The Division of Neonatology at The Children's Hospital of Philadelphia is making significant advances in patient care and research. We're proud of the work highlighted here because, like our colleagues across the country, we're devoted to the children to whom we provide care. We hope you find this update interesting and useful. Contact us at **oconnorp@email.chop.edu** for more information.

U.S.News & World Report BEST CHILDREN'S HOSPITALS Honor Roll 2010-11

Today at CHOP: Neonatal Update

FOCUS ON CHRONIC LUNG DISEASE:

New Program Improves Care for Complex Condition

Despite advances in neonatal care, bronchopulmonary dysplasia (BPD), or chronic lung disease (CLD), remains a major source of morbidity and mortality for extremely low birth weight infants. Because of the increasing survival of extremely low birth weight infants, the burden of morbidity from BPD is growing. The Newborn and Infant Chronic Lung Disease (NeoCLD) Program at The Children's Hospital of Philadelphia is one of the first programs in the country devoted to more comprehensive and consistent treatment of infants with this complex condition.

The Newborn and Infant Chronic Lung Disease Program provides comprehensive treatment of infants to achieve the best outcomes.

Housed within CHOP's Harriet and Ronald Lassin Newborn/Infant Intensive Care Unit (N/IICU), the NeoCLD Program was created in response to a steady increase in referrals for infants with BPD to the N/IICU over the past five years. The program brings together diverse expertise across different divisions at CHOP.

"As a neonatologist, I don't have the magic bullet to cure this disease," says Huayan Zhang, M.D., neonatologist and medical director for the NeoCLD Program. "This is a multisystem disease that needs a multidisciplinary team approach to achieve the best outcomes."

The program's integrated team includes attending neonatologists, specialized nursing teams, respiratory therapists, neonatal clinical pharmacists, neonatal nutritionists, physical, occupational and speech therapists, case managers, and a psychosocial support team. This team collectively follows each patient throughout his/her hospital stay, and works closely with the primary care team to ensure patient safety and continuity of care.

Jointly, the team is establishing treatment protocols to improve inpatient safety and outcomes, and facilitate the transition from intensive care to long-term care and outpatient follow-up. The program's comprehensive database will offer high-quality data on the care and outcomes of infants treated for this condition in an effort to develop more definitive, effective treatment and prevention of BPD going forward.

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>
> — Huayan Zhang, M.D., neonatologist and medical director, Newborn and Infant Chronic Lung Disease Program

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DIVISION OF NEONATOLOGY

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Multidisciplinary Care, from Evaluation to Long-term Follow-up

Close collaboration with specialists throughout The Children's Hospital of Hospital — including the Pulmonary Hypertension Program, Neonatal Airway Program, Pulmonary Function Testing, Bone Health Team and Technology Dependence Center — means patients in the Newborn and Infant Chronic Lung Disease (NeoCLD) Program receive the most comprehensive care, all in one place. Regular patient discussion meetings facilitate direct communication between multiple disciplines, promote joint decision-making and aid in the development of consensual, evidence-based patient care protocols.

"Direct communication across disciplines has really helped with care management, understanding the pathophysiology and deciding the best treatment approach for each patient," says Huayan Zhang, M.D., neonatologist and medical director for the NeoCLD Program.

The program employs the most advanced diagnostic modalities, including sophisticated imaging (e.g., ultra low-dose CT angiogram and ventilation/perfusion scan), pulmonary function testing, cardiac catheterization, and laboratory testing for nutrition and bone health. The program takes advantage of the expertise from highly trained bronchopulmonary dysplasia (BPD) nurse champions, neonatal pharmacists and neonatal nutritionists, as well as physical, occupational and speech therapists at CHOP. The team's goal: comprehensive and optimal management of cardiopulmonary diseases and nutritional deficiencies, while minimizing or normalizing developmental delays.

After thorough evaluation, the program's multidisciplinary team devises a unified treatment plan. For many of these patients, an important component of therapy is time. Providing adequate yet gentle ventilatory support, controlling pulmonary hypertension (a significant, life-threatening complication of BPD), and preventing the deleterious effects of gastroesophageal reflux and aspiration on the developing lungs and airways, in addition to providing optimum nutrition, allows for growth and healing of the immature and damaged lungs.

Ex preemie with Trisomy 21, CLD and pulmonary hypertension transferred from N/IICU to Progressive Care Unit for transition to home.

Patients are followed through CHOP's Neonatal Follow-up Program, the Division of Pulmonary Medicine, the Pulmonary Hypertension Program and the Neonatal Airway Program. In the case of infants with tracheostomies, the Technology Dependence Center is also involved. All of these programs seamlessly integrate their investigation and treatment plans with those of the NeoCLD Program, during both hospitalization and outpatient follow-up.

Family support and education are also essential components of the NeoCLD Program, as babies with BPD often have conditions that require prolonged hospitalizations and long-term outpatient care. A psychosocial team consisting of social workers, psychologists and child life specialists works closely with clinicians to support families.

When treatment in the intensive care setting is no longer needed, the team facilitates the transition to home, home hospital or a chronic care facility. Working with social workers, case managers and, when indicated, the Progressive Care Unit, Integrated Care Service and the Technology Dependence Center, the team empowers parents to care for their child at home whenever possible.

Attending Neonatologists on the Chronic Lung Disease team (left to right)

Kathryn Maschhoff, M.D., Ph.D.
Medical Director

Haresh Kirpalani, M.D.
Program Director

David Munson, M.D.
Attending Physician

Huayan Zhang, M.D.
Medical Director

(Not pictured, Soraya Abbasi, M.D.)

Advancing Research to Guide Care

The absence of a definitive treatment or prevention for BPD is due in large part to the lack of high-quality data.

To address this issue, the Newborn and Infant Chronic Lung Disease Program (NeoCLD) at The Children's Hospital of Philadelphia is developing a comprehensive, interdisciplinary database that documents the care and outcome of infants with severe BPD to establish evidence-based standards for management. The database links to databases within CHOP's divisions of Neonatology and Pulmonology, as well as the Pulmonary Hypertension Program, the Progressive Care Unit, the Neonatal Airway Program and the Neonatal Follow-up Program. The database will enable tracking of all patients after discharge to ensure the capture of post-discharge measures of cardio-respiratory function, social and psychometric functioning, feeding progress, and visits to the ED and/or pediatricians.

"The current lack of high-quality data in BPD drives significant practice variations and limits evidence-based prevention and treatment," says Haresh Kirpalani, M.D., neonatologist and program director for the NeoCLD Program. "This program will help develop evidence-based guidelines for both acute and chronic care in these patients and gather outcome data which is crucial in understanding the disease progression and in the development of treatment guidelines."

Research is integral to this program, as it informs clinical practice. The program is working with clinicians and scientists to develop a broad, evidence-based approach to the management of BPD, facilitating research collaborations between clinical trialists, basic researchers and clinicians within neonatology, and promoting collaborations with investigators from other divisions within the Hospital.

Case Study: Bronchopulmonary Dysplasia

An ex 24-week premature infant was delivered by C-section at a community hospital with a birth weight of 660g. He was intubated in the delivery room and given surfactant. A PDA ligation was performed on day of life (DOL) 21. He received mechanical ventilation for 69 days, NCPAP for 8 days and then transitioned to 6L high flow nasal cannula (HFNC) with persistent work of breathing (WOB) and high oxygen requirement.

He was transferred to The Children's Hospital of Philadelphia at 5 months old on 6 L/min HFNC. Soon after admission to CHOP, he was intubated due to severe WOB on 7L HFNC with FiO2 up to 80-100 percent and hypoxia spells. Echocardiogram was concerning for high right ventricular pressures, and inhaled nitric oxide (iNO) was started in an effort to reduce the frequency and severity of spells.

The patient underwent ultra low-dose CT angiography, which showed significant chronic lung disease and a decrease in the caliber of both mainstem bronchi during expiration, but only minimal evidence of pulmonary hypertension. Patient continued to have significant desat/brady episodes despite ventilation with high PEEP (as high as 18 cm of water) and iNO. To further delineate the possible role of pulmonary hypertension in this patient's BPD spells, he was taken to the cath lab and again showed evidence of significant lung disease without overt evidence of pulmonary hypertension. During the cardiac catheterization, it was noted that he had elevated pulmonary vascular resistance at a PEEP of 18 with diminished cardiac output, which improved when the PEEP was dropped to 10.

Based on these findings, the infant was subsequently ventilated with lower PEEP, and the iNO was weaned off. On DOL 189 the infant underwent bronchoscopy, which revealed grade 2 subglottic stenosis and tracheobronchomalacia, and a tracheostomy was placed. Five weeks later, he underwent a laparoscopic Nissen fundoplication to protect his airway from gastroesophageal reflux, and a gastrostomy button was placed to facilitate feeding. He was transitioned to PEEP with pressure support on a home ventilator and transferred to our Progressive Care Unit to begin preparation for discharge to home.

Taking advantage of the advanced diagnostic modalities available at CHOP and the expertise from our specialists, we were able to come up with the best strategy to manage his severe lung disease with significant tracheobronchomalacia. In addition to thorough medical care, our psychosocial team worked closely with the parents throughout the baby's stay at CHOP and helped his mother overcome significant social and emotional challenges.

For more information or to make a referral, please call **215-590-3083** or e-mail **maschhoff@email.chop.edu** or **zhangh@email.chop.edu**.

Case Study: A Difficult Airway

What is this syndrome?

Baby Girl "M" was born by SVD at a local hospital at term to a primigravida. Pregnancy was uncomplicated except for mild diet-controlled gestational diabetes. There was some concern that the fetus had a large head, but this was not confirmed.

No neonatologist was present, so the pediatrician was called after the delivery for respiratory distress and desaturations. The infant was brought to the SCN, a blood culture was sent and antibiotics were started for r/o sepsis. The baby continued to desaturate and was started on oxygen cannula. After worsening respiratory distress, the neonatologist was called to evaluate the infant.

Initial exam was notable for what was thought to be a large head, flat mid face and cleft palate. Lungs were clear and there was no murmur audible. When the neonatologist arrived, he felt there was a significant component of micro and retrognathia and immediately positioned the baby prone. There was relief of the respiratory distress, and the baby was transferred to a level 3 center for evaluation of possible Pierre Robin sequence.

Upon evaluation of the infant by genetics, ENT, ophthalmology and craniofacial surgery, it was determined that the infant probably had Stickler syndrome, not simple Pierre Robin sequence. Furthermore, upon taking a good family history, it was noted that the father has severe nearsightedness, difficulty hearing, large eyes, mild arthritis and scoliosis, but was never diagnosed. His mother recalls him having "a small jaw" and difficulty feeding when he was a baby, but no palate issues.

In the end, both the infant and her father were diagnosed with the autosomal dominant form of Stickler syndrome. Although this was a shock to the family, genetic counseling was accomplished and all the necessary services were put in place for both the infant and her father.

The infant went on to have mandibular distraction by the Craniofacial team at The Children's Hospital of Philadelphia, was discharged to home by 2 weeks and is feeding by mouth without symptoms.

What is Stickler Syndrome?

Stickler syndrome is a group of hereditary conditions and may be the basis for about 40 percent of infants with Pierre Robin sequence. In fact, and as was seen in this case study, many individuals do not know they have Stickler syndrome.

Stickler syndrome affects an estimated one in 7,500 to 9,000 newborns. Caused by underdevelopment of facial bones, there is distinctive flattened facial appearance, eye abnormalities, hearing loss and joint problems which vary widely among individuals. A particular group of physical features called Pierre Robin sequence is also common in people with Stickler syndrome. Pierre Robin sequence includes cleft palate, macroglossia and micrognathia.

The eye findings are specific and include severe nearsightedness (high myopia). In some types of Stickler syndrome, there is abnormal vitreus appearance, glaucoma, cataracts and retinal detachment.

Genetics

There are four types of Stickler syndrome, which are distinguished by their genetic cause and their characteristic signs and symptoms, (eye abnormalities and severity of hearing loss). Three gene mutations have been identified as causing Stickler syndrome: *COL11A1, COL11A2* (non-ocular) and *COL2A1* (75 percent of Stickler cases). Other genes that have not yet been identified may also cause Stickler syndrome. One type, often called non-ocular Stickler syndrome, does not affect the eyes.

These genes are involved in the production of three types of collagen: type II, type IX and type XI, which are components of vitreous, cartilage and other connective tissues. Defective collagen molecules or reduced amounts of collagen disrupt the development of connective tissues, leading to the characteristic features of Stickler syndrome.

Stickler syndrome tends to run in families. There is a 50 percent chance of recurrance if inherited as autosomal dominant.

People with Stickler syndrome have the following characteristics:

- some degree of cleft palate
- cataracts and/or retinal detachment at an early age
- flat face
- small jaw
- skeletal abnormalities
- hearing loss
- severe myopia

FACES: The National Craniofacial Association
www.faces-cranio.org

Stickler syndrome is a group of hereditary conditions and may be the basis for about 40 percent of infants with Pierre Robin sequence.

Advances in Craniofacial Surgery in Neonates: Mandibular Distraction Osteogenesis Revisited

Neonates with upper airway tongue-based obstruction present a diagnostic and therapeutic challenge to the treating medical team. Tracheostomy and prolonged hospitalization have defined treatment in many neonates with airway compromise due to major craniofacial syndromes such as Pierre Robin sequence, and Treacher-Collins, Goldenhar, Nager and Stickler syndromes. These neonates can present with varying degrees of feeding difficulties and respiratory distress secondary to posterior displacement of the tongue, abnormal tongue posture and retrognathia, and traditionally spend months hospitalized undergoing multiple attempts at extubation, tube feedings and sleep studies only to require tracheostomy and gastrostomy tube insertion.

Though many different diagnostic and management algorithms have been advocated for the treatment of neonates with tongue-based obstruction, there are no evidence-based guidelines for the neonatal population. The difficulty in developing guidelines arises from several reasons, mostly due to the variability at presentation — some present as an isolated entity, others as part of a syndrome along with other congenital anomalies. Additionally, a subset of neonates with tongue-based obstruction will resolve their upper airway obstruction with time and mandibular growth, and therefore need only temporizing measures.

CHOP Plastic Surgeon Jesse Taylor, M.D., and our Neonatal Airway Team are dedicated to developing evidence-based guidelines for the treatment of this patient population. One exciting new treatment alternative to tracheostomy offered at CHOP is neonatal mandibular distraction, a procedure whereby the micrognathic mandible is slowly elongated, clearing tongue-based airway obstruction. Dr. Taylor and others at CHOP have considerable experience with this innovative surgery. In fact, the craniofacial team has done three successful mandibular distractions this year alone within a six month period.

Mandibular distraction osteogenesis is a mechanical bone lengthening process by which two small, semi-buried lengthening devices are applied to the mandibular distraction sites. Each device is made up of two stainless-steel components connected to each other by a drive screw, which is the part of the distractor that allows for lengthening of the mandible. A distractive force is applied to the activation screw through a universal joint driven by a transcutaneous barrel with applied traction along a plane parallel to the mandibular body. Osteotomies are performed via a transcutaneous approach and external corticotomy extended diagonally from the posterior edge of the alveolar ridge to the gonial angle, with attention paid to the dental buds. A series of holes are made in the internal cortical layer as care is taken to avoid the inferior alveolar nerve, then four cortical screws are inserted. The osteotome is then rotated, which increases bone length, and the distractor is stabilized. Distraction is usually initiated one or two days after the initial surgical procedure and continued at a certain mm/day rate for two to three weeks.

The entire process is complex and lengthy, often involving two to four weeks of distraction and another four to 12 weeks for bone consolidation. Mandibular bone length upwards of 15 mm can be achieved and the entire process can take several months.

Success has been reported in numerous large academic institutions and children's hospitals. Bronchoscopy at the time of distractor removal often shows correction of airway obstruction at the base of the tongue. Typical X-rays show bilateral ossification at the distraction sites. The larger mandible allows neonates to breathe, and even eat, better.

In selected neonates with significant microretrognathia and tongue-based airway obstruction, mandibular distraction osteogenesis can successfully avoid the need for tracheostomy and the associated mortality and morbidity while still preserving the airway.

Dr. Taylor believes mandibular distraction has the potential to change the lives of thousands of children who live with tracheostomies, as well.

"If a child has a tracheostomy to bypass tongue-based airway obstruction, mandibular distraction may allow them to breathe without the need for their tracheostomy," he says. "In fact, by lengthening a deficient mandible, obstructive sleep apnea (OSA) of the tongue base can be cured at any age. OSA has been linked to developmental delays, poor school performance and ADHD, all of which may subside once the OSA has been treated."

Congenital indications:

- Cleft lip and palate
- Severe micrognathia/retrognathia
- Goldenhars hemifacial microsomia
- Pierre Robin sequence and Stickler syndrome
- Nonsyndromic craniosynostosis – coronal (bilateral or unilateral) or sagittal
- Syndromic craniosynostosis – Aperts, Crouzons and Pfeiffer syndromes


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Professional Education

For information on ongoing professional education events, contact Patricia O'Connor at 215-590-2616 or oconnorp@email.chop.edu.

Welcome

The Division of Neonatology is pleased to announce the addition of **Kevin Dysart, M.D.**, to our team. An attending neonatologist and assistant professor and academic clinician at the University of Pennsylvania School of Medicine, Dr. Dysart is certified in neonatal-perinatal medicine by the American Board of Pediatrics. He received his M.D. from Hahnemann University, Philadelphia, and completed a residency in pediatrics at Thomas Jefferson University in Philadelphia and duPont Hospital for Children in Wilmington, Del. He also completed a fellowship in Neonatal and Perinatal Medicine at Thomas Jefferson University and Christiana Care Health System, Wilmington, Del.

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