

Accelerating Science – Advancing Medicine

This past year witnessed significant growth and expansion within all academic missions in the Department of Pediatrics.

A major clinical initiative in 2014 focused on integrating pediatric services across the Mount Sinai Health System, which encompasses seven hospital campuses and the Icahn School of Medicine at Mount Sinai. The Health System now oversees 18,000 deliveries, 90,000 pediatric ED visits, and 150,000 pediatric outpatient visits per year.

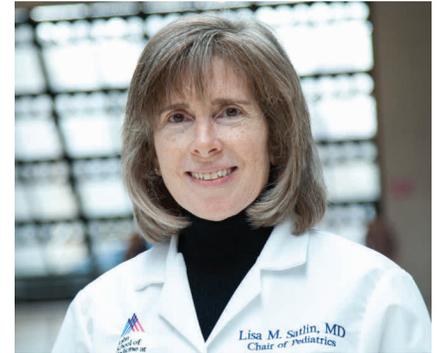
Among our notable achievements in 2014:

- Renovations of the Jo Carole and Ronald S. Lauder Newborn Intensive Care Unit, and the Blau Center for Children's Cancer and Blood Disease at Kravis Children's Hospital at Mount Sinai, are nearly complete.

- *U.S. News & World Report* ranked Kravis in seven specialties in its "America's Best Children's Hospitals" 2014-2015 guidebook: Diabetes & Endocrinology, Gastroenterology & GI Surgery, Neonatology, Nephrology, Neurology & Neurosurgery, Pulmonology, and Urology.

- The Department's robust extramural funding portfolio placed us among the top ten pediatric departments nationwide in National Institutes of Health funding.

This newsletter spotlights a few of the many exciting programs at Kravis Children's



Lisa M. Satlin, MD, Herbert H. Lehman Professor and Chair, Jack and Lucy Clark Department of Pediatrics, and Pediatrician-in-Chief, Kravis Children's Hospital at Mount Sinai

Hospital at Mount Sinai and the Department of Pediatrics at the Icahn School of Medicine at Mount Sinai.

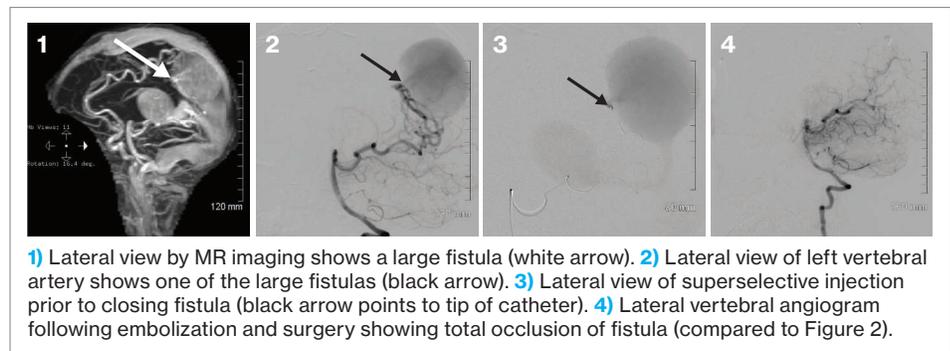
COMPLEX CASES: NEUROLOGY/NEUROSURGERY

Treating a Pediatric Arteriovenous Malformation and Dilated Vein of Galen

In May 2013, a 4-year-old girl born with multiple growing cutaneous vascular lesions from vascular malformations, and a history of gastrointestinal bleeding from gastrointestinal vascular lesions, was evaluated at Mount Sinai.

After a comprehensive workup by Pediatric Neurology and Neurosurgery, a high-flow arteriovenous malformation and/or fistulization in the parasagittal region on the left hemisphere—with a markedly dilated vein of Galen—was found. Vein of Galen malformations are the most severe expression of a vascular malformation of the brain, which, if untreated, frequently result in death or severe disability.

Alejandro Berenstein, MD, Director, Pediatric Cerebrovascular Surgery Program, proceeded with a cerebral angiogram and treatment, with occlusion of a large AV



fistula with Cyanoacrylate. Following the procedure, the child was brought to the PICU awake and responsive. Upon exam, she was not moving the right upper and lower extremity. After an urgent CT scan, an intraparenchymal hemorrhage was diagnosed. Saadi Ghatan, MD, Director, Pediatric Neurosurgery, Mount Sinai Health System, placed an intraventricular drain.

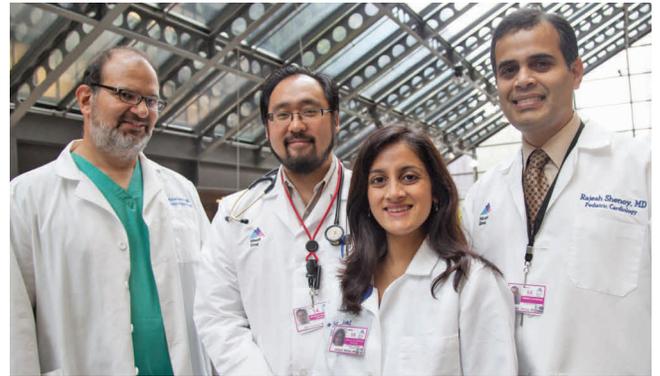
Seven days after surgery, the patient was discharged home where she remained on a course of steroids and continued to show steady clinical improvement. Follow-up treatment between July 2013 and March 2014 included angiograms, embolization with the use of a detachable tip microcatheter, and microsurgical resection to treat residual malformations. The patient is fully recovered and neurologically normal.

Managing Severe Lung Damage After Suspected Dengue Fever

Michell “Oriana” Morillo is a 12-year-old Venezuelan with ongoing medical problems allegedly caused by a severe dengue infection acquired around 2 years of age, resulting in prolonged respiratory failure, several months of hospitalization, several cardiopulmonary arrests, prolonged coma, and severe lung damage. She had very limited activity and required chronic oxygen therapy. She was followed closely by a pulmonologist in Venezuela, but her pulmonary function declined steadily over the next 10 years, and she was referred to the United States to be evaluated for possible lung transplant.

At Mount Sinai, Alfin G. Vicencio, MD, Chief, Pediatric Pulmonology, uncovered several issues, among them a severe tracheal stenosis that had been underappreciated, largely contributing to the severe defects in lung function, and also contributing to the development of severe pectus excavatum, further restricting her pulmonary function. Addressing these issues could potentially obviate or delay the need for lung transplant.

Michael Rothschild, MD, Director of Pediatric Otolaryngology; Rajesh Shenoy, MD, Assistant Professor, Pediatrics (Cardiology); and Aaron Lipskar, MD, Assistant Professor, Surgery (Pediatric Surgery), joined Dr. Vicencio in her care. Balloon dilation combined with cryotherapy relieved the tracheal obstruction, and her previously 3mm airway was converted to a normal caliber, after which she experienced a



From left: Michael Rothschild, MD; Alfin G. Vicencio, MD; Alefiyah Malbari, MD; and Rajesh Shenoy, MD

dramatic improvement in her ability to participate in normal activities, such as walking. A transbronchial biopsy did not identify any progressive disease in the lung parenchyma.

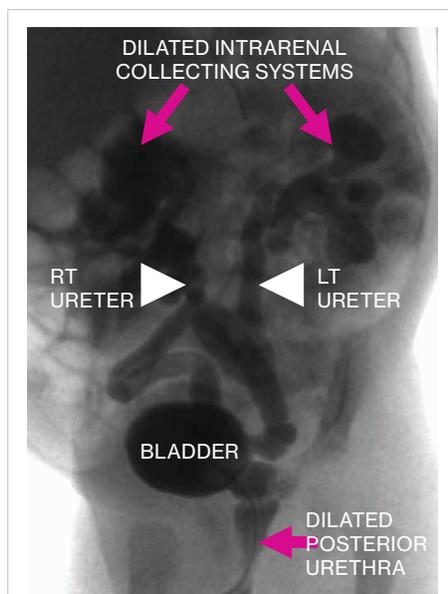
Today, Oriana is exercising regularly and does not require any supplemental oxygen, as had been the case prior to her arrival. Surgical repair of the severe pectus excavatum is likely to be planned in the future. Dr. Vicencio and Alefiyah Malbari, MD, Assistant Professor of Pediatrics, continue to evaluate Oriana as an outpatient.

Treating Urinary Tract Obstruction from Posterior Urethral Valves

In October 2013, Liam Bonilla was a 1.85 kg, 31-week premature infant transferred 9 days after birth to our care with oligoanuric renal failure, hypertension, and a shocking serum potassium level of 10.5 mMol/L. He was ventilator-dependent and had intermittent ventricular tachycardia. Care was quickly coordinated by Mount Sinai’s Ian R. Holzman, MD, Chief, Newborn Medicine; Jeffrey Saland, MD, Chief, Pediatric Nephrology and Hypertension; and Jeffrey A. Stock, MD, Chief, Pediatric Urology.

Management was conservative, and the potassium was lowered by intravenous insulin and glucose with simultaneous calcium infusion to inhibit hyperkalemic arrhythmia. Urine flow was re-established and a catheter was placed to allow for bladder drainage. Clinical sepsis was treated with antibiotics.

Over the following weeks, the NICU team quickly accomplished extubation, initiation of nutrition, and close monitoring.



Bilateral grade V vesicoureteral reflux
Voiding cystourethrogram (VCUG) demonstrates bilateral grade V vesicoureteral reflux with marked tortuosity of the bilaterally dilated ureters, as well as dilatation of the posterior urethra, consistent with a variant of posterior urethral valves.

Henrietta Kotlus Rosenberg, MD, Director of Pediatric Radiology, performed a voiding cystourethrogram (VCUG), which demonstrated posterior urethral valves and bilateral grade V vesicoureteral reflux (see figure). Greyscale/color Doppler ultrasound was also used for evaluation of the baby’s urinary tract at the time of diagnosis, and sequentially thereafter to assess response to treatment. Renal function steadily improved. At 6 weeks of age, the urology team accomplished a successful surgical procedure to endoscopically resect posterior urethral valves.

Now age 15 months, Liam has residual mild dilatation of the bilateral intrarenal collecting systems and ureters with normal renal parenchyma, and subclinical renal disease due to the fetal obstruction, but testing demonstrates compensated and normal renal and urinary function. He is thriving, meeting normal neurocognitive and physical milestones, and is followed by a coordinated team of Mount Sinai faculty members.

Surviving Sudden Cardiac Arrest

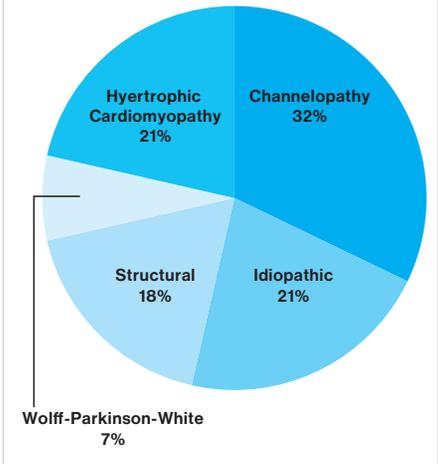
Sudden cardiac arrest (SCA) in an apparently healthy child is a rare event with a reported incidence of 3.5/100,000 per year. However, with the wider availability of automatic external defibrillators, survival with good neurologic outcome after resuscitation from SCA is increasingly common.

The Pediatric Electrophysiology service at Kravis Children's Hospital at Mount Sinai, led by Barry Love, MD, reviewed our experience treating children after resuscitation from cardiac arrest. All patients had stepwise evaluation with ECG, echocardiogram, cardiac MRI, and genetic testing. Additional investigations with stress testing, prolonged ECG monitoring, electrophysiology testing, and cardiac catheterization were undertaken when necessary to clarify the underlying diagnosis.

In the 11-year study period, 9 of 28 (32%) SCA survivors, median age – 15 years, (0.5–20 yrs) had been resuscitated by lay rescuers, and the remainder by trained personnel. Underlying diagnoses are shown in the figure. Twenty-six of the 28 patients (93%) made an excellent neurologic recovery. In 26 patients, an implantable cardiac defibrillator (ICD) was placed with a minimally invasive surgical procedure. During the 1 month – 11 years (mean – 4.4 yrs) follow-up period, 13 patients had subsequent lifesaving ICD therapies. One channelopathy patient who declined ICD replacement at battery depletion died in follow-up.

The prognosis for patients who survive out-of-hospital cardiac arrest is progressively improving. With careful workup, a definitive diagnosis can be made in most patients. ICDs,

Etiology of Resuscitated Pediatric Sudden Cardiac Arrest: an 11-Year Review



combined with medical therapy, as we have demonstrated, can provide excellent protection for secondary events.

Creating a Prognostic Score for GVHD Risk



James L. M. Ferrara, MD, DSc

A team of researchers headed by James L. M. Ferrara, MD, DSc, a renowned investigator and member of Mount Sinai's Departments of Medicine and Pediatrics, has created a prognostic score to improve treatment for acute graft-versus-host disease (GVHD) in adults and children. GVHD is the major cause of non-relapse mortality after allogeneic hemopoietic stem-cell transplantation (SCT).

Because severity of symptoms at the onset of GVHD does not accurately define risk, patients with GVHD are treated alike, most often with high-dose systemic corticosteroids, effective in only half the cases.

Specifically, the investigators used three plasma biomarkers, TNFR1, ST2, and Reg3α, to create an algorithm that calculated the probability of non-relapse GVHD-associated mortality in nearly 500 patients at two study centers. The algorithm produced the same three GVHD risk-group scores in 300 patients from 20 SCT centers, where the cumulative incidence of non-relapse mortality significantly increased as the GVHD score increased.

Dr. Ferrara, Ward-Coleman Chair in Cancer Medicine, and Professor and Director, Hematologic Malignancies Translational Research Center at The Tisch Cancer Institute at Mount Sinai, led a research team that included co-collaborators at the University of Michigan, University of Regensburg, and the Blood and Marrow Clinical Trials Network. The research was published in the January 2015 issue of *The Lancet Haematology*.

Next, researchers plan to specifically test the algorithm in pediatric patients, as well as launch a new study of a Food and Drug Administration-approved protocol to treat high-risk GVHD. Dr. Ferrara's newly created Mount Sinai Acute GVHD International Consortium, comprised of 10 SCT centers, will also adopt the new scoring system to test new treatments for acute GVHD.



Marla C. Dubinsky, MD,

has joined Mount Sinai as Chief of Pediatric Gastroenterology & Hepatology and Co-Director of the Susan and Leonard Feinstein Inflammatory Bowel Disease (IBD) Clinical Center. She will

lead a division that will further advance personalized medicine driven by genetic influences; offer expanded opportunities for patient participation in research; and improve patient care, with a focus on reducing Emergency Department visits, hospitalizations, and complications, and optimizing transition of care to adult IBD programs.

Dr. Dubinsky's primary research focuses on the influence of genetics and immune responses on the variability in clinical presentations, treatment responses, and prognosis of early-onset IBD.

Among Mount Sinai's new IBD initiatives is a collaboration with the Dartmouth-Hitchcock IBD Center, and its Director, Corey A. Siegel, MD, to use a real-time tool that graphically displays a patient's predicted disease course based on a model of clinical and serologic risk factors. The tool also indicates risk of disease-related complications as related to a specific therapy implemented within 90 days of diagnosis.

Previously, Dr. Dubinsky was Director of the Pediatric Inflammatory Bowel Disease Center at Cedars-Sinai Medical Center.



**Mount
Sinai**

Icahn School of Medicine at Mount Sinai
One Gustave L. Levy Place, Box 1107
New York, NY 10029-6574

YOUNG PIONEERS: DIABETES/ENDOCRINOLOGY

Developing a Community-Based Adolescent Diabetes Prevention Program

Nita Vangeepuram, MD, MPH, Assistant Professor of Pediatrics (General Pediatrics), has received a career development award (K23) from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH) to develop a diabetes prevention program for at-risk East Harlem youth in New York City.

Funding will help Dr. Vangeepuram build upon her encouraging preliminary results of a pilot study that had examined the adaptation of a proven effective, peer-led adult diabetes prevention program—Help Educate to Eliminate Diabetes—into an appropriate intervention for pre-diabetic adolescents.

In the study, diabetes risk was assessed by measuring body mass index (BMI). Overweight/obese adolescents (BMI >85th percentile) were offered pre-diabetes screening using oral glucose tolerance testing. Pre-diabetic adolescents were invited to complete 8 weekly diabetes prevention sessions led by youth peer coaches in a community setting.

Overall, 47% of 186 adolescents screened were at risk for diabetes based on BMI, and 64% (n=56) returned for diabetes testing.



Nita Vangeepuram, MD, MPH, second from right, with participants in a diabetes prevention program for at-risk youths, from left: Angel Quintero, Kelvin Tapia, Denise Soledad Cano, and Justice Romero

Nineteen (34%) tested positive for pre-diabetes and 1 (1.8%) tested positive for diabetes. Most (14/19) pre-diabetic adolescents identified enrolled in the workshop; 9 completed >50% of the sessions; and 16 returned for 3-month follow-up. Outcomes were encouraging for adolescents who completed >50% of the sessions compared to those who completed <25% of the sessions (mean change in BMI of -0.3 kg/m² vs. +0.3 kg/m², p=0.3; mean change in fasting glucose of -6 mg/dl vs. +1 mg/dl, p=0.2). Five of 9 adolescents completing the sessions did not have pre-diabetes at follow-up.