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iCi 2013 - Imaging in Structural, Valvular & Congenital Interventions
Jun. 26, 2013; Frankfurt, Germany
www.ici-congress.org

CSI 2013 - Congenital, Structural & Valvular Interventions
Jun. 27-29, 2013; Frankfurt, Germany
www.csi-congress.org

International Academy of Cardiology, 18th World Congress on Heart Disease, Annual Scientific Sessions 2013
Jul. 26-29, 2012; Vancouver, Canada
www.cardiologyonline.com/

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Total Anomalous Pulmonary Venous Connection in the Neonate

By Claudeen K. Whitfield, MD;
P. Syamasundar Rao, MD

Introduction

In the previous issues of this publication, we focussed on several general topics on Congenital Heart Disease (CHD) in the neonate.¹⁻⁵ More recently, we began addressing individual cardiac lesions, namely: Transposition of the Great Arteries⁶ and Tetralogy of Fallot,⁷ Hypoplastic Left Heart Syndrome⁸ and Tricuspid Atresia.⁹ In this issue of *Congenital Cardiology Today*, we will discuss Total Anomalous Pulmonary Venous Connection (TAPVC). Other conditions with similar embryological and clinical findings, as well as therapeutic implications, such as atresia of the common pulmonary vein, cor triatriatum and stenosis/atresia of the individual pulmonary veins will not be reviewed in this paper.

Total Anomalous Pulmonary Venous Connection

In TAPVC, all the pulmonary veins drain into systemic veins; most commonly they drain into a common pulmonary vein which is then connected to the left innominate vein, superior vena cava, coronary sinus, portal vein or other rare sites. Occasionally, individual veins drain directly into the right atrium. TAPVC is the fifth most common cause of cyanotic congenital heart disease (CHD), and the twelfth most common CHD in critically ill infants. TAPVC occurs in 0.6 to 1.2 per 10,000 live births. Sixty-eight percent are diagnosed as neonates.¹⁰ TAPVC is an isolated lesion in approximately two-thirds of patients and

occurs in association with other CHD, as well as heterotaxia syndromes in the remaining one-third of patients. The male to female ratio in the Baltimore-Washington infant study was 18:23.¹⁰ In other reports, a strong male preponderance of 3:1 was observed in patients with infra-diaphragmatic connection. If left unrepaired, 50% of the babies may survive up to 3 months, and 20% up to 1 year of age, depending on the type and degree of obstruction.¹¹

Embryology

During normal development, the lung buds are outgrowths of the primitive foregut, and early in fetal life venous drainage from the lungs is via the splanchnic plexus to the cardinal and umbilicovittelline venous systems. The common pulmonary vein arises from the posterior left atrium as a small pouch that enlarges and connects with the pulmonary venous component of the splanchnic plexus. When pulmonary venous drainage via the common pulmonary vein is established, the connections to the cardinal and umbilicovittelline venous systems involute and eventually disappear. The common pulmonary vein is incorporated into the posterior left atrial wall by differential growth, and the pulmonary veins then connect directly to the left atrium. If the common pulmonary vein fails to develop or fails to connect to the splanchnic plexus, the primitive venous connections persist, and result in total anomalous pulmonary venous connection. The type of TAPVC is determined by which of the connections to the cardinal or umbilicovittelline venous system persists. Drainage of the pulmonary veins may be into the right atrium, the right common cardinal system (superior vena

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cava or azygos vein), the left common cardinal system (left innominate vein or coronary sinus), or the umbilicovortelline system (portal vein, ductus venosus, etc.).¹²

Classification

Darling et al¹³ proposed a TAPVC classification system based on the site of pulmonary venous drainage: **Type I** in which there is a supra-cardiac connection and all four pulmonary veins are connected to the common pulmonary vein, which is then drained by a connecting anomalous vein into the right superior vena cava, left superior vena cava, or their tributaries; **Type II** where there is a cardiac connection and the common pulmonary vein is connected directly to the right heart (coronary sinus or the right atrium); **Type III** is characterized by an infra-cardiac connection and the common pulmonary vein is drained by an anomalous channel which travels caudally anterior to the esophagus through the diaphragm to connect to the portal venous system; and **Type IV** where there are mixed connections, and the right and left pulmonary veins drain to different sites (for example, left pulmonary veins into the left vertical vein and then into the left innominate vein and right pulmonary veins directly into the right atrium or coronary sinus).¹³ Supra-cardiac connection is the most common (45%), followed by cardiac (25%), infra-cardiac (25%) and mixed (5%).¹⁴⁻¹⁸

A simpler classification was proposed by Smith and associates:¹⁹ supra-diaphragmatic without pulmonary venous obstruction and infra-diaphragmatic with obstruction. Although the supra-diaphragmatic forms are generally non-obstructive, obstruction can also occur in these as well, as reviewed elsewhere.²⁰ However, the infra-diaphragmatic forms are almost always obstructive. Connection to the left innominate vein is the most common type of TAPVC.²¹⁻²³ Infra-diaphragmatic type is most common form in neonates.²¹⁻²³

Pathophysiology

In all types of TAPVC, entire pulmonary venous blood eventually returns to the right atrium. Intra-cardiac mixing of systemic and pulmonary venous returns occurs. Therefore, right-to-left shunt across the atrial septum (patent foramen ovale or atrial septal defect) must be present for survival. A restrictive atrial communication is not uncommon. If atrial communication is restrictive, the amount of blood reaching the left atrium is limited, and systemic blood flow (cardiac output) is reduced. If there is wide-open atrial communication, the flow distribution to systemic and pulmonary circuits is dependent on relative compliances of the atria and ventricles; these compliances are eventually linked to pulmonary and systemic vascular resistances.

In babies with a non-obstructive type of TAPVC, as the pulmonary vascular resistance decreases (with age), there is progressive increase in pulmonary blood flow. This causes pulmonary over-circulation and eventually congestive heart failure. Right atrial and right ventricular enlargement and dilatation of main and branch pulmonary arteries are usually seen. If untreated, increased pulmonary blood flow will result in pulmonary arteriolar medial hypertrophy and intimal proliferation, and the patients will develop pulmonary hypertension and eventually pulmonary vascular obstructive disease.

In babies with obstructive types of TAPVC, because of high pulmonary venous pressure, reflex pulmonary arteriolar constriction occurs resulting in high pulmonary artery pressure and decreased pulmonary blood flow. When the osmotic pressure of the blood exceeds the hydrostatic pressure in the capillaries, pulmonary edema develops. This is partly compensated for by increased pulmonary lymphatic drainage, development of alternative pulmonary venous bypass channels and altered capillary permeability.

Obstruction to pulmonary venous return is uniformly present in the infra-diaphragmatic type. It may be extrinsic at the level of the diaphragm as the connecting vein passes through it, constriction of the ductus venosus, high resistance to the passage of the blood through



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the hepatic sinusoids, intrinsic stenosis of the connecting vein or a combination thereof.²⁰ The long connecting vein itself may offer impedance to the pulmonary venous return.²⁰ In the supra-diaphragmatic types, the obstruction can also occur and it may be at multiple sites and with varying degrees of severity. It may be intrinsic, within the connecting vein itself or extrinsic by compression (of the vertical vein) between the left bronchus and left pulmonary artery. The intrinsic stenosis of the anomalous connecting vein may be at its junction with

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The Departments of Pediatrics at the University of Louisville School of Medicine and Kosair Children's Hospital are recruiting for a medical director of heart failure and cardiac transplantation for the Congenital Heart Center at Kosair Children's Hospital in Louisville, Ky.

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the common pulmonary vein, at its entry into the left innominate vein, superior vena cava, azygos vein or right atrium, somewhere within the vein itself or a combination thereof. Also, the left innominate vein, superior vena cava or azygos vein may themselves be narrowed. For further details, the reader is referred elsewhere.²⁰ Obstruction is least likely to occur when the pulmonary veins drain into the coronary sinus. The potential for obstruction at the atrial septal defect level has already been mentioned above.



Figure 1. Chest x-ray of a neonate with total anomalous pulmonary venous connection of an infra-diaphragmatic type demonstrating severe pulmonary venous congestion. Mild cardiac enlargement is also seen.

Clinical Features

Clinical features are largely determined by the degree of pulmonary venous obstruction. If obstruction is present, the majority (~75%) of patients will present within the first few days of life and the remainder at a later time. The presentation is shortly after the first 12 hours of life; this is in contradistinction to Respiratory Distress Syndrome which usually presents at birth. These babies are acutely ill and manifest tachypnea, dyspnea, hypoxemia and metabolic acidosis. These signs and symptoms appear to be related to severe pulmonary venous congestion. Physical examination is significant for rales and rhonchi in both lung fields. Cardiovascular findings include widely split second heart sound with an accentuated pulmonary component and no murmurs. Sometimes a non-specific ejection systolic murmur along the left sternal border may be heard. Hepatomegaly is usually present. Obstructive TAPVC is present in almost all infra-diaphragmatic types and in only 50% of supra-diaphragmatic types.

In the absence of pulmonary venous obstruction, the presentation is within the first month of life in more than half of the patients and the remainder during the first year of life. They usually present with signs of congestive heart failure. Tachypnea, tachycardia, feeding difficulties and failure to thrive are usual presenting symptoms. Findings on physical examination are similar to those in patients with a secundum atrial septal defect in that there is a prominent right ventricular impulse (hyperdynamic), widely split and fixed second heart sound, an ejection systolic murmur at the left upper sternal border and a mid-diastolic flow rumble at the left lower sternal border. In addition, pulmonary component (P_2) of the second heart sound is accentuated, and an ejection systolic click plus third and/or fourth heart sounds (multiple cardiac sounds) may be present. Cyanosis is minimal and may not be clinically detectable because of markedly increased pulmonary blood flow. Signs of cardiac failure are usual. Another clinical feature is a venous hum heard at the left or right upper sternal borders or in the infraclavicular regions in the supra-cardiac types of TAPVC; the venous hum is not altered by changes in the position of the patient.



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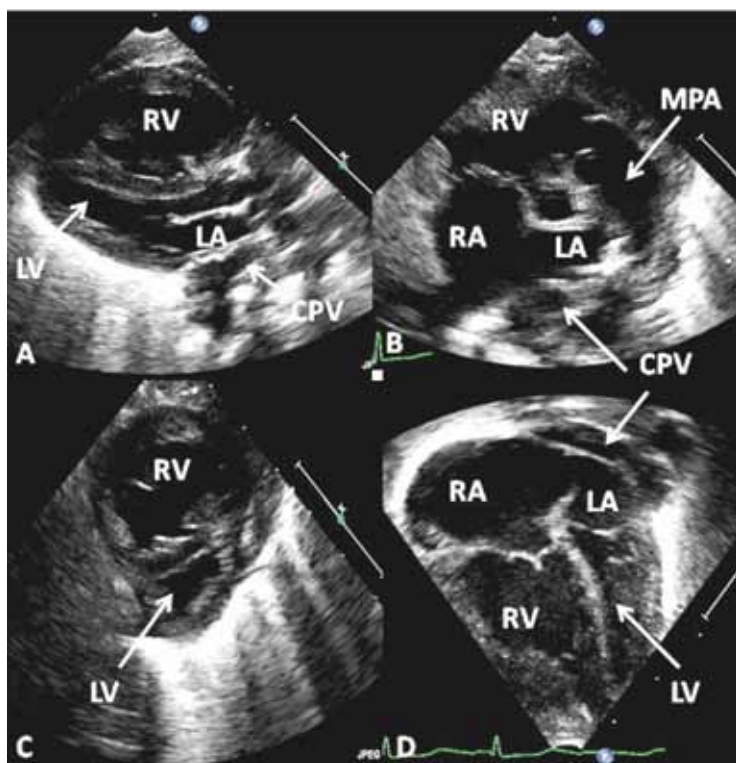


Figure 2. Selected video frames of a 2-dimensional echocardiogram in parasternal long (A) and short (B & C) axis and apical four chamber (D) views demonstrating a large right atrium (RA), right ventricle (RV) and main pulmonary artery (MPA) in an infant with total anomalous pulmonary venous connection. Note that the enlarged RV encroaches onto the left ventricle compressing it posteriorly (A & C) and to the left (D). Common pulmonary vein (CPV) is located behind (A & B) and superior to the left atrium (LA) (D).

Non-Invasive Evaluation

Chest X-ray

In the obstructive type, the size of the heart is small and normal or mildly enlarged. There is evidence of marked pulmonary edema with stippled densities and reticular pattern in the lung parenchyma, partially obscuring the cardiac borders (Figure 1). The reticular pattern may some- toccal infection. In the non-obstructive type where there is unrestricted pulmonary blood flow, there is cardiomegaly and increased pulmonary vascular markings, but usually no pulmonary edema is seen. In the supracardiac type draining into the left innominate vein, a snowman-type of cardiac silhouette may be seen; however, this may take several weeks/months to develop and may not be obvious in the neonatal period.

Electrocardiogram

Electrocardiogram reveals right ventricular hypertrophy in the obstructive type; however, it may be difficult to distinguish it from normal neonatal right ventricular preponderance. In the non-obstructive type, right axis deviation, right atrial enlargement as seen by tall P waves in lead II and right precordial leads and right ventricular hypertrophy, manifested tall R waves in right precordial leads, sometime with rSR pattern are usually seen.

Echocardiogram

Echocardiographic studies are useful in confirming the diagnosis, and in defining various issues germane to the management of these sick babies. Inability to easily visualize the entry of pulmonary veins into the left atrium by two-dimensional (2D) and color flow mapping should

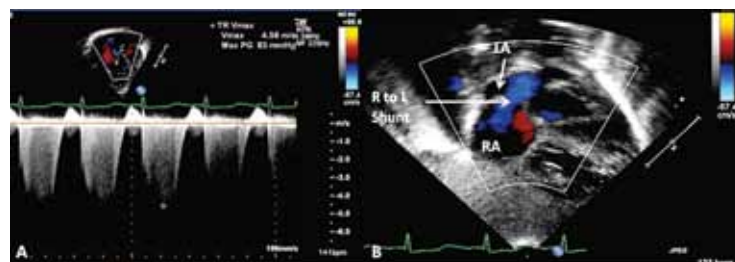


Figure 3. A. High tricuspid regurgitant Doppler flow velocity is shown and is suggestive of elevated pulmonary artery pressure in a neonate with an infra-diaphragmatic type of total anomalous pulmonary venous connection. B. Color Doppler flow mapping demonstrating right to left shunting across the atrial septum. RA, right atrium; LA, left atrium.

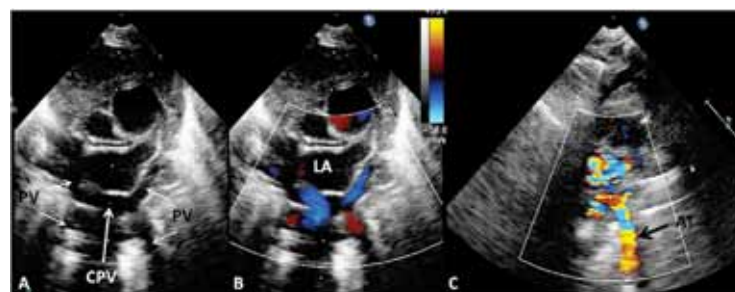


Figure 4. Selected video frames from suprasternal notch views in a baby with infra-diaphragmatic type of total anomalous pulmonary venous connection showing pulmonary veins (PV) draining into a common pulmonary vein (CPV) which is located adjacent to the left atrium (LA); 2-dimensional (A) and color flow mapping (B) images are shown. Anomalous trunk (AT) traversing towards the diaphragm is shown in C.

arouse the suspicion of the diagnosis of TAPVC. Enlargement of the right atrium, right ventricle and pulmonary artery is seen in all types of TAPVC (Figure 2). The left atrium and left ventricle usually appear relatively small compared to the very large right ventricle.^{25,26} The enlarged right ventricle encroaches onto the left ventricle, compressing it posteriorly (Figure 2 A & C) and to the left (Figure 2D). The left atrium is smaller than normal (because of lack of contribution of the common pulmonary vein), but is easily seen (Figure 2 A, B & D).

The right ventricular and pulmonary artery pressures are elevated, as demonstrated by high tricuspid valve regurgitant velocity (Figure 3A). The right ventricular and pulmonary artery systolic pressure may be estimated by modified Bernoulli equation:

$$\text{Right ventricular and pulmonary artery systolic pressure} = 4V^2 + 5 \text{ mmHg}$$

Where V is peak velocity of the regurgitant tricuspid jet, and 5 is the estimated right atrial pressure.

Right to left shunt across the patent foramen ovale is also seen in all types of TAPVC (Figure 3B).

The common pulmonary vein is seen behind the left atrium (Figure 2 A & B) and every effort should be made to demonstrate the entry of all pulmonary veins into this chamber by using a combination of 2D imaging and color flow mapping (Figures 4 & 5) in multiple views. Parasternal, subcostal and suprasternal notch views are most helpful in this regard. The size and orientation (horizontal or vertical) of the common pulmonary vein should also be determined. Careful color flow imaging should be used to demonstrate the anomalous connecting vein and the site of its drainage.

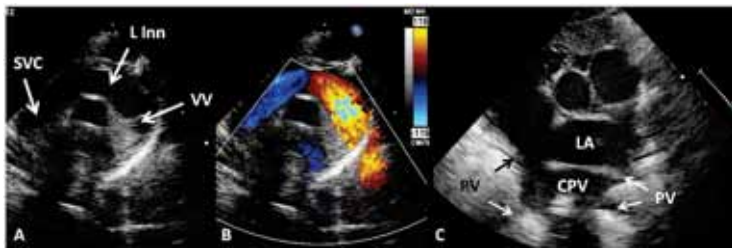


Figure 5. Selected video frames from suprasternal notch views in a baby with supra-diaphragmatic type of total anomalous pulmonary venous connection showing dilated vertical vein (VV), left innominate vein (L Inn) and superior vena cava (SVC); 2-dimensional (A) and color flow mapping (B) images are shown. 2-dimensional images of pulmonary veins (PV) draining into a common pulmonary vein (CPV) which is located adjacent to the left atrium (LA) are also shown (C).

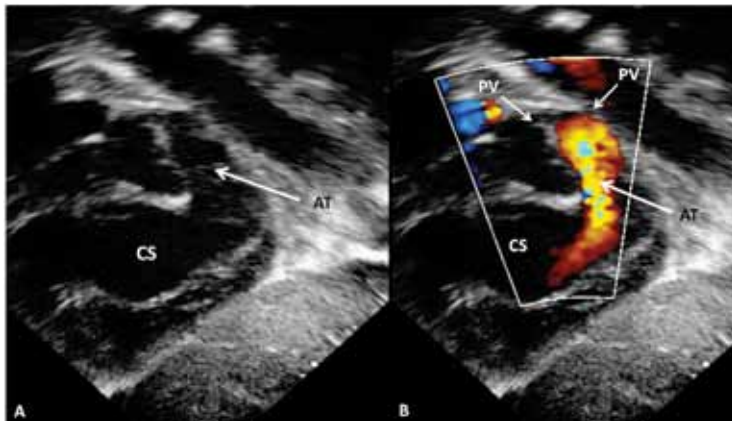


Figure 6. Two-dimensional (A) and color flow mapping (B) images in a baby with total anomalous pulmonary venous connection to coronary sinus (CS) demonstrating dilated CS. An anomalous trunk (AT) connects the pulmonary veins (PV) to the CS.



Figure 7. Continuous wave Doppler recordings from the obstructed anomalous trunks demonstrating high velocities in two different patients with total anomalous pulmonary venous connection, infra-diaphragmatic (A) and supra-diaphragmatic (B).

Examples of TAPVC with connection to infra-diaphragmatic (Figure 4), left innominate (Figure 5) and coronary sinus (Figure 6) sites are shown. Stenosis of the connecting vein can occur and may be demonstrated by imaging actual narrowing, by dilated proximal portion of the connecting vein, by turbulent, continuous and increased Doppler flow velocity (Figure 7) or a combination thereof.

If the ductus arteriosus is patent, right to left shunt across it is usually seen, particularly in patients with obstructed TAPVC; this might partially bypass pulmonary circuit with high pulmonary vascular resistance in the obstructed TAPVC and support the cardiac output.

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Magnetic Resonance Imaging

Because precise anatomic details are often outlined by echocardiographic studies in the neonate, there is little need for MRI in this age group irrespective of pulmonary venous obstruction. When echo-Doppler studies can't, for certain, demonstrate all pulmonary veins,²⁶ particularly when connection to multiple sites (mixed type of TAPVC) is suspected or in patients with poor echo windows, MRI can provide vital anatomic information.



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Cardiac Catheterization

Cardiac catheterization is not usually necessary to confirm the diagnosis in the neonate. However, beyond infancy, it may be indicated in order to measure the pulmonary vascular resistance and study its responses to vasodilators.

Management

The initial management of neonates with TAPVC is similar to that of any cyanotic/distressed infant with suspected serious heart disease and is discussed in depth elsewhere⁴ and will not be detailed here. Maintenance of neutral thermal environment, normal acid-base status, normoglycemia, and normocalcemia should be undertaken by appropriate monitoring and correction as needed.⁴ No more than 0.4 FIO₂ is necessary unless Pulmonary Parenchymal Disease is present. Metabolic acidosis, defined as pH < 7.25 should be corrected with sodium bicarbonate (usually 1-2 mEq/kg diluted half and half with 5% or 10% dextrose solution) immediately. In the presence of respiratory acidosis, appropriate suctioning, intubation and assisted ventilation should be undertaken.

Almost all patients have a large pulmonary venous confluence behind the left atrium. This structure is horizontal in babies with supra-cardiac and cardiac connection and vertical in those with infra-diaphragmatic connection. The surgical repair usually involves making an anastomosis between this pulmonary venous confluence and the posterior wall of the left atrium under cardiopulmonary bypass and/or hypothermia. In TAPVC connected to coronary sinus, surgical excision of the common wall between the coronary sinus and left atrium is performed along with closure of orifice of the coronary sinus and the PFO.

In the obstructive type, initial stabilization by intubation and ventilation with high airway pressure should be initiated. Prostaglandin E₁ (PGE₁) infusion to open the ductus may decompress the pulmonary vascular bed and augment systemic blood flow. In addition, it may open the ductus venosus, thus decreasing pulmonary venous obstruction. This effect is not as certain as with ductus arteriosus and is not reliable. Intravenous infusion of PGE₁ may be started at a dose of 0.05 to 0.1 µg per kilogram of body weight per minute and the rate of infusion is reduced to 0.02 µg per kilogram once the ductus is open. This lower dose has been most helpful in reduc-

ing the incidence and severity of some of the drug's bothersome side effects, namely, apnea and hyperpyrexia. It is important to emphasize, however, that most patients with infra-diaphragmatic type have severe obstruction and the main treatment mode is surgical correction. After initial stabilization, emergent surgical correction by anastomosis of the common pulmonary vein to the left atrium is mandatory. High mortality seen in early years with surgery has decreased over the years.²⁷

In non-obstructive type, elective surgery is recommended after control of cardiac failure is achieved and the patient is stabilized. Congestive heart failure is managed with inotropic support and diuretics. The entire systemic flow must pass through the patent foramen ovale (PFO) and therefore, if the PFO is restrictive, systemic perfusion is significantly reduced. These patients with supra-diaphragmatic type of TAPVC with a restrictive PFO will benefit from a balloon atrial septostomy.^{28,29} Surgical correction involves anastomosis of the common pulmonary vein with the left atrium. Ligation of the connecting vein is routinely performed. Depending on surgical preference, the PFO is usually, but not always, closed.

In the presence of mixed type of TAPVC, a single large posterior pulmonary venous confluence is absent. Therefore, if the patient is stable and without significant pulmonary hypertension or pulmonary venous obstruction then one management option is to follow these patients medically until individual anomalous veins are large enough to be anastomosed to the left atrium.²⁶

Clinical and echocardiographic follow-up is recommended to detect development of pulmonary venous obstruction.

Summary and Conclusions

In TAPVC, all pulmonary veins drain into systemic veins, most commonly they drain into a common pulmonary vein which is then connected to the left innominate vein, superior vena cava, coronary sinus, portal vein or other rare sites. TAPVC is the fifth most common cyanotic CHD and occurs in 0.6 to 1.2 per 10,000 live births. Irrespective of the type, all pulmonary venous blood eventually gets back into right atrium, mixes with systemic venous return, and gets redistributed to the systemic (via patent foramen ovale) and pulmonary (via tricuspid valve) circulations. The TAPVC is classified based on the ana-



Program topics will include management strategies of acute heart failure syndromes, methods of hemodynamic and physiologic monitoring, renal protective techniques, and updates on mechanical circulatory support in children.

When: October 10-12, 2013

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tomic location to which the connecting veins drain, namely, supra-diaphragmatic (supra-cardiac and cardiac) or infra-diaphragmatic and physiologic based on obstruction to the pulmonary venous return, namely, obstructive or non-obstructive. The supra-diaphragmatic forms are generally non-obstructive, and the infra-diaphragmatic forms are almost always obstructive. Connection to the left innominate vein is the most common type of TAPVC. Infra-diaphragmatic type is most common form in the neonate.

The obstructive types present within the first few hours to days of life with signs of severe pulmonary venous congestion and manifest severe tachypnea, tachycardia and cyanosis. Examination reveals rales in the lung fields and a loud pulmonary component of the second heart sound. The non-obstructive TAPVC patients, on the other hand, usually present with symptoms of congestive heart failure later in the first month of life. On examination, they have very mild or no visible cyanosis and may have clinical signs of heart failure. Other findings on examination are similar to those seen in patients with secundum atrial septal defect. Clinical and chest x-ray findings are suggestive of the diagnosis and can be confirmed by echocardiographic studies.

In the obstructive type, initial stabilization by intubation and ventilation with high airway pressure should be undertaken. This is followed by emergent surgical correction by anastomosis of the common pulmonary vein with the left atrium. In the non-obstructive type, control of congestive heart failure and stabilization of the patient, followed by elective or semi-elective surgery is recommended. Follow-up to detect development of pulmonary venous obstruction is recommended.

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The Congenital Heart Intervention Mission Support Project: Aiming To Help Kids With CHD Around The World

By Karim Diab, MD; Damien Kenny, MD

For many years there have been rumblings in the congenital interventional community about consolidating our approach to mission work in developing countries. A significant proportion of interventionalists in developed countries are involved in one way or another in supporting mission trips; however, challenges exist with regard to coordinating these trips, acquiring and transporting equipment, as well as successfully navigating it through erratic border and custom inspection. It is estimated that there are well over one hundred separate charities and missions supporting congenital heart interventions in North America alone, however, these act independently of each other, often confronting similar problems without any exchange of information to rationalize the organizational quagmire experienced by other evolving missions.



Left to right Drs. Damien Kenny and Karim Diab.

These mission trips which usually originate from North America and Europe mainly come as a result of certain personal collaborations with specific programs or hospitals. They represent a very pure desire to help those who are less fortunate than ourselves and exist purely due to the unquestionable commitment of a limited few who are willing to donate so much time. However, there has been a persistent lack of coordination for such missionary work resulting in mission trips organized to similar regions, and limited coordination with various programs in many developing countries that are in need for such help and support. This is largely due to the lack of an infrastructure that allows such programs to have access to mission trips, and of a centralized effort that can help bring support to such missions in terms of providing personnel or equipment needed for such sustainable charitable work. In addition, mission trips have resulted in little or no sustainable improvement of many local programs as they can be limited in their ability to improve the local skills in providing cardiac care or in providing equipment needed for such care.

The potential need is endless. In 2012 at the *PICS-AICS Symposium*, Dr. Bharat Dalvi speaking at a special Round Table Discus-

sion session indicated that in India alone there are an estimated 250,000 children born annually with Congenital Heart Disease (CHD). Eighty thousand of these young patients require some form of surgical or catheter intervention. At present 5,000 children receive the care they need!

As a consequence, the Congenital Heart Intervention Mission Support (CHIMS) project was recently launched at the *Pediatric Interventional Cardiology Symposium*, which took place in Miami in January 2013. The project aims at helping children with CHD who need interventions in developing countries by adopting a new and innovative strategy.

The CHIMS project was conceived to help centralize and consolidate pre-existing charitable mission work. Its main aim is to centralize and distribute donated interventional devices, catheters and other equipment necessary for congenital heart catheterization to be used for mission work in developing countries around the world. As this evolves, the aspiration is to build a registry of mission groups and of congenital heart interventionalists, nurses and technologists involved in such work, as well as a registry of developing programs in need of mission trips in order to provide a platform for both groups to have access to one another. We already have a list of 18 mission trips requesting personnel support! The ultimate goal of the project is to foster appropriate knowledge and technical skills in local physicians and provide them with the equipment needed in order to support development of sustainable self-sufficient interventional programs in developing countries. The organization has no desire or intent to interfere in any way with pre-existing missions and has, as one of its founding tenets, a commitment to ensuring that each mission retains its independence. CHIMS exists to provide support and a platform for sharing personnel, equipment and knowledge.

The team involved at CHIMS is largely a volunteer group of physicians, nurses and technicians who are involved in caring for children with congenital heart disease. This growing group currently includes: name should be followed by a capitalized title ex. Dr. Damien Kenny, Director (and the person who launched the project this past January); Dr. Karim Diab, Executive Secretary; Dr. Andrew Lashus, industry liaison coordinator, Karen Lacono, nursing representative, Kathleen Nolan, technologist representative, and Jane Reich, philanthropic liaison coordinator. The members of the team are committed to working together to make sure this project succeeds.

The concept is straightforward. We are asking all interested catheter laboratories to register and donate surplus inventory. This will be itemized on the website prior to shipping and then, thanks to support from the International

Children's Heart Foundation (ICHF), sent via Fed-Ex to a central warehouse. Charity missions will then have the opportunity to also register and request the donated equipment to be shipped to a location of their choice that may include the country where the mission will take place. CHIMS requests no input or control over any charity mission and fully respects the independence of all established missions. Our organization has already launched a website to support mission trips and developing countries that will list: mission trips, the needs of developing countries, as well as available equipment donations. It can be accessed at www.chimsupport.org. Since its conception, the project has received organizational support through the PICS Foundation, as well as from the International Children's Heart Foundation, the CCISC and *Congenital Cardiology Today*. The launching of the CHIMS project at *PICS 2013* in Miami, included a 5K race sponsored by Siemens in an effort to help support the funding of the project. Almost 100 participants signed up for the run and 80 participated. Dr. Ralf Holzer was the winner! Dr. Ziyad Hijazi announced that this will be an annual event at *PICS* in an effort to continue to help support this initiative and help children with CHD around the globe.

The overwhelming response from the congenital heart community has been one of support. However, our aim is to channel that goodwill into a meaningful effective support service to ensure that the heroic individuals who donate their time and efforts to mission work are able to maximize as much benefit as possible from their work abroad. We hope this project will make a major impact in helping to support mission trips to developing countries and as such help improve the outcome and life quality of children with CHD around the world. You can check out the website, volunteer, donate or request equipment after you register at the website. This endeavor cannot survive without your support, but may flourish with it!

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Do Not Close the Door on Closing the Door!

By Stefan C. Bertog, MD; Laura Vaskelyte, MD; Ilona Hofmann, MD; Marius Hornung, MD; Simon Lam, MD; Sameer Gafoor, MD; Horst Sievert, MD

The foramen ovale, a remnant of the fetal circulation remains patent in approximately 25% of the population based on autopsy and echocardiographic studies.^{1,2} Though population-based longitudinal studies do not support a higher risk of stroke in the presence of a patent foramen ovale (PFO),^{3,4} patients with cryptogenic stroke are more likely to have a PFO (at least 40%) than the general population.⁵ Moreover, passage of thrombus originating from the venous system via a PFO into the systemic circulation is physiologically plausible and has been demonstrated in a number of case reports unequivocally demonstrating paradoxical embolism via an interatrial communication.⁶⁻⁹ Intuitively, anticoagulation, antiplatelet therapy or closure of a PFO should abolish or reduce the risk of stroke from paradoxical embolism. Nevertheless, significant controversy remains as to how a patient should be treated who has experienced a stroke in the absence of an identifiable cause with the exception of a PFO.

For the affected individual, there are four options: no therapy at all, anticoagulation, antiplatelet therapy and surgical or percutaneous closure. Unfortunately, a study that provides us with a definitive answer does not exist.

Let us briefly examine the evidence for either of the available approaches. For the first option, no therapy, we do not know what the risk of a recurrent event is because the natural history (no therapy) of individuals with a PFO and cryptogenic stroke is unknown. Regarding the second and third options, we do not know if either anticoagulant or antiplatelet therapy reduces the rate of recurrent events, as neither has ever been compared with no therapy in a randomized controlled trial. Likewise, we do not have any conclusive evidence to support anticoagulant therapy over antiplatelet therapy or vice versa. Finally, percutaneous or surgical closure has never been compared to no therapy in a randomized controlled fashion. To conclude, in the absence of a randomized controlled trial comparing therapy to no therapy, we do not know if any therapy is better than no therapy. Does this imply that our response to the individual with a cryptogenic stroke and PFO should be that no therapy is required?

If we believe that a patient who has experienced a cryptogenic stroke in the absence of a PFO should be treated with antiplatelet therapy because the most likely mechanism of the event (with the exception of the rare pure atherosclerotic debris, fat, tumor or air embolism) is platelet aggregation and throm-

“To conclude, in the absence of a randomized controlled trial comparing therapy to no therapy, we do not know if any therapy is better than no therapy. Does this imply that our response to the individual with a cryptogenic stroke and PFO should be that no therapy is required?”

bus formation with or without embolization, then we should, likewise, favor antiplatelet therapy for the patient in question because these mechanisms may also be present in patients with cryptogenic stroke *in the presence of a PFO*. The data in support of this approach stems from trials in patients with strokes regardless of mechanism who benefit from aspirin administration. Hence at least an aspirin should be recommended. However, some would argue that, in patients with cryptogenic stroke and PFO, aspirin might not be sufficient because it does not provide adequate protection against thrombus formation in the venous circulation and paradoxical embolization via a PFO. On a theoretical basis, only PFO closure or anticoagulation may have merit in preventing venous thrombus and paradoxical embolism. No dedicated randomized trials comparing aspirin and anticoagulation with warfarin in patients with PFO and cryptogenic stroke exist. Available data stems from subgroup analysis of patients with PFO in stroke trials comparing aspirin and warfarin. Though there was a trend favoring warfarin over aspirin, this was not statistically significant.^{10,11} However, the trials were underpowered to detect a difference. Hence, in the absence of more convincing data, there is no conclusive evidence to favor warfarin over aspirin for the prevention of recurrent events in patients with PFO and cryptogenic stroke. How about PFO closure? There are non-randomized studies comparing percutaneous PFO closure to medical therapy suggesting a lower stroke recurrence rate after closure,^{12,13} and there is surgical data that suggests a very low rate of event recurrence after surgical PFO closure.^{14,15} More importantly, there are now three trials comparing percutaneous PFO closure to medical therapy, CLOSURE 1 (Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack Due to Presumed Paradoxical Embolism through a Patent Foramen Ovale),¹⁶ PC

sure of the Patent Foramen Ovale Using the Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism)¹⁷ and RESPECT (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment)¹ in patients with cryptogenic stroke and PFO.

In CLOSURE 1, patients were randomized to closure with the STARFlex device (NMT Medical) and in PC and RESPECT to closure with the Amplatzer PFO occluder (St. Jude Medical) versus medical therapy. In CLOSURE 1, nine hundred and nine patients (mean age 45 years) were enrolled. After 2 years, though the rate of the primary event (stroke, transient ischemic attack and 30-day all cause and 30-day to 2 year neurologic mortality) and rate of recurrent strokes were numerically lower in patients who underwent PFO closure, the difference was not statistically significant.¹⁶

Three important aspects regarding CLOSURE 1 are worth mentioning. First, the closure rates were lower with the STARFlex device (no or minimal residual shunt: 86%) than with the Amplatzer PFO occluder in both PC (96%) and RESPECT (94%). Second, the follow-up was limited to 2 years. Third, the rates of thrombus formation and atrial fibrillation appear to be higher after STARFlex implantation than after implantation of the most commonly used Amplatzer devices.¹⁸ This may reduce or (in the case of device associated thrombus or atrial fibrillation) offset the potential benefits of PFO closure. In PC, 414 patients (mean age 44-45 years) were enrolled. After a mean of 4 years of follow-up, there was no difference in the primary endpoint (composite of death, nonfatal stroke, transient ischemic attack or peripheral embolism) in an intention-to-treat analysis.¹⁷ However, there was a trend toward a lower rate of strokes (0.5% versus 2.4%) in patients treated with PFO closure ($p=0.13$) by the definition used in the trial and a strong trend towards a reduction in stroke risk based on the definition used in RESPECT ($p=0.07$). Nine-hundred and eighty patients (mean age 46 years) were enrolled in RESPECT.¹ Once again, there was a strong trend towards a reduction in stroke recurrence in patients treated with PFO closure compared to those treated medically (after a mean follow-up time of approximately 2 years) in an intention-to-treat analysis. In addition, there was a significant reduction in stroke recurrence in an as-treated analysis ($p=0.007$). Though this type of analysis may be confounded by non-random factors leading to deviation from the treatment protocol, it is worth mentioning that among the nine patients who experienced a recurrent stroke assigned to the device group, three had not undergone device closure, one of whom had a stroke

JUNE MEETING FOCUS

CSI 2013 and iCI 2013

Frankfurt am Main, Germany

June 26, 2013 (ICI 2013); June 27-29, 2013 (CSI 2013)

www.csi-congress.org or www.ici-congress.org

CSI Course Director: Horst Sievert, MD; CardioVascular Center Frankfurt (Germany)

CSI Co-Course Directors: Mario Carminati, MD; Instituto Policlinio San Donato (Italy); Ilona Hofman, MD; CardioVascular Center Frankfurt (Germany); Shakeel A Qureshi, MD; Evelina Children's Hospital (UK); Neil Wilson, MD; John Radcliffe Hospital (UK);

For the 16th time, **CSI 2013, the annual international Congress on Congenital and Structural Interventions of the Heart**, will take place from June 27th to 29th 2013 in Frankfurt am Main, Germany, with **ICI 2013, the Imaging in Cardiovascular Interventions** meeting taking place one day before on June 26th.

Starting in 1996 as a small one-day workshop on catheter closure of congenital shunts with 77 attendees, the **CSI Congress** has now become an established event for interventional adult and pediatric cardiologists, radiologists, cardiovascular surgeons, catheter laboratory nurses and technicians from all over the world. Over time, the variety of topics grew and, today, our attendees share their experience with procedural techniques, devices and latest technologies in all areas of interventional cardiology. From day one, CSI focused on the transmission of LIVE cases from cath labs around the world, including: CardioVascular Center Frankfurt, Instituto Policlinio San Donato, Sri Jayadeva Institute of Cardiology and Cedars-Sinai Medical Center. With more than 800 participants in 2012, the **CSI Congress** serves as a growing, but still familiar gathering.

In keeping with our tradition, transmission of LIVE cases from various cath labs will continue to be the main focus. Allowing experienced interventionalists, as well as beginners, to profit from the "see one, do one, teach one" concept, **CSI** offers a mixture of complex challenging as well as routine procedures. Every participant at the **Congress** center has the opportunity to directly interact with the interventionalist in the cath lab, assuring that questions directly related to the procedure are answered under real-time conditions. In addition, comprehensive lectures by leading interventionalists allow participants to keep up-to-date on specific topics of interest. Particularly, discussion of controversial topics is fostered. Due to the flexible concept of LIVE transmissions and scientific lectures, attention is directed to every step of the procedure from scientific background, patient selection, planning and execution to postprocedural care.

This year's **CSI** is again accompanied by Imaging in **Cardiovascular Interventions (iCi 2013)**, taking place one day before the CSI conference on June 26th. The main focus of iCi is the introduction and demonstration of new imaging methods and modalities. Main focus is the discussion of the utility of existing and novel imaging techniques in diagnosing congenital and structural heart disease and its application to optimize patient selection. Procedural strategy and choice and sizing of interventional equipment will be discussed in detail. In addition, new imaging methods and modalities (for example 3D-ICE or Echo-Fluoro-Overlay) will be introduced and demonstrated. During iCi, LIVE demonstrations will take place and simulator training will be available.

after enrollment but before scheduled device implantation. The second patient, after treatment assignment, decided not to proceed with device implantation. The third patient underwent bypass surgery and surgical PFO closure after assignment to the device group but prior to planned implantation. Importantly, in subgroup analyses, there was a significant reduction in the primary endpoint in favor of PFO closure (compared with medical therapy only) in patients with an interatrial septal aneurysm or large right-to-left shunt.

Particularly the stronger treatment effect with a larger shunt size is in line with the observed higher event rate in patients with cryptogenic strokes and large shunts,^{19,20} both of which support the notion that PFO's promote strokes via paradoxical embolism and the rationale of its closure. In addition, there was a strong trend toward a reduction in the primary endpoint in patients whose index infarct had been located more superficially favoring an embolic etiology.

The event rates continued to separate further in favor of closure with time. For example, the stroke rates were 1.3%, 1.6% and 2.2% in the closure group and 1.7%, 3.0% and 6.4% in the medically treated group after one, two and five years, respectively. Though the absolute difference in event rates is small, the relative difference at 5 years is 65%. Assuming that the difference between the treatment arms is a true difference and not a result of chance, in young patients this may translate into a large number of strokes prevented. In addition, no device erosion or thrombus formation directly related to the device occurred in either the PC or RESPECT trial supporting the safety of closure with the Amplatzer PFO occluder.

If one focuses on strictly predefined intention-to-treat findings of these trials and allows only results with a p-value of <0.05 to be meaningful, discounts subgroup and as-treated analyses and ignores potential differences among PFO devices, withholding PFO closure from patients with a cryptogenic stroke may be the logical consequence. However, based on above described data, it appears more reasonable to conclude that the risk of harm due to device closure (i.e. device associated thrombus formation and device erosion) is very low. Further, there may be a benefit of closure compared with medical therapy particularly in certain patient subgroups. Therefore, though PFO closure in an unselected population is not appropriate, categorically closing the door to PFO closure is equally inappropriate. For example, mandating no therapy or aspirin therapy only in a young individual with a cryptogenic stroke, PFO with a large interatrial shunt or atrial septal aneurysm and superficial infarct seen on brain imaging seems to be premature. Rather, careful patient selection and a fair discussion with the patient outlining the therapeutic options, risks and limitations to current knowledge, but ultimately respecting the patient's decision seem to be most appropriate.

In this context, we would like to draw attention to our upcoming **ICI/CSI Conference** in Frankfurt Germany this June, where topics such as the above and many others related to congenital and structural heart disease will be discussed at length by experts in the respective subjects. For more information visit: www.ici-congress.org and www.csi-congress.org.

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Medical News, Products and Information

Drug-Resistant MRSA Bacteria -- Here to Stay in Both Hospital and Community

The drug-resistant bacteria known as MRSA, once confined to hospitals but now widespread in communities, will likely continue to exist in both settings as separate strains, according to a new study.

The prediction that both strains will coexist is reassuring because previous projections indicated that the more invasive and fast-growing community strains would overtake and eliminate hospital strains, possibly posing a threat to public health.

Researchers at Princeton University used mathematical models to explore what will happen to community and hospital MRSA strains, which differ genetically. Originally MRSA, which is short for methicillin-resistant *Staphylococcus aureus*, was confined to hospitals. However, community-associated strains emerged in the past decade and can spread widely from person to person in schools, athletic facilities and homes.

Both community and hospital strains cause diseases ranging from skin and soft-tissue infections to pneumonia and septicemia. Hospital MRSA is resistant to numerous antibiotics and is very difficult to treat, while community MRSA is resistant to fewer antibiotics.

The new study found that these differences in antibiotic resistance, combined with more aggressive antibiotic usage patterns in hospitals versus the community setting, over time will permit hospital strains to survive despite the competition from community strains. Hospital-based antibiotic usage is likely to successfully treat patients infected with community strains, preventing the newcomer strains from spreading to new patients and gaining the foothold they need to out-compete the hospital strains.

The researchers made their predictions by using mathematical models of MRSA transmission that take into account data on drug-usage, resistance profiles, person-to-person contact, and patient age.

Published February 28th in the journal *PLOS Pathogens*, the study was conducted by postdoctoral researcher Roger Kouyos, now a scholar at the University of Zurich, and Eli

Klein, a graduate student who is now an assistant professor in the Johns Hopkins School of Medicine. They conducted the work under the advisement of Bryan Grenfell, Princeton's Kathryn Briger and Sarah Fenton, Professor of Ecology and Evolutionary Biology and Public Affairs at Princeton's Woodrow Wilson School of International and Public Affairs.

RK was supported by the Swiss National Science Foundation (Grants PA00P3_131498 and PZ00P3_142411). EK was supported by Princeton University (Harold W. Dodds Fellowship), as well as the Models of Infectious Disease Agent Study (MIDAS), under Award Number U01GM070708 from the National Institutes of General Medical Sciences. BG was supported by the Bill and Melinda Gates Foundation; the Research and Policy for Infectious Disease Dynamics (RAPIDD) program of the Science and Technology Directorate, Department of Homeland Security; and the Fogarty International Center, National Institutes of Health.

Sudden Death in Young Athletes: Important Causes Not Identified by the Screening Process

Even though young athletes are required to receive health screens to be cleared to play sports, those tests failed to detect important cardiovascular abnormalities in cleared players, and many were allowed to play despite suspicions of dangerous cardiovascular conditions, according to a large registry study of patients who died from sudden death. The study results were presented on March 10th by Kevin Harris, MD, Research Cardiologist at the Minneapolis Heart Institute Foundation (MHIF) at the annual *American College of Cardiology Scientific Sessions* in San Francisco.

Aortic stenosis, which occurs when the aortic heart valve does not fully open, is considered a rare, but important, cause of death in young people. Aortic dissection and rupture which occur when the aortic wall tears and ruptures respectively are catastrophic conditions that are not usually associated with the death of younger individuals. However, the role of these very serious conditions is not understood as causes of athletic field deaths, and their identification is often missed during routine pre-participation screening.

"While the majority of these young athletes are being screened, there is unfortunately great variability in the screening process, and we have had very sparse data on the effectiveness of these screening efforts," explains Harris, who is also Co-Director of the Echocardiography Laboratory at the Minneapolis Heart Institute® at Abbott Northwestern Hospital in Minneapolis.

The American Heart Association has recommended specific historical questions and physical examination components which should comprise pre-participation cardiac screening.

For this study, MHIF researchers analyzed the US National Registry of Sudden Death in Young Athletes for occurrences of sudden death due to aortic disease (including dissection, rupture or coarctation) and aortic stenosis.

Of the 2,588 deaths in the registry, 44 events were related to aortic stenosis (19) or aortic disease (25). On average, this group of athletes was 17.6 years old, and 40 were males. The most prominent sports represented in this group were football and basketball, followed baseball and softball.

Eighteen of the 19 deaths related to aortic stenosis occurred just after exercise, reported Harris. Also, 16 deaths attributed to aortic disease occurred during exercise, 6 occurred during sedentary activity, and 2 during sleep.

Data on pre-participation screening were available for 34 of the 44 athletes. Of the 34 deaths, 15 young athletes had been assessed specifically by cardiologists, 3 of the athletes had a known aortic abnormality and 8 had previously been diagnosed with aortic stenosis or bicuspid aortic valves—the latter of which occurs when an aortic valve only has two leaflets instead of three.

Based on their findings, the researchers concluded that aortic stenosis and aortic diseases are uncommon, but important, causes of sudden death among young, competitive athletes, usually while playing basketball or football.

Twenty-five percent of the athletes (11 of 44) complained of symptoms of chest, back or abdominal pain in days prior to collapse. Three of the 11 had been seen in the emer-

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gency room. Two of the 11 had seen a cardiologist the day prior to death.

"We were able to identify the majority of the athletes in this study had been cleared to participate in sports and one-third had been evaluated by a cardiologist," Harris reports. "The widespread screening process failed to detect important cardiovascular abnormalities in 19 of the deaths. In the remaining 15 cases, suspicion of cardiovascular conditions was raised, but the athletes were allowed to continue to compete in competitive sports."

Shalom Jacobovitz Named CEO of American College of Cardiology

The American College of Cardiology Board of Trustees announced in April that Shalom "Shal" Jacobovitz has been selected as the college's Chief Executive Officer.

"Shal has a track record that demonstrates he is the right person to lead a strong organization like the ACC and to take it to the next level at a time when health care is undergoing massive changes," said ACC President John Gordon Harold, MD, MACC. "He is an innovative and proven leader as well as a successful mentor and team builder. Shal brings a unique perspective at a time when the College is ramping up to meet the evolving needs of cardiovascular professionals domestically and around the globe."

Jacobovitz comes to the ACC from Actelion Pharmaceuticals US, a biopharmaceutical company specializing in cardio-pulmonary therapies, where he has served as president since 2004. At Actelion, Jacobovitz developed a strong patient- and customer-centered corporate strategy, which he implemented globally.

"This is an exciting time for the College," said former ACC President William Zoghbi, MD, MACC, who led the CEO Search Committee. "Shal comes to the ACC with more than 25 years in health care, including extensive international and domestic experience. He shares the College's commitment to quality, innovation and strategic management, and we are confident he will advance the ACC's mission to transform cardiovascular care and improve heart health."

Prior to Actelion, Jacobovitz held positions at F. Hoffmann La Roche, where he served as general manager for Central America and the Caribbean, led the Pharmaceutical, OTC and Diagnostic divisions, and served as the global



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Cardiac Imager.

We seek an experienced academic cardiac imager to join our team of 6 dedicated imagers. Candidates must be board-certified in Pediatric Cardiology and ideally have greater than 3 years experience working as an imager in a tertiary heart center. Skills should include transthoracic, transesophageal and fetal echocardiography. Interest and experience in cardiac MRI and/or CT angiography is preferred. Candidates should be academicians with demonstrated research productivity.

Inpatient Cardiologist

Candidates should be prepared to lead a team that includes support from advanced practice nurses and fellows. Candidates would be expected to provide consultative expertise to the care of pre- and post-operative patients in the NICU and PICU. Interest / experience in other aspects of cardiology such as imaging, non invasive electrophysiology and outpatient cardiology is welcome. This position will offer the opportunity to develop research programs pertaining to outcomes, clinical pharmacology and genomics.

We serve a population of over 5 million in the heart of the U.S.A, through our main campus and several additional locations in and around Kansas City, extending to Western Missouri and the state of Kansas. Our team includes 15 (expanding to 20 this year) cardiologists, 2 surgeons, and 17 Advance Practice Nurses. We perform over 400 cardiac operations, 400 hemodynamic / interventional catheterizations and over 130 EP catheterizations, 12,000 outpatient visits, 14,000 echocardiograms and 20,000 EKG's annually. Our preoperative and postoperative ICUs include a 70-bed NICU and a 41-bed PICU (with a new 14-bed Cardiac Wing). The recently inaugurated Elizabeth Ferrell Fetal Health center provides our free-standing Children's Hospital the facility for in-house births of high-risk babies. There is a wealth of opportunity to develop and participate in research programs, quality improvement projects and data collection in many areas related to heart care in children. Our planned integration with the University of Kansas provides the impetus for comprehensive, seamless care and programmatic growth.

Candidates should be qualified for academic appointment at the rank of Assistant or Associate Professor. Salary and academic rank are commensurate with experience. EOE/AAP

For additional information contact:

Girish Shirali, MD (gsshirali@cmh.edu)

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lifecycle leader for cardiovascular products in Basel, Switzerland. He also held positions with Abbott Canada, Nordic Labs and Marion Merrell Dow (now known as Aventis) in Canada. Jacobovitz earned his Bachelor of Science Degree in Biology at the University of Western Ontario in Canada.

"It is a privilege for me to join the ACC," Jacobovitz said. "The College is a thriving medical professional society that is well positioned to be at the center of rapid changes in health care. I look forward to working with the ACC's dedicated professional staff and member leaders to build on the College's legacy of leadership in quality improvement, patient-centered care, clinical education and practice excellence."

Jacobovitz was chosen as CEO following a year-long nationwide search led by the executive search firm, Korn/Ferry International. He will assume the role beginning in May. During the search period, Tom Arend, COO and General Counsel served as Interim Chief Staff Officer.

For more information, visit cardiosource.org/ACC.

Physicians Interactive Introduces Omnio - A Customized, Comprehensive iPad App for Medical Professionals

Physicians Interactive (PI), a leading provider of online and mobile clinical resources and solutions for healthcare professionals, announced in March the launch of Omnio, a versatile, new app that invigorates the medical app market by unleashing the power of the iPad in a personalized point-of care tool.

The free Omnio app is available for download in the App Store: <https://itunes.apple.com/us/app/omnio/id545775601?mt=8>.

From the point of download, Omnio connects clinicians to comprehensive drug and disease references and calculators that are essential in their specialty. Omnio is easy to expand, connecting users to a worldwide medical marketplace of trusted publishers, allowing them to further customize Omnio into the optimal point-of-care companion.

Since its mid-December debut in the App Store, word of mouth and social referral among medical professionals have driven Omnio to top the charts of free medical apps in the App Store, bolstered by a stellar rating near 5 stars.

"With more than 31 million new entrants coming into the American healthcare system under healthcare reform, clinicians have a pressing need for tools to simplify their workflow," said Physician Interactive's CEO and Vice Chairman Donato Tramuto. "Yet, only 5% of medical professionals are satisfied with current medical apps (July 2012 WorldOne Research Survey). Omnio changes everything, allowing clinicians one-tap access to their favorite mobile tools and serving all the diverse roles clinicians now play. We chose the name Omnio because this app will become the omnipresent clinical assistant for the emerging healthcare workflow."

Omnio is designed to be the modern-day digital black bag for clinicians to keep all their most important "must haves" just a tap away on their iPads. The app was developed with extensive user research to ensure it met the needs of medical professionals who have been frustrated with the limitations of other medical apps.



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HOW WE OPERATE

The team involved at C.H.I.M.S. is largely a volunteering group of physicians nurses and technicians who are involved in caring for children with congenital heart disease.

The concept is straightforward. We are asking all interested catheter laboratories to register and donate surplus inventory which we will ship to help support CHD mission trips to developing countries.

The research found that hundreds of apps designed for clinicians on the market today were too overwhelming to manage separately. They often focused on just one function, did not allow clinicians to customize the app for their specialties, and too often failed to provide the relevant information and resources clinicians needed at the point-of-care.

"Clinicians don't have time to scroll through five screens of medical apps to find the one tool they need," said Physician Interactive's Chief Medical Officer and Senior VP of Product Management Gautam Gulati, MD, MBA, MPH. "We provide those core tools, for each specialty, then apply the latest design and technology to make it easy to add, swap, drag and drop to customize Omnio into their optimal point-of-care resource. Clinicians are coming to Omnio to get the latest news in their field, check drug dosing and interactions, review evidence-based guidelines, and perform calculations at the point-of-care. We make it quick and easy for them to access the tools they need."

Omnio's free content includes: drug look-up, dosing recommendations, medical calculators, drug interaction, formulary information, disease reference materials, curated specialty news feeds, and much more with ongoing releases of new updates. All the offerings are personalized by profession and specialty to identify the most relevant resources from publishers, peers in healthcare, and professional associations. Clinicians can bookmark and tag these key resources—which can range from books to medical calculators to entire Web sites—so they are just one tap away on the iPad. With Omnio, clinicians can spend less time looking for information and more time practicing medicine.

"I can use Omnio on my iPad every day to answer questions specific to my branch of cardiology," said Jordan Safirstein, MD, FACC, FSCAI, RPVI, who specializes in cardiac and peripheral vascular intervention. "It is personalized information chosen by me that is always accessible on my iPad. This type of functionality is part of the appeal of the iPad—so it's great to finally have this in a medical app."

For more information - visit www.omnio.com.

Carnitine Supplement May Improve Survival Rates of Children with Heart Defects

A common nutritional supplement may be part of the magic in improving the survival rates of babies born with heart defects, researchers report.

Carnitine, a compound that helps transport fat inside the cell powerhouse, where it can be used for energy production, is currently used for purposes ranging from weight loss to chest pain.

New research shows it appears to normalize the blood vessel dysfunction that can accompany congenital heart defects and linger even after corrective surgery, said Dr. Stephen M. Black, cell and molecular physiologist at the Vascular Biology Center at the Medical College of Georgia at Georgia Regents University.

"My hope is this is going to have a major, major impact on survival of babies," Black said. About half the babies born with heart defects have excessive, continuous high pressure on their lungs from misdirected blood flow. Early surgery can prevent full-blown pulmonary vascular disease, but scientists are finding more subtle disruptions in the signaling inside blood vessels walls that can be problematic – even deadly – up to 72 hours after surgery.

The good news is the changes are reversible and that carnitine speeds recovery and can even prevent the damage in a lamb model of these human heart defects, according to studies published in the *Journal Pediatric Research*.

Normally, most blood flow bypasses the lungs in utero when the placenta provides blood and oxygen for the baby. Baby's first breaths naturally expand the lungs and blood vessels, activating a process inside the lining of vessels that enables them to accommodate the initial blood surge, then reduce pressure quickly, dramatically and permanently.

This natural transition doesn't occur when heart defects misdirect blood flow. "It's kind of like a chronic fetal-to-newborn transition," said Black, the study's corresponding author. Lungs get pounded with about three times the normal flow and, even when surgeries are done as early as possible to repair the defect, correct blood flow and protect the lungs, the 20% death rates from acute pulmonary hypertension have remained unchanged for a decade. "That's 1 in 5 kid (with this condition)," Black said.

Left unchecked, the barrage thickens blood vessels, making them unresponsive, much like those of an elderly individual who has lived for years with uncontrolled high blood pressure. The comparatively brief periods of pounding these babies experience impairs the ability of the endothelial cells, which line



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blood vessels, to produce nitric oxide, a major dilator of blood vessels.

The shear force disrupts carnitine homeostasis, weakens the mitochondria and impairs nitric oxide production. To make bad matters worse, the precursor to nitric oxide instead makes more peroxynitrite, prompting endothelial cells to grow and thickening blood vessels. Black was also corresponding author of a recent study in the *Journal of Biological Chemistry* that showed peroxynitrite does this by turning on the cell survival protein kinase Akt1.

The new study indicates that even without fixing the heart defect, high daily doses of carnitine in the first four weeks of life can prevent endothelial dysfunction. In fact, the laboratory lambs' ability to make nitric oxide is preserved even without the benefit of heart surgery and the responses to the chemical activity that enables blood vessel dilation is normalized, Black said.

Study co-author Dr. Jeffrey Fineman, a whole-animal physiologist and physician at the University of California, San Francisco, developed the model, a lamb whose four-chambered heart is very similar to humans. In utero surgery that misdirects too much blood to the lungs, means that, like children, the lambs are born with the defect.

Black is now working with Fineman, who is pursuing additional funding to resolve questions such as the optimal dosage and timing for giving carnitine. The researchers also plan to examine carnitine homeostasis in the blood of children with heart defects to see if it's disrupted. If it is, they plan to start clinical trials.

The research was funded by the National Institutes of Health, the Foundation Leducq and the American Heart Association.

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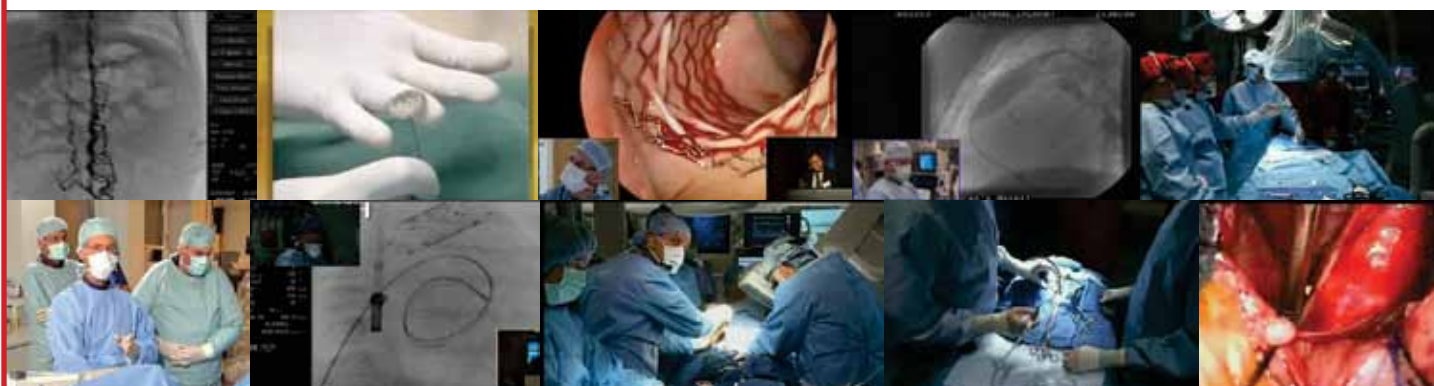
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