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DEPARTMENTS

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IN UTERO CATHETER INTERVENTION FOR CONGENITAL HEART DISEASE

By Audrey C. Marshall, MD and Wayne A. Tworetzky, MD

Advances in diagnostic imaging and surgical technique have allowed most congenital heart disease to be anatomically repaired, even in infancy. However, until recently, the possibility of prevention of congenital heart disease seemed remote. Widespread use of sonographic obstetrical screening, in combination with improved acquisition and interpretation of fetal echocardiograms, now allows us to diagnose many cardiac anomalies by midgestation, and also to observe their prenatal progression. Not unexpectedly, the capacity for early diagnosis has generated considerable interest in prenatal therapeutic intervention.

Several fundamental principles underlie the field of fetal intervention. The fetal diagnosis must be certain, and there must be an understanding of how the disease will evolve through the remainder of gestation. The resultant condition at birth must be associated with significant mortality or morbidity. Finally, a procedure must be available that can correct the initial lesion and thereby improve the outcome at birth; this procedure must offer sufficient benefit to the child to justify the risk to both mother and fetus.

Hypoplastic left heart syndrome (HLHS), though rare, remains the congenital cardiac defect associated with the most deaths in the first year of life. Characterized by a left ventricle (LV) inadequate to support the systemic circulation, the syndrome may result from one of a number of primary left heart lesions. Included among this list of causative primary lesions is valvar aortic stenosis (AS). In fact, fetal echocardiographic observation has demonstrated that AS associated with LV dysfunction, when diagnosed in the second trimester, progresses to HLHS[1]. Thus, critical AS diagnosed in the mid-trimester fetus presents an ideal target lesion for prenatal intervention.

The mechanisms through which AS begets HLHS are poorly understood. It is hypothesized that increased LV afterload and decreased coronary perfusion lead to LV myocardial damage. Initially, this LV injury is manifest as LV dilation and systolic dysfunction. With impaired LV filling, pulmonary venous return is diverted at the atrial level. The resultant decrease in left heart flow leads to growth arrest, and ultimately, hypoplasia. Consistent with this hypothesis, the echocardiographic hallmarks of critical AS of the fetus include:

1. primary AS as evidenced by thickened valve tissue and a narrowed antegrade flow jet,
2. severe LV dysfunction,
3. echogenicity of the LV myocardium,
4. left to right flow at the atrial septum, and,
5. retrograde flow in the ascending aorta (Figure 1).

Authors had described a percutaneous fetal aortic valvuloplasty procedure as early as 1991[2]. Although the work of several groups had resulted in a total of 12 procedures reported through the year 2000, the experience yielded limited technical success and a high rate of fetal mortality[3]. The procedure did, however appear to be technically feasible. With the benefits of improved imaging, instruments, and intraoperative obstetrical management, we believed the procedure could be performed more safely and with better technical results.

In March 2000, we began to offer fetal aortic valvuloplasty to mothers of fetuses with critical AS at less than 26 weeks gestation, as part of an innovative therapy protocol at the Children's Hospital, Boston, and the Brigham and Women's Hospital. Candidates were required to meet all of the echocardiographic criteria described above, with at least 3 experienced fetal echocardiographers attributing a high likelihood of progression to HLHS. Furthermore, the LV had to be deemed "salvageable", that is, without significant hypoplasia (length within 2 S.D. of normal for gestational age) at the time of diagnosis.

Between March 2000 and March 2004, twenty mothers elected to undergo the procedure. All

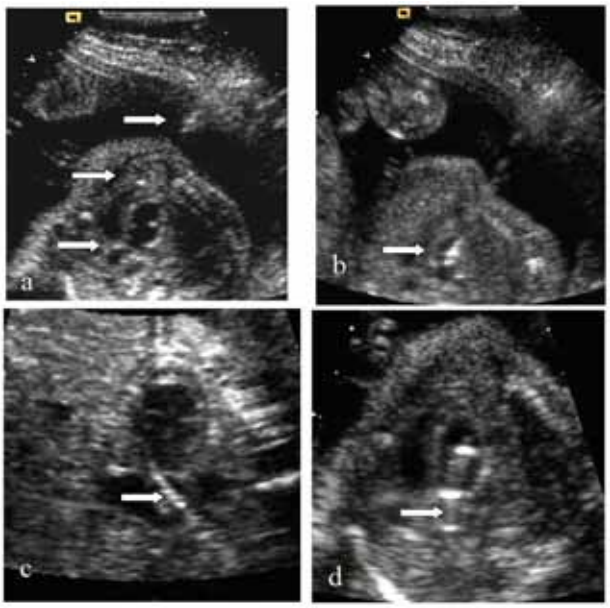

Figure 1. Transabdominal ultrasound imaging of fetal aortic valve dilation. A) The introducer cannula is seen advancing through the myometrium and into the amniotic cavity (first arrow) toward the fetal chest wall (second arrow), with the aortic valve in view (third arrow). B) The needle is advanced into the LV cavity until the tip is in the subaortic region. C) The wire is advanced through the valve and into the ascending aorta. D) The balloon is advanced over the wire and inflated while straddling the valve.

gave informed consent for the procedure after meeting with pediatric cardiologists, fetal surgeons, perinatologists, and anesthesiologists. The aortic valvuloplasty was performed successfully in 14 cases, giving a technical success rate of 70%.

The procedure is performed with the mother under general anesthesia. In many cases, the procedure can be performed percutaneously. When transabdominal fetal positioning fails, a limited laparotomy is performed. Not only does the laparotomy afford greater access for fetal manipulation, but it also allows higher resolution imaging directly on the uterine surface.

Once ideal fetal position is established, the fetus is given intramuscular anesthetic and muscle relaxant. A 19 G needle introduced into the maternal abdomen is guided under ultrasound through the fetal chest wall and into the LV cavity. Once inside the LV, the needle is used as an introducer for a standard PTCA catheter over a wire. The balloon diameter is intended to be ~120% the diameter of the valve annulus. The wire is used to probe for the aortic valve orifice. Once the wire has crossed the valve, the balloon is advanced, and the balloon is inflated straddling the valve (Figure 2). All of the equipment is then withdrawn.

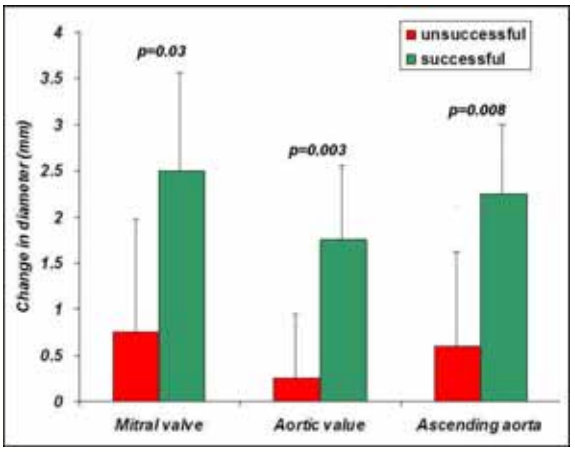

Figure 2. This graph depicts the change in dimension of left heart structures (mitral and aortic valves and ascending aorta) in fetuses that had a technically successful in-utero aortic valvuloplasty compared to those with an unsuccessful procedure and those that declined the procedure. Only fetuses with pregnancies carried to near term delivery (>33 weeks gestation) were included. The data reflects the first and last measurements made during gestation.

Using this technique, we have not observed maternal complications related either to anesthesia or to the catheterization procedure. A variety of fetal complications have occurred; the most common complications being bradycardia and small pericardial effusions. The fetal bradycardia responds to either intramuscular or intracardiac epinephrine. Effusions often resolve spontaneously, but can also be drained at the conclusion of the procedure. Although we have not seen fetal demise intraoperatively, 3 fetuses were found to have expired within 72 hours of the procedure.

Of 14 fetuses who underwent successful aortic valve dilation between 21 and 29 weeks gestation, 3 were born with 2 ventricle circulations. The remainder of the liveborn fetuses who underwent either successful or unsuccessful aortic valvuloplasty procedures had a diagnosis of HLHS at birth. Although only 3 fetuses did not require a Stage I palliation, technically successful fetal aortic valve dilation was associated with significant growth of left heart structures including the mitral valve, aortic valve, and ascending aorta (Figure 3)[4].

The lack of maternal complications and the possible prevention of HLHS in 3 fetuses have encouraged us to cautiously pursue this intervention. We are in the process of developing a protocol to investigate more closely the impact of successful aortic valve dilation on the growth of left heart structures in utero.

While critical AS is currently the most common diagnosis referred for fetal cardiac intervention, indications will likely expand as additional procedures become available and practiced. One additional disease that has been proposed as a target for fetal therapy is pulmonary atresia with intact ventricular septum. Perforation and dilation of the pulmonary valve can be performed using a technique similar to that used for aortic valve procedures. The difficulty in offering intervention to this group of fetuses lies

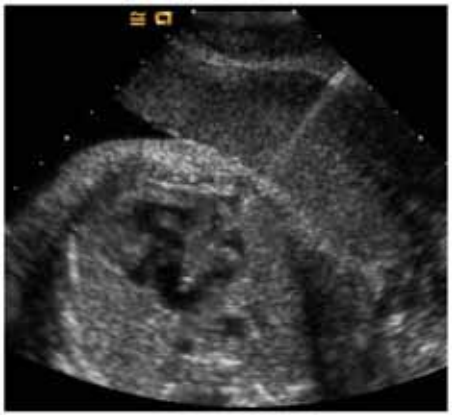

Figure 3. Transabdominal ultrasound imaging of a fetus during puncture through atrial septum. The needle traverses the maternal abdominal wall, the uterine myometrium, the fetal chest wall, and the free wall of the right atrium. Here, the tip of the needle distorts the intact atrial septum, driving it leftward, prior to needle entry into the left atrium.

in the clinical spectrum of the disease, and our inability to predict the postnatal morbidity based on prenatal appearance. Although it seems likely that pulmonary atresia can be treated prenatally, we first need to be able to identify those fetuses who would have the poorest postnatal outcomes, and would therefore have the most to gain from fetal intervention.

In fact, the emergence of a second indication for fetal intervention has, in our center, been driven primarily by the identification of a uniquely high risk set of neonates. Infants born with HLHS and an intact atrial septum have a failing circulation until left atrial (LA) decompression can be achieved. These infants as have markedly elevated mortality rates, compared to others with HLHS. We hypothesized that a prenatal procedure to create an atrial septal defect would aid in postnatal stabilization and thereby improve neonatal outcomes. By decompressing the LA in utero, one might attenuate secondary tissue/organ damage occurring in the lung, and might favorably impact longer term survival.

We have performed 7 of these procedures; 6 of 7 have been technically successful. As with the aortic valve procedure, we have not experienced any maternal complications. Furthermore, we have been able to access the atrial septum in all cases without the use of a laparotomy. Due to the technique and equipment used, the newly created atrial defects are small, but appear to persist through gestation[5]. Although we have not yet demonstrated clinical effect, we expect that the introduction of equipment and techniques dedicated to this procedure will improve our ability to make large defects in the atrial septum, and will ultimately lead to clinical benefit.

Fetal cardiology is emerging as one of the most rapidly growing fields in our specialty. The potential for echocardiographic diagnosis in utero has already favorably impacted care of children with congenital heart disease. A therapeutic arm has been added to the field with regard to management of fetal arrhythmias. Now we are developing the means of modifying structural disease in utero. It is our hope that with the continuing collaborative efforts of fetal imagers, obstetricians, fetal surgeons, and interventionalists, we can add prevention to the management of some forms of congenital heart disease.

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NEW IMAGE ARCHIVING SYSTEM MAKES GOOD BUSINESS SENSE FOR COLUMBUS CHILDREN'S HOSPITAL

By Dave Melvin, Manager, Information Services and John P. Cheatham, MD

Columbus Children's Hospital is a 112-year-old pediatric healthcare network that annually provides more than 575,000 patients with a multitude of services. Long known as a high-quality community hospital in Central Ohio, the hospital aspires to become a nationally-known academic medical center and is in the middle of expansion of facilities and services that will help achieve its goal. The $145 million expansion has resulted in a children's research institute, a pediatric education institute, and the growth of its outpatient care center.

Figure 1. Columbus Children's Hospital Heart Center Cath Lab

Building a World-Class Pediatric Cardiology Center

Developments in the cardiology department have also been part of the hospital's growth spurt. When the hospital board and administrators decided to develop a national presence, part of the plan was to expand the cardiology department into a dedicated, world-class heart center that could provide advanced care to a greater number of patients. Columbus Children's Hospital improved its heart program by recruiting a highly-regarded team of cardiologists and researchers, centralized its cardiology facilities, and is in the process of adding additional space for the Heart Center.

One of the most significant improvements in the pediatric cardiology department has been the upgrade of imaging technology. In May, the Heart Center added two cardiac catheterization labs that contain state-of-the-art imaging equipment for both diagnostic and interventional procedures. Physician recruitment, new facilities, and the new cardiac cath labs have helped the Heart Center attract new patients and increase its workload.

"When the hospital ... decided to develop a national presence, part of the plan was to expand the cardiology department into a dedicated, world-class heart center that could provide advanced care to a greater number of patients."

For example, the number of cardiac patients served by Children's Hospital has increased nearly 150 percent since 2001. The number and type of cath procedures has increased as well. Before 2001, the department annually performed around 200 cath procedures and only about 33 percent of them were interventional. Now the Heart Center performs nearly 500 cath procedures a year, and approximately 75 percent of them are interventional.

Image Archiving Technology Critical to Expansion

The increase in quantity and difficulty of cardiology procedures could not have occurred without a change in patient image and data archiving technology. Columbus Children's Hospital realized that a state-of-the-art image archive is imperative for an organization that wants to grow its cardiology department.

The hospital's legacy system was adequate for a community hospital that performed a small number of interventional procedures, but not robust enough to meet the hospital's aggressive growth targets. They only could store between ten and twelve cases on a disk; once the disk was filled, the studies had to be archived to tape and deleted from the disk. If the case was needed again, the correct tape had to be identified, located and the study had to be loaded back into the disk before it could be viewed.

The need for a new cardiology image archive increased with the growing workload at the new Heart Center. In 2002, the department exceeded its online storage capacity of ten cases in about two weeks. By 2003, online storage capacity was surpassed after only about two days. However, as workload increased, online storage capacity was surpassed after only about two days. In addition, Heart Center staff knew that the installation of the two new cath labs would completely overload the legacy system, and that they needed to upgrade their imaging archive for higher performance, more flexibility, and greater expandability.

Heartlab Encompass: Image Archiving as a Business Advantage

About a year before the new cath labs opened, the Heart Center installed a new archiving system – Encompass from Heartlab, Inc. Very quickly, Encompass proved its ability to meet the needs of a growing institution with national aspirations. As expected, image and information storage is now virtually unlimited – thousands of cases can be stored online. As a result, patients at Columbus Children's Hospital have seen a positive difference in the quality of care.

Figure 2. HeartLab Workstation

The new image and information archiving system has provided much more than increased storage, better workflow, and improved patient care. Administrators and clinicians at the Heart Center quickly discovered that one of the Heartlab system's greatest strengths is that it provides the Heart Center with a business advantage enabling it to achieve its goal of building its reputation beyond central Ohio. The Heart Center's administrative and medical staff found that having a better imaging archive provided multiple business-related benefits:

- *Competitive advantage.* Cardiology patients, potential patients, and referring physicians perceive that institutions with state-of-the-art technology provide better service than those without. A demonstrated commitment to innovation helps an organization maintain, and even increase, market share.
- *Marketing tool*. Improved technology, such as state-of-the-art image archiving systems like Encompass, is a powerful marketing tool. A new archiving system, along with other new imaging equipment, gain attention in community and national marketing promotions such as mailings, brochures, or news articles. Open house events featuring the new system provide effective regional outreach.
- *Increased referrals*. A critical attribute of the Heartlab system is the ability to provide access to the image archive from any Internet-connected computer – with image quality that is on par with a diagnostic workstation. Any referring physician with an Internet-enabled PC can be given secure access to cases in the Children's Heart Center database. Remote access increases referrals because it provides referring physicians with the immediate ability to review cases.
- *New business opportunities*. Remote access can be expanded beyond traditional phy-

sician referrals to create a multitude of new business opportunities. For example, the Children's Heart Center offers consultations from its pediatric cardiologists to hospitals that are as much as 150 miles away, by providing them with easy-to-use software and a secure Internet connection to the Heart Center's image archive. Thus, smaller institutions with limited technology and staffing resources can offer their patients the benefits of a larger institution. Because the service is not limited by physical distance, the Heart Center can expand this service to other hospitals as its reputation grows.

- *Recruitment tool*. Top pediatric cardiologists are well-versed in technology and understand the positive relationship between technology, workflow, and their own work-life balance. Recruiting the best doctors is easier when a hospital can publicize the benefits provided by an easily-accessible, flexible, high-performance, scalable image and information archiving system.

These benefits make good business sense, but they also enable the Heart Center to provide better care for children throughout the region and support the Heart Center's goal of achieving a national presence.

Conclusion

When Columbus Children's Hospital made the decision to increase patient volume and enhance patient care in their cardiology department, its staff and administrators knew that improvements in imaging technology would help transform its Heart Center into a world-class diagnostic and treatment facility. It required an image archiving system that could keep up with an increased workload and more complicated interventional studies.

Figure 3. Columbus Children's Hospital

"The Columbus Children's Hospital expects its investment in cutting-edge image and information archiving technology to enable its Heart Center to become one of the top-rated pediatric cardiology facilities in the nation."

As expected, the image archiving system it chose, Heartlab's Encompass, dramatically enhanced image storage capability, departmental workflow, and patient care. It also provided a number of business advantages that are helping the Heart Center reach its business growth goals. The Columbus Children's Hospital expects its investment in cutting-edge image and information archiving technology to enable its Heart Center to become one of the top-rated pediatric cardiology facilities in the nation.

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MEDICAL NEWS

Mending a Broken Heart . . . With Stem Cells

A $6 million, five-year grant from the Parisian Foundation Leduq has set up a transatlantic effort to study ways to help damaged hearts repair themselves, using stem cells from bone marrow, bloodstream, and adult heart tissue.


Dr. Michael Schneider.

Dr. Michael Schneider, professor of medicine at Baylor College of Medicine, is the U.S. coordinator of the program, which will involve European and American scientists and physicians in Frankfurt, Rome, and Houston. Schneider and Dr. Robert Schwartz, co-directors of BCM's Center for Cardiovascular Development, both are members of the research effort, dubbed the "Transatlantic Network of Excellence for Cardiac Regeneration." The research will start with determining the source of these stem cells for the heart early in life. It will progress to engineering the cells to enhance their ability to repair damaged heart muscle, and then to study the effects of such optimized cells in patients with heart disease.

"This is a bench to bedside effort that demonstrates translational medical research at its best," said Schneider. "The opportunity to work closely with European colleagues in the field, including those most expert anywhere in human trials of stem cells for the heart, will help us solve this challenging problem faster."


Dr. Robert Schwartz.

Schneider and Schwartz have long been interested in applying knowledge of how the heart is normally made to generating new heart muscle cells for diseased or damaged hearts. Schneider discovered a rare and unexpected population of adult heart-forming cells, and Schwartz studies the way in which genes that create the heart are first turned on and function. They are founders of Kardia Therapeutics, a start-up company for novel treatments of heart failure created through BCM Technologies, the incubator for commercialization of discoveries by Baylor College of Medicine faculty.

Coordinating the European efforts will be Dr. Stefanie Dimmeler, Director of Molecular Cardiology at the J. W. Goethe-University in Frankfurt, Germany. Other members of the network are her collaborator Dr. Andreas Zeiher at the same institution, stem cell biologist Dr. Giulio Cossu of the Stem Cell Research Institute San Raffaele in Milan, Italy and mouse geneticist Nadia Rosenthal, head of the European Molecular Biology Laboratory at Monterotondo, Italy.

http://www.bcm.edu/ and http://www.embl.org/

February Conference Focus:

Eighth Annual Update on Pediatric Cardiovascular Diseases

Sponsored by the Cardiac Center at the Children's Hospital of Philadelphia

The Eighth Annual Update on Pediatric Cardiovascular Diseases will be held February 16-20, 2005 at the Disney Beach and Yacht Club Resort, in Lake Buena Vista, FL. The meeting will mix plenary sessions aimed at a multidisciplinary audience with breakout sessions for in depth review of imaging, interventional catheterization, electrophysiology, cardiovascular nursing, heart failure and transplantation, intensive care and pediatric perfusion.

* Dr. Roberto Canessa - a pediatric cardiologist from Montevideo, Uruguay - will give an inspiring talk on Team Building and Group Dynamics in Crisis Situations. Dr. Canessa was a member of his national rugby team that crashed in the Andes in 1972. Dr. Canessa will give the true story behind the movie ALIVE! with direct application to Pediatric Cardiovascular Teams.

* There will be a special networking/career planning session for medical students, residents and fellows interested in a career in pediatric cardiovascular care.

* Once again, abstracts will be accepted for presentation of original research in competition for the 2nd Annual Outstanding Investigator award.

* Special sessions will be held on Patient Safety and Reducing Error in Cardiovascular Care (with special CME contact hours), Cardiac ECMO, Pulmonary Atresia and Challenges Facing Survivors of Surgery for Complex CHD. For the first time, an audience response system will be in place for interactive sessions.

* Hands-on Sessions will take place in 3D Echo, Temporary Pacing at the Bedside, and Advanced Pacemaker Programming.

* The 6th Annual C. Walton Lillehei Lecture will be given by Dr. Ed Bove (Ann Arbor); the 4th Annual William J. Rashind Lecture will be given by Dr. Norman Silverman (Stanford). The Featured Nursing Lecturer is Elisabeth C. Smith, R.G.N., R.S.C.N., M.Sc. from Great Ormond Street, London, England

* Flights to Orlando are considerably less expensive if booked now compared to December or January. In addition, there is a 5-15% discount if booked on USAir and referring to GoldFile 87183183.

The faculty includes over 65 professionals from 25 heart centers in the USA, UK, Canada and South America, representing specialists in imaging (14), intensive care and heart failure (14), cardiothoracic surgery (11), cardiovascular nursing (9), cardiac catheterization (5), pediatric perfusion (5) and electrophysiology (4).

For more information: www.chop.edu/cardiology2005

OutFoxed! New Research May Redefine Late-Stage Cardiac Development

A team of University of Pennsylvania School of Medicine researchers, led by Edward E. Morrisey, PhD, Associate Professor of Medicine, have been investigating how the heart develops from its earliest stages of development to its late stages, with the hope of learning why some hearts don't develop correctly. Dr. Morrisey's latest finding, published in the September 10th issue of Science, may redefine current models of how the heart develops in mammals. "Understanding the earliest steps in heart development gives us insight into the possible genetic causes of the dramatic heart defects exhibited by so many newborn babies, " says Morrisey.

During normal embryonic development in mammals, pre-cardiac cells form the bilateral cardiac primordia - two symmetrical, tube-shaped regions located on both sides of the early embryo. As cardiac development progresses, these two regions fuse, forming one large tube which, in turn, further develops into the four-chamber heart.

Using genetically engineered mice, Penn researchers successfully inactivated the Foxp4 binding protein, which resulted in the inability of the bilateral tubes to fuse. They found that each region of pre-cardiac cells still developed into a single tube, and then further developed into a four-chamber heart. This resulted in the mouse embryos developing two, four-chambered hearts exhibiting most aspects of advanced heart development. Eventually these embryos succumbed due to the lack of correct blood flow with two hearts pumping into the same set of blood vessels.

Foxp4 belongs to a class of DNA binding proteins called transcription factors that turn other genes on and off. Interestingly, Foxp4 is not expressed in heart muscle cells themselves but rather in the primitive gut tube, which will develop into the stomach and intestines. In the early mammalian embryo, the gut tube helps direct the fusion of the two tubes of pre-cardiac cells into one tube. Dr. Morrisey thinks that expression of Foxp4 in the gut tube may be responsible for this lack of fusion: "Other mutations in genes expressed in the gut tube have led to similar results in simpler organisms such as zebrafish. What is remarkable about Foxp4 mutant mice is that their hearts develop to such a late stage. We have never been able to determine in mammals whether fusion of the bilateral heart tubes was required for later stages of development including formation of all four-heart chambers. Now we know it's not necessary."

Another aspect of the work that is remarkable is that both of the hearts that form in Foxp4 mutant embryos show the same ability to distinguish left and right "sidedness". Many organs in the mammalian body have distinct left and right sides such as the heart and lung. In Foxp4 mutant embryos, both hearts show the correct "sidedness" regardless of whether they were on the right or left side of the embryo.

The researchers suggest this work may be crucial in determining what gene mutations might lead to congenital cardiovascular de-

fects. Cardiac development is conserved in mammals so defects in early cardiovascular development may lead to malformations in the human heart.

Other Penn researchers contributing to this study are Shanru Li, Deying Zhou and Min-Min Lu. This study was funded by grants from The NIH (National Institutes of Health) and the AHA (American Heart Association).

Parental Willingness to Have Children Participate in Clinical Trials Depends on Many Different Factors

When asked directly, only one in four U.S. adults (25%) would consider allowing their children to participate in clinical research studies. However, many factors can increase the willingness to participate, possibly at a higher rate than this. The most powerful reasons for participation would be the hope that the drug would cure their children (75%) or that their children had a terminal illness (73%).

These are some of the results of a Harris Interactive® poll of 5,822 U.S. adults conducted online between May 10th and 17th, 2004 for the Wall Street Journal Online's Health Industry Edition.

Additional factors that would greatly increase the likelihood of allowing their children to participate in clinical trials include: if there were no risks involved (72%), if their children's current treatment options were no longer effective (70%), and if participating would benefit their children or someone else's children (69%).

The likelihood of allowing participation also increases greatly if their children were to be diagnosed with a serious or potentially terminal illness. Yet another factor that would increase the likelihood of parents allowing their children to participate in clinical trials is the probability that their children would not receive a placebo. Of those who would consider having their children participate in a study, 80% would be likely to allow participation if there was a zero percent chance of receiving a placebo. As the chance of receiving a placebo increases, the likelihood of allowing participation decreases (15% chance = 74% likelihood, 50% chance = 62% likelihood).

"Only a quarter of all adults say they would consider allowing their children to participate in clinical research studies, says Humphrey Taylor, chairman of The Harris Poll®. However, this survey shows that there are many factors which can greatly increase or decrease participation rates. The most powerful arguments (when valid) can be made for trials that may provide very sick children with better treatment than they would be likely to receive otherwise, particularly for a potentially terminal illness."

Downloadable PDFs of Wall Street Journal Online/Harris Interactive Health-Care Polls are posted at:

http://www.harrisinteractive.com/news/newsletters_wsj.asp

Highlights from the PICS-VIII & ENTICHS-II (Pediatric Interventional Cardiovascular Symposium & Emerging New Technologies In Congenital Heart Surgery): Addendum to the November Issue

Dr. John P. Cheatham and Ms. Sharon Hill, his nurse practitioner, performed live cases on Monday, September 20th, 2004:

- Newborn with PA/IVS - performed RF perforation of atretic pulmonary valve using Nykenan RF catheter and BMC generator followed by balloon valvuloplasty.
- Twenty-three month old with severe long segment thoracic coarctation of the aorta, s/p balloon angioplasty with residual coarctation. Performed balloon angioplasty using new large diameter Cutting Balloon (first time in U.S.)
- Fourteen month old with Type A PDA - used 7x6 medium Nit-Occlud (still under FDA sponsored clinical trials).

Next year's symposium will take place in Buenos Aires, Argentina, immediately preceding the World Congress of Pediatric Cardiology and Cardiac Surgery from Sept. 15-18, 2005.

Live cases for now are scheduled to be performed from Columbus Children's Hospital where Drs. John P. Cheatham, Mark Galantowicz and Sharon Hill and their team will be performing live cases on Friday Sept 16th, 2005. Also live cases will be transmitted from Mexico City with Dr. Carlos Zabal, Sao Paolo with Dr. Carlos Pedra and Cesar Esteves, Santiago with Dr. Felipe Heusser, from Omaha Children's Hospital with Dr. Zahid Amin, Texas Children's with Dr. Ron Grifka and Miami Children's with Drs. Evan Zahn and David Nykanen and of course from two hospitals in Buenos Aires with Drs. Horacio Faella and Miguel Granja. We are also looking at other sites that want to be involved with PICS.

It is promised to be an unforgettable meeting with its educational content and of course the social events in a beautiful city. Ms. Colene Diodati and Ms. Sally Cook from M2 Meeting are busy arranging the social events and they always proved to us, it will be superb Gala night. We have signed an agreement with the organizers of the World Congress to have reduced registrations fees for those attending both PICS and World Congress. For registration, visit the PICS website at: www.picsymposium.com

So, we hope to see you all there and do not miss the opportunity.

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