[CLINICAL FOCUS] SLCH REACHES 30-YEAR ANNIVERSARY FOR LIVER TRANSPLANTS

In 1985, both St. Louis Children’s Hospital (SLCH) and Barnes-Jewish Hospital performed their first liver transplants. For the last 30 years, patients have come from across the country to these premier institutions for the expertise of the multidisciplinary teams that make up the liver transplant programs and provide care for patients of all ages. Led by Washington University transplant surgeons and hepatologists specializing in liver diseases, both institutions have grown to be leaders in the field.

The Liver Care and Transplant Center at SLCH cares for children with all forms of liver disease. Since its inception in 1985, the center’s liver transplant program has performed hundreds of pediatric liver transplants on patients ranging in age from 10 days old to teens.

“One aspect that makes our program so unique is that we do transplants on very small babies, which can be incredibly challenging, requiring great focus and intensity,” says Washington University surgeon and SLCH liver transplant director Majella Doyle, MD. “We often receive referrals from other hospitals because some programs don’t feel comfortable performing liver transplants on smaller children.”

Most pediatric liver transplant patients have liver failure, whether acute when the liver fails suddenly or from end-stage liver disease, such as biliary atresia, the most common cause of chronic liver disease in a newborn.

“Caring for children with liver disease requires the expertise of a multidisciplinary team. You need the physicians and surgeons on the team to have been properly trained and the experience that comes with being in a center with sufficient patient volumes like ours,” says Yumirle Turmelle, MD, Washington University pediatric hepatologist and medical director of the SLCH Liver Care and Transplant Center.

The center has three certified pediatric transplant hepatologists—Dr. Turmelle, Alexander Weymann, MD, and Janis Stoll, MD.

“A center like ours ensures a seamless transition through all stages of liver transplantation,” Dr. Turmelle says. “The first step is to properly diagnose the liver condition, while providing appropriate care for the end-stage liver disease complications. Our goal is to keep the patient as healthy as possible during the wait period for donor organ and finally perform a successful transplant.”

Pediatric patients diagnosed with liver cancers, such as hepatoblastoma and hepatocellular carcinoma, also are often candidates for liver transplant.

“At Children’s Hospital, the liver transplant program collaborates with oncology colleagues to coordinate the care of these patients and plan for the ideal time for transplantation,” Dr. Turmelle adds.

With its long history, the SLCH liver transplant program is among the most successful in the United States, with three-year survival rates continued on next page
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of more than 90 percent, consistently above the national average, Dr. Doyle says. The liver transplant surgeons at SLCH use multiple liver transplant options, including whole liver, segmented/reduced liver, split liver and living donor transplants.

Helping to navigate the pediatric liver transplant patients and their families is a team of transplant coordinators and nurse practitioners. Transplant coordinators follow their patients from the time of evaluation for transplant through pre- and post-op, explains Jill Seys, RN, SLCH Transplant Center program manager. In addition, the hospital has a dedicated inpatient nurse practitioner who stays with the patient during surgery and collaborates with the transplant coordinator.

“The transplant coordinators and nurse practitioners at Children’s Hospital continuously demonstrate dedication and commitment to providing a superior patient experience for patients and families,” Seys says. “It is a privilege to work with a team dedicated to going the extra mile to ensure we always do what’s right for our kids.”

To speak to a member of the liver transplant team, call Children’s Direct at 800.678.HELP (4357).
Children's Asthma/Bronchiolitis Score (CAB)—will be used in the emergency department and inpatient areas to assess respiratory status and help assess use and effect of bronchodilator treatments on children who come to the hospital with bronchiolitis.

Another focus of SIB will be to address avoidance of tobacco smoke exposure for children who present to the hospital with bronchiolitis, by providing family members with resources for smoking cessation.

Lastly, the initiative will focus on increasing the use of NG tubes for hydration of infants with bronchiolitis.

“For bronchiolitis, we are not taking enough fluids orally and need non-oral hydration. Both the AAP and Children’s Hospital’s guidelines recommend nasogastric or intravenous fluids for infants with bronchiolitis who cannot maintain hydration orally,” says Washington University physician Mythili Srinivasan, MD, a pediatric hospitalist at SLCH. “However, currently at Children’s only intravenous hydration is used for providing fluids to these patients, and we do not utilize the option of NG hydration.”

Dr. Srinivasan explains that NG tube placement often requires fewer attempts compared to IV placement. Intravenous access in children with dehydration and poor peripheral circulation can sometimes be difficult and require multiple attempts. Use of an NG tube in such children will be especially useful and can often be accomplished in one attempt. Furthermore, infants may be fed with breast milk or formula via the NG tube, which provides better nutrition compared to intravenous fluids and satiates hunger in the infants.

“A large randomized trial in Australia and New Zealand found no significant differences in length of stay, rates of admission to ICU, need for ventilator support or adverse events between infants 2 months to 12 months old assigned to NG hydration versus those assigned to IV hydration. There was no aspiration in either group of children,” says Dr. Srinivasan.

A smaller pilot study in Israel also showed no significant differences in length of stay, duration of oxygen administration, and time to resume full oral feeding in infants less than 6 months old randomized to NG hydration or IV hydration. Again, no aspiration was noted in either group of children.

“Since NG tube feeding for bronchiolitis is not routinely used at Children’s Hospital, it will require a cultural change not only for our clinicians, but also for families and our nurses who do not use NG tubes for hydration,” says Dr. Srinivasan.

Dr. Srinivasan and her team are currently planning a quality improvement initiative to increase the use of NG tubes for hydration of infants with bronchiolitis who are not in severe respiratory distress. The QI initiative will include such actions as:

- Educate nurses, physicians and parents on the option of NG tubes for hydration of infants with bronchiolitis.
- Determine the impact of education by measuring the increase in the use of NG tubes for hydration of infants with bronchiolitis.
- Obtain feedback from all physicians and nurses throughout the winter on their experience with the use of NG tubes for hydration and make changes in the initiative based on the feedback.

For copies of the new guidelines, visit StLouisChildrens.org/DD.
Gary A. Silverman, MD, PhD, has been named the Harriet B. Spohrer Professor and head of the Department of Pediatrics at Washington University School of Medicine (WUSM). With the new appointment, effective in April, Dr. Silverman will become pediatrician-in-chief at St. Louis Children’s Hospital (SLCH) and executive director of the Children’s Discovery Institute, a partnership of the school and hospital.

A highly regarded neonatologist, Dr. Silverman comes to St. Louis from the University of Pittsburgh School of Medicine, where he is vice chair for basic research in the school’s Department of Pediatrics and at Children’s Hospital of Pittsburgh. He also is the Twenty-Five Club Professor of Pediatrics, Cell Biology and Physiology at the School of Medicine and division chief of newborn medicine at Children’s Hospital of Pittsburgh and Mage-Womens Hospital. Both hospitals are part of the University of Pittsburgh Medical Center (UPMC).

Dr. Silverman succeeds Alan L. Schwartz, PhD, MD, who has led the Department of Pediatrics since 1995. Dr. Schwartz will remain on the faculty and devote more time to national leadership commitments, mentoring faculty and trainees, and to his research. Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine announced Dr. Silverman’s appointment.

“I am pleased to welcome Gary Silverman, a national leader in newborn medicine, especially in the treatment of premature and critically ill infants,” Dr. Shapiro said. “I am confident that under his leadership, the Department of Pediatrics will continue to grow and distinguish itself as a top pediatric program in clinical, research and educational excellence. I am grateful to Alan Schwartz for his commitment to the university and his steadfast guidance of the department over the past 20 years.”

Dr. Silverman is no stranger to Washington University. He completed a fellowship in newborn medicine at SLCH in 1989 and was a postdoctoral research fellow at the School of Medicine from 1988-91, training in the laboratory of the late Stanley J. Korsmeyer, MD, an internationally known cancer researcher.

“It is a great honor to be returning to WUSM and SLCH,” Dr. Silverman said. “These are world-class institutions with exceptional talent, and I can’t wait to roll up my sleeves and join this team of outstanding professionals.

“I hope to expand upon the delivery of exceptional cutting-edge care to all children in need and to continue this institution’s excellence in medical education and community outreach,” Dr. Silverman said. “Another crucial mission is to build upon the expertise of the Children’s Discovery Institute while leveraging the entire Washington University biomedical research enterprise to help usher in a transformative era of child health care.”

Earlier, while studying molecular genetics in the Korsmeyer lab, Dr. Silverman also was an instructor of pediatrics and, later, an assistant professor of pediatrics before moving to Harvard Medical School in 1992. There, he served on the faculty for 12 years and was also director of the division of newborn medicine at Boston Children’s Hospital.

Dr. Silverman then joined the University of Pittsburgh medical faculty, where he merged his clinical expertise with his love for basic science discovery to aid young patients.

Dr. Silverman’s research program has been at the forefront of elucidating the genetic basis of diseases, especially those affecting newborns. Most recently, his laboratory established disease models in the primitive roundworm C. elegans and developed high-throughput screening platforms to identify causative factors and novel therapeutic drugs.

This approach has led to several new drugs for the genetic disease alpha-1 antitrypsin deficiency, which can cause liver and lung disease in children and adults. These drugs potentially may be effective treatments for other diseases caused by misfolded proteins, including neurodegenerative disorders. The screening platform also is being used to discover new therapeutic drugs for necrotizing enterocolitis, a devastating intestinal disease that affects premature infants.

Dr. Silverman has conducted research in collaboration with David H. Perlmutter, MD, the School of Medicine’s incoming dean, a fellow professor of pediatrics and cell biology at the University of Pittsburgh School of Medicine and physician-in-chief and scientific director at Children’s Hospital of Pittsburgh.

“Many rare and old pediatric diseases will be redefined by their genetic underpinnings, thereby leading to dramatic new therapies that could not have been imagined a few years ago,” Dr. Silverman said.

Learn more about Dr. Silverman’s background and awards at StLouisChildrens.org/DD.

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Jennifer Ikle, MD

Each month, St. Louis Children’s Hospital’s Chief Residents honor a resident who shows exceptional dedication to his or her patients, colleagues or profession. In September 2015, the SLCH Chief Resident Award was presented to Jennifer Ikle, MD, a second-year pediatric resident. Dr. Ikle was recognized for her impressive initiative, creativity and hard work in going above and beyond the expectations for her advocacy project.
[FACULTY UPDATE] WHITE NAMED JAMES P. KEATING, MD, PROFESSOR OF PEDIATRICS

Andrew J. White, MD, director of the Division of Pediatric Rheumatology at Washington University School of Medicine, has been named the James P. Keating, MD, Professor of Pediatrics.

Dr. White was installed by Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine, and Alan L. Schwartz, PhD, MD, the Harriet B. Spoehrer Professor, head of the Department of Pediatrics, and pediatrician-in-chief at St. Louis Children’s Hospital (SLCH).

“Andy White is the ideal person to hold the James P. Keating Professorship,” Dr. Shapiro said. “He shares the same values of excellence and commitment to the best possible patient care that Jim Keating exemplified throughout his long career at Washington University and St. Louis Children’s Hospital. Andy is a consummate educator and mentor, just like Jim Keating.”

The installation ceremony paid homage to Dr. Keating, an internationally recognized pediatrics professor at the School of Medicine who created one of the country’s first pediatric intensive care units, pioneered the pediatric gastroenterology subspecialty and introduced the concept of pediatric diagnostic medicine. Dr. Keating died in late 2014 at age 76.

“It is most fitting that Andy White is now the James P. Keating, MD, Professor of Pediatrics,” Dr. Schwartz said. “Dr. Keating is a legend and was simply the finest physician in the history of SLCH and the finest physician with whom I have ever worked, and Andy White is the next Jim Keating.”

Dr. White directs the pediatric residency program at St. Louis Children’s Hospital, a post held by Dr. Keating for 33 years.

“Holding this professorship is particularly meaningful to me because I worked very closely with Jim in the diagnostic center, on the wards and in residency education,” Dr. White said. “Dr. Keating was a titan of medicine, who crafted, molded and mentored hundreds of students, residents and physicians here and across the country. He was, and continues to be, a tremendous inspiration to us all.”

Dr. White, who was named the Philip R. Dodge, MD, Scholar in Pediatrics in 2013, also serves as co-director of the Hereditary Hemorrhagic Telangiectasia Center of Excellence at Washington University, which treats the genetic blood disorder also known as Osler Weber Rendu.

Dr. White received a bachelor’s degree from Brandeis University near Boston and a master’s in physical sciences from the University of Chicago. He earned his medical degree at University of Texas Southwestern Medical School in Dallas before completing an internship and residency at SLCH and a pediatric immunology and rheumatology fellowship at the School of Medicine.

[FACULTY UPDATE] CONSTANTINO, LUBY RECEIVE AWARDS FROM CHILD PSYCHIATRY ACADEMY

The American Academy of Child and Adolescent Psychiatry (AACAP) has honored two Washington University child psychiatrists at St. Louis Children’s Hospital (SLCH).

John Constantino, MD, director of psychiatry at SLCH and the Blanche F. Ittleson Professor of Psychiatry and Pediatrics at the School of Medicine, received the organization’s 2015 George Tarjan Award for Contributions in Developmental Disabilities. Joan Luby, MD, director of the early emotional development program at the hospital and the Samuel and Mae S. Ludwig Professor of Child Psychiatry, was awarded AACAP’s Irving Phillips Award for Prevention.

Dr. Constantino directs the William Greenleaf Eliot Division of Child and Adolescent Psychiatry and the Intellectual and Developmental Disabilities Research Center at the School of Medicine. He was recognized for his work in determining risk and mechanisms of inherited susceptibility in the autism spectrum disorders. The Tarjan Award recognizes significant contributions to the understanding or care of those with mental retardation and developmental disabilities.

Dr. Luby was recognized for her work with very young children who have depression. Her research includes brain-imaging studies that may point to treatment windows during particular stages of brain development.

The Phillips Award was established in honor of Irving Phillips, MD, who served as the AACAP president from 1985-1987 and was well known for his work in the field of prevention. Both awards were presented in October at the academy’s annual meeting in San Antonio.

[FACULTY UPDATE] GUTMANN APPOINTED TO NIH ADVISORY BOARD

David Gutmann, MD, PhD, the Donald O. Schnuck Family Professor and director of the Washington University Neurofibromatosis (NF) Center, recently was appointed to the Advisory Council for the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH). The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

David Gutman, MD, PhD
Respiratory infections are common in preschoolers, but while most children recover fairly easily from the typical coughs and congestion, a significant number develop illnesses severe enough to interfere with breathing and warrant trips to urgent care clinics and emergency rooms. In children whose colds tend to progress and lead to severe wheezing and difficulty breathing—such that they are given oral corticosteroids as rescue therapy—researchers have shown that giving a common antibiotic at the first sign of cold symptoms can reduce the risk of the episode developing into a severe lower respiratory tract illness.

The new study, led by researchers at Washington University School of Medicine, appeared online Nov. 17 in the *Journal of the American Medical Association (JAMA)*.

“Oral corticosteroids such as prednisone have become the standard of care for these situations,” said lead author Leonard B. Bacharier, MD, professor of pediatrics. “But there are some studies that suggest these treatments don’t consistently work for young children. That’s why we want to find ways to prevent upper respiratory infections from progressing to lower respiratory tract illnesses. Once the episode gets going, standard interventions are less effective than would be desired.”

The investigators tested the antibiotic azithromycin against placebo in 607 children at nine academic medical centers nationwide. The children were ages 12 months to 6 years and had histories of developing severe lower respiratory tract illnesses but otherwise were healthy. About equal numbers of respiratory infections were reported in both the antibiotic and placebo groups. But there was a significant difference in the severity of the infections experienced between the two groups. Of the 92 illnesses deemed severe because they required oral corticosteroids, 57 were in the placebo group compared with 35 in the group receiving azithromycin.

For this study, Dr. Bacharier and his colleagues chose to give the antibiotic at the highest FDA-approved dose for treating infection.

“We chose this antibiotic dose in order to try to maximize the anti-inflammatory effects,” said Dr. Bacharier, who treats patients at St. Louis Children’s Hospital (SLCH). “But we don’t know if this is why we saw less severe disease in children receiving early azithromycin treatment. It also could work because it is preventing or treating bacterial infections.”

The protocol for dispensing the antibiotic also differed from typical courses of these drugs. Parents were given the antibiotic to have on hand at home so they could give it at the earliest signs of cold symptoms. The investigators worked with each family to identify a set of early symptoms that would indicate to parents to begin the treatment course.

“We helped families identify the collection of symptoms that triggers that internal alarm parents have that says, ‘Here we go again,’” Dr. Bacharier said. “That’s when we wanted them to start giving the antibiotic. We think the earlier you get it going, the more effective the intervention will be.”

Because of concerns over the development of antibiotic-resistant organisms, Dr. Bacharier and his colleagues studied azithromycin resistance in a subset of 86 patients seen at SLCH.

“We saw that there were children who received azithromycin during the study who, at the end of the study, had azithromycin-resistant germs in their throats,” Dr. Bacharier said. “But we also saw, at nearly but not quite the same rate, azithromycin-resistant bacteria in children who did not receive any of the antibiotic. So we don’t fully understand the effect of azithromycin on antibiotic resistance.”

Dr. Bacharier said a larger study is necessary to determine whether the difference in the rates of developing azithromycin resistance is statistically or clinically meaningful. He also noted that those children shown to have bacteria resistant to azithromycin did not fare any differently in the study than those who did not have azithromycin-resistant organisms.

Dr. Bacharier added that about one in six visits to doctors for asthma symptoms in the United States results in the child being prescribed an antibiotic. But this is usually after the episode has become severe.

“We want to be prudent with our antibiotic use,” he said. “We don’t want to overdo this. On the other hand, these are children having severe episodes for which we don’t have a lot of effective therapy. A significant number are getting an antibiotic therapy anyway and have to be very sick to get it. Our study suggests we can reduce the risk of severe respiratory illnesses by giving azithromycin treatment earlier.”

Dr. Bacharier also pointed out that even among children who developed severe illnesses while on azithromycin, overall symptoms were less severe than in those who received placebo. The study also demonstrated that despite the benefit in reducing episode severity, this treatment strategy does not lengthen time between infections or prevent them from happening.

He said one of the next steps for this particular intervention is to see if it is similarly effective in children who are receiving daily asthma therapy.

“We showed this worked for the children we studied who did not need daily asthma therapy,” he said. “Now we would like to investigate what will happen in a group of children at the next step of the disease severity ladder.”

Visit StLouisChildrens.org/DD for article references.
CASE STUDY  MOODY IN SOUTH DAKOTA

The following case study was used by Andrew J. White, MD, the James P. Keating, MD, Professor of Pediatrics and division director of pediatric rheumatology, Washington University School of Medicine, and director of the St. Louis Children's Pediatric Residency Program, as part of the “Patient of the Week” (POW) series. Many of the POW case studies cover uncommon illnesses, or common illnesses with unusual symptoms that can be overlooked. If you would like to be added to the POW email distribution, send an email to white_a@kids.wustl.edu.

This case was submitted by Saquib Lakhani, MD, (SLCH Resident 1996-1998), who is now in Pediatric Critical Care, Sanford School of Medicine at the University of South Dakota.

3-year-old boy with CC: “mood spells.”

He is a healthy boy who six months ago began having “mood spells.” They occur on average once a week, though frequency has increased to about every other day over the past month. They typically begin with an odd comment, which alerts parents that an episode of moodiness is about to begin. Mother pulls out a camera and shows a video to the physician.

Episode description: He was sleeping in the back seat of the minivan when he abruptly sat up, exclaimed, “Mom, is it ok if I sleep?” and began staring. When the recording begins he is sitting upright looking hyper alert and a bit worried when he suddenly begins laughing uncontrollably and almost maniacally. This lasts for about 20 seconds and then he begins tearfully sobbing for another 5-10 seconds. After this he lays his head on the armrest and promptly falls asleep.

Parents report that this recorded episode is fairly typical and he usually sleeps for at least an hour and up to a few hours after each spell. The spells have no specific trigger. The spells are not interruptible; they simply run their course. He had a normal routine EEG a few weeks ago, though he did not have a spell during the EEG.


A diagnostic test was obtained:

MRI Brain: There is a 1.5x1.7x1.7-cm mass centered at the level of the floor of the third ventricle in the region of the tuber cinereum. The signal of the mass follows gray matter on all pulse sequences and there is no associated enhancement on post contrast images. The optic tracts are located just lateral to the mass on each side and the mammillary bodies are located just inferior to the mass.

There is no diffusion abnormality. No evidence of intracranial hemorrhage. No hydrocephalus. The major intracranial flow voids are intact. There is no abnormal enhancement identified. The hippocampal formations appear normal with no evidence of mesial temporal sclerosis. The sulcal and gyral pattern appears symmetric and within normal limits. No evidence of a migrational abnormality. The posterior fossa structures appear normal.

Impression: Mass at the floor of the third ventricle centered at the tuber cinereum of the hypothalamus, most likely a hamartoma.

Diagnosis:

1. Hypothalamic hamartoma
2. Gelastic seizures, secondary to No.1 (Gelos = Greek for laughter)

Treatment: Surgical resection vs. thermocoagulation vs. gamma knife therapy (for which he is currently being evaluated).

Neither levetiracetam nor valproic acid seem helpful in controlling his seizures, but symptoms typically do improve/resolve with resection of the mass.

He has no signs of precocious puberty (known to occur in this syndrome).

The mechanism of the laughter is unknown.

SLCH PARTICIPATING PROVIDER OF MISSOURI CARE

On December 1, St. Louis Children’s Hospital (SLCH) and Washington University (WU) Physicians, along with Barnes-Jewish Hospital, became participating providers in Missouri Care, a managed care network serving Missouri Medicaid patients.

“We are pleased to participate in Missouri Care, and we appreciate the opportunity to partner with our referring physicians in providing exceptional care to children who need specialty care and hospital services,” says Joan Magruder, SLCH president.

In addition to Missouri Care, SLCH and WU Physicians continue participating in standard Missouri Medicaid as well as Aetna for Better Health (formerly HealthCare USA) and Home State Health Plan.

For specific questions regarding the hospitals and physicians’ participation in Missouri Care, contact Andy Fleming, 314.273.0416.

SLCH NEWS
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CONTINUING EDUCATION

2016 EARLY BIRD ROUNDS
Fridays, 8 a.m., St. Louis Children’s Hospital Executive Boardroom, 3-S36, or online at StLouisChildrens.org/Med_Ed.

• Jan. 8 - Adolescent Medicine
• Jan. 15 - Preparing for Office Emergencies
• Jan. 22 - Radiology
• Jan. 29 - General Surgery

For additional information about continuing education opportunities, go to StLouisChildrens.org/Med_Ed.

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