



UCSF Children's Hospital



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Case Study: Pediatric Neurosurgery Relieves Lifetime of Seizures

Nine-year-old Aarika Rodriguez had been suffering seizures since infancy, regularly emerging from sleep trembling and disoriented. Yet in her short life, she had failed with seven different medications, either because they were ineffective or because of severe side effects. In February 2008, her central California neurologists referred Rodriguez to UCSF Children's Hospital epileptologist Joseph Sullivan, MD.

"The single-type seizure and a single, subtle abnormality on her MRI made her a surgical candidate," says Sullivan, who over the next few months conducted a series of tests to map the seizure activity against critical brain functions.

He began with a video EEG that indicated the seizures occurred in the left frontal lobe – the same locale as the lesion that had been revealed on the MRI. The next step was magnetoencephalography (MEG), which showed spikes that also appeared close to the MRI abnormality. "But we were unable to map speech with the MEG, and speech was a concern," says Sullivan.

Next up was a functional MRI, but that too failed to disclose speech location. And when they tried a Wada procedure, the young girl could not tolerate it. That left Sullivan and pediatric neurosurgeon Kurtis Auguste, MD, with one option: invasive strip and grid monitoring. In July 2008, Auguste performed a craniotomy, opening the dura and laying down a subdural grid that contained 64 electrodes in an 8x8 pattern.

The grid effectively revealed the speech centers as well as a more precise location for seizure activity. "Speech was a short distance away from the seizures, and we were convinced resection would not run the risk of causing speech problems," says Auguste. (CONTINUED ON PAGE 5)

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Sam Hawgood, MB, BS Diana Farmer, MD

Perspective

For those who treat children, childhood vulnerability is not a tired cliché, but raw motivation to do more and do better. It is precisely because UCSF Children’s Hospital offers some protection for our most vulnerable children that we take unabashed pride in our work. This place teems with people who – working in partnership with you – improve children’s lives with remarkable consistency.

Consider how the Pediatric Intestinal Rehabilitation and Transplantation Program enhances the lives of children who suffer from conditions that make daily nutrition a frightening challenge. Or how the pediatric sleep lab offers explanations for baffling learning and processing disorders – and often can treat the source. Or the way the pediatric epilepsy program taps new technology to cure seizures more safely than previously believed possible. Or how the pioneering NF/Ras pathway clinic is transforming genomic advances into more effective, tailored treatments.

UCSF Children’s Hospital fosters a culture that allows such innovations to grow. There is no more concrete example than the new hospital going up at Mission Bay. Among other benefits, a new helipad has been proposed for Mission Bay that would facilitate faster and safer emergency transport for critically ill children.

Safer and faster emergency transport, a convenient location and an increase in pediatric hospital beds will enable us to strengthen and broaden our partnerships with so many of you. In turn, children and their families will gain another level of protection against conditions we are rapidly learning to better prevent and treat.

Sam Hawgood
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Physician in Chief
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Reaping the Benefits of Genetic Advances: Pathway Clinic Devises Unique Care and Research Opportunities

When a teen arrived at UCSF Children’s Hospital with a diagnosis of Noonan syndrome, medical geneticist Katherine Rauen, MD, PhD, and genetic counselor Michelle Strecker recognized that something didn’t add up.

“She had severe and chronic gastrointestinal problems, which is not typical of Noonan,” says Strecker, who manages the hospital’s NF/Ras pathway clinic. “The sparse eyebrows and early feeding difficulties were a better fit for CFC (cardiofaciocutaneous) syndrome – and we found

more effective treatment as well as unique translational research opportunities.

A leading expert on the clinical implications of mutations along the Ras/mitogen-activated protein kinase (MAPK) pathway, Rauen has seen firsthand the role these mutations play in one of the most common groups of inherited genetic syndromes.

The group includes neurofibromatosis (NF), Noonan, CFC, LEOPARD, Costello and other genetic syndromes. Clinical conditions



Earnest Jackson, pathway clinic patient, is examined by Katherine Rauen, MD, PhD.

a mutation in the BRAF gene, which is associated with CFC.”

The finding opened the way for more aggressive GI treatment, and demonstrates the advantages of a pathway-based approach to this group of genetic syndromes.

Unifying Diagnoses Lead to More Effective Treatments

The NF/Ras pathway clinic, Rauen’s brainchild, operates on this belief: If genetic pathway dysregulation is responsible for syndromes that predict a wide range of debilitating conditions, then a pathway-based clinic should offer

associated with these syndromes run from cancer and cardiac abnormalities to hydrocephalus, headaches, epilepsy, and learning and processing disorders.

“Because of multisystem involvement and resulting specialty care needs, providing comprehensive care for these individuals is a challenge,” says Rauen.

To meet that challenge, the NF/Ras pathway clinic offers comprehensive case management, prenatal and obstetric care, and multidisciplinary referrals to a network of more than 50 specialists. And because these syndromes are lifetime afflictions, the center also facilitates the transition from pediatric to adult care. (CONTINUED ON PAGE 8)



Michelle Strecker, genetic counselor, speaks with Jackson and his family.

“The advantage is a unifying diagnosis that helps providers know what to be mindful of and facilitates more personalized medicine.”

Clinical Indicators for an NF/Ras Pathway Referral

NF1

- Skin spots (café au lait macules, armpit and groin freckling)
- Neurofibromas
- Developmental delay and learning disabilities
- Short stature or macrocephaly

NF2

- Bilateral vestibular schwannomas (tinnitus, hearing loss and balance dysfunction)
- Schwannomas of other cranial and peripheral nerves
- Meningiomas

Noonan and LEOPARD syndromes

- Dysmorphic features
- Skin spots (lentigenes, café noir spots)

- Short stature
- Pulmonary stenosis or other heart defect

Cardiofaciocutaneous syndrome

- Dysmorphic features
- Heart defects
- Skin rashes and sparse hair
- Developmental delay
- Severe GI problems and failure to thrive

Costello syndrome

- Coarse facial features
- Heart defects
- Failure to thrive
- Developmental delay
- Deep palmar and plantar creases

Intestinal Rehab Programs STEP Up Outlook for Short Bowel Patients

Patients diagnosed with short bowel syndrome have traditionally faced disheartening survival rates and painful quality-of-life compromises. Today, however, evolving clinical approaches have improved the outlook, especially when patients arrive at intestinal rehabilitation centers before they experience severe complications.

Such centers see a disproportionate number of these rare syndromes, and engage multidisciplinary teams that include pediatric gastroenterologists, pediatric surgeons and transplant surgeons, pediatric hepatologists, dietitians, pharmacists, and social workers. This ideally positions them to balance considerations of total parenteral nutrition (TPN), medications and potential surgeries – including serial transverse enteroplasty (STEP), the latest tool in the armamentarium.

“We tailor the therapy to each individual child, depending on their underlying condition, and coordinate care with the patient’s pediatrician,” says Sue Rhee, MD, medical director of the Pediatric Intestinal Rehabilitation and Transplantation Program at UCSF Children’s Hospital.

Managing Complications

The causes of short bowel syndrome range from congenital conditions (e.g., intestinal atresias and gastroschisis) to acquired causes such as necro-

tizing enterocolitis. “Regardless of cause, though, our first concern is to support growth and nutrition, using TPN, which we can administer both as an inpatient and at home,” says Rhee.

One challenge is managing TPN’s two major risks: infection and liver disease. “To prevent line infections, one strategy we use is antibiotic lock therapy for our catheters,” says Rhee. Managing the risks of infection and liver disease also tends to involve complex adjustments of medications and TPN content. That’s why Rhee’s program is part of an NIH-funded consortium researching how to better identify those at risk for complications – and devise better ways to prevent and treat those complications.

Ultimately, however, the goal in all cases is to wean patients from TPN, using their remaining bowel and a specialized diet. And sometimes, when a patient is not progressing or complications become severe, there are surgical options.

Serial Transverse Enteroplasty and More

One recent surgical option is the bowel lengthening procedure STEP. This novel surgery, which has become standard procedure for pediatric intestinal rehabilitation programs, involves simultaneously cutting and stapling

sections of the intestine to hasten intestinal growth and improve motility. Surgeons Tippi MacKenzie, MD, Doug Miniati, MD, and Kerilyn Nobuhara, MD, at UCSF Children’s Hospital have completed a number of STEP procedures, including one on a 6-week-old.

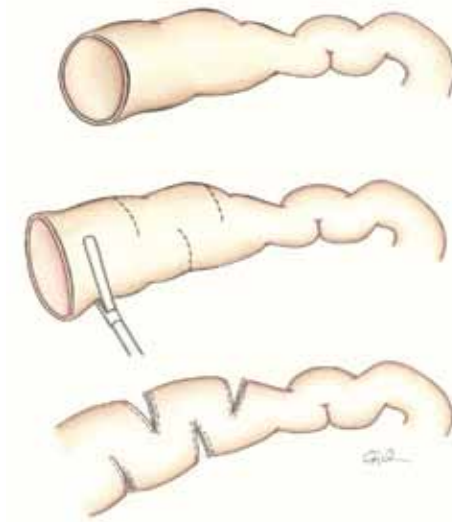
“It’s a real improvement over the past and can improve the chances of weaning patients from TPN,” says Rhee.

Transplantation is another surgical option. Typical indicators include liver failure, frequent sepsis or running out of places for a central line.

“We have top transplant surgeons here and a renowned abdominal transplant program, but our goal is to avoid transplant because, though it can be life-saving, it also can have many potential complications,” says Rhee, who is triple board-certified in pediatrics, transplant hepatology and pediatric gastroenterology.

The transplant hepatology certification is especially important for management of intestinal transplant patients with concurrent liver disease. It is yet another example of why quick referral to an expert center is such a crucial consideration for young people with GI concerns. ★

For more information, contact Dr. Rhee at (415) 476-5892.



In serial transverse enteroplasty, the surgeon simultaneously cuts (see dotted lines) and staples the intestine to encourage growth and improve motility. The procedure creates a “crooked street” effect that helps achieve those goals.

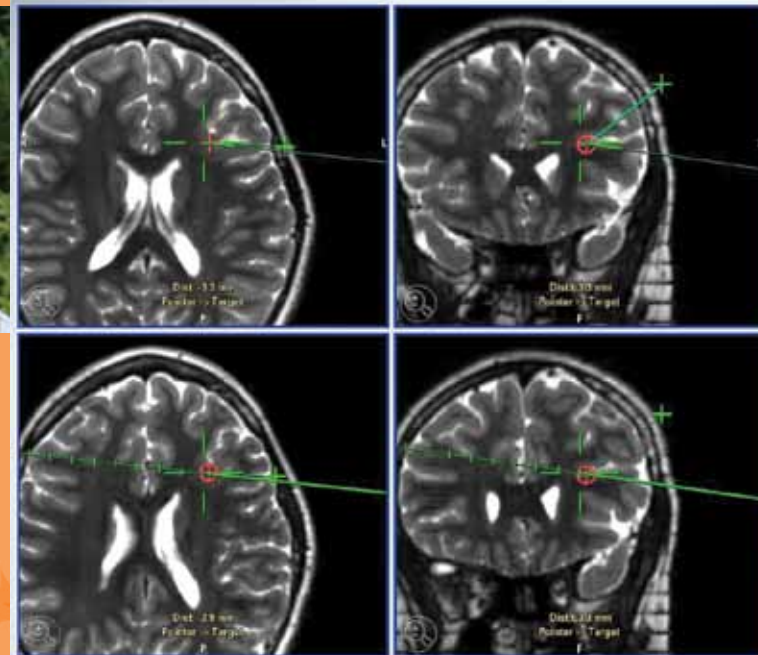


Sue Rhee, MD

“The neuronavigation was invaluable because it allows us to be much more precise.”



From top:
Kurtis Auguste, MD;
Joseph Sullivan, MD



Pediatric neurosurgeons use an intraoperative neuronavigation machine for precise targeting. A camera attached to a computer detects a wand that surgeons point along the surface of the brain. Here, cross-hairs reveal suspected sources of the patient’s seizures.

PEDIATRIC NEUROSURGERY (CONTINUED FROM FRONT COVER)

Using intraoperative neuronavigation – where the surgeon works from computer images that provide four different, adjustable views of the targeted area – Auguste resected the lesion as well as other electrically active tissue. “The neuronavigation was invaluable because it allows us to be much more precise,” he says.

Rodriguez emerged from the procedure with pristine speech and, as of April 2009, is back in school. She has remained seizure-free in the months since her surgery.

Except for a January 2009 follow-up with Sullivan and Auguste, and one scheduled for 2010, she has returned to the care of her referring neurologists, who will maintain her medication for a year postoperatively. If she remains seizure-free, Sullivan and her home neurologists will discuss titrating her off her medications.

“Aarika’s case is a strong illustration of the advantages of a center that has, among other things, an epileptologist, who can expertly evaluate when it is time to move from medications

to surgery; the ability to perform any necessary procedure (temporal lobectomy, lesional frontal lobe, nonlesional frontal lobe, corpus callosotomy, multiple subpial transection, hemispherectomy); and access to the most up-to-date equipment and collaborative expertise, including pediatric craniofacial plastic surgeons to help address cosmetic concerns with neurosurgery,” says Auguste. ★

For more information, contact Dr. Auguste at (415) 353-2348 or Dr. Sullivan at (415) 353-8440.



Gwynne Church, MD

Sleep a Missing Link in Many Childhood Disorders

“Sleep disorders are often overlooked, but in children, they can be a significant factor in processing and learning disorders, attention deficit hyperactivity disorder, and aggressive behavior,” says sleep specialist Gwynne Church, MD, director of the pediatric sleep lab at UCSF Children’s Hospital.

Missing the role of sleep in these disorders can be a dropped clinical opportunity because sleep problems are common. One in four children experiences a sleep disorder at some time during childhood. Obstructive sleep apnea alone may afflict as much as 1 percent to 3 percent of all children and a higher percentage of children who are obese, have craniofacial anomalies or have neuromuscular weakness.

“Moreover, treatments for sleep disorders have fairly high success rates and can often substantially alleviate academic problems, behavioral disorders or mood dysfunction,” says Church.

Be Aware

The challenge for busy pediatricians is that parents rarely discuss their children’s suspected sleep problems, and a wide variety of sleep disorders emerge from many causes and manifest in different ways. “Sleep problems can be caused by anything from enlarged tonsils to disorders that affect only 16 children

in the world,” says Dennis Nielson, MD, PhD, medical director of the UCSF pediatric sleep lab.

Nielson and Church believe, however, that heightened awareness among pediatricians can help uncover a suspected sleep disorder, after which physicians can refer the patient to an expert center.

Such centers have numerous advantages. At UCSF, Church is board-certified in sleep medicine, pediatrics and pediatric pulmonology, which enables her to understand the full range of potential diagnoses and treatments. In addition, the sleep lab has access to specialists that include pediatric neurologists, pediatric craniofacial surgeons, pediatric neurosurgeons, pediatric otolaryngologists/head and neck surgeons and pediatric anesthesiologists.

“We can diagnose the problem, and then work with the referring physician and the family to create an ideal treatment plan,” says Nielson. “If, after something like a tonsillectomy, a sleep problem isn’t improving, we can move people to CPAP therapy, with follow-up provided by experts.”

“In one case, a physician suspected that a patient with restless sleep and tonsillar hypertrophy had obstructive sleep apnea,” says Church. “But a sleep study showed periodic limb movement disorder, which is often associated

with iron deficiency. We discovered low ferritin levels, and treatment with iron supplementation solved this common problem.”

In another instance, a child was admitted to UCSF Children’s Hospital with carbon dioxide narcosis. He also had severe scoliosis, restrictive lung disease and a previously undiagnosed myopathy.

“A sleep study revealed severe nocturnal hypoventilation and obstructive sleep apnea,” says Church. “Subsequent bilevel titration improved his nighttime ventilation sufficiently that his daytime carbon dioxide levels returned to normal, and he felt dramatically better.” He then returned to his normal routine with the help of other members of the medical team, including pediatric intensivists, orthopedic surgeons and neurologists.

“These are clear examples of how a center can make a dramatic difference for children with sleep disorders,” says Church. ★

The UCSF Children’s Hospital sleep lab conducts studies every night of the week and on week-ends. The sleep clinic is held every other Tuesday from 9 a.m. to 3 p.m. on the second floor of the Ambulatory Care Center at 400 Parnassus Ave., San Francisco.

For more information, contact the pediatric sleep lab at (415) 353-1957 or Dr. Church at (415) 476-8629.



The pediatric and neonatal critical care transport team stands in front of the new, dedicated CALSTAR MD 902 Explorer.

New Helicopter Speeds and Eases Emergency Transport of Children and Neonates

As pediatric beds disappear from California hospitals, the need for expert emergency transport to rush severely ill children to specialty care heightens. In response, UCSF Children’s Hospital has added a state-of-the-art helicopter air ambulance to its fleet. That fleet, which also includes a dedicated ground ambulance and a fixed-wing aircraft, is one of the few transport programs in the region to work with critically ill pediatric and neonatal patients.

“The new helicopter enables us to get to many places sooner and be in and out the door faster,” says Christa Thomas, RN, patient care manager of the UCSF Children’s Hospital transport team.

Expert Team with Expert Equipment

Adding a helicopter became possible when CALSTAR, a nonprofit air ambulance organization, agreed to dedicate one of its newly purchased

this is urgent-type care, where sometimes you need to improvise.” The entire crew received additional training in everything from how to approach the vehicle to looking for obstacles in flight, flight physiology and communication with helmet mikes.

The specialty equipment includes a transport incubator, a dedicated critical care stretcher with nitric oxide therapy, and the ability to do limited lab work such as blood gases and electrolytes. “CALSTAR’s retrofitting allows us to slide all our specialty equipment in and out, with our goal to be en route in 30 minutes or less,” says Thomas.

The helicopter itself contains all of the latest safety equipment recommended by the National Transportation Safety Board and is relatively quiet, due to robust noise mitigation and the absence of a tail rotor.

How the Transport System Works

Use of the craft depends on strict clinical criteria as well as on weather conditions, distance – there is about a 150-mile radius – and the presence of a helipad at the referring hospital. “We estimate we’ll use it about 30 to 40 times a month,” says Thomas. Landing on a helipad at referring hospitals means the UCSF team will not have to tie up their local ambulances for transport to and from an airport.

When referring physicians need transport, they should call the UCSF Children’s Hospital Access Center – (877) UC-CHILD [(877) 822-4453] – which is staffed 24/7 by a pediatric critical care nurse. “We triage, get in contact with the appropriate attending and determine whether transport needs to take place,” says Thomas.

If the helicopter is the choice, the transport team will meet the helicopter at San Francisco International Airport and travel from there. When the new hospital at Mission Bay opens in 2014, a proposed helipad would enable the team to depart immediately from there. ★

For more information, contact Christa Thomas at (415) 353-1246.



MD 902 Explorers exclusively to UCSF Children’s Hospital. CALSTAR also agreed to retrofit the craft for UCSF’s specialized equipment and a team of pediatric and neonatal critical care experts.

“Collectively, the physicians, nurse practitioners and nurses on our team have hundreds of years of pediatric and neonatal experience as well as ongoing access to pediatric specialists at UCSF Children’s Hospital,” says Thomas. “That’s important because

When is a pediatric patient an appropriate candidate for a sleep study?

- Difficulty falling asleep or maintaining sleep
- Frequent or loud snoring
- Apneic pauses, episodic choking, gasping and snorting
- Nocturnal enuresis
- Restless sleep or frequent leg movements during sleep
- Chronic mouth breathing or adenoid facies
- Excessive daytime sleepiness
- Sleep complaints in the presence of behavioral disorders, performance impairment or mood dysfunction
- Sleep complaints in the presence of a family history of a primary sleep disorder

Children's Hospital Access Center

Our dedicated admission, transfer and transport hotline, staffed 24/7 by experienced pediatric critical care nurses, ensures that access to our inpatient services is always just a phone call away.

For maternal, neonatal and pediatric transfers and transport, please call 877-UC-CHILD (822-4453).

Referral Liaison Service

Our Referral Liaison Service provides you with improved access to our physicians and medical services. Liaisons can expedite the referral process, assist in obtaining follow-up information and are available to help resolve difficulties.

To contact the Referral Liaison Service, please call (800) 444-2559.

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Obstetrics and Gynecology Update: What Does the Evidence Tell Us?	October 7-9, 2009	InterContinental Mark Hopkins Hotel	San Francisco

Ras/MAPK Syndromes Symposium

On August 1-2, 2009, at the Doubletree Hotel in Berkeley, California, six patient advocacy groups will join clinicians and researchers for a two-day research symposium, titled "Genetic Syndromes of the Ras/MAPK Pathway: From Bedside to Bench and Back." Katherine Rauen, MD, PhD, of UCSF and Lisa Schoyer of the Costello Syndrome Family Network will chair this forum for discussion of the basic science and clinical issues surrounding these syndromes.

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PATHWAY CLINIC (CONTINUED FROM PAGE 2)

After a phone intake that includes a complete medical history and family tree, a patient's first visit is with a medical geneticist and genetic counselor, who review the history and conduct a thorough physical exam.

"We look for phenotypic markers that form a recognizable pattern of dysmorphism," says Rauen. "A skin manifestation, for example, can help tie the clinical diagnosis down." A molecular diagnosis, which requires patient consent, can confirm the clinical diagnosis, help family members understand the overall impact on the family and help them make decisions.

The next step is to tap into the clinic's extensive network of subspecialists. "If it's Noonan, for example, we know they

may be more prone to hypothyroidism, so we begin a workup and call in Endocrinology," says Rauen. "The advantage is a unifying diagnosis that helps providers know what to be mindful of and facilitates more personalized medicine."

"Throughout the process, we work with the family and their primary care provider to create a joint set of goals that can include nonclinical issues," says Strecker. "We care for the whole person – and, many times, the entire family – and make sure there are no gaps in care." ★

For more information, contact Michelle Strecker at (415) 476-9321 or Dr. Rauen at (415) 514-3513 or the NF/Ras pathway clinic at (415) 476-2757.