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Pediatric Heart-Lung Transplants - Underutilized?

By Pirooz Eghtesady, MD, PhD

Introduction

Combined adult heart-lung transplants have declined steadily since a high of approximately 200 cases per year in the early 1990s to 50 or so cases per year more recently. We've seen the same trend in the pediatric realm: a steady decline from 50-60 cases per year to 10 or less today. In the last two years, there was only one pediatric heart-lung transplant performed: it was for a 15-year-old patient who presented to our institution, St. Louis Children's Hospital, in the fall of last year. Simultaneously, the number of adult heart (~4,000/year), adult lungs (~4,000/year), pediatric heart (~100/year) and pediatric lungs (~100/year) transplants have remained steady. Few centers perform pediatric heart-lung transplants and a majority perform no more than 1 or 2 per year. Why these statistics?

Certainly, the indications for these procedures have not changed. Approximately a third of the recipients are patients with end-stage Congenital Heart Disease (CHD), a third with pulmonary arterial hypertension, and a final third belong to a group of other indications, such as interstitial lung disease, retransplantation, and unique cardiomyopathies, etc. For children, however, the scenery has changed. Early on, Congenital Heart Disease was the most common indication, accounting for 50% or more of the cases. Today, isolated pulmonary arterial hypertension is the most common indication (~75%). Interestingly, in Europe, adolescents with Cystic Fibrosis still account for a third of the recipients. Of note, over the last three

decades, the overall age distribution has not changed world-wide: adolescents still make up 60-70% of the recipients.

"In the last two years, there was only one pediatric heart-lung transplant performed: it was for a 15-year-old patient who presented to our institution, St. Louis Children's Hospital, in the fall of last year.

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Figure 1 provides the first glimpse as to the reason why overall outcomes for patients have been suboptimal, particularly for patients with Congenital Heart Disease and especially for younger patients (Figure 2). Figure 3 clearly explains the rationale: in earlier eras, median survival was barely more than a year, with a significant portion of that time spent in the hospital. More recently, there has been significant improvement in survival, though there is still a steep drop-off in survival immediately after surgery. For patients who survive this perioperative risk, however, and who survive to 1-year after transplant, their expected median survival is more than a decade (Figure 4). Not surprisingly, in transplant literature, the 1-year conditional survival is predicated by the immediate perioperative outcomes: patients who have a difficult and complicated post-operative course are less likely to make it to their 1-year anniversary. This self-fulfilling prophecy then impacts the long-term outcome of the patients.

The Case

At 16-months old, the patient was diagnosed with rhabdomyosarcoma. For a year, he went through chemotherapy, radiation and multiple surgeries before entering remission. The boy continued to develop at the same pace as his peers, but in 2012, he collapsed while playing hockey with friends.

At first, the patient's pediatrician thought it was asthma and prescribed him an inhaler, but his symptoms did not improve. The family went for a second opinion, and the patient was given antibiotics for pneumonia.

Later tests revealed scarring in the patient's lungs resulting from the chemotherapy and radiation he received as a child. The scarring slowly progressed, and by 2015, the patient needed oxygen each night. By 2016, he needed round-the-clock oxygen, a wheelchair to get around, and he had some mild symptoms of heart failure as well.

The patient's local medical center began planning for a lung transplant, but doctors discovered that the patient's heart was also problematic with elevated end-diastolic pressures (high teens). Since combined heart-lung transplantation was not offered at the local facility, the patient's family was given a short list of children's hospitals with expertise in pediatric heart-lung transplants.

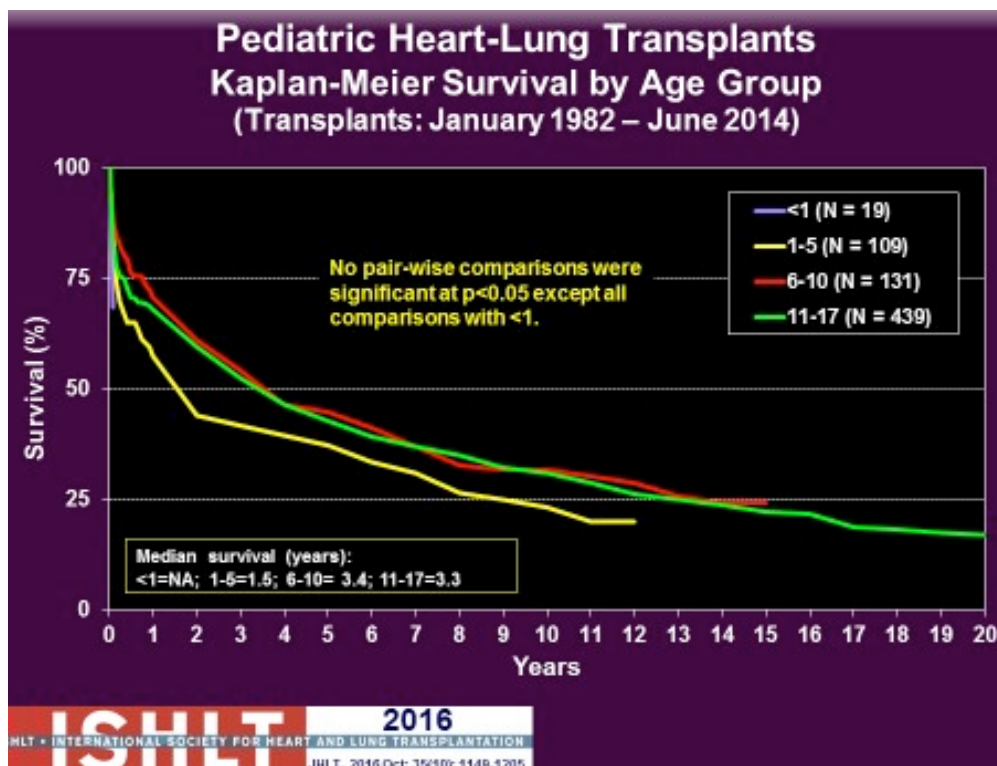
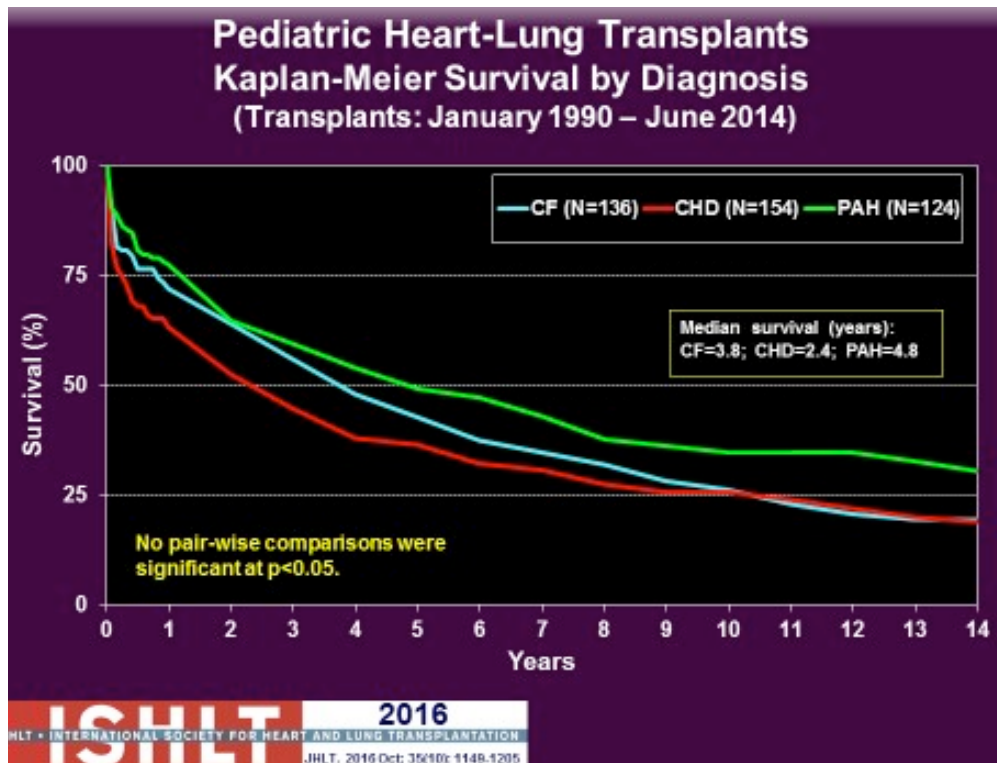


Figure 1. (Top); Figure 2 (Bottom)

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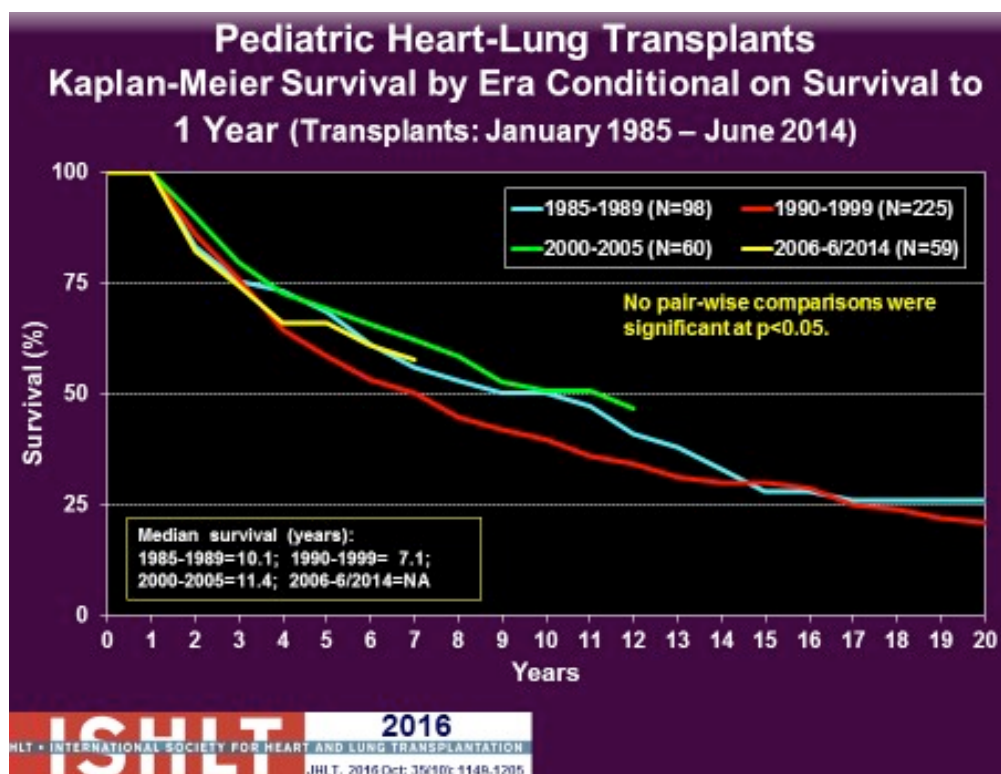
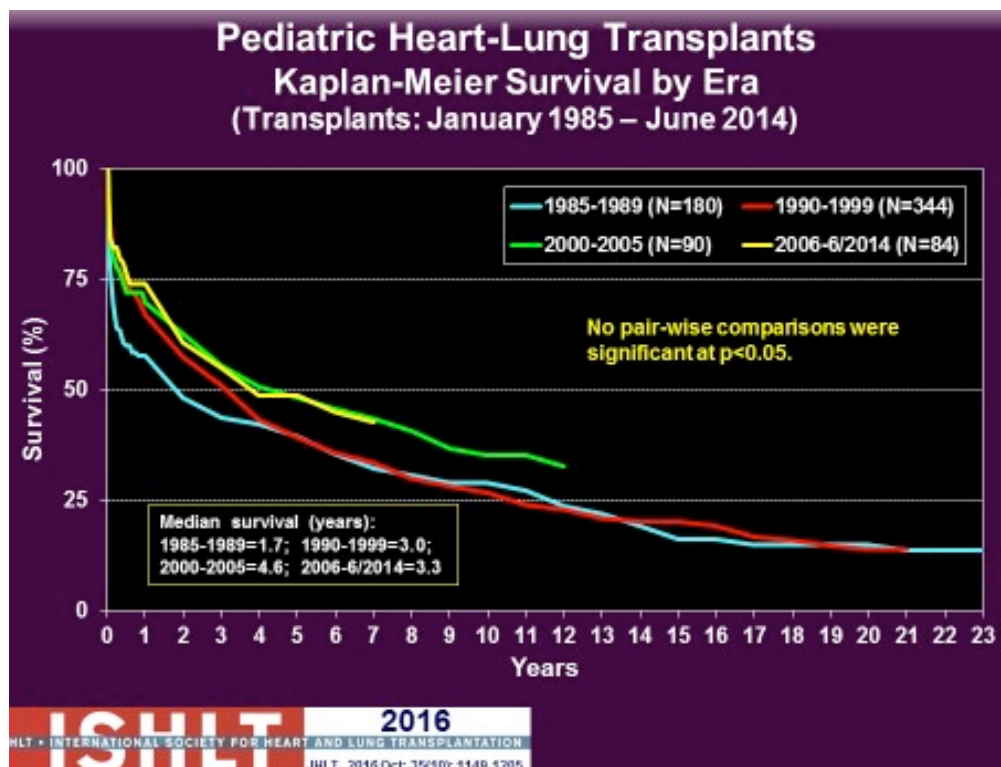


Figure 3. (Top); Figure 4 (Bottom).

The patient's family first approached a program in a city where they had family in the area. The hospital's heart failure and pulmonary services program, in a separate evaluation, concluded that the patient's cardiac status was stable and that he only needed a lung transplant. The lung transplant team believed that the degree of adhesions noted on radiographic findings (thickened pleura) made him a too-high risk candidate. Also, the ability for an ailing heart to be able to deal with the aftermath of a complicated surgery would further add to the risk.

The patient was then referred to St. Louis Children's Hospital for a third opinion. At this point, the patient was in extremis, consuming on average one tank of oxygen every couple of days. He was severely tachypneic and also cachectic at baseline. We elected to list the patient for a combined heart-lung transplant.

While waiting for a donor the patient's health started to deteriorate even further, leading to emergent readmission in just a couple of weeks. Due to concerns with possible further decompensation requiring ECMO (extracorporeal membrane oxygenation) support (with limited long-term support options), the patient was put on a ventilator. Fortunately, a suitable donor became available in a timely manner and the patient underwent a successful combined heart-lung transplant. The pleural adhesions turned out to be minimal and trivial in nature and the patient underwent the procedure without requiring an intraoperative blood transfusion.

Discussion

The first successful adult heart-lung transplant was performed in March 1981, and its success in adults led to it being performed in children with comparable, if not better results. In 1986, a 15-year old female received the first successful pediatric heart-lung transplant. In general, the overall trajectory and biology of heart-lung transplanted patients follows a path similar to patients with isolated lung transplantation. Of note, however, most readers likely do not realize that, indeed, the outcomes in particular for recipients with pulmonary hypertension, are superior (>12 years 50% survival) to other etiologies such as cystic fibrosis, likely in part because of an absence of underlying baseline infections or secondary organ problems (Figure 5). A similarly quality of life and functional status follows a similar pattern. Figure 6



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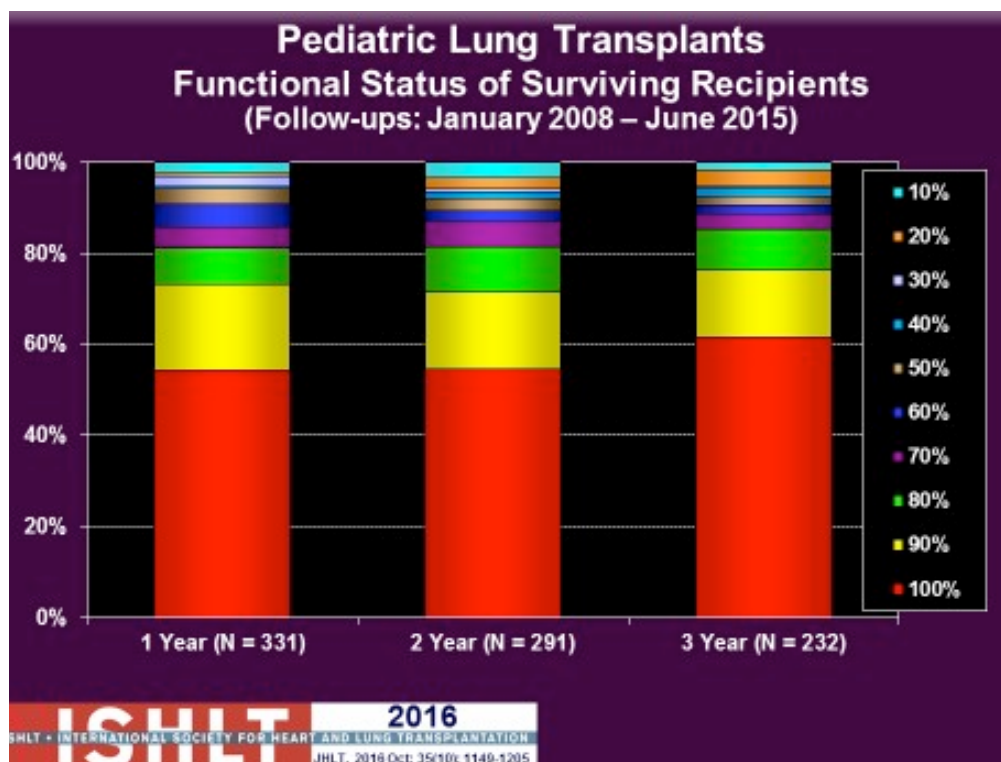
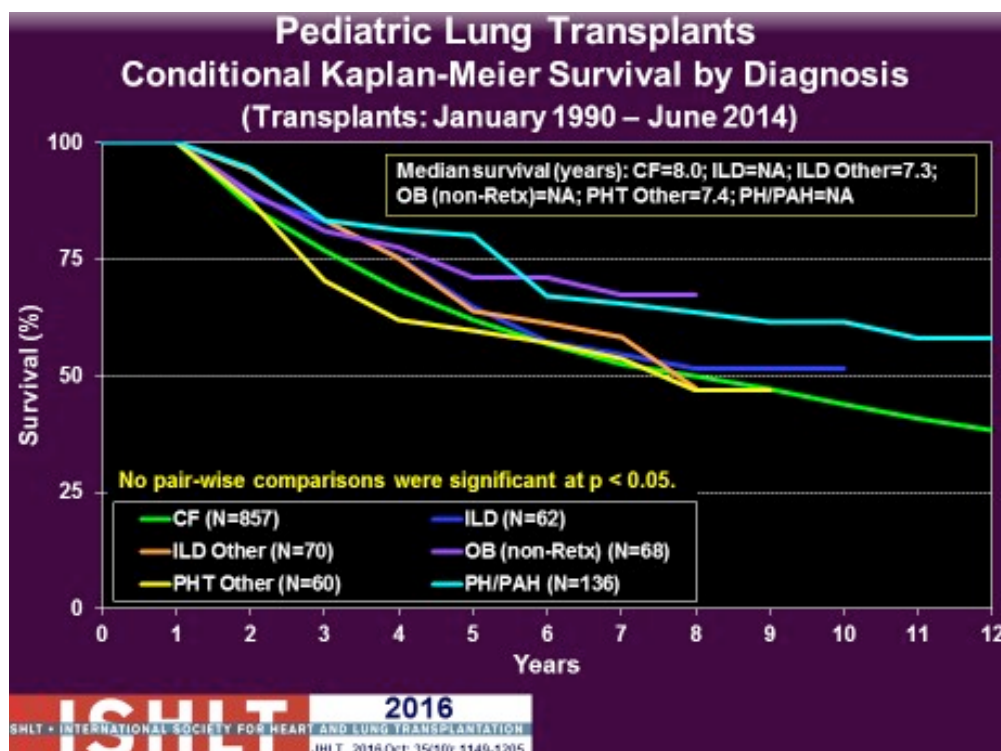


Figure 5. (Top); Figure 6 (Bottom).

demonstrates the functional status of surviving patients. Contrary to common perception (based on inpatient experiences), the patients can actually do quite well, especially if they do well during that first year after transplant. An increasingly smaller fraction of patients require hospitalization after the first year (Figure 7). This means kids can go back to doing things that every child does,

including going to school and playing sports.

According to UNOS Reports (United Network for Organ Sharing - www.unos.org), in 2015, six patients were added to the heart-lung waitlist, and three transplants were performed. In 2016, two patients were added to the waitlist, and the only transplant was performed at our institution. The rarity of heart-lung transplants is multi-factorial; part is due to simple impression or assumption of poor

Pediatric Cardiologist

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outcomes based on historical results noted above. There is also the fact that fewer conditions today necessitate such a surgery, especially in view of the number of donor organs available. In general, there are fewer donor heart-lung organ blocks than donor hearts alone because brain death may be associated with neurogenic pulmonary edema. In addition, aspiration into the lung or

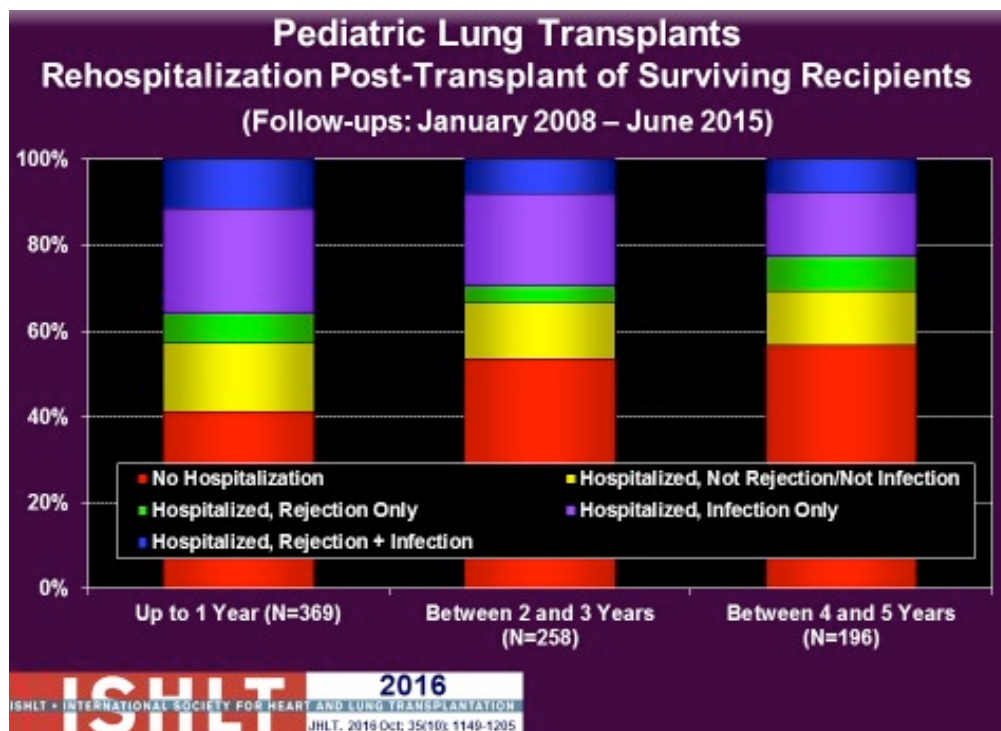
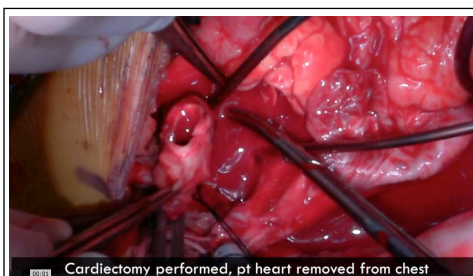


Figure 7.

other forms of pneumonitis is common with severe trauma and resuscitation. Prolonged ventilatory support may also predispose the potential donor to nosocomial infection, and direct thoracic trauma may result in pulmonary contusion. Consequently, a smaller fraction of overall potential heart donors have lungs suitable for heart-lung transplantation.

Nevertheless, there are still many clinical scenarios where combined heart-lung transplants could be or perhaps should be considered. Not infrequently at our center, we receive referrals for patients with acquired pulmonary vein stenosis who have undergone prior sutureless repair, and not infrequently, repeat sutureless repair. Some of these patients also have other complicating cardiac conditions such as heterotaxy that preclude lung-only transplantation. Unfortunately, often these patients have undergone attempts at "suture-less" repair, often followed by repeat "suture-less" repair, and the hospital course is then complicated by need for repeated interventions, tracheostomy and a multitude of transfusions. In 2011, Dr. Nicola Viola and his colleagues reported a 47% mortality for this approach in one of the larger reported series. The 10-year survival was only 31% for all-comers.² The same can be said for a select subset of patients with pulmonary atresia-VSD

and multiple aortopulmonary collaterals. In 2016, Dr. Anu Kaskinen reported on long-term outcomes from a nationwide study of more than 100 children: Palliated patients had a survival rate of only 34% at 10 years. These results were further impacted by the initial size of the true central pulmonary arteries (smaller-worse).³ Not surprisingly, the repeated operative interventions lead to formation of pre-formed reactive antibodies negating the



Watch the Video

"St. Louis Children's Hospital Heart-Lung Transplant: 15-Year Old Boy"

<https://vimeo.com/201031487>

possibility of transplant or reducing the chances of long-term success from an immunologic perspective. Accrued morbidity, as well as inevitable scarring from repeat surgery, also create a situation that is too prohibitively risky for transplantation. Primary heart-lung transplantation may offer superior results. Often transplant is thought of as a salvage operation (instead of an alternative option), which unfortunately, is a recipe for disaster.

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2. Viola et al. The Journal of Thoracic and Cardiovascular Surgery, Volume 142, Issue 2, August 2011, Pages 344-350).
3. Kaskinen et al. Eur J Cardiothorac Surg. 2016 May;49(5):1411-8.

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About the Author

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Study Shows Probiotics Can Prevent Sepsis in Infants Findings Reported in *Nature*

Newswise — A research team at the University of Nebraska Medical Center College of Public Health has determined that a special mixture of good bacteria in the body reduced the incidence of sepsis in infants in India by 40% at a cost of only \$1 per infant. The findings are reported in the Aug. 16, 2017 issue of the journal *Nature*.

Pinaki Panigrahi, MD, PhD, Professor, Epidemiology and Pediatrics, Center for Global Health and Development, and his colleagues in the College of Public Health, led the international research team. The results reflect a culmination of 15 years of research and could seriously impact infant health worldwide.

The special mixture included a probiotic called *Lactobacillus plantarum* ATCC-202195 combined with fructo-oligosaccharide (FOS), an oral synbiotic preparation developed by Dr. Panigrahi.

Probiotics are live bacteria and yeasts that are good for your health, especially your digestive system. Synbiotics are combinations of probiotics with an FOS supplement that promotes growth and sustains colonization of the probiotic strain. FOS, naturally found in breast milk and such plants as onion, chicory, garlic, asparagus, banana, artichoke and others, is food for the probiotic bacteria.

Sepsis is a severe complication of bacterial infection that results in around one million infant deaths worldwide each year, mostly in developing countries. It occurs when the immune system stops fighting germs and begins to turn on itself and can lead to tissue damage, organ failure and death.

It is estimated that 40% of patients with severe sepsis in developing countries do not survive. When children and adults are included, the inpatient cost for managing patients with sepsis in U.S. hospitals is nearly \$24 billion each year.

"This is the largest clinical trial of probiotics in newborns funded by the National Institutes of Health," Dr. Panigrahi said. The team enrolled more than 4,500 newborns from 149 villages in the Indian province of Odisha and followed them for their first 60 days, the most critical period when they get sick and die.

During their first days of life, the newborns were administered the oral preparation for seven days.

Results of the randomized, double-blind, placebo-controlled study showed that sepsis and deaths in the first two months of infancy were reduced by 40%, more than twice the anticipated reduction of 20%. The synbiotic treatment also lowered respiratory tract infections.

The effectiveness demonstrated in Dr. Panigrahi's study was so successful the study was halted early.



Division Head, Pediatric Cardiology and Co-Director, Congenital Heart Center

The Department of Pediatrics at the University of Illinois College of Medicine at Peoria and the OSF Healthcare Children's Hospital of Illinois seek an outstanding academic leader to direct the Division of Pediatric Cardiology as the Division Head, Pediatric Cardiology and Co-Director, Congenital Heart Center.

OSF Healthcare Children's Hospital of Illinois (CHOI) is a 144-bed, full-service children's hospital, with more than 115 pediatric specialists in 40+ subspecialties. Children's Hospital is the major pediatric teaching affiliate of the University of Illinois College of Medicine at Peoria (UICOMP). UICOMP is one of four regional campuses that make up the nation's largest public medical school. The Peoria campus is the sponsoring institution of 11 residency programs and eight fellowship training programs.

Principle responsibility of the Division Head and Co-Director is growth and enhancement of the state of the art clinical programs in pediatric & congenital cardiology, echocardiography, electrophysiology, interventional cardiology, and advanced imaging. Working with the surgical co-director, UICOMP Department of Pediatrics and leadership of CHOI, he/she will also work to increase the footprint of the program, develop interdisciplinary services to enhance current programs and increase the regional, national and international reputation of the program. The Division Head will be responsible for recruitment and retention of physicians, advanced practice providers and staff needed to expand the program and provide outstanding family-centered care to patients of the pediatric Congenital Heart Center. Currently, the Division of Pediatric Cardiology has 11 physicians and two APNs located in Peoria and two physicians located in Rockford, IL.

The Division Head will be a physician leader with a record of professional leadership in an academic institution. The Division Head reports to the Head of Pediatrics. He/she must be BC in Pediatrics and/or Pediatric Cardiology.

Interested candidates should contact:

Jennifer Schaulin,

Vice President MillicanSolutions, LLC,
at 682-223-5782

or via email: Jennifer.Schaulin@MillicanSolutions.com
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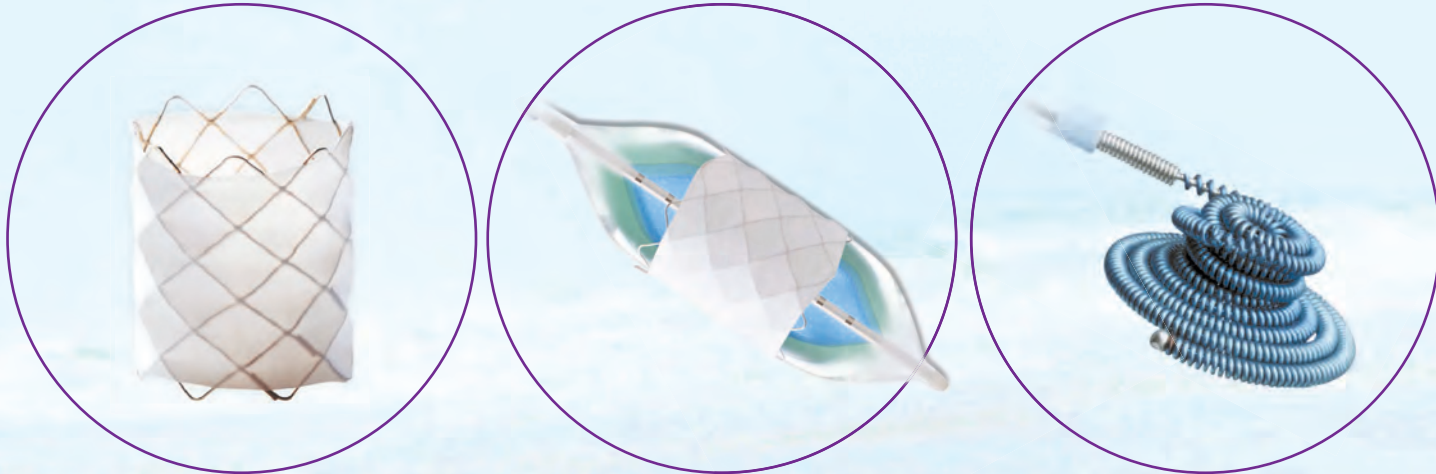
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The probiotic formula could be a “very cheap oral sepsis vaccine,” Dr. Panigrahi said.

Few trials on the use of probiotics to prevent sepsis have focused on newborns, whose largely naive immune system and less complex intestinal environment would allow the probiotic to grow.

“We were concerned when the data safety and monitoring board stopped the study prematurely. We had enrolled just about half of our proposed subjects. Typically, a study is stopped when something is wrong.

“But, it was a moment of superlative thrill when we learned it was stopped due to early efficacy. We were surprised a second time when the complete data analysis showed that respiratory tract infections also were reduced – something we did not anticipate in our population,” Dr. Panigrahi said.

A country's health is measured by its infant mortality. India has one of the highest rates of infant mortality in the world. Of the one million newborns who die at birth worldwide, India accounts for 700,000 such deaths, according to UNICEF. For every 1,000 live births in India, 40 babies die.

By comparison, the infant mortality rate in Sri Lanka, Nepal, and Bangladesh are 9, 29, and 33, respectively, according to the World Health Organization (WHO).

Dr. Panigrahi wants to bring these numbers down and the results of his study are a big first step.

“This study has to be replicated in different countries and under different circumstances. We maintained tight controls on the administration of the synbiotic and conducted a rigorous follow-up which will not be available in real life,” he said.

“We have to find out why respiratory infections went down. How does this treatment affect the lungs?”

The intestinal system is the largest immune organ in the body, Dr. Panigrahi said. “If you took it apart and spread out the villi – small, finger-like projections that extend into the small intestine – it would cover a tennis court. And, it's loaded with lymphoid cells. So, if you want to stimulate the body's immunity, go to the intestine.”

Also known as “blood infection,” sepsis is a global health care problem that is more common than heart attack and claims more lives than any cancer. In the least developed countries, it is a leading cause of death.

In the developing world, sepsis accounts for 40% of all neonatal lives lost per year and more than 100,000 women contract sepsis in the course of pregnancy and childbirth.

In children and adults, sepsis occurs when the body's attempt to fight an infection results in the immune system damaging tissues and organs. This chaotic response, designed to protect us, causes widespread inflammation, leaky blood vessels and abnormal blood clotting resulting in organ damage. In severe cases, blood pressure drops, multiple organ failures ensue and the patient can die rapidly from septic shock.



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General Pediatric Cardiologist

The Heart Center (THC) at Nationwide Children's Hospital (NCH) is recruiting a cardiologist, at the assistant or associate professor level, to attend on our Cardiac Step-Down Unit and participate in our robust outpatient/satellite outreach program. This individual would join a team of dedicated academic cardiologists, nurse practitioners, specialty nurses and allied healthcare specialists who provide care to patients in our 24-bed cardiac step-down unit and outpatient clinic system. Candidates must be board-eligible or certified in pediatric cardiology. The successful applicant would work closely with the team members of our cardiac step-down unit, out-patient services, and national referral partners to ensure effective care delivery and safe transition of care for our patients. Our step-down unit is vigorously engaged in family centered care and quality improvement initiatives focused on the institutional pillars of Treat Me Well, Navigate My Care, Do Not Harm Me, Heal Me, and Treat Me with Respect.

Nationwide Children's Hospital is the primary pediatric teaching facility for The Ohio State University in Columbus Ohio. THC, a top USNWR program, embraces a culture of patient safety and quality, transparency, engagement in translational/outcomes research, excellence in education, value-based care and community health awareness. This creates ample opportunities for professional growth and leadership development. THC is comprehensive with services that include a single ventricle program, neurodevelopmental and cardiogenetic services, thoracic organ transplantation program, fetal cardiac intervention, blood conservation strategies, as well as a comprehensive outreach network. Annual clinical metrics for THC include: 500 cardiothoracic surgeries, 700 cardiac interventional and EP procedures, and 15,000 cardiology outpatient encounters. We have a well-established pediatric cardiology fellowship with advanced training opportunities in ACHD, interventional catheterization, and non-invasive imaging along with options to pursue master's degrees in statistics/study design, healthcare administration and medical education at OSU. We participate in numerous multicenter clinical trials and quality initiatives including the ACC QNet and JCCHD QI collaboratives. We are directly linked to our Center for Cardiovascular Research which has an NIH T-32 training grant.

Interested candidates are encouraged to submit their curriculum vitae to:

Rob Gajarski, MD, Cardiology Section Chief at:
robert.gajarski@nationwidechildrens.org

The Ohio State University is an Equal Opportunity, Affirmative Action Employer. Women, minorities, veterans, and individuals with disabilities are encouraged to apply.

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CONGENITAL HEART INTERNATIONAL PROFESSIONALS

The congenital heart professionals network exists to facilitate communications between congenital heart professionals locally, regionally, and globally.

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Funded by Cincinnati Children's Heart Institute

The study's team from UNMC included: Pinaki Panigrahi, MD, PhD, Professor and Principal Investigator; Lorena Baccaglini, DDS, PhD, Associate Professor, Epidemiology; and Dinesh Chandel, PhD, Research Assistant Professor, Environmental, Agricultural & Occupational Health, Center for Global Health and Development in the College of Public Health.

Other collaborators on the study were:

- Sailajanandan Parida, SCB Medical College, Cuttack, Odisha, India.
- Nimai Nanda, Ispat General Hospital, Rourkela, Odisha, India.
- Radhanath Satpathy, Arjit Mohapatra, Pravas Misra, Asian Institute of Public Health, Bhubaneswar, Odisha, India.
- Lingaraj Pradhan, pediatrics, Capital Hospital, Bhubaneswar, Odisha, India.
- Rama Chaudhry, microbiology, All India Institute of Medical Sciences, New Delhi, India.
- Hegang Chen, epidemiology and public health, University of Maryland School of Medicine, Baltimore.
- Judith Johnson, J. Glenn Morris Jr, Emerging Pathogens Institute, University of Florida, Gainesville.
- Nigel Paneth, Epidemiology, Pediatrics & Human Development; and Ira Gewolb, Neonatology, College of Human Medicine, Michigan State University, East Lansing.

The study was funded by a \$3 million, five-year grant from the National Institutes of Health - Eunice Kennedy Shriver National Institute of Child Health and Human Development. An earlier \$4.5 million grant awarded to Dr. Panigrahi provided funds to build the field sites, clinical trial setup, labs and data management infrastructures at two sites in India. Funding also was provided by the Bill & Melinda Gates Foundation.

Children's Hospital of Philadelphia to Lead New Pediatric Data Resource Center for Research in Childhood Cancer and Structural Birth Defects

Funds from the Gabriella Miller Kids First Pediatric Research Program will establish a "first-in-kind" data discovery and sharing platform to support collaborative pediatric research

Newswise – The Center for Data Driven Discovery in Biomedicine at Children's Hospital of Philadelphia (CHOP) will lead a new, collaborative effort funded by the National Institutes of Health Common Fund to discover the causes of pediatric cancer and structural birth defects through the use of big data. The Center will be known as the "Kids First Pediatric Data Resource Center" (DRC).

Investigators at CHOP, in partnership with the Ontario Institute for Cancer Research, the University of Chicago, Children's National Health System, the Oregon Health and Science University and Seven Bridges, will create a centralized, cloud-based database and discovery portal of well-curated clinical and genetic sequence data from dozens of childhood cancer and structural birth defects cohorts, comprising thousands of patients and their families. Partner organizations will provide expertise in the following areas:

- The Ontario Institute for Cancer Research will support the innovative design and development of the Kids First Data Resource Portal (DRP) and associated web-based analytic tools for Kids First's disease-specific data sets.

Pediatric Cardiac Intensivist

The Congenital Heart Collaborative (TCHC), an affiliation between University Hospitals Rainbow Babies & Children's Hospital (Cleveland OH) and Nationwide Children's Hospital (Columbus OH) heart programs, seeks candidates at the Assistant or Associate Professor rank for a faculty position in the Division of Pediatric Critical Care at UH Rainbow Babies & Children's Hospital in the role of Pediatric Cardiac Intensivist. Candidates should have dual training in Pediatric Critical Care and Cardiology, or Pediatric Critical Care with an additional year of Pediatric Cardiac Critical Care training. The successful candidate will be expected to perform at the highest level, with dedicated clinical service and night call in the Pediatric CTICU. The candidate will also have opportunities to participate in quality improvement initiatives, clinical research, and education of medical students, residents, and fellows.

The successful candidate will be well-supported at a world-class children's hospital with over 60 years of experience in the care of pediatric and adult congenital heart disease patients; an outstanding educational and research enterprise at Case Western Reserve University School of Medicine and an internationally recognized program partner with the Nationwide Children's Hospital Heart Center. TCHC is a dedicated service line with a common executive administration and functions as one program on two campuses with the commitment to expand access to high-quality comprehensive cardiac care regardless of patient age to the communities we serve while equally embracing a scholarly and educational mission. TCHC provide excellent cardiothoracic surgical, cardiac interventional, electrophysiologic, and non-invasive services. The candidate would be immediately accountable to the Pediatric Critical Care Division Chief and to TCHC senior leadership.

Please send letter of interest and curriculum vitae to:

Alexandre Rotta, MD, FCCM

Division Chief of Pediatric Critical Care

UH Rainbow Babies & Children's Hospital,

Alex.Rotta@uhhospitals.org

*Equal Opportunity Employer – minorities/females/
veterans/individuals with disabilities/sexual orientation/
gender identity.*

**The Congenital
Heart Collaborative**

University Hospitals
Rainbow Babies & Children's
Nationwide Children's Hospital



Archiving Working Group
International Society for Nomenclature of
Paediatric and Congenital Heart Disease
ipccc-awg.net

- University of Chicago will partner in the management and optimization of large-scale, genomic data processing for the Kids First initiative. They will also support the data coordination efforts by establishing cloud-based, open-source software needed for the operations of the Data Coordination Center within Kids First.
- Children's National Health System will support project-specific efforts for the Administrative and Outreach Core within Kids First, and will also coordinate additional foundation and consortia-based partnerships for the generation of new, large-scale pediatric cancer and birth defects data.
- Oregon Health and Science University will provide resources and new technologies to the Data Coordination Center to support community standards and frameworks for reproducible genomic analysis. They also will provide a deep knowledge of cross-disease analysis, especially in cancer.
- Seven Bridges will further develop the scalable, cloud-based data analysis platform using the infrastructure the company co-developed and deployed CAVATICA platform with CHOP. This platform will help researchers collaboratively analyze genomic data sets and provide access to Kids First data to the entire scientific community.
- "Scientists are beginning to recognize the developmental biology connections between structural birth defects and pediatric cancers, and building on that shared understanding, we can now leverage new technologies, cloud computing, and sophisticated algorithms for collaborative discovery to develop improved, less toxic therapies," said Adam Resnick, PhD, Director of the Center for Data Driven Discovery in Biomedicine (D3b) at Children's Hospital of Philadelphia.
- The Kids First Data Resource Center will allow researchers to instantly search large genomic datasets using new data visualization tools and cloud-based data-sharing platforms. Researchers will be able to identify genetic pathways that underlie and may possibly link childhood cancer and structural birth defects, such as congenital heart defects, hearing loss and cleft palate. Additionally, the DRC will develop new analytical tools to provide the research community with access to this large-scale data for use in the discovery of novel and improved treatments for children diagnosed with cancer or structural birth defects.
- A lack of available resources and access to large-scale pediatric disease data limits the ability of research scientists to uncover new clues for biological discoveries of childhood cancer and structural birth defects, slowing the development of new diagnostics, less toxic treatments, or cures. The Kids First Data Resource Center will provide for non-siloed and integrative access to both genomic and clinical data across cancer and birth defects, a first in the pediatric research community.

The National Institutes of Health Common Fund's Gabriella Miller Kids First Pediatric Research Program recently announced the award to establish the DRC. Contingent on available funds, the award is expected to provide funding for five years of up to a total of approximately \$14.8 million. Within the NIH, the Kids First program is primarily led by four Institutes and Centers (ICs) – the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Cancer Institute (NCI), the National Human Genome Research Institute (NHGRI) and the National Heart, Lung and Blood Institute (NHLBI), in partnership with the Office of the NIH Director and with additional involvement of several other key NIH Institutes and Centers.

"NICHD is committed to supporting research on birth defects as part of its overall focus on improving the health of children," said Dr. Diana



We Treat Kids Better



USC University of Southern California

Chief for its Division of Cardiology and Co-Executive Director of The Heart Institute

Children's Hospital Los Angeles (CHLA), in partnership with University of Southern California (USC) and the Keck School of Medicine of USC (KSOM), seeks to recruit a Chief for its Division of Cardiology and Co-Executive Director of The Heart Institute. We seek a visionary leader to further develop a successful clinical, research and academic program that serves a large and diverse patient population in our world-class children's hospital. The Division Chief provides leadership for the Division, overseeing clinical care delivery and quality, budget and financial performance, strategic planning, recruitment and program development, and ensuring the integration of training and research programs with clinical services throughout the hospital. The Chief will also lead the Division's support of the departmental academic goals in research, education and faculty recruitment and development and join the Department of Pediatrics Leadership team.

The successful candidate will have strong academic, clinical, and leadership/management experience in either a research-oriented children's hospital or an academic pediatric department affiliated with a university medical school, with a minimum of 10 years of progressive medical and research experience and an increasing scope of responsibility including faculty and trainee mentoring and program development. The candidate will have a track record of scholarly accomplishment, ideally with extramural funding.

The candidate must have an MD, DO or MD/PhD degree, must have completed at least three years of post-doctoral or clinical fellowship training, and must be board-certified by the American Board of Pediatrics and board-certified in Pediatric Cardiology. The candidate should have clinical as well as research experience in a pediatric setting and qualify for appointment as Associate Professor or Full Professor at KSOM.

To apply, please direct inquiries, nominations, and applications, including resume and a letter of interest, in confidence to:

Children's Hospital Los Angeles
Attn: Valerie Campana, Director of Faculty Affairs and Development
4650 Sunset Blvd., M/S #71
Los Angeles, California 90027
Vcampana@chla.usc.edu

Electronic submission is encouraged.

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Bianchi, Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. "The Kids First initiative provides a unique opportunity to use DNA sequencing information to gain a better understanding of the underlying causes of birth defects and childhood cancers."

Analyzing data from different disease types is crucial to the biological understanding and precision treatment of pediatric diseases, as studies suggest that children born with birth defects are at a higher risk of developing childhood cancer, currently the leading cause of disease-related death in children.

"For clinicians, structural birth defects and cancer have been some of the most challenging areas of Pediatric Medicine. For the first time, clinicians and researchers, along with academic, government and commercial partners, are coming together to fully harness the power of emergent technologies, shared data, and precision medicine. This collaboration will lead to improved outcomes for every child across all of these diseases," said N. Scott Adzick, MD, Surgeon-in-Chief of Children's Hospital of Philadelphia and Director of the Center for Fetal Diagnosis and Treatment at CHOP.

Approximately 6,000 patient samples will be ready for analysis at the inception of the Kids First project, growing to more than 25,000 by 2018, making it the largest pediatric data cohort of its kind.

In addition to the development of the Kids First Data Resource Center, CHOP investigators will also contribute to the generation of large-scale data from associated Kid's First Program sequencing efforts across pediatric cancer and structural birth defects, including data from neuroblastoma samples collected by CHOP oncologist Dr. John Maris through the Children's Oncology Group and structural birth defect and cancer samples collected by Dr. Hakon Hakonarson of the Center for Applied Genomics at CHOP.

The Kids First DRC will also integrate data from consortia-based efforts including the Children's Brain Tumor Tissue Consortium (CBTTC) and the Pacific Pediatric Neuro-Oncology Consortium PNOC), which will contribute data collected from more than 2,000 children with brain tumors.

"It is only through an authentic partnership with patients and families and the integration of efforts across disciplines, from surgery to oncology to genetics, within and across institutions, that these efforts are made possible," noted Phillip (Jay) Storm, MD, Chief of the Division of Neurosurgery at Children's Hospital of Philadelphia. "The Kids First DRC will continue to work closely with partnered foundations, disease-specific consortia and other partners in support of patients and their families."

The "Kids First Act" was established in April 2014, less than six months after 10-year-old Gabriella Miller, an advocate for childhood cancer research, died from an inoperable brain tumor. Her efforts to raise awareness of childhood cancer raised hundreds of thousands of dollars for children's cancer charities and launched Smashing Walnuts, a foundation dedicated to childhood brain cancer research. As a result of these advocacy efforts, Congress passed the Gabriella Miller Kids First Research Act to direct funding into the NIH Common Fund over a 10-year period in support of pediatric research.

For more information about Children's Hospital of Philadelphia, visit www.chop.edu



PEDIATRIC INTERVENTIONAL CARDIOLOGIST FACULTY POSITION

The Division of Pediatric Cardiology at the University of Utah School of Medicine and based at Primary Children's Hospital is recruiting a BE/BC Pediatric Cardiologist with subspecialty training in Interventional Cardiology, providing focused care to patients with congenital heart disease needing cardiac catheterization for diagnosis and management. The interventional cardiologist will join a division of 29 faculty and a team of 2 pediatric interventional cardiologists, a dedicated nurse practitioner, and experienced cath lab personnel, while working in a growing, nationally ranked Heart Center. The division has a flourishing catheterization program (640 cases last year) and coordinates care with cardiothoracic surgery, cardiac intensive care, and cardiac anesthesia. In addition, the division's thriving programs in fellowship training and research will provide the candidate with tremendous opportunities for teaching and participation in basic, translational, and/or clinical research (our program is one of the core participating centers in the Pediatric Heart Network funded by the NIH).

The successful candidate will receive a faculty appointment in the Department of Pediatrics on the Clinical or Tenure track at the academic level commensurate with experience and qualifications. The University of Utah offers an excellent benefits package, including 20.2% retirement contributions that vest immediately and excellent health care choices. The Department also offers an education loan repayment program. The local area provides an exceptional quality of life with immense cultural and recreational opportunities.

To read more about this opportunity and apply, please visit:

- **Pediatric Interventional Cardiologist:**
<http://utah.peopleadmin.com/postings/69669>

For additional information, please contact Lloyd Tani, M.D., Division Chief, at Lloyd.Tani@hsc.utah.edu.

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Cardiology and Professor of Radiological Science and Medicine
University of California at Irvine
19 Mistral Lane
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Penn Researchers Closer to Uncovering a New Feature in Heart Failure

Newsweek — Each cell in the average human body contains 23 pairs of chromosomes, with four telomeres on each pair. Telomeres cover the end of the chromosome, protecting it from deterioration or fusion with adjacent chromosomes, much like the plastic tip at the end of a shoelace protects it from unraveling. While there is a length range for classifying a healthy telomere, researchers found, for the first time ever, that people with heart failure have shorter telomeres within the cells that make up the heart muscle (known as cardiomyocytes).

A team of researchers from Penn Medicine, in collaboration with the University of Connecticut, published their findings recently in the *Journal of the American Heart Association*, building on a methods paper which was published recently in *Nature Protocols*. The team is the first to have developed a method for measuring the length of telomeres using human heart tissues.

"Once we had established the method for measuring the telomeres in heart cells, which was tricky because human cardiac cells are rarely taken from a living person, we acquired heart tissue samples from patients receiving heart transplants and organ donors in order to evaluate telomere length," said the study's lead researcher, Foteini Mourkioti, PhD, an Assistant Professor of Orthopaedic Surgery and Cell and Developmental Biology, and Co-Director of the Musculoskeletal Regeneration Program in the Penn Institute for Regenerative Medicine. "Using samples from the Penn Heart Tissue Biobank meant we were also able to acquire patient data for the samples, so we knew useful information like the patient's age, sex, and heart function."

Researchers were able to measure the telomeres in the samples of patients who had heart disease and those who did not, and group the findings into categories based on patients' age. They found that in the samples for healthy people, age did not play a role in telomere length, since the telomeres of both young and old healthy individuals were not affected. However, patients with heart failure had shorter telomeres regardless of their age. In comparing diseased and healthy samples, researchers were able to draw a correlation between shorter telomeres and the presence of heart failure. Patients with the shortest telomeres in their cardiac cells also had the most severely decreased cardiac function. The team also found that the cardiomyocytes were the only heart cells affected by the telomere length in disease samples, but the telomere length of other cells within the same diseased heart samples were not different.

"This human tissue research is critical, as it may open the door for future telomere-preserving therapies to help protect heart failure patients" said co-author Kenneth B. Margulies, MD, a Professor of Medicine and Research Director for Heart Failure and Transplantation. "While there is a need to better understand how heart disease induces telomere shortening, this is an important step in the research process, one that brings us closer to a better understanding of heart failure."

Leaning on this human data to inform basic science studies, Mourkioti and her team are now working to pinpoint pathways



Boston Children's Hospital
Until every child is well™

Division of Cardiac Imaging Faculty Position Available

The Division of Cardiac Imaging, Department of Cardiology at Boston Children's Hospital is actively recruiting a faculty physician to join our world-renowned cardiac imaging team. Candidates must be Board Certified or Eligible in Pediatric Cardiology. Candidates at all career stages who possess strong clinical, research, and teaching abilities are encouraged to apply. Valued clinical skills include echocardiography, cardiac magnetic resonance, and computed tomography. Faculty will be eligible for appointment at Harvard Medical School.

The Division of Cardiac Imaging at Boston Children's Hospital is one of the largest imaging programs for children and adults with congenital heart disease in the United States. Its activities include transthoracic echocardiography, transesophageal echocardiography, fetal echocardiography, cardiac magnetic resonance, and cardiac computed tomography. A high proportion of cases have complex disease and undergo image-guided interventions. Equipment includes state-of-the-art imaging, reviewing, and reporting technology. Resources for conducting clinical, basic science, and translational research are abundant throughout the Department. Academic advancement through research and teaching activities is strongly encouraged and supported. We have a highly-regarded senior fellowship program in cardiac imaging and train 2-3 senior fellows each year.

Interested candidates should forward their CV to:

Andrew J. Powell, M.D.
Chief, Division of Cardiac Imaging
Department of Cardiology
Boston Children's Hospital
300 Longwood Avenue
Boston, MA 02115

Email: andrew.powell@cardio.chboston.org

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that specifically target cardiomyocytes, in order to track the disease progression, and identify areas for therapeutic interventions that can later be tested in in-human clinical trials. "The important thing is that we now have a new lead to follow and test how cardiac-specific telomere interventions can improve heart function," Mourkioti said.

Additional Penn authors on the studies mentioned in this release include: Maryam Sharifi-Sanjani, Nicholas M. Oyster, Elisia D. Tichy, and Kenneth C. Bedi. These studies were funded by start-up funds and a Pilot and Feasibility Grant from National Institutes of Health (P30 AR069619) and procurement of human heart tissues were enabled by grants from the National Institutes of Health (HL089847 and HL105993).

Penn Medicine is one of the world's leading academic medical centers, dedicated to the related missions of medical education, biomedical research, and excellence in patient care. Penn Medicine consists of the Raymond and Ruth Perelman School of Medicine at the University of Pennsylvania (founded in 1765 as the nation's first medical school) and the University of Pennsylvania Health System, which together form a \$6.7 billion enterprise.

The Perelman School of Medicine has been ranked among the top five medical schools in the United States for the past 20 years, according to *U.S. News & World Report's* survey of research-oriented medical schools. The School is consistently among the nation's top recipients of funding from the National Institutes of Health, with \$392 million awarded in the 2016 fiscal year.

The University of Pennsylvania Health System's patient care facilities include: The Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center -- which are recognized as one of the nation's top "Honor Roll" hospitals by *U.S. News & World Report* -- Chester County Hospital; Lancaster General Health; Penn Wissahickon Hospice; and Pennsylvania Hospital. Additional affiliated inpatient care facilities and services throughout the Philadelphia region include Good Shepherd Penn Partners, a partnership between Good Shepherd Rehabilitation Network and Penn Medicine.



Congenital Cardiac Intensivist

The Heart Center (THC) at Nationwide Children's Hospital, the primary pediatric teaching facility for The Ohio State University in Columbus Ohio, is recruiting an attending physician, at any academic level, for the Cardiothoracic Intensive Care Unit (CTICU). This individual would join a group of seven multi-background academic cardiac intensivists and eight dedicated nurse practitioners devoted to the CTICU providing 24/7 in house coverage.

Our current independently-managed free-standing CTICU is a 20 bed unit with approximately 800 total admissions per year (medical and surgical) and an average daily census of 12. Candidates must have completed fellowship training in pediatric cardiac anesthesia, critical care and/or cardiology that includes advanced cardiac intensive care training. Preference will be given to those with experience and are boarded in pediatric cardiology.

THC embraces a culture of patient safety and quality, transparency, translational/outcome research, education, cost-containment and public health awareness. These create ample participation and leadership opportunities for the candidate's professional growth. THC is comprehensive with services including an active hybrid palliation center, a comprehensive single ventricle program, thoracic organ transplantation program, blood conservation strategies, and cardiac mechanical support team. The CTICU is supported by world-class and innovative interventional cardiology, cardiac imaging, cardiothoracic surgery and adult congenital heart experts. Current annual clinical metrics for THC includes: over 500 cardiothoracic surgeries, over 700 cardiac catheterizations and EP procedures, and over 13,000 cardiology outpatient visits. We have a pediatric and pediatric/adult combined cardiology fellowship programs. We participate in numerous multicenter clinical trials and quality initiatives including the JCCHD QI Collaborative. We are directly linked to our Center for Cardiovascular and Pulmonary Research which has an NIH T-32 training grant.

Interested candidates are encouraged to submit their curriculum vitae to:

Janet Simsic, MD
Director of the Cardiothoracic Intensive Care Unit,
Nationwide Children's Hospital, T2296
700 Children's Drive
Columbus, OH 43205
or janet.simsic@nationwidechildrens.org

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The ACHA website offers resources for ACHD professionals as well as for patients and family members.

Explore our website to discover what ACHA can offer you.

www.achaheart.org/home/professional-membership-account.aspx



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Pediatric Cardiology Division Chief

The Department of Pediatrics at The Ohio State University and The Heart Center at Nationwide Children's Hospital is seeking a Division Chief of Pediatric Cardiology. The Chief will oversee all missions of the Division including accountability for clinical excellence and timely access to care, strategic growth, quality improvement, education, and original, innovative research. Applicants for this position must be highly motivated with a distinguished academic record, reputation as an effective and motivated leader, and ability to mentor. A track record of proven leadership experience and skill in career development, research, operations, communication, conflict resolution, time management, and ability to work with departmental and hospital personnel is necessary. The Chief must support the diversity and equity values of our organization. Academic rank will be at the associate or full professor level.

The Chief will be directly accountable to the Department Chair and the Chief Medical Officer at Nationwide Children's Hospital. The chief will work closely with the Co-Directors of The Heart Center at Nationwide Children's Hospital to develop and execute the strategic plan for the center. The Chief will partner with the Director of the Center for Cardiovascular Research to advance the Heart Center's research strategic plan which includes basic laboratory science, clinical and translational components. The Section Chief of Pediatric Cardiology, along with medical directors of each of the cardiology sub-specialties (outpatient, in-patient services, cardiothoracic intensive care, adult congenital heart, catheterization and intervention, transplant/heart failure, non-invasive imaging), will report directly to the Division Chief. The Division Chief will work closely with the Vice President of The Heart Center on personnel, budgetary, operational issues. The Division Chief will be expected to work closely with nursing administration within The Heart Center.

The Division of Pediatric Cardiology has 33 outstanding pediatric cardiologists with categorical and subspecialty cardiology fellows in adult congenital heart disease, advanced imaging, heart failure/transplantation, and interventional catheterization. The division has an NIH T-32 training grant with The Ohio State University along with various masters training opportunities. The Heart Center performs approximately 500 cardiac surgical cases, 700 catheterization/interventional cases, and 15,000 outpatient encounters per year. The world-class surgical and medical teams work closely to develop innovative hybrid approaches to patient care, and we are committed to caring for the patient with congenital heart disease from fetus through adulthood. Some of our highlighted programs include a hybrid approach to congenital heart disease, our regional partnerships, seamless transition to our COACH (ACHD) program, comprehensive single ventricle care team, and cardiogenetics research. We have a 20 bed dedicated cardiothoracic intensive care, 24 bed stepdown unit, two state of the art hybrid catheterization laboratories, and two hybrid operating rooms along with an extensive off-campus network of regional outpatient care sites.

Nationwide Children's Hospital is a perennial USNWR Honor Roll hospital. It employs a medical staff of over 1,100 and more than 11,000 employees, providing state-of-the-art pediatric care for 1.2 million patient visits annually. Nationwide Children's Hospital has 68 facilities extending out across Ohio and beyond. In addition, the Research Institute at Nationwide Children's is one of the top NIH-funded freestanding pediatric research facilities in the United States. Columbus, the Ohio state capital and the 15th largest city in the United States, is a thriving, diverse, technologically sophisticated city with a population of 1,800,000. Quality of life is exceptional and cost of living is affordable.

Please submit nominations to:

John Barnard, MD, Department Chair,
700 Children's Drive, T6D A6421
Columbus OH 43205
or john.barnard@nationwidechildrens.org

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