sheet can be found online at: www.hormone.org/Resources/upload/congenital-adrenal-hyperplasia-bilingual-081310.pdf.

To learn more about the Society and the field of endocrinology, visit our site at www.endo-society.org.

Pioneer of Modern-Day Neonatology Celebrates over 50 years of Premie Care

Professor Emeritus Philip Sunshine, MD, has been very busy since he first came to Stanford in 1957, back when the School of Medicine was actually located in San Francisco. And what this humble and gentle man has accomplished not only forms a narrative of modern-day neonatal care, but makes him clearly "a pioneer and one of the creators of our discipline," says David Stevenson, MD, Professor of Pediatrics, who proudly acknowledges Sunshine's mentoring. "He's one of our history's best."

It's a history that's seen a revolution in saving lives. "When I first started seeing patients in the intensive care nursery, premie survival was less than 50%," recalls Sunshine. "Now, it's well over 90%."

Sunshine has been both author and witness to an explosion of research and care. "In 1963, when I finished my fellowship, there had been only a few papers published even talking about neonatology," Sunshine remembers. "And the term neonatology had only been around since 1960."

Stevenson, Director of the Johnson Center for Pregnancy and Newborn Services at Packard Children's, cites Sunshine's "intellectual versatility and extraordinary clinical insight" as a researcher. For example, he was a member of the team that first implemented mechanical ventilation at

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FEBRUARY MEETING FOCUS

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Annual Legends of Neonatology Award

Ceremony: 2011 Honorees - Stanley Dudrick, MD and Forrest Bird, MD

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Stanford, and devised the first scoring system for selection of infants to be treated with assisted ventilation. He was the first in the US to describe a child with ornithine transcarbamylase deficiency, a rare and deadly metabolic disorder. He was part of the team that documented for the first time the occurrence of hyperammonemia, a dangerous rise of ammonia in the blood, accompanying intravenous feedings of newborns.

Sunshine has also led groundbreaking research in developmental gastroenterology and nutrition, including one landmark 1964 study that was the first to show that lactose malabsorption can result from acute gastroenteritis. The list of his research accomplishments continues, all very deep, all very scientific, and all very lifesaving.

Looking back, Sunshine remembers one key practice he helped to advance that is now so customary it would seem bizarre to do otherwise. "Up until around 1966, parents weren't allowed to even come into the nursery with their babies," he says. "But we discovered that parents provide care that doctors and nurses could not. Parents get to know their babies at an early stage of life and the babies relate well to this."

Decades later, Sunshine is a comforting, unpretentious presence in the Intermediate Intensive Care Unit, where he prepares preemies and families for the transition home. The big-time Sudoku fan has made only one concession: He's trimmed his workweek to around 30 hours, leaving him more time for biking, tennis, grandkids and dancing with his wife, Beth.

Sunshine is famously unflashy. In the 1970s, while he was leading several divisions in neonatology and gastroenterology at Stanford, serving on national neonatology boards and associations, creating exam certification measures and more, he was tooling around Palo Alto in a clunky old Dodge Dart to the tune of 275,000 miles, Stevenson recalls. "We also used to joke about the way he dressed, with lots of keys and stuff. People mistook him for a night janitor," he says.

The awards from his peers have piled up, including the Alwin C. Rambar-James B.D. Mark Award for Excellence in Patient Care, presented May 27 at Stanford's student clinician ceremony. He is also the recipient of the prestigious Virginia Apgar Award in Perinatal Pediatrics from the American Academy of Pediatrics, as well as dozens of other honors the Denver native is too modest to mention. "I don't know why they give me these things," says Sunshine.

"He's launched an unbelievable number of careers," says William Benitz, MD, Chief of Neonatology and also the Philip Sunshine, MD, Endowed Professor in Neonatology, a position Benitz calls "a tremendous honor." Benitz notes Sunshine's coast-to-coast influence on leaders such as Josef Neu, MD, Professor of Pediatrics at the University of Florida, who salutes Sunshine as "a terrific mentor both clinically and scientifically, one who will always be remembered as truly special."

Sunshine turned 80 on June 16, and he has no plans to leave the institution he has been a part of since 1957, minus a two-year stint in the Navy in the late 1950s and four years in leadership positions at Children's Hospital Los Angeles and the University of Southern California School of Medicine.

"Phil is an amazing contributor," Benitz says. "He's out on the road and involved in regional outreach programs, visiting community hospitals and providing ongoing medical education. From my perspective, Phil just might work forever. He's still fully-engaged in babies and their care, not as a detached authority figure but in a very intimate way. He is extraordinarily important to our mission as neonatologists, and his perspective and achievements are timeless."

"I've been lucky," Sunshine says. "I grew up in an exciting new sub-specialty, I have five healthy children and six healthy grandkids, my wife still puts up with me, and if my health stays OK, I'll keep working. My agreement with the division chief is that as long as I do an excellent job, he'll keep me on."

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