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THE HELEX SEPTAL OCCLUDER - A UNIQUE ASD/PFO CLOSURE DEVICE

By Larry A. Latson, MD

Atrial septal defect (ASD) closure using a transcatheter device instead of open heart surgery has become the standard of care in most large pediatric cardiology centers around the world. Although the first successful percutaneous ASD closure was described in 1974, the precursors of today's ASD occlusion devices were first used in a significant number of patients in the late 1980's. Design ideas proliferated and, over the last 15 years, a number of different device designs and methods for device delivery have been developed. Some remain in widespread use today, and we have learned important lessons from these and other devices that did not achieve longstanding success. An ideal ASD occlusion device would render all ASD's clinically irrelevant in the safest possible way for both the short and the long term. Experience has now shown, however, that patients and ASD's are highly variable, and it is therefore, valuable to have different types of devices available. It has also become clear that physicians are not perfect in device selection and placement, so the ideal devices will have recovery features built in.

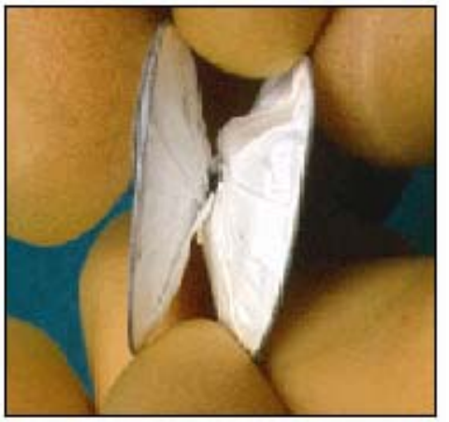

Figure 1. The Helex Septal Occluder is a double disk device designed to be deployed with one disk on the left side of the septum and the other on the right. It is formed by a nitinol frame draped with ultrathin ePTFE membrane.

A relative newcomer to the transcatheter ASD occlusion device armamentarium is the Helex Septal Occluder. This is a unique device that consists essentially of an expanded polytetrafluoroethylene (ePTFE) draped wire that forms a double disk shape when fully configured. (1)(Figure 1) For delivery, the Helex can be elongated into the spiral shape suggested by its' name – a helix – and then further elongated into a nearly straight single wire. (Figures 2A, 2B) To accomplish this transformation the wire frame and ePTFE are threaded onto a central shaft called the mandrel. The proximal end of the device can be pulled back over the mandrel until the frame is nearly straight for delivery through a 9 French delivery catheter (equivalent to a 7 French delivery sheath). The "shape memory" of the nitinol frame results in the device forming the desired double disk configuration when the frame is advanced, in a stepwise manner, to the tip of the mandrel.

It takes a little practice to get used to the delivery technique for the Helex device since it does not simply spring open as it is pushed out the end of the delivery catheter. (2) First, the device is loaded by alternately advancing the mandrel slightly, and then pulling the elongated portion of the frame into the catheter. The catheter is soft and pliable even with the Helex loaded (since the frame has been elongated into a relatively straight single wire) and can be maneuvered directly across the ASD without the need of a previously placed transseptal sheath (though a transseptal sheath can be used if desired). The distal disk is deployed in the left atrium by repeatedly advancing the frame and mandrel together for a short distance and then pulling the mandrel back to near the tip of the delivery catheter. When the distal disk is completely formed, the entire system is withdrawn until this left atrial disk is against the septum. (Figure 3A) At this point, the delivery catheter is withdrawn to the IVC-RA junction and the right atrial disk is formed by simply advancing the wire

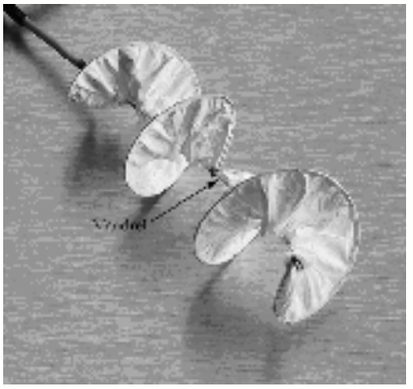

Figure 2A. The helical shape of the device frame when it is partially deployed is seen in this photo. The frame and ePTFE membrane are threaded onto a mandrel for delivery of the device.

frame on the mandrel (Figure 3B). One of the attractive features of the Helex is that, if the device appears to be improperly positioned or is the incorrect size, it can easily be non-destructively withdrawn back into the catheter and repositioned or removed until it is released from the mandrel. When the Helex is in good position, the mandrel is further withdrawn until it "pops off" of the frame. This maneuver uncovers the locking loop that helps keep the device stable in its final configuration. As an added safety feature of the Helex, a thread or safety cord remains looped through the right atrial eyelet during the lock release. (Figure 4) As with other devices, there is often some change in the exact configuration and positioning of the device when the mandrel (or release cable of other devices) is freed. If there are any concerns about the adequacy or positioning of the Helex after lock release, the safety thread can be used to remove the entire device (though destructively) back out through the delivery catheter. This safety thread is a feature that enhances confidence when contemplating the risks of a potentially difficult or risky procedure. When all is well, the safety thread is easily pulled through the right atrial eyelet to completely free the device.

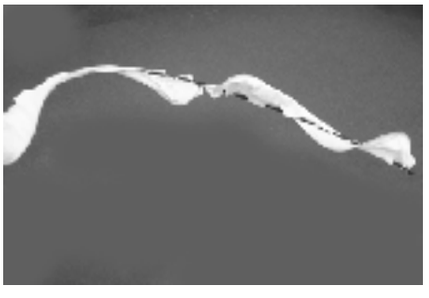

Figure 2B. Further elongation of the device frame on the mandrel results in a nearly linear device that can be readily pulled into the delivery catheter.

The Helex device has been available in Europe for approximately four years and has been implanted in over 1,000 patients outside of the United States. Trials of the device in the United States began with a feasibility trial at the Cleveland Clinic Foundation and Miami Children's Hospital in 2000. After encouraging early results in the initial 57 patients, the trial was expanded to a multi-center pivotal trial including 14 centers in 2001. That trial completed enrollment in 2003, and collection of the one-year follow-up information is ongoing at this time. Final data on these trials is not anticipated to be available until late 2004, but some preliminary data obtained in a recent interim review directly from the implanting centers is encouraging. It must be stressed that this data has not been confirmed by completed audits of the Data Safety and Monitoring Board or the independent echocardiographic core lab which will be the final judges for data to be presented to the FDA. A total of 183 patients underwent attempted implantation of the Helex Septal Occluder in the Feasibility and Pivotal Trials. The device was successfully implanted in 161 (88%) of these attempts. Some of the 22 failures to

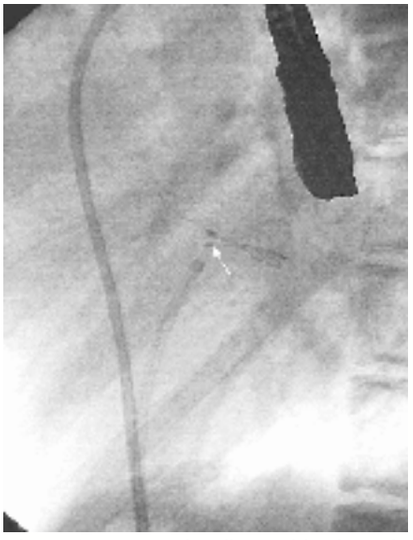

Figure 3A. Lateral radiographic view of the Helex Septal Occluder after the left atrial disk has been deployed and pulled lightly against the atrial septum. The white arrow points to the middle of the three eyelets of the device.

implant were due to lack of availability of the larger size devices early in the trials, uncertainty as to the correct device size (since this was a new device), and the learning curve as new investigators were added. There was only one major adverse event deemed to be related to the procedure and that event was a retroperitoneal hematoma apparently due to an intracardiac echo probe inserted in the femoral vein opposite the Helex insertion site. Although entry criteria allowed attempted device placement in ASD's as large as 22 mm, it appears that the Helex will probably not be the device of choice for most large ASD's (those exceeding 20mm stretch diameter).

Potentially serious complications after device implantation have been few. Four devices embolized after the patient left the catheterization laboratory. These patients had minimal or no signs or symptoms. It was determined in the

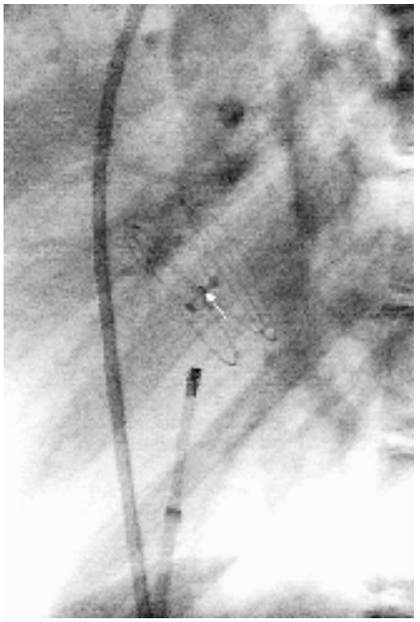

Figure 3B. The device has been fully deployed and released from the mandrel.

initial animal testing that the Helex device is very flexible and can be re-elongated into a relatively straight wire during retrieval with a snare or grasping catheter. In each of the four human cases, it was possible to remove the embolized device in a subsequent catheterization procedure and no patient required surgical removal. In one case the device was not removed until 6 months after implantation when the early embolization was first noticed. Two devices were electively removed surgically in follow-up. One patient had new onset eczema and there was concern that this could be an allergic reaction (however, the skin condition did not resolve with device removal). Another device was apparently inappropriately large and was poorly configured enough that it was felt removal should be undertaken with surgical closure of the ASD at the same procedure. No attempt was made to remove the device in the catheterization lab, since it was not felt that any other device was more suitable. There have been no deaths or adverse events more serious than those mentioned above in the patients enrolled in these studies. Importantly, this is the only one of the major devices in use around the world today that has not had any instances of late erosion of the device into the aorta or pericardial space. The Helex device has been used in patients with widely varying anatomic features including absent rims, aneurysms, and multi-fenestrations. (3,4)

The effectiveness of the Helex Septal Occluder in eliminating the need for surgical ASD closure has been very good. Because the device does not have a strong "clamping" action, it is not surprising that at least a small leak is seen immediately after implant in approximately 50% of ASD patients. The expected biological reaction to the device often results in a decrease or elimination of small residual leaks over the first 6-12 months. (5) The preliminary data indicates that clinically significant residual leaks will be rare in patients with successfully implanted devices. At the last available follow-up of the patients enrolled in these trials with a device still in place, the implanting centers have detected residual leaks that they feel may be hemodynamically significant in fewer than 2% of the subjects.

"Trials of the device in the United States began with a feasibility trial at the Cleveland Clinic Foundation and Miami Children's Hospital in 2000."

The Helex Septal Occluder is not currently being tested for closure of patent foramen ovale (PFO) in the United States. In other countries however, PFO closure in patients who have suffered a presumed embolic stroke is a major indication for use of the device. Apparent reductions in recurrent stroke rates have been evident (in uncontrolled trials) compared to historical rates in medically treated patients in several trials with different devices. In these trials, the Helex device has consistently been among the devices that seem to have the lowest rate of asymptomatic thrombus accumulation or recurrent stroke. (6,7,8)

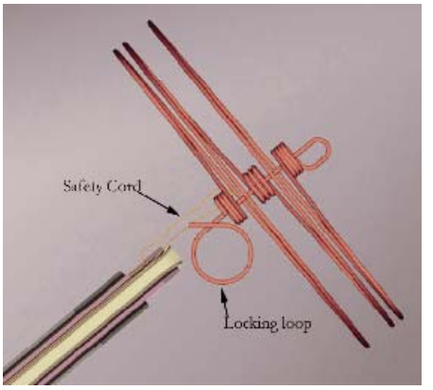

Figure 4. Illustration of the frame of the device after it has been released from the mandrel. The locking loop holds the three central eyelets of the device together. The safety thread is still looped through the right atrial eyelet so the device could be removed at this point with the delivery system if necessary.

An Expanded Access trial of the Helex Septal Occluder is currently underway and allows for continued implantation of a slightly modified Helex device at investigational sites in the U.S. Two changes to the device have been made for the Expanded Access Trial. The first is a change in the processing of the ePTFE that makes the device much less echo reflective than the original device. A major technical issue with the original device (used in the trials mentioned above) was the extreme

echo reflectivity of the ePTFE material. Once the left atrial disk was deployed, it was usually very difficult to visualize the right atrial disk by trans-esophageal echocardiography (TEE) because of "shadowing" or inability of the ultrasound to penetrate the material of the left disk. The entire device is much more easily seen by either TEE or intracardiac echo with the newer version.

"Final data collection for the U.S. trials of the safety and efficacy of the device compared to a surgical cohort is underway."

The other alteration in the device was a change in the direction of the locking loop. With the original model, it was not uncommon for the transient torsion on the device caused by lock release to result in an unfavorable change in position or conformation of the device. In some cases, the change was enough to result in the need to remove the device and replace it. With the newer Helex device, this effect has been greatly reduced. Overall, the newer device is subjectively easier to use with the two modifications and an analysis will be done to be certain that the changes do not adversely affect any of the other characteristics.

In summary, the Helex Septal Occluder is a unique new transcatheter closure device with several worthwhile characteristics. It is composed of materials that are intuitively favorable for an intravascular prosthesis. It is round and very flexible compared to most other devices, and appears to have a lower chance of causing late erosions into the aorta or pericardium. It does not work well for large ASD's, but does work well for small to moderate sized ASD's, even with deficient rims, aneurysms, or multi-fenestrations. The inherent safety features of the Helex make it attractive for use in small children in whom most other devices may be difficult or impossible to remove if misplacement or embolization should occur. Final data collection for the U.S. trials of the safety and efficacy of the device compared to a surgical cohort is underway. A newer model of the device with changes that improve visualization and final positioning of the device is currently available at the investigational sites enrolled in the Expanded Access Trial. If final data analysis (anticipated late this year) justifies FDA approval, the Helex Septal Occluder will be a worthwhile addition to our armamentarium of transcatheter closure devices.

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Caution: Currently the Helex Septal Occluder is limited by United States law to investigational use.

For comments to this article, send email to: MARLL@PediatricCardiologyToday.com

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THE FIELD OF PEDIATRIC CARDIOLOGY LOSES ONE OF ITS PIONEERS

Dr. Samuel Kaplan, a pioneer in congenital heart disease research and emeritus professor of pediatrics at the David Geffen School of Medicine at UCLA, died of cancer on January 21, 2004 at UCLA Medical Center in Los Angeles. He was 81 years old.

Kaplan graduated from the University of Witswatersrand School of Medicine in

Dr. Samuel Kaplan

Johannesburg, South Africa, in 1944 and completed his residency training before being awarded a scholarship to continue his postgraduate training in cardiology at Hammersmith Hospital in London in 1949.

He moved to the United States in 1950 to join the cardiology department at Cincinnati Children's Hospital, where he began his pioneering studies in congenital heart disease. As Chief of the Division of Pediatric Cardiology, he was among the first in the world to establish the specialty and is considered among the founders of this discipline. Kaplan made many experimental contributions to the field; his laboratory studies were instrumental in developing the membrane oxygenator that is still an essential part of the surgical procedure for open-heart surgery on both children and adults.

At the time of his retirement from his position in Cincinnati in 1987, he was widely recognized as among the top five most constructive and productive academic cardiology leaders in the United States. In 1998, in recognition of his outstanding service, the University of Cincinnati established an annual Kaplan Cardiology Society Lecture Series, which continues to this day.

Dr. Kaplan joined UCLA in 1987 where he became the leader of a multi-institutional research program funded by a $9 million grant from the National Institutes of Health to study the effects on the heart and lungs of HIV transmitted from mother to infant. This work alone has contributed more than 30 scientific reports, has identified important heart and lung complications associated with HIV, and has identified appropriate treatment and follow-up for these infants and children.

Kaplan was the recipient of numerous honors and awards throughout his career including election to Alpha Omega Alpha, the medical honor society; the Susan and Theodore Cummings Humanitarian Award from the American College of Cardiology; the Cincinnati Pediatric Society Founder's Award; the American Academy of Pediatrics Founder's Award; and the Visionary Award from the American Heart Association. He served on the editorial boards of most major cardiology journals, and served as president of the California Society of Pediatric Cardiologists. The impact of Kaplan's career in pediatric cardiology will forever be felt within the framework of that clinical discipline. He was a revered figure in both pediatrics and pediatric cardiology.

"Kaplan made many experimental contributions to the field; his laboratory studies were instrumental in developing the membrane oxygenator that is still an essential part of the surgical procedure for open-heart surgery on both children and adults."

"Sam Kaplan was an extraordinary, gentle leader, who gave so much of himself to his patients, students and colleagues. His artful and quiet approach to problem-solving was important to his success in all areas of his career," said Edward R. B. McCabe, Executive Chair of UCLA's Department of Pediatrics and Physician-In-Chief of UCLA's Mattel Children's Hospital. "He was a marvelous influence on all of us who were fortunate enough to know him."

For comments to this article, send email to: MARSK@PediatricCardiologyToday.com

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LEADERS IN PEDIATRIC CARDIOLOGY TODAY INTERVIEW SERIES: AGA MEDICAL CORPORATION

With the March 2004 issue, Pediatric Cardiology Today (PCT) starts a new editorial feature entitled, "Leaders in Pediatric Cardiology Today Interview Series." Throughout the year PCT will interview people in business, associations and the medical community serving pediatric cardiology. Our first interview is with Mike Smithson, *U.S. Sales & Marketing Director*; Jodi Raus, *Director of Regulatory Affairs*; Ken Lock, *Director of Clinical Affairs*; and Mark Cibuzar, *Director of International Sales & Marketing* from the AGA Medical Corporation.

Q: ***Briefly describe the company and its major products and markets.***

A: AGA Medical Corporation based in Golden Valley, Minnesota, U.S. is dedicated to the development, design, manufacture, and market of minimally invasive nitinol-based occlusion devices and accessories for the treatment of cardiovascular defects and peripheral vascular disease.

We estimate that AMPLATZER devices have treated more than 50,000 patients worldwide. Our major products and markets include: (1) AMPLATZER Septal Occluder ® - U.S., Europe, Australia, Canada; (2) AMPLATZER Duct Occluder - U.S., Europe, Australia, Canada; (3) AMPLATZER PFO Occluder ® - U.S. (limited indication), Europe, Australia, Canada; and (4) AMPLATZER Membranous VSD Occluder ® - Europe, Australia.

Q: ***Please give a short history of the company and the company's founders.***

A: The company was founded in 1995 by Kurt Amplatz, MD. AGA Medical Corporation owes its namesake to its three original owners: Kurt Amplatz, MD, Franck Gougeon, and Michael Afremov. The company is privately held.

Q: ***The AMPLATZER Septal Occluder is FDA approved. Is the FDA requiring any further data for follow up of patients?***

A: AGA Medical is required to follow those patients enrolled in the primary Phase of the Clinical trial (Phase IIB) as well as patients enrolled in the Continued Access phase: (1) Who received devices < 10mm and > 28mm, and, (2) patients under the age of ten.

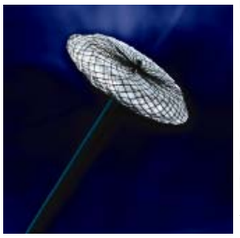

Figure 1. AMPLATZER Septal Occluder ®

Q: ***There have been a few reports of erosion of the ASO into the pericardial space and cardiac tamponade. Can you tell us anything more about this complication and its risk?***

AGA Medical has convened an Advisory Board to review these complications. The reported event rate is low (approximately 0.18%), making it difficult to detect any sort of trend for these events. The Board will meet again in March.

Q: ***The AMPLATZER Duct Occluder is FDA approved. Is the FDA requiring any additional data or follow up for this device?***

Yes. The FDA required a five year follow-up on the 435 patients enrolled in the primary Phase of the Clinical trial (Phase II).

Q: ***The AMPLATZER PFO Occluder has HDE approval from the FDA. Does the company have any responsibility in monitoring its use?***

A: AGA Medical is responsible for verifying that IRB approval is obtained and remains in place while the device is being used at the institution.

Figure 2. AMPLATZER PFO Occluder ®

AGA Medical is also responsible for verifying that the number of devices implanted does not exceed 4,000 per year. AGA is also required to report malfunctions, serious injury and death occurring under the HDE approval.

Q: ***What is the status of the RESPECT Trial (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment)? Is it***

enrolling patients yet? How long will the study take to complete?

A: Patients are being enrolled in the RESPECT trial. It is anticipated that the trial will be completed in three years. To find the RESPECT Trial nearest to you or for additional information visit the AMPLATZER website at: www.amplatzer.com.

Q: ***What is the status of the AMPLATZER Muscular VSD Occluder? Do you expect FDA approval soon? When will it be available to operators?***

A: We reached the maximum number of patients in the clinical trial and are in the process of assembling the pre-market approval application for the Muscular VSD Occluder. Once submitted, FDA review will take a minimum of six months. We continue to review compassionate and emergency use situations on a case-by-case basis. A high-risk protocol has been approved by the FDA to handle any compassionate use requests. The AMPLATZER Muscular VSD Occluder has CE Mark approval and is available in most countries world-wide.

Figure 3. AMPLATZER Muscular VSD ®

Q: ***What is the status of the AMPLATZER PeriMembraneous VSD Occluder? Is it in a FDA clinical study in the US?***

A: The Membranous VSD Occluder is currently in Phase I clinical study in the U.S. The AMPLATZER Membranous VSD Occluder received CE Mark in 2003. It is currently marketed in over 20 countries world-wide.

Figure 4. AMPLATZER PeriMembraneous VSD Occluder ®

Q: ***Is the AMPLATZER Vascular Plug FDA approved? Is it available for use? What are the indications?***

The AMPLATZER Vascular Plug is 510K cleared by the FDA. We are currently conducting an initial limited market evaluation. We have forecasted to market release the device during the 3rd quarter of 2004. The AMPLATZER Vascular Plug is indicated for arterial and venous embolizations in the peripheral vasculature.

Figure 5. AMPLATZER Vascular Plug ®

Q: ***What other devices have been designed by AGA? What others are being pursued?***

A: Several new products, as well as Iterations of our current devices, are being evaluated for further study.

Q: **Does AGA plan to improve the delivery sheaths for the ASO and other devices (i.e. make them more kink resistant, marker tip, etc.)?**

We are currently developing an improved delivery sheath that will feature several design enhancements to aid in AMPLATZER device placement and retrieval. The design enhancements will include improved kink resistance, torque-ability, and visibility. We anticipate the release of the new delivery system by the end of 2004.

Q: ***Do you have a website, a newsletter, or catalogue for your pediatric products?***

A: Please visit AGA Medical Corporation's website at: www.amplatzer.com to learn more about transcatheter closure of heart defects with AMPLATZER Occlusion devices. If you would like to receive more information pertaining to the AMPLATZER family of occlusion devices or if you would like to receive a copy of the next issue of the *AMPLATZER Focal Points Newsletter*, please send an e-mail request to: salesmarketing@amplatzer.com. Please include your name, title, organization, address, phone number and email.

Q: ***How do our readers contact an AGA representative?***

A: You can reach a representative of the AGA Medical Corporation by calling 1-888-546-4407 (toll-free in the U.S.) or 1-763-513-9227. You can also reach us by sending an e-mail to: salesmarketing@amplatzer.com.

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HIGHLIGHTS FROM CARDIOLOGY 2004: THE 7TH ANNUAL UPDATE ON PEDIATRIC CARDIOVASCULAR DISEASE—FEBRUARY 25TH-29TH, 2004, BUENA VISTA, FLORIDA

By Gil Wernovsky, MD

Providing optimal care for neonates, children and young adults requires a multidisciplinary team approach, including physicians (from cardiology, cardiac surgery, cardiothoracic anesthesia, neonatal and pediatric critical care medicine, and multiple consulting services), nurses, perfusionists, respiratory therapists, social workers, and many others. All of these various practitioners must be expert in their own area, but should also be knowledgeable in what the other members of the team add to the overall care of the patient. With this "team approach" in mind, The Cardiac Center at The Children's Hospital of Philadelphia (CHOP) presented the 7th Annual Post-Graduate Course in the Conference Center at the Contemporary Hotel and Resort in Walt Disney World. While there are many successful meetings for sub specialists who care for children with heart disease, this annual course provides a multidisciplinary faculty from multiple institutions to present a varied approach to diagnosis and management. The conference attendance roster reflected the multidisciplinary nature, with over 770 attendees from all aspects of the field, who came from all around the globe. In addition to a faculty of over 70 physicians and allied professionals from 24 centers, 58 poster presentations were on display from 38 different centers.

One thread, which ran throughout the course, was a "soup to nuts" review of common congenital heart disease. These sessions were of variable length and depth of topic, but always followed the same basic theme: anatomy, initial diagnosis and management, surgical intervention, postoperative care, and mid-term results. Professor Robert Anderson, from the Great Ormond Street Hospital for Children in London, introduced each of the lesions with his preferred nomenclature and pertinent aspects of the anatomy. This was followed by Dr. Paul Weinberg (wearing a head cam) showing detailed anatomy of heart specimens shipped to Orlando from the Cardiac Registry at CHOP. Of course, Drs. Anderson and Weinberg would frequently disagree on what to call the defect, but all in the audience could see exactly what it looked like. Surgeons and cardiologists then presented "what they do" to diagnose and treat these lesions, and available outcome studies were summarized. These nine sessions (transposition of the great arteries, total anomalous pulmonary venous return, truncus arteriosus, interruption of the aortic arch, vascular ring, hypoplastic left heart syndrome, tetralogy of Fallot, aortic stenosis and ventricular septal defect) were spread over the 5-day course, and were presented to a "packed house".

"The 8th Annual Post Graduate Course will be held at Disney's Yacht and Beach Club, February 16-20, 2005."

Dr. Martin Elliott, also from Great Ormond Street, opened the meeting with a spirited review on strategies to reduce morbidity following neonatal cardiac surgery, emphasizing that expert surgical techniques are a 'necessary, but insufficient' component of success. Drs. Betsy Goldmuntz (CHOP) and William Mahle (Sibley Heart Center, Emory) reviewed the genetic and environmental causes of congenital heart disease, followed by an update on mortality and morbidity in low birth weight infants from Dr. David Rubenstein (Babies Hospital, NYC), who emphasized how similar the survivors appear to be. The evening session was closed by Dr. Thomas Spray (CHOP), who critically reviewed the methods by which cardiac surgeons change operative techniques in response to preliminary results from prominent surgeons throughout the world. His closing remarks emphasized the importance of data collection, self-criticism, resisting dogma, and always keeping an open mind.

Cardiac and non-cardiac abnormalities associated with the 22q11 microdeletion syndrome were reviewed in depth, with an entire session devoted to tetralogy of Fallot. The importance of screening families whose children have tetralogy, interrupted aortic arch, truncus arteriosus and aortic arch anomalies was constantly re-emphasized by the faculty. The second day of the meeting also featured a special meeting of the Pediatric Cardiac Intensive Care Society (www.pcics.com), which included a comprehensive review on clinical trials by Dr. David Wessel from Boston Children's Hospital. At the Business Meeting, the membership agreed upon Level I and Level II training guidelines in cardiac intensive care, which will be incorporated into the upcoming Pediatric Cardiology Training Program Guidelines (see the January issue of *Pediatric Cardiology Today* at www.PediatricCardiologyToday.com for details).

The second day of the conference also featured hands-on demonstrations of temporary pacing by Dr. Mitchell Cohen (Phoenix Children's Hospital), live imaging of the fetus with CHD by Drs. Jack Rychik and Zhiyun Tian (CHOP), and the

kick-off session for the newly formed pediatric cardiac administrators consortium. Topics in this track included issues related to work hour restrictions, interactions with information systems, risk stratification, marketing and strategic planning.

The third day of the congress included three mini-symposia which featured in depth reviews of hypoplastic left heart syndrome (HLHS), brain injury in patients with CHD, and new frontiers in pediatric cardiac transplantation. In the HLHS session, newborn management strategies were discussed in detail, including a comprehensive review of preoperative management by Dr. Anthony Chang (Texas Children's Hospital) and postoperative management by Dr. James Tweddell (Children's Hospital of Wisconsin). Dr. Spray discussed newborn surgical interventions, including the standard Norwood operation and the recent Sano modification using a right ventricular to pulmonary artery conduit. Dr. Mark Boucek (Denver Children's Hospital) discussed newborn catheterization palliation by ductal stenting and internal pulmonary artery banding. Dr. Timothy Feltes (Columbus Children's Hospital) described a combined newborn strategy of catheterization for ductal stenting and surgical pulmonary artery banding, followed by a combined Norwood-Glenn procedure in early infancy. All of the presenters reported similar 1-year survival (~70-80%), and emphasized that the next big hurdle is to reduce the long-term morbidity associated with either strategy.

The HLHS symposium segued into the Brain Injury Mini Symposium, where school age learning disabilities and behavioral problems were reported to be the single most common long-term morbidity in survivors of complex CHD surgery. Following an overview of developmental testing by Dr. David Bellinger (Boston Children's Hospital), the prenatal and preoperative risk factors for central nervous system injury were reviewed by Drs. Jonathan Kaltman and Bill Gaynor from CHOP, and Dr. Bill Mahle. Drs. Ross Ungerleider (Doernbecher Children's Hospital, Portland) and Bill DeCampli (CHOP) reviewed the laboratory and clinical data related to bypass and surgical techniques. The combination of preoperative events, intraoperative hypoxic-ischemic injury, and postoperative hypotension or hypocapnia result in white matter injury, which translates into the learning and behavioral difficulties seen years later. Dr. Gaynor presented data on the genetic predisposition to brain injury, resulting from carrying two copies of the apolipoprotein epsilon allele ε2.

Conference Attendee Statistics

Physicians - 45%
Registered Nurses - 31%
Advanced Practice Nurses - 11%
Perfusionists - 4%
Physician Assistants - 1%
Respiratory Therapists - 1%
Sonographers - 2%
Other - 5%

On the 4th day of the meeting, the First Annual Outstanding Investigator Award was given to Meredith Allen, MBBS, FRACP for her presentation on Cytokine polymorphisms which influence the inflammatory response following cardiac surgery. As the first recipient of this award, she received a 3-day Caribbean cruise aboard the Disney Wonder, and complimentary registration to Cardiology 2005. The 5th Annual C. Walton Lillehei Memorial Lecture was presented by Dr. William Williams from the Hospital for Sick Children in Toronto, Canada. His lecture on data management compared academic databases and voluntary registries, pointing out the relative strengths and weaknesses of each. This was followed by the Featured Nursing Lecture given by Mary Fran Hazinski, RN, MSN, internationally recognized as a pioneer in the field of pediatric critical care nursing and the author of the seminal textbook in the field. Her review of critical care medicine and nursing emphasized the collaborative approach that has evolved, and was full of historical photos and vignettes. The 3rd Annual William J. Rashkind Memorial Lecture was given by Dr. Jane Newburger (Boston Children's Hospital). Dr. Newburger reviewed Kawasaki Disease, including the clinical features in the diagnosis, our current treatment strategies, the ongoing trail of steroid therapy in addition to intravenous gamma globulin, and emphasizing that further research is necessary to determine the cause.

On the final day of the meeting, a number of excellent presentations in cardiovascular nursing and intensive care were given, culminating in Dr. Bill Williams' thoughtful review on the future directions and systems necessary to manage the growing population of adults with congenital heart disease, a group that now outnumbers their pediatric counterparts.

A full conference CD with all 135 presentations will be distributed to the congress attendees in late March. The 8th Annual Post Graduate Course will be held at Disney's Yacht and Beach Club just prior to Presidents' Day Weekend, February 16-20, 2005. Hope to see you in Orlando!

For comments to this article, send email to: MARLGW@PediatricCardiologyToday.com

~PCT~

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CLINICAL TRIAL ABSTRACTS (CLINICALTRIALS.GOV)

Family Studies of Hypertrophic/ Dilated Cardiomyopathy

~ currently recruiting patients ~

Sponsor: National Heart, Lung, and Blood Institute (NHLBI)

Purpose: This study will examine blood cells of patients (and their relatives) with hypertrophic cardiomyopathy or dilated cardiomyopathy for genes that may cause or modify the disease. Cardiomyopathy causes thickening or stretching of the heart muscle that can cause chest pain, shortness of breath, palpitations, and fainting. Cardiomyopathy sometimes runs in families and is caused by an abnormal gene or genes.

Patients diagnosed with hypertrophic cardiomyopathy or dilated cardiomyopathy, or both, may enroll in this study. Relatives of patients will also be studied.

Participants will have a review of their medical history and a brief physical examination, including and electrocardiogram (ECG) and echocardiogram-an ultrasound test of the heart. A small blood sample will be obtained for DNA (genetic) study.

Condition: Hypertrophic Cardiomyopathy, Congestive Cardiomyopathy

Study Type: Observational

Study Design: Screening

Further Study Details: Hypertrophic cardiomyopathy (HCM) is an important cause of sudden death in apparently healthy young individuals but its clinical manifestations are highly variable both within and between families. Linkage analysis and/or a candidate gene approach has been used to localize 10 genes, which when mutated, can cause HCM. Recently, mutations in disease genes for HCM have been shown to cause dilated cardiomyopathies. Thus, biased screening studies with HCM genes against patients with either hypertrophic or dilated cardiomyopathies are warranted. Clinical observations as well as experiments in our laboratory have demonstrated the contribution of modifier genes to the severity of any one individual's disease. Both biophysical and genomics studies in our laboratory are yielding a list of candidate modifier genes. The purpose of this protocol is to determine allele frequency of existing and newly identified genes for which there is mechanical, genomic or conceptual evidence that these genes modify or cause cardiac hypertrophy/dilation. Evidence for the effect of any one allele is established through a combination of association, linkage and/or mechanical analysis studies. The latter studies involve analysis of normal and transgenic animal skeletal/ cardiac tissue from animals produced under the oversight of the Animal Use Committee.

Eligibility: Both genders

Criteria: Individuals enrolled into this protocol have been referred on the basis of a diagnosis of hypertrophic cardiomyopathy and/or dilated cardiomyopathy, or have relatives carrying such a diagnosis. There is no age, gender, or racial criteria applied to inclusion or exclusion.

Expected Total Enrollment: 1000

Location and Contact Information: National Heart, Lung and Blood Institute (NHLBI), 9000 Rockville Pike, Bethesda, MD 20892; Patient Recruitment and Public Liaison Office: 1-800-411-1222; prpl@mail.cc.nih.gov

Study ID Numbers 020283; 02-H-0283
Study Start Date August 21, 2002
Record last reviewed October 23, 2003
Last Updated October 23, 2003
NLM Identifier NCT00045825
ClinicalTrials.gov processed this record on 2004-01-16

Study of Energy Expenditure in Infants With Ventricular Septal Defects

~ currently recruiting patients ~

Sponsor: National Center for Research Resources (NCRR) Indiana University

Purpose: Compare the total daily energy expenditure in infants with ventricular septal defects vs. healthy control infants.

Condition: Heart Septal Defects, Ventricular

Study Type: Observational

Study Design: Natural History

Further Study Details: Protocol Outline: Height, weight, and vital signs (including oxygen saturation by pulse oximetry) are measured on Day 1. Resting energy expenditure, oxygen consumption (VO2), carbon dioxide production (VCO2), and resting respiratory exchange quotient (RQ) are measured using open circuit respiratory calorimetry on Day 1. Patients undergo assessment of total daily energy expenditure using the doubly labeled water method comprised of oral deuterium and oral oxygen O 18 with the next scheduled feeding on Day 1. Urine samples are collected prior to isotope administration, then serially for approximately 12 hours after isotope administration on Day 1, and then daily on Days 2-7. These samples are analyzed by mass spectrometry. On Day 1, patients also undergo echocardiogram to confirm size of defect and measure the degree of pulmonary/systemic blood flow ratio and pulmonary artery pressures.

Eligibility: Ages: 3 - 4 months, both genders; accepts healthy volunteers

Criteria: Protocol Entry Criteria:

--Disease Characteristics--

Infants with moderate to large ventricular septal defect (VSD) by most recent echocardiogram who meet the following conditions: no other concurrent heart or lung disease; no chromosomal defects or congenital anomalies.
OR
Healthy control infants without VSD who meet the following conditions: clinically well; no heart disease; no chromosomal defects or congenital anomalies.

--Prior/Concurrent Therapy--

Surgery: VSD infants -- No prior cardiac surgery or palliative procedures; VSD and control infants - greater than 6 weeks since prior surgery.

Other: VSD and control infants: greater than 6 weeks since prior hospitalization.

Expected Total Enrollment: 20

Location and Contact Information: Indiana University, Indianapolis, IN 46202-5167, Recruiting, Catherine A. Leitch, Study Chair, 317-274-4920

Study ID Numbers NCRR-M01RR00750-9045; IU-9607-08; IU-9511-16
Study Start Date August 1994
Record last reviewed December 2003
NLM Identifier NCT00006272
ClinicalTrials.gov processed this record on 2004-01-16

Study of Triostat in Infants during Heart Surgery

~ currently recruiting patients ~

Sponsor: FDA Office of Orphan Products Development

Purpose: This is a study to determine the safety and efficacy of liothyronine sodium/ triiodothyronine (Triostat), a synthetic thyroid hormone, when given to infants with congenital heart disease during cardiopulmonary bypass surgery.

Condition: Heart Defects, Congenital

Treatment or Intervention: Drug: Liothyronine sodium/triiodothyronine; Procedure: Cardiopulmonary bypass and cardiac surgery.

Study Type: Interventional

Study Design: Treatment, Randomized, Double-Blind, Placebo Control, Safety/Efficacy Study

Further Study Details: Patients will be randomized to receive study drug or placebo and randomization will occur stratified to each diagnostic category. All patients undergo preoperative echocardiograms to provide preoperative cardiac function data. The study drug or placebo will be provided in the operating room as an iv bolus just prior to cardiopulmonary bypass and as a bolus delivered on release of the aortic cross-clamp. This will be followed by iv for 12 hours. Operative data will be collected including CPB time, aortic cross-clamp time, length and degree of hypothermia. These data will be extracted from the anesthesia record.

Eligibility: Ages up to 2 years, both genders

Criteria: Inclusion criteria: Diagnosis of one of the following:

• Ventricular septal defect (VSD)

• Infant coarctation of the aorta

• Transposition of the great arteries

• Tetralogy of Fallot

• Complete atrioventricular canal defect

• Hypoplastic left heart, including patients who undergo a Norwood type procedure for aortic or mitral atresia

Patient must be scheduled for surgery.

Exclusion criteria: Certain additional defects and/or requirement for additional surgery.

Expected Total Enrollment: 225

Location and Contact Information: Children's Hospital and Regional Medical Center, Seattle, WA 98105; Recruiting — Kendall Magnuson, 206-528-5181; resadmin@chmc.org; Michael A. Portman, MD, Principal Investigator

Study ID Numbers FD-R-1971-01; FD-R-001971-01
Study Start Date April 2001
Record last reviewed October 2001
NLM Identifier NCT00027417
ClinicalTrials.gov processed this record on 2004-01-16

For comments to this article, send email to: MARCT@PediatricCardiologyToday.com

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