



# Neonatal News

Fall 2009

Neonatology at The Children's Hospital of Philadelphia

## Picture Perfect

### CHOP pioneers use of ultra-low-dose CT angiography with 3-D reconstruction

Increasing numbers of babies are being referred to The Children's Hospital of Philadelphia's Harriet and Ronald Lassin Newborn/Infant Intensive Care Unit (N/IICU) with severe chronic lung disease (CLD). The referring physician and family are always looking for answers and guidance about the baby's condition and available treatments.

With the rise in neonatal referrals with significant and often debilitating CLD, CHOP has increased capacity to offer these infants timely and extensive pulmonary diagnostic evaluations.



Jeffrey Hellinger, M.D.

Recently, CHOP introduced a novel technology that makes evaluation and diagnosis quicker, more efficient and less risky. Jeffrey Hellinger, M.D., a pediatric radiologist specially trained in multidetector computed tomography angiography (MDCTA, or CTA), has worked since 2006 to perfect a new application of CTA with ultra-low-dose radiation (one-tenth that of conventional CT or about 10 chest X-rays) for the neonate. According to Hellinger, current protocol routinely yields less than 1 mSv tissue exposure with a dose-length product (DLP) of 3 to 4. Routine chest CT exams can have a DLP between 50 and 100, yielding 2-4 mSv for a neonate.

The use of traditional technology, including chest X-rays, plain CT and ventilation-perfusion scans, often provides an incomplete assessment in the evaluation of severe CLD. The wide anatomic variations in lung destruction, airway abnormalities and parenchymal scarring often can't be captured with these conventional forms of evaluation.

At Children's Hospital, CTA has replaced conventional CT and MRI for evaluation of infants with bronchopulmonary dysplasia. CHOP radiologists frequently use CTA to diagnose cardiac and vascular congenital disease in the neonatal period. Airway and lung parenchyma are evaluated with high-resolution detail along with the cardiovascular structures. This makes CTA an excellent modality for comprehensive evaluation of airway and lung parenchyma and cardiovascular structures in neonates with

bronchopulmonary dysplasia and CLD. In addition to assessing the airway and lung parenchyma, a baseline study is performed to assess the right cardiac chambers, exclude intra- and extracardiac shunts, and evaluate the pulmonary arteries. 3-D reconstructions of the thoracic cardiovascular and noncardiovascular structures are generated and used for radiologist interpretation, clinical treatment planning and patient counseling.

*Story continued on next page*

### Case Study



*Significant Pruning of the Pulmonary Vasculature*

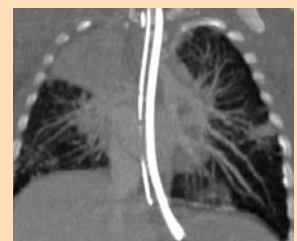
In an infant with right congenital diaphragmatic hernia and pulmonary hypertension, CTA can depict enlarged central pulmonary arteries with peripheral pruning and loss of vasculature. 3-D reconstruction of the lung demonstrates compensatory emphysematous changes of the right lung with collapse of the left lower lobe. Conventional chest CT would

not elucidate this information as precisely as the multidose CTA. Additionally, we are able to alter the PEEP and get lung inflation measurements, measure heart chamber size and obtain a virtual bronchoscopy all in one rapid study.

*Below: CTA of congenital diaphragmatic hernia lung with 3-D reconstruction showing severe loss of pulmonary parenchyma with atelectasis and volume reduction and accompanying airway disruption.*



*3-D Reconstruction — CDH*



*Axial View of Airways*

Story continued from cover

In comparison to other modalities currently used for evaluation of this population, CTA:

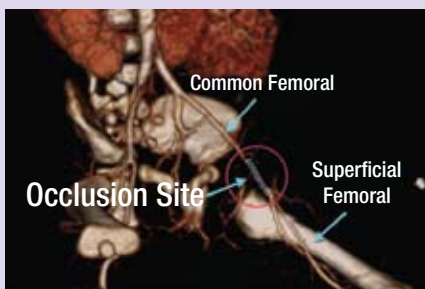
- provides greater detail and understanding than a chest radiograph
- helps reduce the number of daily chest radiographs
- quickly provides key anatomical cardiac and vascular information
- may obviate the need for or reduce the procedural extent of a cardiac catheterization

CHOP is currently the only pediatric hospital in the region to offer this new therapy. This low-dose protocol is crucial for neonates because they are far more susceptible than older, healthier babies to the effects of radiation. Neonates, by nature, receive more radiation because they receive many tests in the course of their diagnosis and treatment, resulting in the repeated use of plain-film X-rays and exposure to cumulative high-dose radiation without the benefit of a certain diagnosis.

The novel use of ultra-low-dose CTA for this group of infants with severe and progressive CLD has proven to be a milestone in pediatric radiology at CHOP. This specialized imaging allows more rapid planning for future care needs, such as evaluation for tracheostomy or medical treatments for severe CLD.

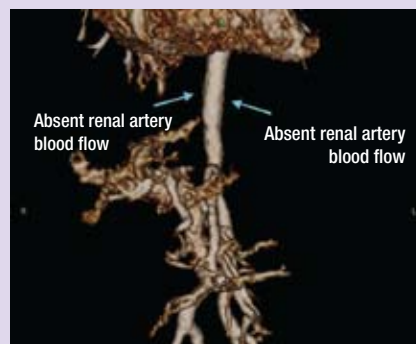
## Other Uses for CTA in Neonates

Several recent N/IICU referrals to CHOP made use of CTA. Here are descriptions of two of them:



When a full-term infant with a white leg was transported to CHOP, Bill Fox, M.D., ordered a relatively new test, CTA with 3-D reconstruction. In less than an hour, the results (left) showed a

spontaneous, occlusive thrombus in the femoral artery with some collateral circulation surrounding the clot. Fox ordered immediate heparin therapy, and the baby showed improvement in the following days. The N/IICU team was then able to use bedside ultrasound to monitor the therapy because CTA had elucidated the exact anatomic defect. The result was less radiation for the patient and more convenience for the family, whose baby did not



need to be moved for another CTA.

A premature twin was referred from Pennsylvania Hospital with sudden significant hypertension and rising creatinine. Within hours of admission to CHOP, a CTA of the aorta and renal arteries

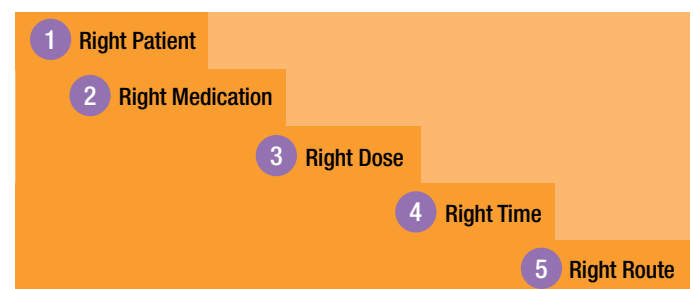
(above) showed almost complete calcification and obliteration of both renal arteries and the mid-aorta. The technology allowed for an immediate diagnosis of idiopathic calcinosis and mid-aortic syndrome, allowing appropriate therapy to begin earlier than it otherwise would have.

## John Chuo Joins Division of Neonatology

Previously of the Robert Wood Johnson Medical School, John Chuo, M.D., M.S., joined the faculty here in 2008 to lead the Quality Control Team for the N/IICU. He is the Q.I. Patient Safety Officer and directs many N/IICU Q.I. committees, including Unit Quality and Patient Safety, Infection Control, and Discharge and Patient Flow. Chuo has already been instrumental in developing a Q.I. model for minimizing medication errors that counts ownership, communication and data among its key elements. At the bedside, he runs weekly patient safety walk-rounds with each team, focusing on issues such as central line usage and infection, unplanned extubation and the establishment of “clean zones” in each patient’s environment.

Chuo is the recent associate editor of the book *Improving Medication Use and Outcomes with Clinical Decision Support: A Step-by-Step Guide*.

### Minimizing Medication Errors Model



# Advances in Neonatal Genetics at CHOP

When a baby is referred for a genetics evaluation, Elaine Zackai, M.D., director of Clinical Genetics, and her team are usually waiting at the entrance to the N/IICU long before the transport team arrives. As fast as Zackai appears, she disappears with the patient's blood sample in hand. The sample is delivered to the CytoGenomics Laboratory, where it undergoes complete Genome-wide SNP Array Testing.

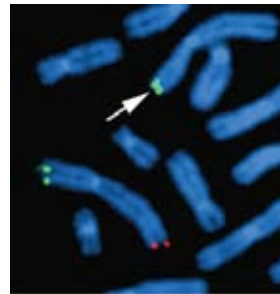
The SNP array uses the information available from genotyping more than 600,000 single nucleotide polymorphisms (SNPs) to create a picture of the deletions and duplications present in a patient's genome. The resolution of this test is about 100- to 200-fold higher than standard chromosome analysis. Often, these babies have had prior genetic testing and were thought to be "normal." But the microarray-based tests available in the CHOP laboratory can identify genetic abnormalities that are frequently missed with other technologies and in other laboratories.

The CytoGenomics Laboratory has also been able to diagnose genetic disorders caused by single gene deletion or duplication. This opens the door for diagnosis with new clinical indications for testing, such as hearing loss or ocular abnormalities, which may not be accompanied by the developmental delay that was always a hallmark of chromosome abnormalities.

The technology provides several direct benefits:

- Better coverage of the genome, with more than 400 dosage-sensitive genes analyzed
- Precise delineation of breakpoints of the abnormalities, revealing gene content
- Enhanced diagnosis of mosaicism (only some cells having the abnormality)

CHOP's program in CytoGenomics combines our world-class cytogenetic, genomic, bioinformatic and clinical expertise to vastly improve the diagnosis of genetic abnormalities. This test allows us to increase our diagnostic rate and map the abnormalities at the genomic level with increased precision, for better diagnosis and prognosis. In some cases, a genetic diagnosis can be made before the full clinical phenotype is appreciated, leading to a "genotype first" approach for infants with only subtle or no dysmorphisms.



*Area of gene deletion diagnosed by fluorescent in situ hybridization (FISH)*

---

## CHOP Launches Intestinal Rehabilitation Program

CHOP is a major referral center for infants with severe necrotizing enterocolitis. Often, these infants end up with substantial loss of the small bowel after surgery and experience major feeding difficulties and long hospitalizations.



*Clockwise from top left: Michael Posencheg, Brenda Waber, Rose Graham and Joy Collins*

CHOP has introduced a comprehensive, multidisciplinary intestinal rehabilitation program (IRP) for these patients. The goal of the IRP is to provide consistent, consultative care across both the inpatient and outpatient settings for patients with short bowel syndrome to unify care and improve patient outcomes. Under the direction of gastroenterologist Rose Graham, M.D., M.S.C.E., neonatologist Michael Posencheg, M.D., neonatal nutritionist Brenda Waber, R.D., C.S.P., C.N.S.D., L.D.N., and surgeon Joy Collins, M.D., F.A.A.P., will direct the neonatal care of infants referred to CHOP for treatment of short bowel syndrome.

Eligible infants are those who:

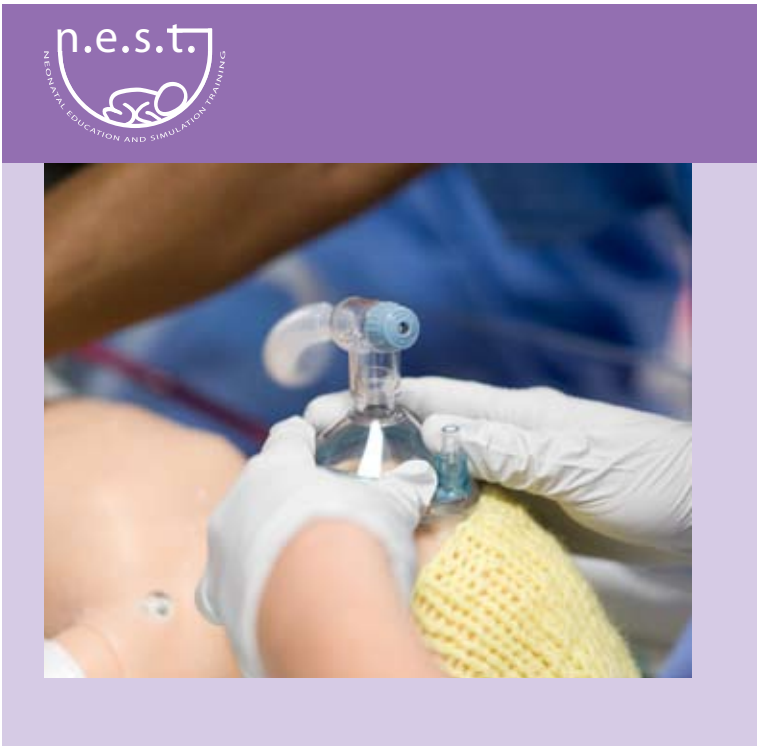
- have undergone surgical bowel resection
- are dependent on TPN for more than 30 days
- have lost their ileocecal valve (ICV)
- have less than 40 cm remaining bowel with or without the ICV

The outpatient IRP clinic is held weekly, and all infants are followed closely. All referrals are done through the N/IICU with an inpatient evaluation.

# Simulation Training: New Space, New Approach

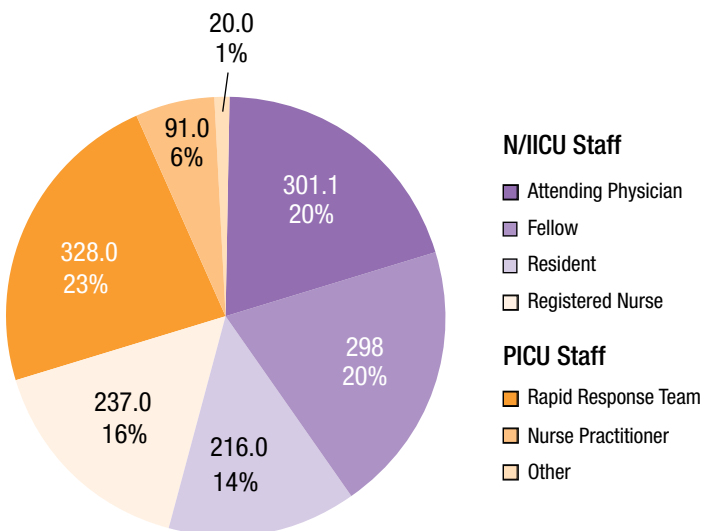
Teamwork is essential in any medical endeavor — but it's especially important in the delivery room. Anne Ades, M.D., who directs the N/IICU's simulation training program, recognized that the Garbose Family Special Delivery Unit was the ideal venue for this type of training. Designed to produce a more consistent team approach for the nurses, fellows and attendings, organized and planned

simulations translate into seamless precision at the most complex and high-risk deliveries at CHOP. This team simulation training has been pivotal in shaping the way the SDU is organized and run. In addition, there is now a dedicated space in the N/IICU for most simulation training sessions called the Neonatal Education and Simulation Training center (the NEST).

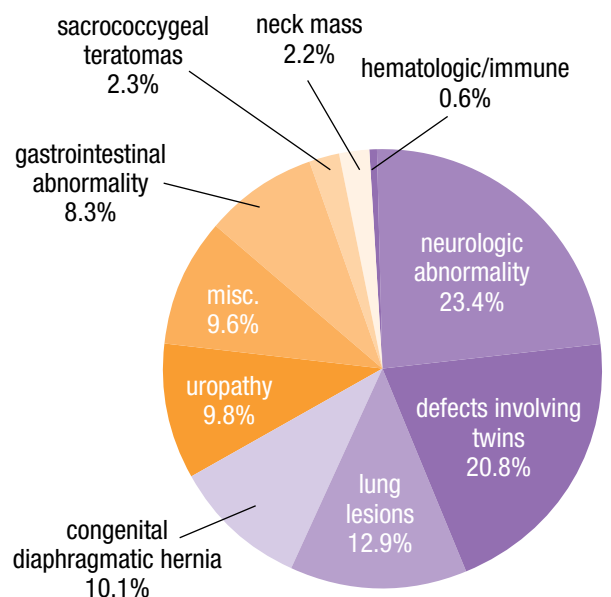


Anne Ades, M.D., directs the N/IICU's simulation training program

## Simulation Contact Hours by Discipline



## Cases and Deliveries — Center for Fetal Diagnosis and Treatment/SDU



## Research Corner

### CHOP Helps Create First-of-Its-Kind Database

Under the direction of Jacquelyn Evans, M.D., F.R.C.P. (c), F.A.A.P., and Michael Padula, M.D., CHOP's Division of Neonatology has spearheaded an initiative among large U.S. children's hospital NICUs to create a first-ever database, the Children's Hospitals Neonatal Consortium (CHNC), to benchmark quality of care and outcomes for the specialized patient population of older infants in tertiary and quaternary NICUs.

This database allows participating hospitals to collect and compare information on patients who come to these large NICUs from community hospitals and therefore are not eligible for the Vermont-Oxford Network.

CHNC was formed as an informal group in 2006 due to a need for high-quality clinical data that could be used for quality-improvement projects and research in this population.

CHNC is working collaboratively with the support of the Child Health Corporation of America to improve care for the hospitals' highest-risk patients.

#### Initial improvement opportunities identified by CHNC:

- improve diagnosis-specific outcomes in >1,500 gram babies
- reduce disease-specific infection rates and unnecessary variations in cost of care
- improve variations in discharges and readmission rates
- improve diagnosis-specific outcomes in surgical care

### Enrollment Continues for Neonatology Clinical Trials

The two ongoing funded clinical trials in the Division of Neonatology, the Canadian Oxygen Trial (COT) and the Nasal Intermittent Positive Pressure Ventilation (NIPPV) study, are increasing their enrollment at a steady rate. Our first community hospital, Virtua Voorhees, has joined the NIPPV study this year under the direction of Jane Ierardi, M.D.

COT: 799 Infants Enrolled

NIPPV: 324 Infants Enrolled

For more information on joining clinical trials at CHOP, please contact Barbara Schmidt, M.D., F.R.C.P. (c), M.S.C., director of Clinical Research.

## Staff Honors and Accomplishments

**David Munson, M.D.**, recently passed his boards in Palliative Care Medicine. Munson attends on the Pediatric Advanced Care Team (palliative care) throughout the Hospital and has been instrumental in assisting many N/IICU families through end-of-life decisions.

**Anne Ades, M.D.**, was featured as a "Rising Star" in *Philadelphia* magazine's 2009 Top Doctors issue for her work with simulation. Also featured was **Scott Lorch, M.D., M.S.C.E.**, for his work with neonatal outcomes research.

**Jacquelyn Evans, M.D.**, received the prestigious Master Clinician Award at CHOP this year in recognition of her hard work and her dedication to the N/IICU.

**Janet Liroy, M.D.**, received the March of Dimes Salute to Bucks County Women of Achievement Award. She will be participating in several events for the organization throughout the upcoming year.

Fellow **Sara DeMauro, M.D.**, received the NRP Young Investigator Award and fellow **Clyde Wright, M.D.**, received the Boggs Award at the Philadelphia Perinatal Society this year.

## Case Report: Neonatal Infectious Disease

A 1,100-gram infant was born to a 24-year-old G3P2 at 27 5/7 weeks, delivered by c-section due to breech presentation in labor. The last reported prenatal ultrasound was at 20 weeks and was normal. This was the mother's first baby with a new father and all prenatal labs were negative. The infant received surfactant for respiratory distress but was noted to have a persistent metabolic acidosis, denuding skin rash and large cranium at birth. The infant was transferred to CHOP for management with a preliminary diagnosis of epidermolysis bullosa, macrocephaly and persistent metabolic acidosis.



Upon arrival to CHOP, the baby immediately had a head U/S, and antiviral and antifungals were started for suspicion of congenital infection.

Dermatology and Neurology were consulted and direct fluorescent antibody (DFA) of the skin lesions was sent for herpes and varicella tests, as well as scrapings for KOH and yeast. A skin biopsy was also sent. An ophthalmologic exam revealed microphthalmia and cloudy corneas.

*Continued on back panel*

Questions:

1. What is the differential diagnosis of the rash?
2. What does the head U/S represent?
3. What tests would confirm the diagnosis? What are the tests' sensitivities?
4. What are the transmission rates for the diagnosis?
5. What is timing of transmission for the diagnosis?
6. What is the mortality?

Discussion:

*In utero* HSV occurring before 20 weeks of gestation is a rare and mostly fatal disease. As opposed to the 85 percent of cases of neonatal HSV occurring at the time of delivery, less than 5 percent of cases are classified as *in utero* transmission, with most caused by HSV-2. Since most cases occur in younger women, one must entertain a high suspicion of fetal maldevelopment early in order to anticipate the diagnosis. Since most infections occur around midgestation, these cases may not be picked up until after delivery. Humans are the only reservoirs of HSV-2, which is highly neurotropic and latent. Approximately 60 percent of women who acquire genital HSV during pregnancy have no symptoms and before pregnancy, many have had a new sexual partner during a primary outbreak. Several factors increase the risk substantially: a lack of passive antibody transfer, young parity, ROM and use of fetal-scalp electrodes. As a rule, a triad of severe cutaneous manifestations, ophthalmologic findings and severe neurologic involvement are present with *in utero* HSV transmission. Of the few survivors, most have severe neurologic morbidities. High-dose acyclovir should be started initially if the clinician notes these findings at birth.

1. Congenital candida, HSV, varicella, bacterial sepsis; epidermolysis bullosa/hyperkeratosis, collagen membrane rupture, histiocytosis, mastocytosis; other noninfectious transient erosions
2. Severe hydranencephaly with brain destruction
3. Fresh open vesicle swab: Tzanck-poor-67 percent; DFA-better-77 percent; PCR-best-99 percent
4. 50 percent-primary outbreak; 30 percent-nonprimary but first clinical episode; 1-3 percent-recurrent
5. Transmission: 5 percent *in utero*; 85 percent peripartum; 10 percent postnatal
6. Mortality: 80 percent without treatment; 57 percent with treatment. 70 percent mortality with dissemination to CNS. Survivors: 80 to 90 percent neurologic impairment with dissemination

Answers:

# Calendar of Events

## Advances in Neonatology: Full-day CME

Leonard and Madlyn Abramson Pediatric Research Center

Wednesday, Oct. 14, 2009

Featured national and international speakers:

Steven Abman, M.D., University of Colorado School of Medicine and The Children's Hospital: "The New BPD — A Neonatal Dilemma"

Jay P. Goldsmith, M.D., Tulane University: "Advances in Neonatal Resuscitation"

Barbara Schmidt, M.D., The Children's Hospital of Philadelphia: "Interpreting Neonatal Clinical Trials"

Richard Shannon, M.D., University of Pennsylvania School of Medicine: "Creating a Culture of Safety in Medicine"

## Dinner Lectures

Presented by the Neonatal Outreach Program

Wednesday, Sept. 16, 2009

Thane Blinman, M.D.: "Minimally Invasive Surgery in Neonates"

Presented by the Cardiac Center

Wednesday, Sept. 30, 2009

"Outcomes and Current Surgical Options for the Neonate with CHD"

Thursday, Nov. 5, 2009

"Transposition of the Great Arteries"

Presented by the Center for Fetal Diagnosis and Treatment

Wednesday, Oct. 28, 2009

"Abdominal Wall Defects"

## Neonatal Fellows Conferences:

Tuesdays at 11 a.m., CHOP Main Bldg.

Coming Soon: WebEx conferencing for the community

For more information, please contact Patti O'Connor at 215-590-2616.

### Editor:

Janet Liroy, M.D.

### Contributing Editors:

Sulagna Saitta, M.D.

Jeffrey Hellinger, M.D.

Jacquelyn Evans, M.D.

John Chuo, M.D.

### Contact Us:

For transport, call 215-590-3083.

For more information, visit [www.chop.edu](http://www.chop.edu).