EMERGING MINDS

V2N1
2013

INNOVATIONS IN THE JANE AND JOHN JUSTIN NEUROSCIENCES CENTER AT COOK CHILDREN'S

Leading Advances *in* SAFETY for Surgical Treatment of Pediatric Chiari Malformation

PAGE 4

Neuroimaging: The Cartography of Seizure Control

PAGE 8

Demystifying Causes of Stroke in Young Patients

PAGE 13

CookChildren's℠

Meet the Medical Directors

Angel Hernandez, M.D., medical director of Neurology and co-director of the Jane and John Justin Neurosciences Center at Cook Children's

John Honeycutt, M.D., medical director of Neurosurgery, medical director of Neuro-Trauma and co-director of the Jane and John Justin Neurosciences Center at Cook Children's

Get to know the personal side of two of our top neuroscience experts.

Q: What is your idea of happiness?

DR. HERNANDEZ: For me, it includes spending time with my family, including my daughters, Victoria, 14, and Isabela, 11, and helping keep patients seizure free.

DR. HONEYCUTT: I think of happiness as being content. To be truly happy, you should know your place in the world, while being able to balance your work and responsibilities with family.

Q: For you, what would be the greatest misfortune?

DR. HERNANDEZ: The hardest thing for me personally is telling families that their children will likely continue to have seizures.

DR. HONEYCUTT: I think the greatest misfortune for me would be the loss of family and friends. In my position, I see families losing their kids or having their kids get hurt and needing surgery, and that's probably the saddest thing I see. But I also have the opportunity to see lives turned around.

Q: When you were young, what did you want to be when you grew up?

DR. HERNANDEZ: I always wanted to be a doctor; my mom was a science teacher for 50 years and my dad was a physician—a child neurologist. I didn't want to be a child neurologist initially because I saw myself more as an intensive care physician. It wasn't until I started my pediatric residency and rotated with a pediatric neurologist that I found it fascinating.

While completing my child neurology fellowship, I felt I needed to do more for patients with epilepsy and did an epilepsy fellowship. I always knew I wanted to take care of children, so there wasn't really any other thought about treating adults.

DR. HONEYCUTT: Growing up, I always enjoyed studying science. Before pursuing medicine, I considered becoming a marine biologist.

Q: If you could make one change in medicine, what would it be?

DR. HERNANDEZ: I would like to be able to find specific medications to treat patients for the specific gene mutations causing epilepsy.

DR. HONEYCUTT: I would like to make sure all health networks have universal access, so patients don't have to worry about getting medical care.

Q: What would your colleagues be most surprised to learn about you?

DR. HERNANDEZ: I am not only dedicated to treating patients with epilepsy, but I'm also a dedicated father and love my family very much.

DR. HONEYCUTT: I broke my neck when I was 15 and that had an impact on me wanting to be a physician. I have pretty much worked my whole life—to where I am today. I also enjoy practicing yoga.

Q: What do you learn from your patients?

DR. HERNANDEZ: My patients reaffirm how important compassion and patience are while dealing with new treatments.

DR. HONEYCUTT: Patients and parents put a lot of trust in their surgeon, and I'm honored to take care of them.

INSIDE THIS ISSUE

OUR PROMISE

Knowing that every child's life is sacred, it is the promise of Cook Children's to improve the health of every child in our region through the prevention and treatment of illness, disease and injury.

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John Honeycutt, M.D., medical director of Neurosurgery, medical director of Neuro-Trauma and co-director of the Jane and John Justin Neurosciences Center at Cook Children's

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Please Recycle

To refer a patient to Cook Children's Neurosciences team, call 682-885-2500.

SPECIAL THANKS

Jane and John Justin Foundation
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XTO Energy, Inc.
The Dodson Foundation

Cook Children's

Conquering the Unknowns of Genetic Epilepsy

As an increasing number of genetic mutations are causing epilepsy syndromes never before seen by medical researchers, pediatric care providers will be looking to experts in neurology and genetics to make sense of the data. The Cook Children's Genetic Epilepsy Clinic is providing just that—expertise, new technology and fresh insight—to pave the way for better outcomes in genetic epilepsy.

THE GENETIC EPILEPSY CLINIC brings together the expertise of pediatric epileptologist and medical director of the Epilepsy Monitoring Unit and Tuberous Sclerosis Complex Clinic M. Scott Perry, M.D., and metabolic geneticist Alice Basinger, M.D., to provide better screening and targeted treatment for specific forms of genetic epilepsy. After reviewing a child's medical history, Dr. Perry and Dr. Basinger can offer additional testing to establish a more precise diagnosis based on the genetic components of the epilepsy. Genetic counseling and treatment plans are then tailored to address the needs of each child's individual condition.

EARLY, ACCURATE, EFFECTIVE

Correctly diagnosing genetic epilepsy early in a child's life can eliminate unnecessary, invasive testing and rule out treatments and medications that might aggravate symptoms. According to Dr. Perry, early diagnosis of genetic epilepsy can also mean better long-term outcomes.

"Genetic epilepsy is rare, but we know there are patients out there who haven't been diagnosed," Dr. Perry said. "With our advanced understanding of genetics and the epilepsy syndromes associated with these mutations, we approach the disease at a gene level and can provide earlier diagnoses and specific treatment plans."

DIGGING DEEPER

The Genetic Epilepsy Clinic can also help children who previously received confusing or unclear test results for a genetic epilepsy syndrome, for example, children who fit the physical or biochemical characteristics of a well-known genetic epilepsy syndrome, but received negative test results or results with "variants of unknown significance."

"For many providers and parents, genetic epilepsy is full of unknowns," Dr. Perry said. "Dr. Basinger and I work closely together during the diagnostic and treatment process to get to the bottom of each child's condition."

For referrals and consultations, call 682-885-2500.

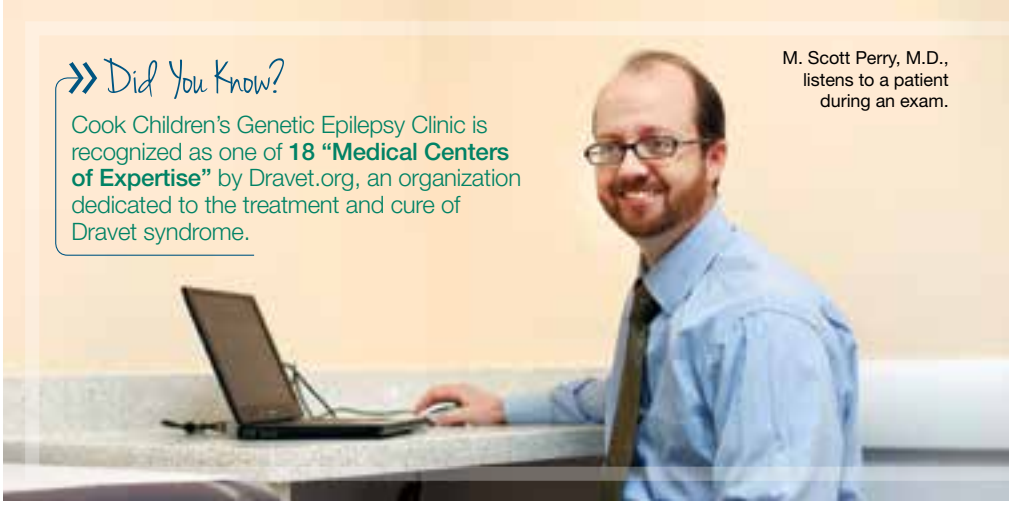
Common Syndromes

Well-known genetic syndromes associated with epilepsy include:

- **Dravet syndrome**—The most severe form of sodium channel disorder, Dravet syndrome is characterized by febrile seizures in infancy leading to more unprovoked seizures and cognitive decline as the child ages. A similar syndrome, PCDH19, resembles Dravet, but is found only in females. (To learn more about Dravet syndrome, turn to page 12.)
- **Potassium channel disorders**—These disorders often cause seizures within the first few days of an infant's life. Some varieties of potassium channel disorders are relatively benign and disappear with time, but others continue on through childhood and can substantially impair cognitive development.
- **Glucose-transporter mutations**—Also known as Glut1, these mutations result in a spectrum of epilepsy syndromes that can cause developmental delays. Glut1 may also present with microcephaly, a neurodevelopmental disorder that hinders a child's brain and skull growth.

Did You Know?

Cook Children's Genetic Epilepsy Clinic is recognized as one of **18 "Medical Centers of Expertise"** by Dravet.org, an organization dedicated to the treatment and cure of Dravet syndrome.

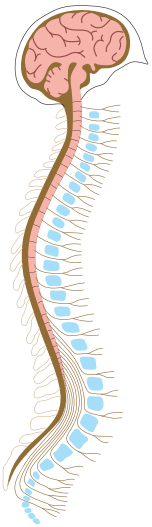


M. Scott Perry, M.D., listens to a patient during an exam.

Advancing Safety

in Pediatric Chiari Malformation Surgery

> "Top minds have been looking for years for a schema that explains which patients need duraplasty and which ones don't, and some debate whether it is necessary at all because they can't always tell if there's enough space after the decompression. Most of the research into this has been performed using ultrasounds, and they have mixed results. We use iMRI to get a better picture and decide during the surgery if we have to open the dura."
>
> —John Honeycutt, M.D., medical director of Neurosurgery, medical director of Neuro-Trauma and co-director of the Jane and John Justin Neurosciences Center at Cook Children's



Using intraoperative magnetic resonance imaging (iMRI) to complement Chiari malformation surgery, neurosurgeons at the Jane and John Justin Neurosciences Center at Cook Children's achieve optimal safety in the surgical suite.

WHILE CHIARI MALFORMATIONS (CMs) can vary in type, they can all be categorized as cerebellar defects. CMs occur when a lower portion of the cerebellum, whether the cerebellar tonsils, the medulla, the brain stem or the undersurface of one of the cerebellar hemispheres, is displaced in such a way that it slips into the spinal canal.

"When the cerebellum slips past the foramen magnum into the spinal canal, it crowds the area and can lead to compression on the brain stem or blockage of spinal fluid," said John Honeycutt, M.D., medical director of Neurosurgery, medical director of Neuro-Trauma and co-director of the Jane and John Justin Neurosciences Center at Cook Children's. "It's a condition that varies quite a bit; sometimes a malformation that looks awful on an MRI scan causes no clinical symptoms at all, but others can lead to chronic problems."

The symptoms—or lack thereof—resulting from CMs aren't the only way in which these conditions vary; they also have unique causes. Many come from genetic mutations such as myelomeningocele or hydromelia or from problems in prenatal development, but injuries and infections can also trigger CMs later in life.

A SAFER PROTOCOL

Because of variations in both cause and presentation of CMs, neurosurgeons have been unable to gather statistical evidence for best practices regarding CM surgery. Recognizing the practical issues inherent in this conundrum, the neurosurgery team at Cook Children's expanded safety measures during the surgery to ensure that children can still be healed even while the medical community continues its research.

"We have a protocol in which we use intraoperative MRI scans to help with the decision-making process as we operate," Dr. Honeycutt explained. "Our experience finds that the less you change the anatomy while still getting clinical improvements, the better the outcome is for the patient."

CM surgery usually requires a pairing of two separate procedures in one. First, the neurosurgeon performs a posterior fossa decompression to make more room around the parts of the cerebellum that have descended. Because neurosurgeons debate the safety of the next step, many espouse compunctions about moving beyond the decompression, but research hasn't shown that decompression alone is enough to treat every case of CM. Clinical evidence suggests that some patients also require an opening of the dura.

"Top minds have been looking for years for a schema that explains which patients need duraplasty and which ones don't, and some debate whether it is necessary at all because they can't always tell if there's enough space after the decompression," Dr. Honeycutt said. "Most of the research into this has been performed using ultrasounds, and they have mixed results. We use iMRI to get a better picture and decide during the surgery if we have to open the dura."

DARING THE DURA

Cook Children's adds safety measures to CM surgery with the addition of the iMRI scan. The team takes an iMRI scan at the beginning of the procedure, another between decompression and duraplasty, and additional scans as they progress through the layers of the dura and into the spinal canal. Each scan checks if the spinal canal has enough room to free the patient from the associated CM symptoms.

Because the dura has multiple layers, neurosurgeons thin it as they progress through surgery. This weakens it and releases some of the pressure it puts on the spinal canal. However, some CMs are so complex that surgeons are compelled to go even beyond thinning the dura.

"If at this point, we have made enough room, we stop the procedure and close up the surgical area, but if not, we open the dura, explore the area to make sure everything's in order, and sometimes, we perform electrocautery to shrink the cerebellar tonsils," Dr. Honeycutt said. "This procedure itself is well tolerated, and we've been using the iMRI scans to make sure the anatomy is suited for it."

Once the nerve tissue has been sufficiently decompressed, cerebrospinal fluid can once again flow properly around and behind the cerebellum. By relieving these problems, patients are safe not only from the frustrating symptoms of headaches and numbness, but also from the potential of other problems that would interrupt everyday activities. The surgery prevents brain and spinal cord damage that can result in poor control of arm and leg movement, swallowing control, and hand-eye coordination.

To refer a child for diagnostic testing or surgery for a Chiari malformation, call 682-885-2500.

BETTER R
Better Care

You may assume only a facility with an academic affiliation conducts the most advanced research while also delivering the best patient care. At Cook Children's, we challenge that assumption.

M. Scott Perry, M.D., discusses a case in an epilepsy conference.

"MANY PARENTS AND referring physicians are surprised to find we're deeply involved in clinical trials and research of all kinds," said M. Scott Perry, M.D., pediatric epileptologist and medical director of the Epilepsy Monitoring Unit and Tuberous Sclerosis Complex Clinic at Cook Children's. "I joined Cook Children's in 2009 specifically because I was drawn to the leading-edge research taking place here."

Dr. Perry is one of dozens of physicians with Cook Children's who is either leading or participating in a total of more than 200 research projects. Some of these projects are nationwide trials for innovative new drug therapies and treatment devices, while others are independent studies unique to Cook Children's.

BASED ON EXPERIENCE, FOCUSED ON PATIENTS

Database studies are one of the leading forms of research being conducted. Researchers at Cook Children's perform studies to determine what specific treatment plans produce the best outcomes, both on a large scale and in relationship to varying factors such as gender, age, heredity and medical history. As an epileptologist, Dr. Perry said the epilepsy program has benefited from Cook Children's epilepsy surgical database, which specifically monitors outcomes of patients who undergo surgical treatment to correct certain types of epilepsy. As a result of these disease-specific databases,

ESEARCH

physicians are able to sharpen their understanding of certain treatments and apply the most effective therapies to the appropriate patients.

Cook Children's Health Foundation recently began an endowed chair program to provide physicians with an opportunity to conduct research, create new programs and publish studies. Warren Marks, M.D., was one of two physicians selected for the program. The funding has allowed him to create a comprehensive movement disorder center at Cook Children's with deep brain stimulation at the center of the program. The scope of service stretches from the earliest diagnosis to the last stage of rehabilitation and return to normal function. (You can read more about Dr. Marks' program on page 14.)

The endowed chair program is a significant commitment to Cook Children's promise and will provide the funding physicians need to support their efforts to improve the health of children in our community.

LEADING MEDICINE

Because of research, patients also have access to treatment options beyond what is commonly available. Dr. Perry points specifically to a recent research trial on intranasal therapy for epilepsy. This therapy delivers the antiepileptic medication midazolam intranasally to treat acute seizures. Intranasal therapy is one of many innovative treatments made available to patients through research.

Dr. Perry also stresses the humanitarian nature of participating in these trials.

"Seeking treatment at a research hospital provides patients and their referring physicians the opportunity to give back by participating in studies that will eventually uncover better treatments for complex diseases," Dr. Perry said. "We solve problems that arise in these treatments. We then compile and publish these cases so other physicians and their patients can benefit from our research."

To learn more about research efforts at Cook Children's, call 682-885-2103.

> "Much of our research is derived from registries and databases, which allows us to extrapolate outcome predictors and develop different evaluation models that may be more effective than the current standard."
>
> —M. Scott Perry, M.D., pediatric epileptologist and medical director of the Epilepsy Monitoring Unit and Tuberous Sclerosis Complex Clinic at Cook Children's

Neuroscience Publications

Perry, M.S., Bailey, L., Malik, S., Gilson, C., Kotecha, A., & Hernandez, A. (2013). Clobazam for the treatment of intractable epilepsy in children. *Journal of Child Neurology*, 28(1), 34-39.

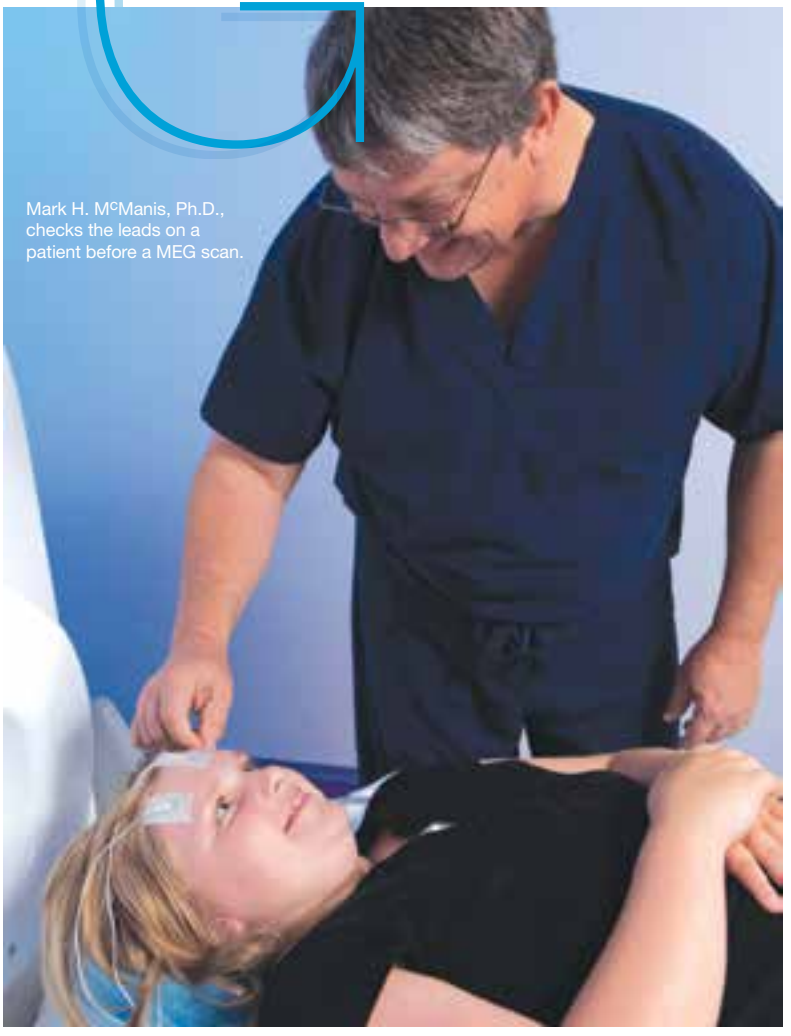
Malik, S., Galliani, C., Hernandez, A., Donahue, D. (2013). Epilepsy surgery for early infantile epileptic encephalopathy (Ohtahara syndrome). *Journal of Child Neurology*, (in press) Date of Electronic Publication: 2012 Nov. 8.

Marks, W.A., Bailey, L., Reed, M.A., Pomykal, A., Mercer, M., Macomber, D., Acosta, Jr., F.A., & Honeycutt, J. (2013). Pallidal stimulation in children: comparison between cerebral palsy and Dyt-1 related dystonia. *Journal of Child Neurology*, 2013 Jul; (28)7:840-8. Date of electronic publication: 2013 May 10.

MEG for Epilepsy

> "Cook Children's is one of only five children's centers with magnetoencephalography technology [MEG]. Approximately half of focal epilepsy patients who have undergone MEG and who were not previously thought to be good candidates for surgery have undergone successful procedures due to MEG's ability to pinpoint the exact location of focal seizures."
>
> —Angel Hernandez, M.D., medical director of Neurology and co-director of the Jane and John Justin Neurosciences Center at Cook Children's

Parents and children can find epilepsy a frustrating disorder because, so many times, it is difficult to locate the root cause or to keep seizures under control. In fact, seizure control becomes a lifelong quest for many families.



Mark H. McManis, Ph.D., checks the leads on a patient before a MEG scan.

IMAGINE A MULTILAYERED map marked by roads and state boundaries as well as topographical lines showing mountains, valleys and ravines. A good geographic information system could allow topographers to manipulate all these overlays at their convenience and view the map in three dimensions.

Still, the map is static and doesn't reveal real-time changes in terrain and weather. In contrast, advanced imaging technology provides neurosurgeons multiple layers of information, creates 3-D views and even displays electromagnetic activity as it occurs within the brain.

Epilepsy evaluation and treatment relies heavily on neuroimaging. This is especially true for focal epilepsy, which originates in limited areas of the brain. Common imaging techniques include CT, for identifying head injuries and calcifications, and MRI, which reveals brain structure.

Magnetoencephalography, or MEG, displays magnetic fields created by brain activity. It's a map of the brain's electromagnetic weather, and it can help physicians pinpoint the spots where seizures originate with extreme accuracy. In turn, this nuanced record of brain activity generates opportunities for some patients to undergo surgery that can reduce or eliminate focal seizures who otherwise would not receive this treatment option.

Nearly half of the epilepsy patients at Cook Children's who were previously not good surgical candidates have been helped by MEG through successful brain surgery. Cook Children's is one of only five children's centers with this advanced type of imaging.

Focus on Focal Epilepsy

Resulting from electrical disorders in the brain, epileptic seizures may manifest as generalized tonic-clonic seizures or partial (focal) seizures. Focal seizures, rather than occurring throughout the brain, take place in a single part of the brain, though they may then expand throughout the brain.

Focal seizures may result in muscle contractions, staring spells, hallucinations, blackouts and many other physical and mental abnormalities. Children often find them frightening to experience.

Focal epilepsy may be treated by surgery to remove the part of the brain where seizures are originating, a process requiring detailed information about the location of a particular patient's brain function. Otherwise, the patient may lose important capabilities.

"In normal brains, generalized principles tell us where functions such as speech and hearing are located," said Mark H. McManis, Ph.D., MEG administrator in the department of Neurosciences at Cook Children's. "People with epilepsy have more variety in the functional organization of their brains. It's important to know these cases very accurately and to localize function to within a couple of millimeters. MEG imaging, combined with MRI, allows physicians to distinguish areas to be removed from functional areas in the brain with pinpoint accuracy."

Angel Hernandez, M.D., checks on a patient in the EMU.

HOW DOES IT WORK?

A functional imaging technology, MEG captures an image of the brain in motion.

"We combine an image of the brain structure with an image of what different sections are doing, and it can show us very clearly what parts of the brain are responsible for what function," said Mark H. McManis, Ph.D., MEG administrator in the department of Neurosciences at Cook Children's. "We can separate those functional areas from parts of the brain where seizures might be originating."

When a brain cell fires, it creates an electromagnetic field. MEG, one of the world's most sensitive magnetic field detectors, records this activity.

Wearing headgear that contains 306 sensors, patients first perform a series of simple tests, such as looking at a picture or listening to words. This allows MEG technicians to localize functional brain activity. Then, for an amount of time ranging from half an hour to an hour, the patient wears the MEG headgear while relaxing or even sleeping. Images taken of the brain record seizure activity.

"It looks like an old-fashioned hairdryer," said Angel Hernandez, M.D., medical director of Neurology and co-director of the Jane and John Justin Neurosciences Center at Cook Children's. "Because it exposes the face, it's not scary or confining like an MRI. The machine doesn't make any noise."

And, as a passive sensor system, MEG is completely safe.

Afterward, technicians combine MEG images with MRI and other images to create a 3-D mathematical model that a physician uses to plan for surgery.

"Technicians can then transmit the 3-D planning model to the surgery suite, where physicians use it in conjunction with a probe they move around the patient's head," said Dr. McManis. "Before a doctor makes a cut, he or she can replicate the measurements from the planning stage and confirm an accurate surgical path."

WHO'S A CANDIDATE?

Patients with difficult-to-control focal epilepsy are ideal candidates, especially if their seizures are coming frequently and they're not responding to medication.

"MEG is helpful in identifying where seizures are taking place," said Dr. Hernandez. "It's an integral part of the evaluation of patients with difficult-to-control focal epilepsy because it increases the chances of localizing seizure focus, allowing more patients to become candidates for surgery."

To watch a video about MEG at Cook Children's, visit cookchildrens.org/neuro or scan this QR code.

Kiera, with her mom at her side, begins shaving the head of Brian Aalbers, D.O., after winning a bet that she would walk again after surgery.

Unlocking a Child's Hope

Through Deep Brain Stimulation

Like most 9-year-olds, Kiera Hurtado likes to get her own way. So when this petite, feisty fireball made a bet with her neurologist, Brian Aalbers, D.O., pediatric neurologist specializing in movement disorders at Cook Children's, that she would walk again and win the battle over her dystonia, it was "winner-takes-all"—which meant shaving Dr. Aalbers' head.

WHEN KIERA FIRST VISITED Cook Children's Neurosciences department and the Pediatric Movement Disorder program, she could barely walk. However, Kiera was determined not to let that slow her down. Diagnosed with generalized dystonia, secondary to a metabolic disease, Kiera had developed a permanent deformity in her spine and a crippling tightness in her toes and feet, which affected her motor abilities and prevented her from walking.

"I had never before seen dystonia progress so rapidly in a child," explained Dr. Aalbers. "Here was this intelligent, outgoing child deteriorating right before our eyes. The disease had completely corroded part of her brain and we knew we had to act quickly. She presented as a perfect candidate for deep brain stimulation [DBS]."

From the moment they first met, Kiera carved out a special place for herself in Dr. Aalbers' heart. While some patients often leave a lasting impression on their physicians, Kiera and Dr. Aalbers' unique relationship, built on mutual admiration, humor and trust, would prove to be truly life changing for them both. When the decision was made for Kiera to undergo DBS, Dr. Aalbers knew she was putting her faith and life in his hands—literally.

"She made a bet with me before her surgery that she would walk again and when she did, I would have to shave my head," said Dr. Aalbers. "Sure enough, a few months later she was up and walking. While I

hated to have to shave my head, it was one bet I was very happy to lose."

HOPE FOR KIERA

According to Dr. Aalbers, genetic forms of dystonia like Kiera's that cannot be adequately controlled by medications often respond well to DBS and help reduce symptoms.

"The decision for Kiera to undergo deep brain stimulation was a profound one for me because I knew how desperately she wanted to get better; however, the procedure had a huge risk of making her condition worse," Dr. Aalbers said. "Kiera is a tough, straight-A student who captured our hearts. The staff at Cooks Children's was dedicated to finding a way to offer her relief that would hopefully help her regain her mobility."

It is estimated that fewer than 1,000 patients with dystonia have undergone DBS, and Cook Children's is one of the first pediatric hospitals in the nation to perform this treatment on children. This minimally invasive, neurosurgical procedure requires low-voltage neurostimulators, similar to but smaller than a cardiac pacemaker, to be surgically implanted deep in the brain. Targeted, continuous electrical stimulation blocks abnormal signals and can significantly improve the symptoms of movement disorders such as dystonia and Parkinson's disease.

DBS is performed while the patient is awake in order to test his or her responses to the electrical impulses.

"The Cook Children's team of Child Life specialists were with Kiera during the entire 45-minute procedure. She played on her iPad and texted her mother updates while we were operating. It was amazing," Dr. Aalbers said. "She came through with flying colors."

BETTING ON COURAGE

Today—a year and a half out from surgery—Kiera is going strong and is able to walk. While her dystonia continues to advance due to the severity of damage done to her mitochondrial function, Dr. Aalbers believes Kiera's sheer determination and courage will help her overcome any challenges that may come her way in the future.

"Kiera gives new meaning to the word 'hope,'" said Dr. Aalbers. "While she knows she still has many obstacles to overcome, she is steadfast in her bravery and courage. No matter what happens in her life, she will always be the one standing tall."

The Pediatric Movement Disorder program at Cook Children's treats a wide range of conditions that affect movement. Physicians may refer a patient by calling 682-885-2500.

In the Know

According to the Dystonia Medical Research Foundation, no fewer than **300,000 people** in North America are affected by dystonia.

It is estimated that fewer than **1,000 patients** with dystonia have undergone deep brain stimulation.

Cook Children's is **ONE OF THE FIRST** pediatric hospitals in the nation to perform this treatment on children.

Saleem Malik, M.D., conducts a bedside exam in the EMU.

SPOTLIGHTING a Rare Form of Epilepsy

To maintain the best quality of life possible, children with an uncommon type of epilepsy called Dravet syndrome require individualized management from an epileptologist—precisely the type of care they will find at the Comprehensive Epilepsy Program at the Jane and John Justin Neurosciences Center at Cook Children's.

DRAVET SYNDROME TYPICALLY develops according to a specific seizure pattern. Beginning during the first year of life, a child experiences febrile seizures, followed by afebrile seizures. Then, myoclonic seizures, which cause the body to jolt, are followed by status epilepticus—lengthy seizures that require emergency intervention to control.

Neurologists typically diagnose Dravet syndrome based on clinical examination and electroencephalography readings. Another diagnostic clue: up to 80 percent of Dravet syndrome patients possess a mutation in the SCN1A gene, according to the Dravet Syndrome Foundation.

Currently, no cure for Dravet syndrome exists.

"Clinicians haven't developed a standard treatment protocol for Dravet syndrome because patients' experiences with the condition vary widely," said Saleem Malik, M.D., director of the Comprehensive Epilepsy Program at the Jane and John Justin Neurosciences Center at Cook Children's. "However, certain anticonvulsants and the ketogenic diet help manage seizures in some patients."

CASE STUDY

One of the first children Dr. Malik diagnosed with Dravet syndrome illustrates the disorder's typical progression.

Referred to Dr. Malik when the child was approximately 4 years old, the patient had been taking anti-seizure medication since infancy. Her history of febrile and afebrile seizures prompted Dr. Malik to recommend genetic testing, which confirmed the diagnosis of Dravet syndrome. Now 12 years old, the patient has experienced deterioration in her gait that is typical of Dravet syndrome patients and takes multiple medications daily to manage seizures.

"Children who enter our Comprehensive Epilepsy Program are placed under the direct care of one of four epileptologists; this clinician works with families to determine the best management strategy for patients," Dr. Malik said. "We offer a level of personal care here I haven't seen in other large epilepsy centers in which I've worked."

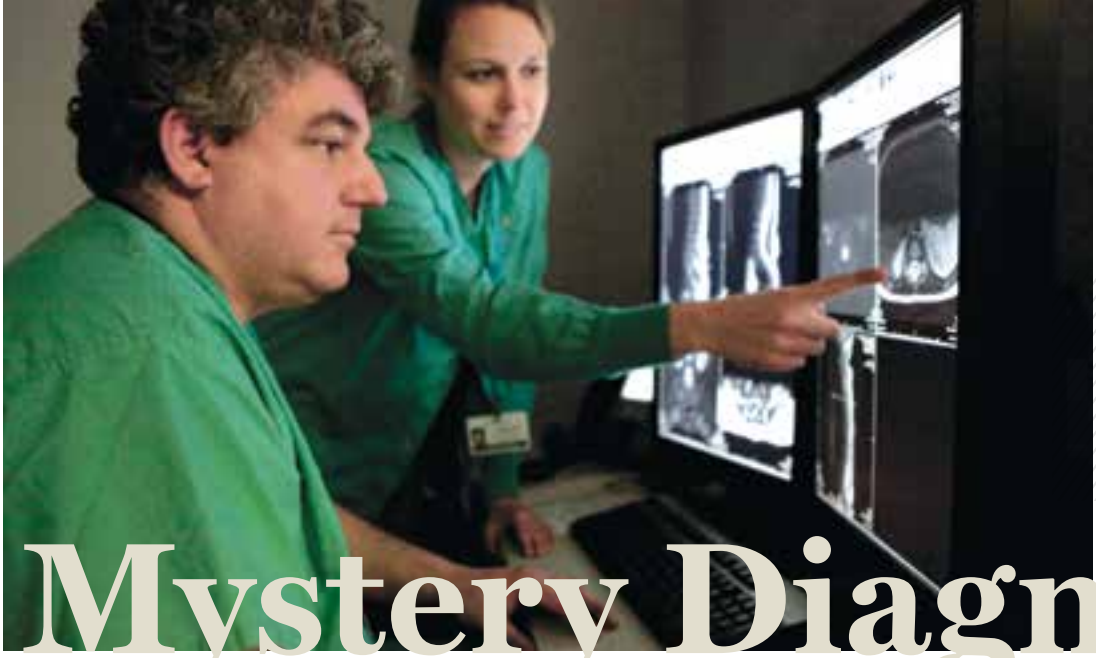
If an infant or toddler suffers frequent febrile seizures that, over time, give way to other seizures, visit cookchildrens.org/neuro for information about referring him or her to the Cook Children's Comprehensive Epilepsy Program for evaluation.

Long-term Consequences of Dravet Syndrome

Children with Dravet syndrome can struggle with cognition, as well as communication and social skills; some can even develop autism, according to the Dravet Syndrome Foundation.

"Most patients' seizures persist throughout life," said Saleem Malik, M.D., director of the Comprehensive Epilepsy Program at the Jane and John Justin Neurosciences Center at Cook Children's. "As a child with Dravet syndrome grows, he or she might develop an abnormal gait, dysmorphic facial features and a smaller head than would be expected for his or her age."

Cook Children's Genetic Epilepsy Clinic allows physicians to study the genetic profiles of pediatric patients to help diagnose Dravet syndrome and guide treatment decisions (see "Conquering the Unknowns of Genetic Epilepsy," on page 3). By bringing together advanced resources, Cook Children's helps patients function to the best of their abilities despite the challenges they face.



Richard Roberts, M.D., reviews scans with Grace Crotzer, P.A.

What makes a child have a stroke?

Mystery Diagnosis

ZACHARY, AGE 5, had been playing his recorder nonstop since he brought it home from kindergarten. A few minutes later, his mother noticed that Zachary was acting strangely. He slurred his words, and his face seemed to droop. At first, she thought he was being silly, but his behavior didn't improve.

She hurried him to the emergency room, where his symptoms of slurred speech and weakness along one side of his face and body prompted the physician on call to order a brain computed tomography (CT) scan, which led to a diagnosis of stroke.

THE PHYSICIAN'S CHALLENGE

"Any time a child experiences stroke, we try to rule out potential causes," said Richard Roberts, M.D., pediatric neurosurgeon at Cook Children's Jane and John Justin Neurosciences Center. "For instance, fibromuscular diseases and clotting problems may cause a child to have a stroke. Sickle cell disease may also be related to stroke in children. Once we rule out known conditions, we investigate what's left."

Though rare, moyamoya can be one reason a child might experience a stroke.

In moyamoya, progressive narrowing of the carotid artery leads other vessels to grow in compensation as the body tries to increase blood flow to the brain. These tiny blood vessels in the area of the basal ganglia appear in angiography as a cloud-like formation, resulting in the name "moyamoya," which is Japanese for "puff of smoke."

Reduced blood flow to the brain may result in stroke, often in response to stress or, as in Zachary's case, to hyperventilating or playing a wind instrument. Transient ischemic attack, epileptic seizures and headaches are other symptoms of this arteriopathy. While primarily found in children, moyamoya can occur in adults, as well.

Moyamoya may also occur as part of another disease process, such as Down syndrome or sickle cell anemia. Moyamoya is typically fatal if not treated, leading to mental decline, further strokes and brain hemorrhage.

TREATMENT AND PROGNOSIS

"Medically, we treat moyamoya with blood thinners and anticoagulants," said Dr. Roberts. "Surgically, we perform revascularization, taking vessels from the head's external circulatory system and internalizing them in order to provide alternative pathways for blood flow."

Dr. Roberts performs these surgeries in stages laterally, on the left and right sides, in separate surgeries, which allows for redundancy in blood flow as one side heals.

These surgeries are merely attempts to increase blood flow to the brain and reduce the frequency of stroke in the patient, but Dr. Roberts warns: there is no permanent cure for moyamoya.

"However, the important thing is that there are surgical options to mitigate the effects of this disease," said Dr. Roberts. "We can fortify the child's blood supply to the brain, making strokes less frequent and hopefully eliminating them."

To learn more about neurosurgery at Cook Children's, visit cookchildrens.org/neuro.

» Delicate Diversions

Cook Children's offers a variety of surgical treatment options for moyamoya:

Indirect revascularization includes two procedures, **encephalo-duro-arterio-synangiosis** (**EDAS**) and **encephalo-myo-synangiosis** (**EMS**).

EDAS involves placing a branch of a temporal artery over the brain's surface without doing a graft. The displaced artery gradually begins to send out new arteries into the brain, improving blood flow. This procedure is more successful in children than adults.

EMS involves moving a section of the muscle on the temple through an opening in the skull and across the brain's surface. Over time, the displaced muscle begins creating blood supply into the brain.

MOVING in the Right Direction

At Cook Children's, we've restructured our existing advanced motion disorder treatments and research into the new Comprehensive Motor Disorders Center, an initiative that creates more opportunities for us to spearhead advances in the field.

A movement disorder patient is examined by Warren Marks, M.D.

DEEP BRAIN STIMULATION, a treatment that disrupts abnormal neuron firing with electrical impulses, has been used primarily in adults with essential tremor or Parkinson's disease. Research suggests it may be successful in treating other conditions, such as Tourette syndrome and epilepsy. The Comprehensive Motor Disorders Center will continue developing additional applications for this life-changing treatment.

"Motor disorders are extremely widespread among children. The most common, cerebral palsy, is found in one in every 300 children at age 8," said Warren Marks, M.D., medical director of the Movement Disorder and Neurorehabilitation Program at Cook Children's Jane and John Justin Neurosciences Center. "That represents a tremendous need in the medical community. Our center will improve the quality and availability of care for children with a variety of motor disorders."

BUILDING AN INTERNATIONAL DEEP BRAIN STIMULATION REGISTRY

Working with major academic institutions across the United States and around the world, Cook Children's is laying the groundwork to develop an open database of pediatric deep brain stimulation patients. This represents collaboration on a global scale, designed to improve outcomes for patients everywhere.

INCREASING REHABILITATION SERVICES

"Our team already provides targeted rehabilitation services to children with brain injuries, with specialized programs for children with dystonia and neuromuscular disorders," Dr. Marks said. "Expanding will allow us to become a center for spinal cord rehabilitation in children and adolescents."

MOTION ANALYSIS LABORATORY

The first step toward introducing new technology in the treatment and management of motion disorders is Cook Children's new multi-modality motion analysis lab, scheduled to open in early 2014.

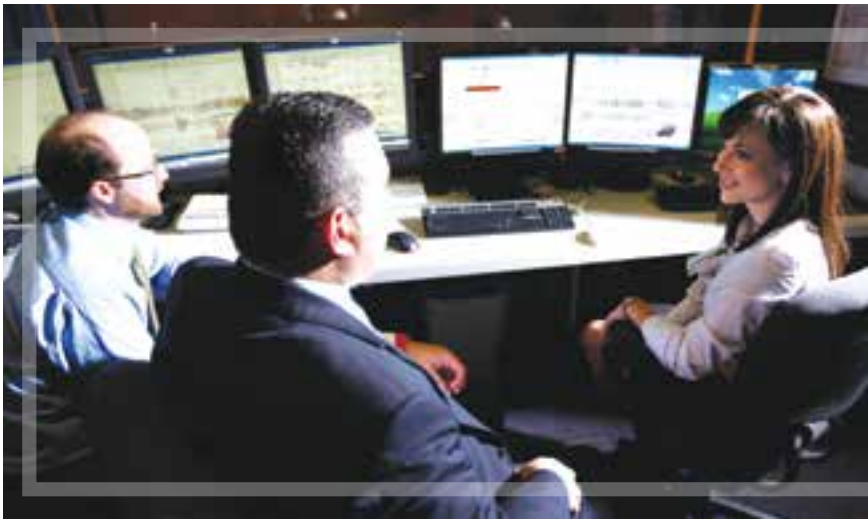
"This new system utilizes high-speed infrared cameras, electromyography machines and a pressure-monitoring floor system," Dr. Marks said. "The information from this system will allow us to better partner with orthopedics and neurosurgery to meet the needs of highly complex patients with cerebral palsy and other movement disorders. By combining with our sports rehabilitation program, we will have a unique service for children."

To learn more about how the Jane and John Justin Neurosciences Center at Cook Children's plans to improve lives for young people with motor disorders, visit cookchildrens.org/neuro or scan the QR code.

"The ketogenic diet is for children who are truly medically refractory. It involves regular follow-up, as well as monitoring for vitamin levels and bone growth. Additionally, when effective, the slightest cheating—even a jelly bean or a bit of toothpaste—can break ketosis and cause seizure breakthrough."

—Cynthia Guadalupe Keator, M.D., epileptologist at Cook Children's Jane and John Justin Neurosciences Center

WHEN SEIZURES DON'T Respond to Medication



M. Scott Perry, M.D., Angel Hernandez, M.D., and Cynthia Guadalupe Keator, M.D., discuss the ketogenic diet for a patient.

EPILEPSY CAN PROVE a frustrating journey for children and their caregivers. Epidemiological data indicates that 20–40 percent of newly diagnosed patients with epilepsy will become refractory to treatment, and many of those are children. Treatment resistance is a due to a multifactorial phenomenon.

STARVE THE SEIZURE

In these cases, dietary changes that cause people to burn fats instead of sugars for more energy may reduce seizures.

The most commonly known such diet is called a ketogenic diet, for the ketosis state it creates. The ketogenic diet has been around since the 1920s in its current form.

"Physicians have used approaches similar to the ketogenic diet for centuries because they perceived the connection with seizure control," said Cynthia Guadalupe Keator, M.D., epileptologist at Cook Children's Jane and John Justin Neurosciences Center. "In fact, there is ancient reference in the 5th century BCE documented in the Hippocratic collection of a man being cured with epileptic convulsions by abstinence from food and drink.

"The brain uses sugar as its primary energy source, but the body only maintains about a 24–36-hour supply of glucose. By depriving the body of carbohydrates, we force it to burn fat for energy, which results in ketone bodies getting into the brain to be used as its main source of fuel. Through a mechanism we don't fully understand, this process can reduce seizures in some people."

APPROACH WITH CARE

The ketogenic diet consists of three- or four-to-one ratio of fats to carbohydrates and proteins. This diet must be carefully monitored, and typically starts with an initial stay in a medical facility. Side effects can include lethargy, nausea, vomiting, dehydration and constipation. People who spend an extended period of time on the ketogenic diet are also at risk for kidney stones, poor bone health, vitamin deficiency and elevated triglycerides. The patients (and families) are asked to try the diet for a minimum of three months to see if it will be effective. The ketogenic diet does not necessarily take the place of seizure medications, but in some instances patients do become seizure free and come off medications. There is no set time in which the diet must be stopped; however, due to long-term risks of being on the diet, some children come off after being on it for two years, even in successful cases. There are times that seizure control continues once the patient is weaned from the diet, according to Dr. Keator.

It is important for children beginning the ketogenic diet to undergo counseling and initial monitoring at a tertiary care center, like Cook Children's, that is fully staffed with nutritionists, counselors and other support staff, as well as physicians experienced with the diet.

Not all children respond well to the ketogenic diet, but about one-third of children initiated on the diet will have a greater than 90 percent improvement in seizures. Another third will have some seizure improvement, and another third have no response or find it too hard to continue.

"We treat the ketogenic diet like any other medication," Dr. Keator said. "If a child is seizure-free for two years, we consider taking him or her off the diet. Another beneficial effect is that we can lower doses of other seizure medications for children on the ketogenic diet if it is effective. Best of all, some children can come off the diet and have freedom from seizures."

To refer a patient for an appointment at Cook Children's Jane and John Justin Neurosciences Center, please call 682-885-2500.

Cook Children's Medical Center

801 7th Avenue
Fort Worth, TX 76104

More Than Medical Know-how

Receiving a neurological diagnosis such as epilepsy can be hard on even the strongest families. **The Jane and John Justin Neurosciences Center at Cook Children's** offers extra support to patients, their parents and other family members as they begin their treatment journeys. From a resource library where parents can get the most accurate information about their child's condition and treatment options to a social worker who can help parents evaluate their financial needs, no need is too great or too small.

"Many times, parents are overwhelmed, so we help them organize all important information in a binder they can take with them to appointments. Support groups and camps are also available to help parents connect with others who understand what they're going through. We even offer a program where a Child Life specialist will visit the patient's school and educate both school staff and students about what a patient's condition means—and doesn't mean."

— Julie Schmidt, patient liaison at Cook Children's Jane and John Justin Neurosciences Center

To learn more about patient liaison services, visit cookchildrens.org/neuro.

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