The Cardiac Neurodevelopmental Program: Addressing the learning and behavioral needs of children with congenital heart defects

Just 30 years ago, prospects for babies born with the most serious forms of congenital heart disease were grim: only 20 percent reached adulthood. Recent advances in prenatal and pediatric cardiovascular care and cardiac surgery have brightened the long-term outlook, as today, more than 90 percent of children with congenital heart disease survive well into their adult years. In the United States alone, this new trend can be classified as “a tsunami of survivors,” says Jane W. Newburger, MD, MPH, associate cardiologist-in-chief for Academic Affairs at Children’s Hospital Boston.

But in tandem with this increase in survivorship comes a significant risk of lifelong developmental difficulties that can impact survivors’ learning, behavior, mental health and interpersonal relationships. Such problems can range from nutritional deficiencies and early motor delays to struggles with higher-order thinking. “This isn’t just an issue that affects patients and their families,” says Dr. Newburger. “It’s also a societal issue, an educational issue and an economic issue. We want these kids to reach their full potential at school and at work and to feel good about their achievements—to realize the very best of themselves.”

Dr. Newburger has spent several years collaborating with David Bellinger, PhD, senior research associate in Neurology at Children’s, to study the long-term neurological, psychological and psychosocial outcomes for children and adolescents with cardiac disease. Incorporating aspects of their work—and recognizing the lack of specialized resources for this burgeoning population—Dr. Newburger began referring her cardiovascular patients to Janice Ware, PhD, senior psychologist in Children’s Developmental Medicine Center.

CONTINUED ON PAGE 6

New hope for infants with hydrocephalus

Problem
Endoscopic third ventriculostomy (ETV)—in which a small perforation is made in the third ventricle of the brain, allowing cerebrospinal fluid (CSF) to circulate—can often be a permanent treatment for hydrocephalus that avoids the complications of shunt dependence. But this procedure has been less successful in infants, most likely because it requires competent CSF circulation and absorption pathways that may not have had time to develop.

Solution
A treatment pioneered by Children’s Hospital Boston’s Benjamin C. Warf, MD, combines ETV with choroid plexus cauterization (ETV/CPC), decreasing the amount of CSF produced and thereby reducing the demands the ETV places on the structure of the developing brain.

Results
Research has shown that ETV/CPC can obviate the need for a shunt in infants with hydrocephalus, in association with spina bifida or encephalocele more than 75 percent of the time, in association with neonatal infection more than 60 percent of the time and in association with other causes of congenital hydrocephalus around 70 percent of the time. Preliminary data in Dr. Warf’s current investigation indicates that ETV/CPC could allow half of infants with post-hemorrhagic hydrocephalus of prematurity to forego shunt dependence.


See clinical trial on page 7.

What’s inside
• Q&A: Acute otitis media PAGE 3
• Program spotlight: Transport Team PAGE 4
• Research news: EEG to predict autism PAGE 5
Ambulatory enhancements coming soon!

This summer, Children’s Hospital Boston will begin a major improvement project—one that will provide our patients and families with an even more welcoming environment and easier access to our world-class clinicians and care. We will be making extensive enhancements to our clinic entrances, lobbies and elevators in Fegan. We will also be adding a new ambulatory lobby that will allow patients and families to access these areas without using the stairs off the main lobby.

Watch overview video: http://on.chbos.org/eWPvpe

A facelift for Plastic Surgery’s home in Hunnewell

Our Plastic Surgery Department’s clinic space in the Hunnewell Building started showing off its new face in February. The new state-of-the-art treatment center will include one of the most advanced imaging centers in the country, featuring a cone beam CT scanner, high-tech treatment rooms and clinical photography (incorporating both 2D and 3D digital photography). The space will also add a nursing station, height and weight room, improved waiting area for patients and families and additional exam room space.

Plastic Surgery launches condition-specific app

The Plastic Surgery Department has a new iPhone/iPad mobile application—specific to cleft lip and palate—available in the Apple App Store. It is the first and only app on the market in this field and is already getting great reviews on Facebook. The team is currently developing a Plagiocephaly app.


Children’s legal eagles

Children’s recently announced the Medical-Legal Partnership (MLP) available in the Children’s Hospital Primary Care Center (CHPCC) to aid vulnerable patients by helping ensure that their basic needs—such as food, housing, utilities, education and employment, health care, and personal and family stability and safety—are met. The program offers families and providers access to legal information and support in identifying and addressing unmet legal needs and navigating public services and service protection. Left unaddressed, these needs, which are important determinants of health, can hinder a patient’s clinical progress.

With the newly established MLP triage phone line, clinicians and social workers can refer a patient or family they feel needs legal expertise and expect a response within five minutes. MLP attorney, Kristin Small, Esq., holds legal clinics in the CHPCC once a week and arranges pro-bono consultations through the MLP’s network of Boston law firms, who are called upon to litigate cases when necessary. The emphasis, though, is on preventive measures intended to resolve a situation before it needs to be taken to court.

Children’s receives $8 million to create Center of Excellence for Quality Measurement

Last month, Mass. Senators John Kerry and Scott Brown, along with Congressman Stephen F. Lynch, announced that Children’s will receive $8 million over 4 years from the U.S. Department of Health and Human Services to establish the Children’s Hospital Boston Center of Excellence for Quality Measurement to improve how healthcare is delivered to children in America. Under the guidance of Director Mark A. Schuster, MD, PhD, Chief, Division of General Pediatrics at Children’s, the new center will provide research expertise, clinical experience and direct access to diverse healthcare delivery settings and patient populations that are needed to produce meaningful measures that can significantly advance the quality of children’s health care.

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Book Corner

Operative Techniques: Pediatric Orthopaedic Surgery

by Mininder S. Kocher, MD, MPH, associate director of the Division of Sports Medicine, and Michael B. Millis, MD, professor in Orthopedic Surgery at Harvard Medical School

This text provides a step-by-step guide to pediatric orthopedic surgery, focusing on femoral lengthening, Sofield procedure, distal radius fracture and more. Includes a dedicated Web site and companion DVD with select procedural videos.

Encyclopedia of Sports Medicine

edited by Lyle J. Micheli, MD, director of the Division of Sports Medicine

This four-volume resource provides comprehensive and accessible information on sports medicine. The text describes all aspects of the field with perspectives, concepts and methods from the medical, behavioral and social sciences and physical education.

Glasscock-Shambaugh’s Surgery of the Ear

by Dennis S. Poe, MD, FACS, Department of Otolaryngology, A. Juliana Gulya, MD, and Lloyd B. Minor, MD

The coverage in this 6th edition book integrates all the latest research in genetics, biotechnical advancements in laser and image-guided systems and clinical innovations and techniques of the past 7 years. Coverage includes scientific foundations and fundamentals, clinical evaluation and rehabilitation, and sections on the external ear, inner ear, tympanomastoid compartment, internal auditory canal/ cerebellopontine angle/petrous apex and skull-based surgery.
Acute otitis media has been the subject of increased discussion in recent months. The American Academy of Pediatrics recommends waiting a few days before starting antibiotics in a child with an ear infection, as some cases of acute otitis media may clear up on their own without the use of antibiotics.

Once acute otitis media has been diagnosed, when do you start antibiotics?

If a child comes in with signs and symptoms, as previously noted, and is subsequently diagnosed with acute otitis media, I would start her on antibiotics at that office visit. Which antibiotic to start with is somewhat controversial, but at this time I would still start with amoxicillin unless there were other clinical reasons not to. Amoxicillin is reasonable to start with, and I recommend treating children for ten days.

When should a pediatrician consider referring to a specialist?

There are two different categories of patients whom pediatricians might consider referring:

- A child who has an acute active ear infection and has undergone multiple trials of antibiotics on a broad spectrum, but continues to have acute otitis media that might need surgical drainage. Or if a child has gone on to develop complications from an ear infection, such as mastoiditis, meningitis or facial nerve paralysis.
- A child with recurrent acute otitis media. I think the minimum for which I would ever consider placing tubes is four infections in a six-to-nine-month period. If a child has four or more in that period, consider a referral. You may want to make the criteria less strict if the child is immunocompromised, displaying speech or language delays that may suggest a problem with hearing, developing multiple allergies to antibiotics or having severe complications from antibiotic therapy.

What treatments does Children’s offer for acute otitis media?

There are a few paths I take, depending on the history:

- Counseling patients regarding potential risk factors that could be modified to reduce the number of ear infections a child gets, e.g., child is in day care, exposure to smoke
- Continued observation and medical therapy, with or without possible prophylactic antibiotics. Prophylactic antibiotics are somewhat controversial because of the potential for developing resistant bacteria. I consider prophylaxis in children who are being seen near the end of cold and flu season, and I am trying to bridge them to spring.
- A medical workup to determine why a child is having recurrent ear infections, e.g., immunodeficiency, gastric reflux
- Placement of tubes

A lot depends on a child’s medical history and social situation when considering the appropriate workup and management of children with acute otitis media. I generally consider the placement of ear tubes a last resort, but if the proper patient population is chosen, then the results are generally excellent.

Make a referral: 617-355-6462

childrenshospital.org/oto
About Us

Advances in pediatric and neonatal intensive care and the regionalization of services require the availability of high-quality, efficient and safe inter-hospital transport services for critically ill or injured infants and children. The transport team is responsible for the resuscitation, stabilization and interfacility transfer of patients ranging from preterm infants to young adults.

- 1,000 patients transported per year
- Commission on Accreditation of Medical Transport Systems (CAMTS)-accredited
- experience with low birth weight (1-2.5 kg) and extremely low birth weight (<1 kg) premature infants
- nitric oxide available when needed (e.g. newborns with persistent pulmonary hypertension, children with acute respiratory distress syndrome and acute lung conditions)
- available 24 hours per day, seven days per week
- serves Children’s critical care areas: Neonatal ICU, Cardiac ICU, Medical/Surgical ICU, Medicine ICU and Emergency Department (ED)
- 15 dedicated nurses
- five dedicated EMTs and paramedics
- eight communication center dispatchers

Goals

Through improved access, system efficiency and expert patient care, our goals are to reduce morbidity and mortality, improve patient and family satisfaction and support the tertiary care programs at Children’s.

Quality of Care

We are committed to improving the quality of acute neonatal and pediatric care in the region through outreach education and support of community programs. Furthermore, we plan to contribute to the field of transport medicine through research and participation in system improvement and policy development on a regional and national level.

How to Transfer or Transport a Patient

Children’s Emergency Communications Center facilitates and coordinates emergency patient transport to Children’s. With one phone call, community pediatric providers can:

- request Children’s Critical Care Transport Team
- arrange transfer to Children’s ED or ICU
- access Children’s specialists for urgent consultation

The center is staffed by trained communication specialists dedicated to handling emergency referrals for medical, surgical, trauma, neonatal and cardiac patients. The center’s staff works closely with community providers (physicians, nurses, administrative staff) to mobilize the Critical Care Transport Team, discuss the availability of a bed and plan for interim stabilization.

Program spotlight: Critical Care Transport

The Children’s Hospital Boston Critical Care Transport Program coordinates and provides transport services for critically ill or injured patients referred to Children’s.

MEET THE TEAM

Monica E. Kleinman, MD,
Medical Director, Transport Program
617-355-7327

Aimee Lyons, RN, BSN, MSN,
Nursing Director, Critical Care Transport Team
617-355-6700

Michael O’Melia, RN,
Co-Clinical Care Coordinator, Critical Care Transport Team

Robert Shields, RN, BSN, NREMT-P,
Co-Clinical Care Coordinator, Critical Care Transport Team

For transport: 1-866-771-KIDS (toll-free)
For information: 617-355-2170
childrenshospital.org/criticalcaretransport
Could autism be predicted with an EEG?

EEG, BRAIN CONNECTIVITY AND AUTISM
Autism is thought to be associated with abnormal connectivity patterns in some parts of the brain. Drs. Bosl and Nelson are using EEG readings to try to detect differences in brain connectivity between infants at risk for autism and typically developing infants. This schematic shows how local connection patterns between neurons form clusters to create a complex network.

Many neuroscientists believe that autism reflects a miswiring in the brain, which may be reflected in its electrical activity. In a pilot study at Children’s, researchers William Bosl, PhD, in the Children’s Hospital Informatics Program, and Charles A. Nelson, PhD, research director of the Developmental Medicine Center, examined this activity by combining standard EEGs and machine-learning algorithms.

EEG recordings were made from 64 electrodes in each of 79 babies from a larger study aimed at finding very early risk markers of autism; 46 had an older sibling with a confirmed diagnosis of an autism spectrum disorder (ASD) and 33 had no family history of ASDs. When possible, tests were repeated at 6, 9, 12, 18 and 24 months of age.

Dr. Bosl then analyzed the EEG readings and computed their modified multiscale entropy (mMSE)—a mathematical property of a signal that is believed to contain information about the density of neural connections near each electrode.

The mMSE had 80 percent accuracy in distinguishing 9-month-olds at high risk for autism from controls of the same age. Although this work needs validation and refinement, including long-term follow-up of the infants, it suggests a safe, practical way to identify infants at high risk for autism by capturing very early differences in brain organization and function.

Omega 3’s work in preventing retinopathy

Several years ago, omega-3 fatty acids were shown to prevent retinopathy in a mouse model of the disease: Mice fed omega-3-rich diets had nearly 50 percent less pathologic blood vessel growth in the retina.

Now, Children’s ophthalmologist Lois E. H. Smith, MD, PhD, and colleagues have isolated the ultimate source of this protection—the omega-3 metabolite 4-HDHA and the 5-lipoxygenase enzyme that produces it—and shown that the protection is double-pronged. Omega-3s not only reduce inflammation, they also have a direct effect on angiogenesis that selectively promotes growth of healthy retinal blood vessels and inhibits growth of pathologic vessels.

The study also provides reassurance that aspirin and nonsteroidal anti-inflammatory drugs don’t negate these benefits. It even suggests that omega-3s may be beneficial in diabetes: 5-lipoxygenase acts by activating the PPAR-gamma receptor, the same receptor targeted by “glitazone” drugs.

Omega-3s are highly concentrated in the retina, and premature infants are often deficient in them, predisposing them to retinopathy. Dr. Smith is collaborating with a Swedish group that is testing omega-3 fatty acids in premature infants. If results are promising, she will seek FDA approval to conduct a similar clinical trial at Children’s.

New pneumococcal vaccine approach successful in early tests

A new approach to Streptococcus pneumoniae immunization that is potentially cheaper than vaccines like Prevnar® and able to protect against any pneumococcal strain is getting closer to clinical testing.

Six years ago, Richard Malley, MD, of Children’s Division of Infectious Diseases, and colleagues showed that there is a natural mechanism of protection against pneumococcus that doesn’t require antibodies, and that could be exploited for a vaccine: the body’s own TH17 cells, which prevent the bacterium from colonizing the upper respiratory tract.

In a new study, Dr. Malley and colleagues at Genocea Biosciences screened a comprehensive library of S. pneumoniae proteins, finding those that activated TH17 cells in mice. When live mice were immunized with these antigens, they showed near-complete protection from S. pneumoniae colonization. These same antigenic proteins also potently stimulated human TH17 cells from adult volunteers.

In collaboration with the international nonprofit PATH, the researchers will refine and test the most promising vaccine formulation in animals. If it proves effective and safe, they will prepare an Investigational New Drug application to begin human trials.

Congenital heart defects

“Dr. Newburger and Dr. Bellinger’s landmark research identified children with congenital heart disease as a group at very high risk for ongoing developmental, learning and behavioral problems,” says Dr. Ware. “Their work underscored the fact that a child’s development extends far beyond how well the heart is working. Parents go home from the hospital to face a set of problems they were not anticipating. Typically, local services and schools don’t know how to help children with cardiac histories; they have limited understanding and few resources to guide them.”

Determining that an organized clinical approach was necessary, Dr. Newburger and Dr. Ware—together with Frank Pigula, MD, of Children’s Department of Cardiac Surgery—formed the Cardiac Neurodevelopmental Program (CNP) at Children’s in 2008. Today, the program:

• provides neurodevelopment consultation services for every newborn with a cardiovascular condition prior to initial discharge from the hospital
• offers ready access to ongoing, comprehensive neurodevelopment assessment services with an interdisciplinary team experienced in the developmental care of children with cardiac conditions
• includes services for children with a broad spectrum of cardiac diagnoses (see sidebar)

Dr. Newburger describes the CNP as “a strong supporter of early intervention.” In the past, she says, “some doctors, when talking to the parents of a newborn with a heart ailment, would avoid discussing the potential for future learning and development problems. The focus was only on the function of the heart.” However, similar to the way that understanding of preemies’ needs has evolved over time, “we now know that parents shouldn’t wait until neurological and psychological problems become noticeable to start addressing those issues,” she says. “Every baby with a cardiac problem should leave the hospital with, at the very least, an initial consultation with a neurodevelopmental specialist.”

One of CNP’s key initiatives is developing a central registry of children with congenital heart disease who have received neurodevelopmental care. “We ask all of our patient families if they’d consider being added to the registry,” explains Dr. Ware. “Our goal is to build a standard set of data for future clinical and research undertakings.” She and Dr. Newburger have also begun building a network of community resources that includes psychoeducational seminars for parents, adjustment groups for children with ongoing medical needs and their siblings and a strong school consultation program that provides hands-on assistance for families.

Patient populations treated by the CNP at Children’s

• children who have undergone cardiac surgery within the first year of life
• children of any age who have been placed on extracorporeal membrane oxygenation (ECMO)
• children of any age who are pre- or post-heart transplant or heart/lung transplant
• children of any age on ventricular assist devices
• children of any age diagnosed with velo-cardio-facial syndrome

The CNP provides a broad range of services that address the needs of children with cardiac disease and their families, including:

• comprehensive psychological assessments that address cognitive, learning, behavioral and social-emotional concerns
• guidance and support for expectant parents whose babies have been diagnosed with cardiac disease in utero
• interventions for children and families to address regulatory disorders such as feeding, sleeping and behavior difficulties
• school consultations to design and implement special education services

Referrals

The Cardiac Neurodevelopmental Program receives referrals from within and beyond Children’s.

Increasingly, referrals are coming from pediatric cardiologists and cardiovascular surgeons from throughout New England and across the country. “We want our program to serve as a local, national and international resource,” says Dr. Newburger.

Make a referral: 617-355-3401
childrenshospital.org/cnp
Sharon J. L. Levy, MD, MPH, director of the Adolescent Substance Abuse Program, has been appointed incoming chair of the AAP’s National Committee on Substance Abuse.

Mininder S. Kocher, MD, MPH, associate director of the Division of Sports Medicine, and director of the Clinical Effectiveness Research Unit, was elected to the Board of Directors of the American Academy of Orthopaedic Surgeons (AAOS).

Robert C. Shamberger, MD, chief of the Department of Surgery, was recently named the chair of the Section on Surgery of the American Academy of Pediatrics.

David K. Urion, MD, director of the Learning Disabilities/Behavioral Neurology Program, and director of education for the Department of Neurology, is the recipient of the 2011 Martha H. Ziegler Founders Award from the Federation for Children with Special Needs.

Esther Lopez, MPA, executive director of the Martha Eliot Health Center, was named an Emerging Executive by the Greater Boston Chamber of Commerce. The award is one of the Chamber of Commerce’s series of Pinnacle Awards, honoring business and professional women who have demonstrated excellence in entrepreneurship, management and lifetime achievement.

Donald Ingber, MD, PhD, of Children’s Vascular Biology Program, was inducted into the American Institute for Medical and Biological Engineering’s (AIMBE) College of Fellows in honor of his contributions to cell and tissue engineering, angiogenesis and cancer research, systems biology and nanobiotechnology.

Joel N. Hirschhorn, MD, PhD, director of the Center for Basic and Translational Obesity Research at Children’s, is the co-recipient of this year’s E. Mead Johnson Award for Pediatric Research. The award, given by the Society for Pediatric Research, recognizes outstanding achievements in clinical and laboratory research in pediatrics.

Marc Bernard Ackerman, DMD, MBA, FACP, joins Children’s as the director of Orthodontics.

Outcomes study of combined endoscopic third ventriculostomy and choroid plexus cauterization (ETV/CPC)

The purpose of this study is to determine the outcomes of combined endoscopic third ventriculostomy and choroid plexus cauterization (ETV/CPC) for treatment of post-hemorrhagic hydrocephalus of prematurity. Information will be collected from the patient’s care before, during and after their surgery, as well as information from exams at one, three, six and 12 months after surgery.

Eligibility: Patients who are between zero (corrected age for premature birth) and 6 months of age and are undergoing ETV/CPC surgery can participate.

Contact: Laurel Fleming at 617-448-3072 or laurel.fleming@childrens.harvard.edu.

More information on ETV/CPC: See article on page 1.

Phenotypic and genetic factors in autism Spectrum Disorders

This study is designed to gather cognitive, behavioral, developmental and social findings from children with a diagnosis of an autism spectrum disorder. Participation in the study involves two research visits, one in the home and one at Children’s Hospital Boston. The visits will consist of cognitive assessments, collection of family history, blood drawn from each family member and 3-D imaging of the child’s face. Participants will receive a research report of the observations.

Eligibility: Children over 24 months of age with a diagnosis of an Autism Spectrum Disorder.

Contact: Recruitment coordinator at 617-355-3076 or ASDresearch@childrens.harvard.edu.

Changes in the migraine brain in children and adolescents: an MRI study

The purpose of this study is to investigate how brain structure and activation in children and adolescents with migraines differ from healthy controls. We will explore the effect of chronic migraine pain on normal brain development. Participation involves up to two visits to Children’s at Waltham, and each visit includes a short neurological exam, sensitivity testing to hot and cold temperatures and an MRI. All study participants will receive a free DVD with images of their brain and $30 per visit.

Eligibility: Children 8 to 11 years old and adolescents 14 to 17 years old with either classic/common migraines or no significant medical history and on no medications may be eligible.

Contact: Athena Drosos at 781-216-1199 or athena.drosos@childrens.harvard.edu.
ASK THE EXPERT: SPORTS CONCUSSIONS

As the spring sports season enters full swing at schools across the country, what should pediatricians know about concussions?

Winter and spring sports carry a concussion risk. Football concussions tend to get the most coverage in the news, but kids can also get concussions during hockey, baseball, lacrosse, wrestling and other sports.

It’s important to remember that sustaining a direct hit to the head isn’t the only way to get a concussion. Concussions occur when the brain is sent into a sudden “spin,” which can also happen when there’s a blow to the chest or torso that causes the head to snap forwards or backwards. Any time a child suffers this kind of injury, he should be seen by a medical professional and then monitored closely for the next several hours.

Here at Children’s Hospital Boston, we provide baseline neurocognitive evaluations with a comprehensive computerized test called Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT). These baseline tests can be used to assess the likelihood of future sport-related concussions.

Warning signs of a concussion are usually apparent just after the initial impact. However, we caution parents that it is possible symptoms won’t be obvious right away; they can also be overlooked when associated injuries, like lacerations or fractures, occur at the same time. For this reason, it’s essential that—even if children receive immediate treatment from athletic trainers, EMTs or in the emergency department—they also see their regular doctor.

Kids with concussions most often complain of headaches or insomnia, but they can also experience dizziness, nausea, fatigue, confusion, memory loss and difficulties concentrating and completing their schoolwork. All of these symptoms should start to improve after a few days of rest and avoidance of any strenuous physical or mental activity.

Out of all high school athletes who have a concussion, approximately 85 percent are symptom-free within a week and 98 percent are symptom-free within a month. If a child’s symptoms aren’t getting any better after the first few days, or are becoming worse, he should be referred to a specialist for further tests and treatment.

William Meehan, MD, is director of the Sports Concussion Clinic at Children’s Hospital Boston.

Make a referral to Children’s Sports Concussion Clinic: 781-216-1328

childrenshospital.org/concussions