Innovations in Pediatric Heart Care

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"Innovative care, outstanding outcomes".

It is estimated that 1 percent of infants are born with heart problems. Not all of these infants will require immediate care or surgery, but for those that do, it is lifesaving.

Fortunately for families in the Midwest and beyond, one of the top pediatric heart programs in the country is right here in Kansas City. The Ward Family Heart Center at Children's Mercy has been named one of the best pediatric cardiology and heart surgery programs in the nation by U.S. News and World Report.

With an emphasis on clinical innovation and patient-centered care, The Ward Family Heart Center is advancing pediatric medicine across the globe.

The Ward Family Heart Center is one of the higher volume programs in the country. Each year, the center performs more than 450 cardiac surgical procedures, provides more than 11,000 outpatient visits and performs catheterization and electrophysiology procedures on nearly 700 patients. With that high level of patient activity comes a level of expertise dealing with the common to the complex that cannot be found at many other centers.

Working in state-of-the-art hybrid catheterization suites and operating rooms, the center is able to treat an increasing number of children more safely and less invasively, avoiding open heart procedures and the need for heart-lung bypass.

The Fetal Cardiac Program, offered in conjunction with the Elizabeth J. Ferrell Fetal Health Center, brings potentially lifesaving care to families from the moment of fetal diagnosis, through delivery and beyond.

This advanced level of care is supported by resources that can only be found at a comprehensive pediatric hospital committed to delivering outstanding outcomes through evidence-based medicine, innovative solutions and a family-centered approach to care.

"Melody valve helps some patients avoid surgery."

Children Mercy is now part of an elite group of hospitals nationally to offer the Melody transcatheter pulmonary valve therapy for use in pediatric and adult patients with a regurgitant or stenotic Right Ventricular Outflow Tract (RVOT) conduit.

"The Melody valve allows us to replace a heart valve through a catheter instead of open heart surgery," says Stephen Kaine, MD, director of the Cardiovascular Laboratory at Children’s Mercy, Associate Director, The Ward Family Heart Center and an Associate Professor of Pediatrics at the University of Missouri-Kansas City School of Medicine.

The procedure can also be used to replace the valve as the patient grows.

"Instead of always needing additional surgeries to replace the human valves over time, we can use a stent on which a valve has been placed," says Dr. Kaine. "Without doing open heart surgery, we can put the stent in position and inflate it to place a functioning valve where it’s needed."

This can delay the need for invasive surgery for many years and in some cases, eliminate the need for it altogether. In addition, instead of having to be hospitalized for five to seven days, those who have treatment with the Melody valve go home the next day.

"Like other replacement valves, the Melody will eventually wear out," says Dr. Kaine. "What’s been found is that a second Melody valve can be placed if needed. It is not as though the valve can be used only once and then you have to go back to surgical interventions."

The use of the Melody valve is a collaborative project between Children’s Mercy and the University of Kansas Medical Center.
Thus, the need to identify a more efficient, cost-effective solution for heart valve replacement in children continues to be at the forefront for cardiovascular surgery researchers at Children’s Mercy Hospitals and Clinics in Kansas City, Mo.

“Our central goal is to create a viable personal heart valve suitable for surgical implantation, tissue engineered in a clinically realistic time frame using allogeneic valve scaffolds seeded with patient derived cells that must be capable of growth and adaptation following replacement of congenitally malformed or absent valves,” says Richard A. Hopkins, MD, the Thomas Holder/Keith Ashcraft Endowed Chair in Pediatric Surgery Research, Director of the Cardiac Regenerative Surgery Research Laboratories at Children’s Mercy and a Professor of Surgery at University of Missouri-Kansas City School of Medicine.

“Our success will fundamentally impact surgical therapeutics and essentially initiate a new era of regenerative congenital cardiac surgery for children,” adds Dr. Hopkins.

Once fully developed and approved, a living, growth-capable valve will eliminate the need for multiple reoperations, as is currently required for available valve prosthetics.

“As we move toward the development of the clinical version of the tissue engineered heart valve, we will continue to seek regulatory guidance from the FDA based on the data generated from our preclinical safety and performance studies,” adds Stephen Hilbert, MD, PhD, Deputy Director of the Cardiac Regenerative Surgery Research Laboratories.

The groundbreaking project is just one of several of its kind in development at the Cardiac Regenerative Surgery Research Laboratories (CRSRL) of The Ward Family Heart Center at Children’s Mercy.

The CRSRL is dedicated to the translation of fundamental scientific research into therapeutic strategies for the treatment of congenital and structural cardiac disorders.

Striving to improve the care of patients with congenital cardiac disease through innovative translational research, the CRSRL fosters focused research and the development of collaborations by leveraging expertise in the fields of cardiac surgery, cardiology, cardiac anesthesiology, cardiac imaging, bioengineering, tissue engineering, cell biology, developmental biology, molecular biology, cardiovascular pathology, biotechnology and regenerative medicine.

The team – which works out of the academic and discovery laboratory at Children’s Mercy and through multiple collaborations with university partners in the Kansas City area as well as with a full-time Good Laboratory Practices (GLP) compliant testing facility located in Maryland – also is working on projects that include a range of cell, tissue, polymer, drug eluting and gene engineered constructs for surgical and catheter based cardiovascular repairs.

“Combining excellence in clinical surgery with translational research and development generates unique research projects and collaborations,” says Dr. Hopkins. “As evidenced by our published work during the past two years, we are adding to the body of knowledge regarding tissue engineering that goes well beyond heart valves. Our work in the CRSRL is leading to multicenter cutting edge clinical trials, and a leadership role in defining regulatory criteria that, ultimately, gives us the potential to vastly improve the lives of children.”
UNRAVELING THE GENETICS OF CONGENITAL HEART DISEASE

As we learn more about the human genome, our understanding of cardiac disease processes and treatment continues to change. Partnering with our internationally known Division of Clinical Pharmacology and Therapeutic Innovation, the hospital’s unique Center for Genomic Medicine, and a robust Clinical Genetics program, Children’s Mercy physicians and researchers are helping to advance the understanding of genetic causes of cardiovascular disease and how to utilize that knowledge to better treat patients.

Rapid Diagnosis of Disease

Researchers at the Children’s Mercy Center for Genomic Medicine made international headlines recently with a breakthrough that provides rapid (50 hours versus weeks) whole genome sequencing for the diagnosis of genetic diseases. Already this technique has helped identify a novel, recessive gene for viscero-arterial heterotaxy. Such techniques have the potential to revolutionize our diagnostic capabilities in a manner previously unmatched for speed and precision.

“By shortening the time-to-diagnosis, we may markedly reduce the number of other tests performed and reduce delays to a diagnosis,” says Stephen Kingsmore, MB, ChB, DSc, FRCPath, Director of the Center for Pediatric Genomic Medicine at Children’s Mercy. “Reaching an accurate diagnosis quickly can help to shorten hospitalization and reduce costs and stress for families.”

Improving Treatment Effectiveness

Dyslipidemia is a major health concern not only for patients at Children’s Mercy, but for the whole country. Statins, the most common class of drugs used to treat dyslipidemia in children and adults, hasn’t really been tested in the developing child.

Jon Wagner, DO, a fellow in Cardiology and Clinical Pharmacology, and Steve Leeder, PharmD, PhD, Division Director of Clinical Pharmacology and Innovative Therapeutics, are looking at the liver specific protein transporter, OATP1B1, which is the major transporter of statins from the blood to the liver (statins’ site of action), to better understand how children’s bodies distribute statins in the body.

Currently, biospecimens are being collected to perform a genetic analysis specifically for SLC01B1, the gene that encodes the OATP1B1 transporter, and other transporters involved with statin disposition. The overall goal is to establish the role of not only genetic variation, but also age and development on the dose-exposure-response relationship for statins in children.

“Children undergo a lot of developmental changes, or ontogeny, and we know with development, a lot of these drug transporters, drug metabolizing enzymes, do change either through gain of function or loss of function.

“That’s why this is of the utmost importance to look at,” says Dr. Wagner.

Cardiac Genetics

The Children’s Mercy Cardiovascular Genetics Clinic, staffed by cardiologists, geneticists and genetic counselors, provides a coordinated, integrated approach for the diagnosis, care and genetic counseling for syndromic and inheritable systemic disorders, which typically include significant cardiovascular manifestations. The clinic makes use of available gene testing to aid in the patient evaluation and counseling, and is also working with other researchers to develop additional testing methods.

“Over the last 20 years there has been a tremendous amount of information...
uncovered about the genetic causes of disorders, such as DiGeorge, Williams, Noonan and Marfan syndromes. The next big area for the future expansion of pediatric clinical cardiovascular genetics will be the translation of the basic science investigations into the genetic causes of structural congenital heart disease,” says Robert Ardinger, MD, Cardiovascular Genetics Clinic Director.

Dr. Ardinger, along with James O’Brien, MD, Co-Director of The Ward Family Heart Center at Children’s Mercy, developed a DNA repository for all children receiving cardiovascular procedures at the hospital. Dr. O’Brien has used the repository in his ongoing investigation into the genetics of tetralogy of Fallot. Some of his work was recently published in the journal Cardiovascular Genetics.

“My hope is that we can use our general cardiology patients, the patients we see in the Cardiovascular Genetics Clinic, our DNA repository and our clinical genetics laboratories, along with the genomic tools Dr. Kingsmore is developing, to try to elucidate some of the causative gene mutations behind congenital structural heart disease,” says Dr. Ardinger.

Is there a causal effects between small nucleolar RNA (snoRNA) expression and conotruncal heart defects?

James E. O’Brien Jr., MD, FACS, Co-Director of the Ward Family Heart Center and Associate Professor of Surgery, University of Missouri-Kansas City School of Medicine, and Douglas Bittel, PhD, Associate Professor in the Section of Genetics Research, are collaborating with Naoya Kenmochi, PhD, Frontier Science Research Center, University of Miyazaki, Japan, who is using a zebrafish model to alter snoRNAs.

“When you target those snoRNAs in zebrafish, they also get heart defects,” Dr. Bittel says. “That is the very first step in demonstrating that alterations in snoRNA levels may contribute to heart defects.”

Misregulation of snoRNAs and its culpability in other disorders, including cancer and inflammation, is an area of growing interest among researchers, and Drs. O’Brien and Bittel posit that there are more hidden links to be discovered among this class of ncRNAs.

Dr. O’Brien adds, “After looking at the genetic expression, we may be able to identify subgroups that would benefit from different therapeutic interventions and more directed therapies.”
TAKING THE LEAD IN 3D ECHOCARDIOGRAPHY

The live, 3D echo laboratory is the latest addition to the neonatal intensive care unit at Children’s Mercy, and Dr. Shirali, who is also the Melva and Randall L. O’Donnell Chair in Cardiology, Co-Director of The Ward Family Heart Center and a Professor of Pediatrics at the University of Missouri-Kansas City School of Medicine, is working on making this state-of-the-art technology standard in everyday clinical operations.

Clinicians use the advanced imaging to explore the heart inside its outer wall, and from multiple viewpoints, while gathering data unobtainable with conventional 2D echo.

Children’s Mercy is investing in the future with its installation of the Phillips live 3D scanner, and Dr. Shirali is personally involved in the technology, having helped develop its pediatric matrix transducer – the only one of its kind in current use and specifically sized to the small body mass of the pediatric patient.

Two-dimensional imaging is excellent for small, intricate structures, such as the coronary arteries, but for studying the morphology of the heart, and its overall specific function, 3D echo is superior, according to Dr. Shirali.

Three-dimensional echo helps determine the shape and volume of intricate cardiac structures, such as the right ventricle, and it helps clinicians analyze valvular structure and function. It also allows for multiple viewpoints as well as interaction with the digital scan.

“It basically changes the viewing perspective from having a standardized position and image with a customized interpretation, to one that makes sense from the surgeon’s perspective,” explains Dr. Shirali. “We are able to rotate these images and cut away the walls of the subject so we can do virtual dissections of the heart.”

The ability to examine the structures of the heart from different perspectives is key in pre-surgical examination, especially in those cases involving valvular disorders and atrial and ventricular septal defects. The 3D echo lab is also critical in post-surgical assessment in the ICU.

Analysis of complex structures such as the right ventricle, and the validation of advanced measurements are part of the ongoing work at the 3D echo lab at Children’s Mercy. Three-dimensional echocardiography produces images that more closely correlate to real life, and Dr. Shirali intends to push the technology in new directions.

“Some of the things we are trying to measure in 3D are things we never tried to measure before with 2D technology,” adds Dr. Shirali.
Early in 2012, the Cardiovascular Laboratory at Children’s Mercy entered the IMproving Pediatric and Adult Congenital Treatment (IMPACT) Registry, joining about 70 other hospitals, clinics and medical centers throughout the United States to measure outcomes and guide quality improvement initiatives that should lead to better clinical results.

“This is unique in the field of pediatric cardiology because there haven’t been many large, multicenter registries designed to improve quality,” says Stephen Kaine, MD, director of the Cardiovascular Laboratory at Children’s Mercy, Associate Director, The Ward Family Heart Center and an Associate Professor of Pediatrics at the University of Missouri-Kansas City School of Medicine. “We submit information from our procedures and are then provided information on how we are doing in comparison to other centers over time. The feedback from IMPACT is used to enhance our quality improvement processes.”

Less than two quarters of registry data are currently available, but the results have been positive so far.

“Our first summary shows that our catheter lab performance, as measured by both complication rate and quality of interventions, is equal to or better when compared to our colleagues throughout the nation,” explains Dr. Kaine.

IMPACT is sponsored by the participating institutions and the American College of Cardiology Foundation; thus, there is a stable funding source and an independent third party that provides oversight of the data registry.

“Having access to large populations has long been a problem in congenital cardiology,” Dr. Kaine says. “With 70 centers accumulating information, we can make meaningful inferences more quickly to identify appropriate treatment decisions and improve outcomes for our patients.”

Dr. Stephen Kaine and Dr. Jonathan Wagner
When a 20-week ultrasound revealed her son Bryce had hypoplastic left heart syndrome, Jamie Bolen’s thoughts of planning a nursery were overshadowed by thoughts about possibly planning a funeral.

“We walked out of the hospital in a daze,” Jamie says. “It was one of the worst days of my life.”

Immediately after birth, Bryce was transported to Children’s Mercy Hospital where he underwent his first open-heart surgery. By the time Bryce was in kindergarten, he’d braved three major surgeries to reconstruct his heart, as well as numerous other procedures and hospital visits, including a difficult six months treating fluid build-up around his heart.

Now in second grade, Bryce is very active and enjoys playing baseball, flag football and even riding dirt bikes.

Bryce’s biggest hurdles are now behind him, but there will be challenges in the future. He continues to have regular visits to the Cardiology Clinic at Children’s Mercy.

“I would absolutely recommend Children’s Mercy,” Jamie says. “It is a great place with wonderful nursing care and amazing, talented doctors.”

Scan the QR code to view the video of Bryce’s story or visit www.childrensmercy.org/heart.