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Hematological Complications of Cyanotic Congenital Heart Disease: Profile of Unoperated Sudanese Children

By Samia H. Osman, MD; Abdullgadir E Ali, SSMB

Abstract

Introduction

Children with cyanotic heart disease have deficient oxygen transport to tissues that might be complicated by polycythaemia with the potential risk of brain injury and abnormal haemostatic mechanisms: thrombosis or bleeding diathesis.

Patients and methods

A descriptive cross-sectional hospital based study from February 2010 to August 2010 was conducted at Gafaar Ibn Auf specialized hospital. Measurements of complete blood count, INR, bleeding time and serum ferritin was obtained from children with CCHD and correlated to their clinical and echocardiographic data.

Results

Thirty-one patients were seen during the study, 19 were males and 12 were females. The complications were: iron deficiency in two-thirds of the cases, polycythaemia in half of the cases, low serum ferritin and prolonged INR in one third of the cases. Thrombocytopenia and prolonged

bleeding time was detected in 12% of the cases. Significant correlation between polycythemia and the oxygen saturation was detected ($p=0.03$). No significant correlation was found between the prolonged INR and the age, duration of CCHD since diagnosis, type of CCHD and the oxygen saturation.

Conclusion

Polycythaemia was common in our cases, but a thromboembolic phenomenon was not detected. Iron deficiency should be looked for carefully even in the presence of polycythaemia. Coagulation screening for children with CCHD is crucial especially before surgery. In developing countries where surgical intervention is limited due to technical and financial constraints, hematological status needs to be assessed carefully to minimize serious disabling complications.

Preface

Hematologic complications associated with cyanotic congenital heart diseases (CCHD) mainly in unoperated children needs specific attention. In the presence of hypoxemia, adaptive mechanisms to increase the oxygen delivery, like an increase in oxygen content and rightward shift in the oxyhemoglobin dissociation curve occur. Oxygen delivery is enhanced at the cost of a higher hematocrit; as erythropoietin production is stimulated so polycythaemia may result with

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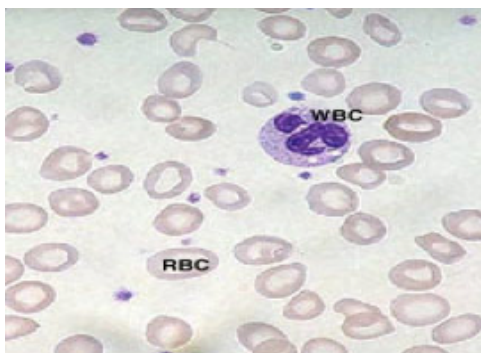
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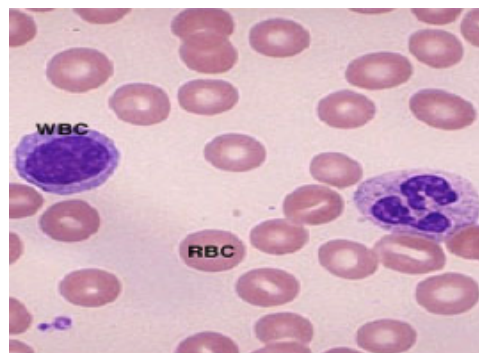
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Type of complications	No. of Patients	Percentage
Polycythaemia	16	51.6
Iron deficiency anaemia	21	67.7
Low serum ferritin	11	35.5
Thrombocytopenia	4	12.9
Prolonged bleeding time	4	12.9
Prolonged INR	11	35.5

Age group	No. of Patients	Percentage
< 1 month	1	4%
< 1 year	3	14%
1-2 years	2	9%
2-5 years	12	58%
> 5 years	3	15%
Total	21	100%



Iron Deficiency Anemia



Normal Blood Smear

Figure 1. Peripheral blood picture of a child with complex cyanotic heart disease and iron deficiency anemia (on the right). RBCs shows microcytosis and hypochromia compared with the normal blood smear to the left.

possible, hyperviscosity and associated iron deficiency (ID). These elevated hematocrit levels and abnormal iron deficient cells increase the risk of thromboembolic phenomena and brain injury.^{1,2}

It has been recognized for decades that patients with CCHD show a significant thrombotic tendency, as well as bleeding tendency; hemorrhagic diathesis is attributed to various haemostatic defects, including

thrombocytopenia, shortened platelet life-time and suppressed platelet aggregation. Deficiency of clotting factors, such as factors II, V, VII, X and von Willebrand factor is also described.¹

Methods

A descriptive cross-sectional hospital-based study was conducted from February 2010 to August 2010 in Gafaar Ibn Auf Specialized Hospital for Children, which is the major central

referral hospital in Khartoum. All children with CCHD proofed by echocardiography from birth to 18 years were included in this study. Patients with a disease which may affect the hematological findings like--chronic liver disease, haemophilia A or B, von Willebrand, haemolytic anemia and malnutrition due to other chronic illness rather than CCHD--were excluded.

Informed consent was obtained, then a questionnaire was completed including demographic details, clinical, hematological and echocardiography data. Measurements of complete blood count, INR, bleeding time and serum ferritin was obtained.

For the CBC: Sysmex analysis automation was used, blood was taken and EDTA was used as an anticoagulant for the sample. Polycythemia was considered present if Hb is > 18 gm/dl and platelet was considered low if < 150,000/cmm.

PT & INR: Trisodium citrate was used as anti-coagulant, the reagent used was Diaplastin, and INR was considered high if it was > 1.5.

Bleeding time: BT was measured by the Duke method, and considered high if it was > 4 minutes.

Serum ferritin level: The serum ferritin was measured by the direct sandwich ELISA method. The sample was taken in lithium heparin-tube, done in automated Biosystem machine, and was considered to be low if < 15 µg/L.

Echocardiography

Echocardiography was performed using Esaote My Lab 30 echocardiograph equipped with 2.5–5.0 MHz transducer.

Results

Thirty-one patients were enrolled in this study: 19 were males and 12 were females; five patients were infants, five were between 1-2 years; 13 between 2-5 years, four between 5-10 years; and 4 were more than 10 years.

Table 1 shows the complications: iron deficiency was found in two-thirds of the cases; polycythaemia was found in half of the cases. One third of the cases had low serum ferritin and prolonged INR. Thrombocytopenia and prolonged bleeding time was detected in 12% of the cases.



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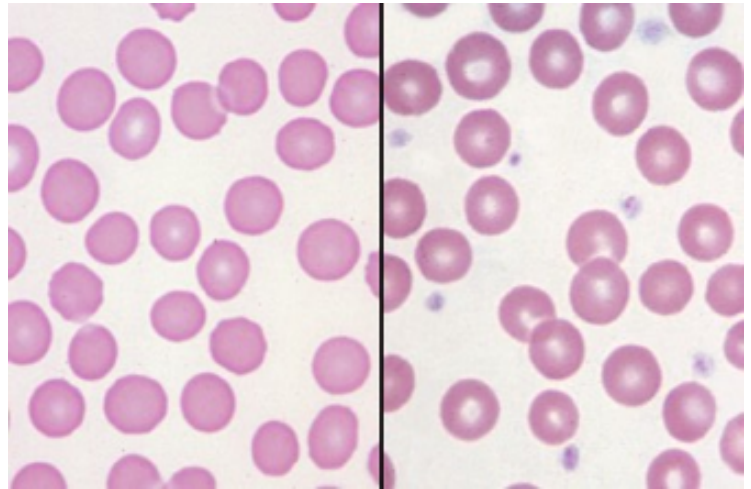


Figure 2. Shows peripheral blood smear of a patient with thrombocytopenia, to the right platelets (smaller blue stained cells with faint granules in the centre) were severely reduced compared with normal platelets to the left.

Table 2 shows iron deficiency according to age group in 21 patients with cyanotic congenital heart diseases. It was found mainly in the age group 2-5 years; 12 cases in this age group were found accounting for 58% of the total sample size.

Figure 1 shows peripheral blood picture of a child with complex cyanotic heart disease and iron deficiency anemia (on the right). RBCs show microcytosis and hypochromia compared with the normal blood smear to the left.

Significant correlation between polycythemia and the oxygen saturation was detected ($p=0.03$). The polycythemia was not correlated to either the specific age groups or the type of CCHD. The P Values were 0.38 and 0.320 respectively. Also, iron deficiency anemia was not correlated to either the specific age groups or the type of the CCHD. The P Values were 0.13 and 0.62 respectively.

Thrombocytopenia was found in four cases; all of them had complex CCHD and their oxygen saturation was less than 85%.

No significant correlation was found between the prolonged INR and the age, duration of CCHD since diagnosis, type of CCHD and the oxygen saturation. The P Values were: 0.056, 0.179, 0.744 and 0.635 respectively.

Figure 2 shows a comparison between normal platelets and those from a peripheral blood smear of a patient with thrombocytopenia. The slide on the right shows the platelets (smaller blue stained cells with faint granules in the centre) were severely reduced compared with normal platelets to the left.

Discussion

Polycythemia was found in almost half of the cases. It was inversely proportionate to the oxygen saturation in the cases ($p= 0.03$). Two-thirds



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of the cases (67.7%) had features of iron deficiency anemia confirmed by the presence of microcytic hypochromic RBCs in the peripheral blood picture and low serum ferritin level. This results in an increase in whole blood viscosity combined with Iron deficient red cells which are known to be relatively rigid microcytes with impaired deformability and thus increase the tendency to thrombosis.¹ However, thrombo-embolic complications were not detected in our cases. In one German study neurological complications were present in 12.7% of patients, indicating severe symptomatic polycythemia.² Many studies found that both polycythemia and iron deficiency were associated with increased risk of neurological complications.^{3,4,5} Also, the association of ID with concomitant extremely high red blood cells was reported with hematocrit of 80%.⁶ The absence of the neurological complications in our cases might be due to that the deeply cyanosed children with complex lesions in developing countries die before they develop the complications or because the number of patients included in this study was small.

Ninety percent of the cases with ID were between 2-5 years. Iron deficiency is described in patients with cyanotic heart disease despite the high hematocrit.^{7,8,9} This might be attributed to a co-nutritional factor in such a developing country or repeated phlebotomy in cases of symptomatic polycythemia. Similar results were described in many countries.^{7,10}

Prolonged INR was found in 11 (35.5%) of the cases; lower levels of procoagulant and anticoagulant factors, especially factors II, V, VII, and X; protein C, and antithrombin III is a known problem with CCHD.^{11,12,13} We only screened for the INR. Individual coagulation factor assays might be more specific and essential, especially for patients planned for surgery.

Thrombocytopenia was found in 4 cases; all of them had complex CCHD. One patient also had platelet dysfunction. It has been recognized for decades that patients with CCHD show a significant bleeding tendency¹⁴ despite their susceptibility to thrombosis. This hemorrhagic diathesis is attributed to various hemostatic defects such as: thrombocytopenia,^{14,15} shortened platelet life-time,¹⁵ suppressed platelet aggregation, and an increase in peripheral destruction of platelet. Platelet-derived microparticles (MPs) were also identified as a sensitive variable of platelet activation, probably triggered by high shear stress due to hyperviscosity and polycythemia.^{16,17,18} This was described by many authors in cases of CCHD and Eisenmenger Syndrome.^{19, 20, 21}

We conclude that hematological status should be assessed carefully in patients with cyanotic heart diseases especially in developing countries where surgical intervention is limited due to technical and financial constraints so as to guard against serious disabling complications which might be preventable if abnormalities were identified early and proper actions performed.

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Cloud-based Medical Information Exchange: Seamless Technology for Sharing Medical Files

By G. Paul Matherne, MD

One of the most promising technological developments to ease medical workflow is now in use at hundreds of facilities in the U.S. It is a cloud-based system for sharing medical information that approximates email in its ease-of-use. This article describes its architecture and our experience in a referral-based cardiology program. The advantages of this approach make it something worth considering in order to improve communication between referral centers and distant practices.

From a broad perspective, it's not hard to imagine how patient care could be improved if hospitals, physician practices, and other medical facilities that see referred patients could receive a patient's prior imaging studies within minutes. Emergency patients could be diagnosed and treated much faster if those studies could somehow be transferred with a simple, fast electronic process like email, instead of the more laborious and time-consuming approaches usually used today. It is also clear that consultations with experts would occur more frequently if files were more easily shared.

From a cost perspective, experts have long speculated about potential savings if sharing between medical information technology (IT) systems could be improved. Nearly every node of our healthcare system would benefit if the inefficiencies of traditional file-sharing methods could be replaced.

Less expensive file transfers would also mean enhanced clinical efficiency. Even with their modest budgets, individual physician practices could provide more advanced care to their patients, including patients they ultimately refer, if they could receive or transfer studies electronically without adding costly infrastructure.

In the Pediatric Cardiology Division of the University of Virginia Children's Hospital (UVACH) we work closely with several other practices across the state and we now use a technology called eMix (one of several such services), that realizes most of the possibilities described above. This cloud-based system for sharing medical information,

is as easy as email to use, and also has multi-layered security architecture to help facilities comply with the Health Insurance Portability and Accountability Act (HIPAA), and it easily handles the large file size of high-resolution imaging studies for cardiology and radiology.

Current Medical Information-Sharing Approaches: A Brief History

When radiological imaging modalities began transitioning to digital two decades ago, it would have been logical to apply the new technology to a major problem in the field: how to share imaging studies between facilities in a timely and efficient manner. After all, for ordinary consumers, it soon enough became possible to download substantial files over the Internet. Surely, cardiology files could be transferred just as easily. But logic doesn't always dictate how a technology develops. Healthcare IT systems such as PACS that stored patient image files are usually proprietary. Thus, a hospital with one vendor's technology was not able to send files to a site with a different vendor's system because the two systems didn't "talk" to each other.

To deal with the crazy-quilt environment, several workaround solutions emerged, some of them employing high technology and others being almost alarmingly low-tech. Two of these solutions are still in wide use today.

The most common high technology solution is the virtual private network (VPN), which effectively is an Internet-mediated "pipeline" that connects two institutions to each other. From the narrow standpoint of transferring files, VPNs work adequately most of the time. But they can never be more than a partial solution because they only connect two institutions at once.

Unless there is a steady flow of files between two institutions, setting up a VPN is not worth the effort. In fact, even if there is that constant flow, VPNs are problematic because of the following drawbacks:

Cost. Setting up a VPN requires hardware and software and skilled IT staff. Each file transfer is also costly from a time perspective. Normally, the sending institution will select the file of interest from a PACS or other digital

archive, burn it to CD, and then upload it to the VPN. This multi-step process often takes 45 minutes or more, and the burning and uploading must be monitored by staff.

Security risks. Recall that a VPN is a digital pipeline between two institutions and although it would be unethical, recipients are able to view files beyond the files of interest. Obviously, this creates a security risk from both a HIPAA and business standpoint.

Limited clinical utility. File transfers by VPN are relatively slow for emergency patients and the method only works if the referring hospital is already connected by VPN.

Given these challenges, medical institutions have resorted to another workaround approach: burning the files to CD, sending them by express mail or courier or, in the case of transfer patients, sending them with the patients themselves.

This method, while primitive, overcomes the universality and security issues with VPNs. But its other problems can be extremely frustrating. Common issues include discs that get lost in transit, CDs that are hard to track down after arrival, and the long time it takes for the CDs to get from one institution to another.

If the discs are received in time and go to the correct office, there still can be problems with the discs themselves, as delineated in a survey published in the January 2011 issue of the *Journal of the American College of Radiology* (JACR):

- Staff can't load the CDs because they are in proprietary formats.
- The CDs may lack embedded viewer software or the files are not in standardized DICOM or IHE PDI formats.
- The files may contain the wrong studies, or crucial portions may be missing.
- The discs may be corrupted.
- Security protocols may stop the recipient institution's workstations from opening auto-run and executable files.

Until about two years ago, medical facilities generally shared imaging files by VPN or CD despite these shortcomings, because no better approach had emerged. When the first cloud-based medical information exchanges



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2 FULL TIME PEDIATRIC CARDIOLOGISTS **Halifax, Nova Scotia, CANADA**

The Division of Pediatric Cardiology, Department of Pediatrics, Dalhousie University and the IWK Health Centre, is expanding. We are seeking two full time General Pediatric Cardiologists. The successful candidate will join an active clinical and academic practice group and bring the total number of cardiologists to five.

The IWK is the sole perinatal and tertiary care pediatric hospital for the Maritime Provinces. It hosts the only pediatric cardiac surgical program in Atlantic Canada. The successful candidates will provide general cardiac inpatient clinical care to infants and children in the NICU, PICU, and inpatient wards; see patients in a dedicated local outpatient cardiology clinic; and participate in a series of outreach clinics throughout the Maritimes on a rotational basis. He or she will also be responsible for interpretation of ECG's, echoes, and exercise tests on a rotational basis. The successful candidate must be competent in all aspects of general pediatric cardiac care, although skill in the performance of cardiac catheterization is not required, in view of divisional expertise.

This position offers an opportunity to pursue an academic career within a stable funding environment. The cardiology database, housed and managed by the Division, contains data on all patients seen in the division extending back to 1966. Linkage studies between this and other databases afford an excellent opportunity for clinical research. There is an established cardiovascular research group in the fundamental sciences at Dalhousie University. Opportunities for educational contributions at all levels, including the RCPSC fellowship training program for pediatric cardiology, provide a stimulating clinical and academic environment. The successful candidates will be expected to have evidence of academic productivity and a strong potential for academic contributions in education and research.

The Division members enjoy a very collaborative, stable working environment with well-established, collegial relationships between cardiology and cardiac surgery. Halifax, the largest city in Atlantic Canada, offers an attractive maritime environment and an enviable lifestyle. Many desirable living areas are within walking distance or a few minutes drive from Dalhousie University and the IWK Health Centre with an opportunity to enjoy a wide variety of leisure time activities.

Academic qualifications include an MD degree (or equivalent) from an accredited university with completed recognized specialty training and RCPSC certification in Pediatrics and in Pediatric Cardiology or equivalent. For one of the positions, training or interest in training in pediatric electrophysiology will be considered essential. Eligibility for medical licensure in the Provinces of Nova Scotia, New Brunswick and Prince Edward Island is also essential.

All qualified candidates are encouraged to apply; however, Canadians citizens and permanent residents will be given priority. Dalhousie University is an Employment Equity/Affirmative Action employer. The University encourages applications from qualified Aboriginal people, persons with disability, racially visible persons and women.

Interested applicants should submit a current CV as well as send a statement outlining their academic interests. They should arrange to have three letters of reference sent under separate cover to the Chair of the Search Committee. At least two of these references must come from academic referees.

Interested candidates should contact:

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Head, Division of Pediatric Cardiology
IWK Health Centre
5850/5980 University Avenue
P.O. Box 9700
Halifax, Nova Scotia, Canada B3K 6R8

Phone: (902) 470-8407
Fax: (902) 470-6616
E-Mail: andrew.warren@iwk.nshealth.ca



began beta-testing their systems in late 2009, it was a revelation.

For instance, the system we use was first beta-tested by a grassroots group of 30 rural healthcare facilities in Montana called Image Movement of Montana (IMOM). IMOM had been searching for a better way to send studies to the urban hospitals to which they transferred their most complicated cases. On behalf of the other members, three IMOM member facilities began testing cloud-based file exchanges. From the beginning, they reported that the exchanges were simple to execute, reliable, and fast. In other words, they were suitable for all clinical applications. Files were transferred between sites in minutes, with no failures.

The first IMOM members went live with the technology before the beta period officially ended, because the test had gone so well. In other parts of the country, similar systems were coming online. A transformation was underway.

Experience at UVACH

Compared to the IMOM facilities, our facility at UVACH was in the second or third wave of those adopting cloud-based medical information exchange. But ours is a prime example of a site that can benefit profoundly from this technology. Roughly two-thirds of our patients are referrals that come from three practices in our region, so we have a continual need for prior studies from those practices.

Our referring practices had varied levels of IT equipment and support, precluding options such as VPNs. To get prior studies on patients from this office in the pre-cloud era, we had to rely on CDs. This was, of course, also true for other facilities that referred the occasional patient to us.

While we never measured the failure rate of CD transfers, experientially it seemed that some kind of problem occurred up to half the time. When we traded files by VPN with our larger referring facilities, the process was prone to all the challenges inherent in that technology.

So we were intrigued to learn about the cloud-based approach. But we were also skeptical. Given how troublesome image-sharing had been historically, it seemed unlikely the new technology could overcome all the problems with other methods.

Our experience has been otherwise. As early adopters like IMOM had discovered before us, the technology works seamlessly. Here are the steps to the process:

At the sending institution, an authorized user:

- Selects the files of interest from a worklist of files electronically stored in their PACS or other archive.
- Uploads the package of files via the technology's simple user interface.
- Selects a recipient from a list of authorized users at the recipient institution.

At the recipient institution, the authorized user:

- Receives an email alerting them that the file is ready to download.
- Logs in via the technology's user interface.

- Clicks on the link embedded in the email to preview or download/view the study (The vendor provides a free DICOM viewer for this purpose).

“The ease and effectiveness of cloud-based medical information exchange have inspired us to imagine new applications at our institution. For instance, we can foresee a time when our cardiologists will use the cloud to provide more consultations and second opinions to other facilities. In a similar vein, the technology can be used to efficiently share files to several sites at once, so that experts can discuss interesting or unusual cases.”

Note: To help ensure security, the technology's vendor requires that user facilities register an administrator who will be responsible for authorizing users. Those users then have to authenticate their identity during every log-in to protect facilities' privacy and confidentiality and enhance HIPAA compliance. As a further layer of protection, the technology audits the details of the transaction, including all parties involved.

While we primarily trade files with facilities in our region, the transfers would work just as easily and quickly if we were sharing files with facilities in India or Africa. As with any Internet-mediated file transfer, all the sending and receiving party needs is a computer with a broadband connection.

It's worth noting that receiving physicians are not restricted to their facility's PACS. They are able to receive files on any Internet-connected device, including mobile devices, and do a full clinical review using only their browser – that is, without downloading an application. The technology can also be used to move files to any enterprise IT system that makes it possible, for example, to include imaging files in an electronic medical record (EMR). The technology is completely vendor-neutral – it works with any computer, IT system, or mobile device, proprietary or not.

We have experienced numerous benefits from cloud-based medical information-sharing, including:

Reliability. If we request a study from a referring facility, we can be sure it will arrive and be readable, and that the transfer can be accomplished in minutes.

Cost and labor savings. Our cloud-based transfers are paid for on a modest per-use basis or monthly subscription fee, easily affordable by



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Dr. Gary Webb, MD

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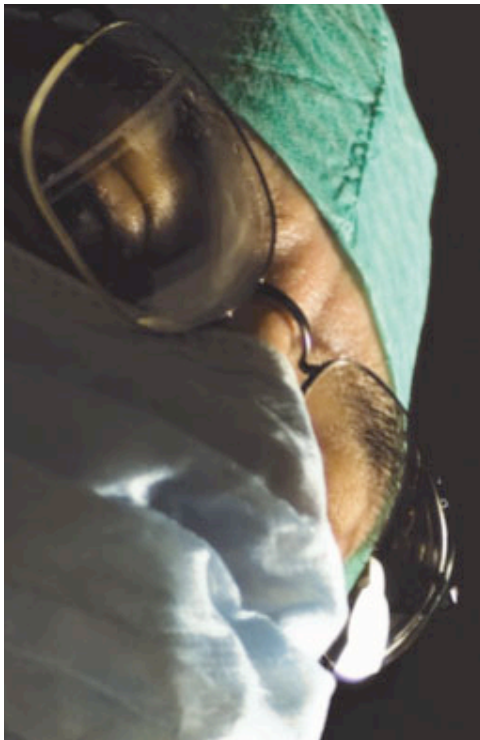
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“Recognizing the benefits of a more digitalized national healthcare system, the federal government has encouraged the acquisition and use of EMRs with its meaningful use incentives. Many of us who realize the benefits of cloud-based medical information exchange feel this technology is helpful in a similar way.... Most importantly, the technology would help advance the dream of a truly national healthcare IT system.”

even small physician practices. No acquisition or installation of software/hardware is required, and as with all cloud-based applications, the provider maintains the service. We save the cost of uploading and troubleshooting CDs, including tracking them down when they cannot be found and requesting resends when they are unreadable or lost in transit. The sending institution avoids the labor costs associated with burning and packaging CDs. Both institutions save the various costs of a VPN. Overall, cloud-based information exchange greatly increases the efficiency of our workflow.

Improved patient care. The ability to quickly and reliably receive prior studies enhances the care we provide our patients and could potentially make a life-saving difference in an emergency case.

Versatility. Although ours is a large, referral institution with few technological barriers, that is not true of all offices that refer to us. Cloud-based information exchange enables us to

share files with small physician offices that have no IT infrastructure beyond Internet-connected computers. The ability to electronically connect in this way with virtually any physician office has us contemplating referral relationships we would never pursue if CDs and VPNs were our only options for file sharing.

Other Applications of the Technology

The ease and effectiveness of cloud-based medical information exchange have inspired us to imagine new applications at our institution. For instance, we can foresee a time when our cardiologists will use the cloud to provide more consultations and second opinions to other facilities. In a similar vein, the technology can be used to efficiently share files to several sites at once, so that experts can discuss interesting or unusual cases. We also imagine using the cloud in our training of cardiology fellows throughout the state.

Recognizing the benefits of a more digitalized national healthcare system, the federal government has encouraged the acquisition and use of EMRs with its meaningful use incentives. Many of us who realize the benefits of cloud-based medical information exchange feel this technology is helpful in a similar way. Perhaps it is time for the federal government to consider incentivizing use of these services. The impacts on patient care would be substantial and the direct and indirect cost savings would be, as well. Most importantly, the technology would help advance the dream of a truly national healthcare IT system.

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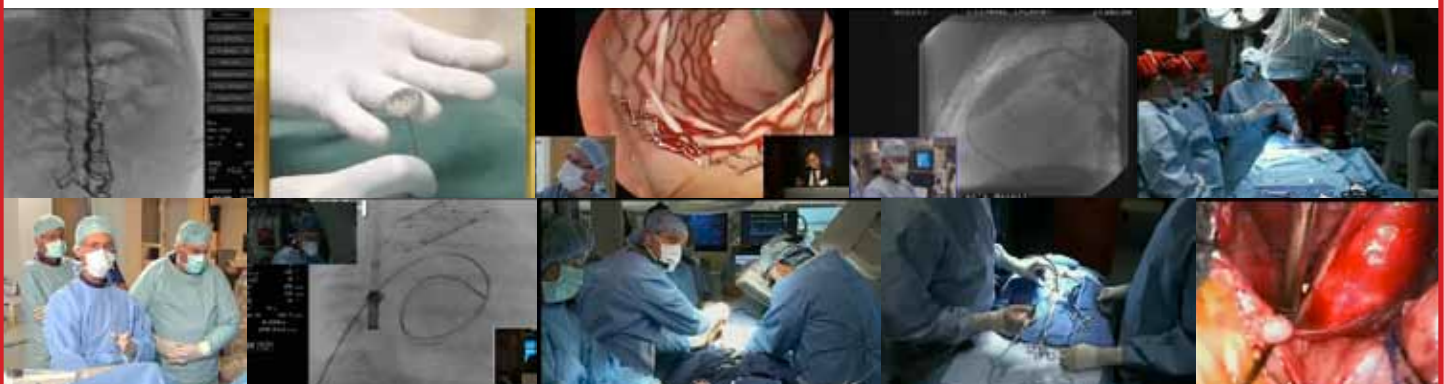
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A New Paradigm in Academic Meetings and Medical Education: Congenital Cardiology Group Summit 2012

By Gira Morchi, MD and Anthony Chang, MD,
MBA, MPH on behalf of the Congenital
Cardiology Group 2012

The typical regional, national, or international pediatric or congenital cardiology meeting currently consists of an immutable formula: an endless parade of speakers accompanied by their requisite 20-minute Powerpoint presentations with little if any time for interaction with the attendees. To make matters worse, most if not all of the speakers usually have given their talks before in other academic venues so the presentations are often mundane. Finally, success of these meetings is often measured in the metric of number of attendees thereby discourages smaller but more intimate meetings. In short, as aptly delineated in the recent *New England Journal of Medicine* article, these academic meetings typify a failed medical education strategy (with its baneful consequences) in

which there is excessive didactic lecturing and little or no interactive process in learning.¹

To address the aforementioned shortcomings and to experiment with a counterculture of academic meeting and educational learning, a different kind of congenital cardiology meeting was planned. The meeting format was also partly inspired by the *TED (Technology, Entertainment, Design) Conferences* which are hosted by a private nonprofit organization formed "to disseminate ideas worth spreading"-brilliant people in various fields give short but inspiring talks on topics they are passionate about. The mission of this new congenital cardiology meeting was to create an open and intimate venue for exchange of new clinical and non-clinical ideas or concepts among leaders in congenital cardiology.

On a beautiful California weekend in February, the first *Congenital Cardiology Group (CCG) Summit* convened, hosted by Dr. Anthony

Chang. The name CCG is a phonetic play on the word syzygy which occurs when multiple celestial bodies align. As Dr. Chang aptly stated, "leaders in congenital cardiology are in our own 'orbits' almost all of the time and lack substantive time together in alignment, or in syzygy." The participants were invited leaders from the top institutions in the various fields of congenital heart disease (pediatric cardiology, cardiac imaging, cardiac catheterization, cardiothoracic surgery, adult congenital heart disease, intensive care, and neonatology) who are known for their creativity or vision. Each leader was accompanied by a junior colleague who was selected to join this uniquely different academic meeting and venture.

The themes at this inaugural CCG conference were Innovation and Mentorship, so each presenter was invited to give two short ten-minute talks followed by a longer fifteen-minute discussion period. The first talk is a best new idea, a clinical concept that has not been



The attendees were treated to a visit and dinner event at the Bowers Museum in Santa Ana, California with a private viewing of *Warriors, Tombs and Temples: China's Enduring Legacy*, an exhibition featuring the terra cotta warriors of three of the most formative dynasties in Chinese history.

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“One of the many benefits of the meeting was having a very small number of attendees (35 total) in a casual and intimate environment to allow for truly meaningful interactions and a special esprit de corps. There was a session on leadership during which each senior faculty member spent a few minutes discussing how they attained (or were sometimes thrust into) the positions they are in. In turn, the junior attendees introduced themselves and talked about their goals. These more personal introductions set the stage for excellent dinner conversations with rotating seating plans.”

previously published or presented, and the second talk is to present a best lesson, based on any theme the speaker felt inspired by or passionate about. Lastly, in order for the attendees to totally conform to the relaxed but intellectually stimulating atmosphere of Laguna Beach, the guests were requested to wear informal attire (no ties, suits, etc) to all the sessions and activities.

Certainly the highlights of the weekend were the myriad of insightful talks. The innovation topics ranged from the newest smart materials for cardiovascular devices to the newest strategies for measuring and managing risk in our quickly progressing field. Dr. Chang spoke of the use of artificial intelligence to navigate and organize the information for ease of clinical application—if we are able to put in the correct information, the computers can give us the answers we need to help make better educated decisions for our congenital cardiology patients. In addition, real life lessons in leadership and mentorship came from stories about coaching high school sports teams, from experience in the military, and even from the various styles of communication and synchronization by jazz musicians. With a study of the various styles of orchestra conductors, the concepts of leadership and team building to work towards a common goal were beautifully demonstrated.

One of the many benefits of the meeting was having a very small number of attendees (35 total) in a casual and intimate environment to allow for truly meaningful interactions and a special esprit de corps. There was a session on leadership during which each senior faculty member spent a few minutes discussing how they attained (or were sometimes thrust into) the positions they are in. In turn, the junior attendees introduced themselves and talked about their goals. These more personal introductions set the stage for excellent dinner conversations with rotating seating plans. There was even a separate lunch for the junior attendees to

exchange ideas and thoughts about being junior faculty in today's environment. In short, this weekend provided the leaders and their junior colleagues an opportunity to reconnect in a meaningful way, and offered a special alchemy of education, entertainment, culture, and friendship, as well as some deserved rest and relaxation.

There is an inveterate tendency in the medical field to overlook the obvious: our academic meetings have become somewhat lackluster and unproductive as these meetings usually lack substantive interaction. There is a current paradigm shift in education promoted by Salman Khan of the Khan Academy to emphasize interaction rather than lecture in the classroom (www.khanacademy.org). In a similar vein, this inaugural CCG meeting of new ideas and life lessons emphasized interactive group discussions and forsook lengthy didactic lectures. The meeting received laudatory reviews and may offer a meaningful antidote to “meeting fatigue” and “Powerpoint paralysis” too often experienced at our congenital cardiology meetings worldwide. Plans are being made for another meeting in one year.

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CCT



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Outstanding Conference on Barth Syndrome Defies Tropical Storm Fury

By Matthew J. Toth, PhD

Rain, wind and electric power losses did not prevent the *6th International Scientific, Medical & Family Conference on Barth Syndrome* going ahead June 25-30, 2012 at the Don CeSar Hotel in St. Pete Beach, Florida. The conference was hailed as an outstanding success by the patients with Barth Syndrome, family members, clinicians and researchers who braved Tropical Storm Debby to attend.

An Essential Gathering to Facilitate Research and Healthcare

These conferences are held every two years and draw many individuals with Barth Syndrome (cardiomyopathy, neutropenia, growth delay, muscle weakness, and extreme fatigue) and their families as well as most of the researchers who work on this rare X-linked genetic disease. The 2012 conference included 44 individuals with Barth Syndrome and their families and nearly 50 physicians and researchers to hear about the progress made in this field. In all, over 330 people attended this seminal event—a new record. This biennial conference is sponsored by the Barth Syndrome Foundation (BSF). The 2012 event was supported, in part, by grants from the National Institutes of Health (NIH) through the National Heart, Lung, and Blood Institute, the Office of Rare Disease Research, and the National Institute of Child Health and Human Development.

Highly Commended Dual-Track Conference Format

BSF conferences are unique because of the way they are organized and have been cited by others as a model to imitate. Following previous BSF conferences, the 2012 meeting was a two-track event that brought together in one location a scientific/medical meeting running concurrently with a patient/family meeting. During several days before the meetings themselves, there also was an opportunity for families to schedule consultations with Barth Syndrome world-leading experts and healthcare professionals. Scientists, physicians, healthcare workers, and affected families from around the world participated. Four IRB-approved studies also were conducted during this time to take advantage of the largest single gathering of Barth Syndrome individuals. One new facet of the 2012 conference was the attendance of six scholarship recipients from the healthcare community. Six medical professionals submitted scholarship applications that detailed their commitment to Barth Syndrome patient care and research and were subsequently awarded stipends to help defray the costs of attending the conference.

Keynote Lecture

Dr. Stephen C. Groft, PharmD, Director of the Office of Rare Disease Research at the NIH, presented the keynote lecture entitled, "A Globalization of Rare Diseases Research." Dr. Groft spoke about the

renewed emphasis on translational research at the NIH which culminated in the establishment of the National Center for Advancing Translational Sciences (NCATS). In addition, Dr. Groft spoke about the international efforts, both public and private, to address the problems of the rare disease community. This included the development of the Global Rare Disease Registry (GRDR) for which the BSF has been selected as a pilot participant. This GRDR will collect medical data (and eventually biological samples) from many different rare disease groups in a format that will allow researchers to easily assemble information across rare diseases. It is hoped that this will increase interest and stimulate new discoveries.

The Scientific/Medical Presentations

The scientific and medical sessions began with an introduction by an individual with Barth Syndrome. Bench level researchers get an enormous boost from seeing and hearing the people most affected by their work.

Featured presentations covered the clinical aspects of the syndrome in which Drs. Kelley [Johns Hopkins University], Steward [Bristol Royal Hospital for Children], and Cade [Washington University] presented their ideas on the underlying pathologies and their experiences with treating individuals who suffer from the resulting symptoms.



Other presentations from Drs. Claypool [Johns Hopkins University], Greenberg [Wayne State University], Vaz [University of Amsterdam], Schlame [New York University], and McMaster [Dalhousie University] covered the biological function of *tafazzin* (the gene whose dysfunction is responsible for Barth Syndrome) and the lipid cardiolipin which is intimately associated with Barth Syndrome. Fourteen posters also were presented, many of whose authors obtained stipends to help attend the conference. Poster presentations by Ann Bowron [Bristol Royal Hospital for Children] and by Dr. Ji Zhang [University of California, San Diego] were selected for oral presentation on the next day.

An important cardiology report from Dr. John Jefferies [Cincinnati Children's Hospital Medical Center] described the cardiology problems faced in Barth Syndrome and reviewed his recent publication in *Pediatric Cardiology* about the Bi-VAD plus oxygenator treatment of a critically compromised Barth Syndrome child. Following that report, the session concentrated on the *tafazzin* knockdown mouse model of Barth Syndrome. Several reports demonstrated the amazing parallels of this mouse model with the human genetic disease. Drs. Phoon [New York University] and Khuchua [Cincinnati Children's Hospital Medical Center], respectively, showed how this mouse model can produce left ventricular non-compaction (LVNC) perinatally, and how adult mice demonstrate impaired fatty acid metabolism during exertion—both aspects pointedly similar to what is found in the human clinical condition. Meghan Soustek [University of Florida], Drs. Kiebish [Washington University] and Chicco [Colorado State University] also used this mouse model to better understand skeletal muscle performance, the lipid pathologies caused by a *tafazzin* dysfunction, and how dietary lipid modifications may affect these parameters.

Varner Award for Pioneers in Research

The Varner Award, presented to an individual(s) with great impact on the study and treatment of Barth Syndrome individuals, was presented to Dr. Colin Steward, PhD, FRCP, FRCPCH. Dr. Steward has been a tireless advocate of increasing the awareness of Barth Syndrome in the UK and in the world. Through his leadership and tenacity, along with the support of the UK affiliate of the BSF, the Barth Syndrome Trust, Dr. Steward started an NHS-sponsored Barth Syndrome clinic at the Bristol Royal Hospital for Children in 2010 which currently helps over 25 Barth Syndrome individuals in the UK and Europe.

Poster presentations selected the day before, along with more talks about the mitochondrial physiology of Barth Syndrome, rounded out the conference. Dr. Ren [New York University] showed that the PPAR-alpha agonist, bezafibrate, appears to reverse the cardiolipin perturbation found in cell lines derived from Barth Syndrome individuals. Dr. Pu [Children's Hospital of Boston] showed that *tafazzin* dysfunctional cells have an altered OX-PHOS metabolism that can be measured in vitro as oxygen consumption rate and acid (lactate) formation rate, and he presented the first results from induced pluripotent stem cells (IPS cells) derived from fibroblasts of two Barth Syndrome individuals. Drs. Hatch [University of Manitoba] and Shi [Pennsylvania State University] demonstrated that other genes can alter cardiolipin levels within the cell while Dr. de Kroon [Utrecht University] spoke to the enzymatic mechanism of acyl chain switching of *tafazzin*.

Final Observations of a Stimulating Conference

The wrap-up brainstorming session for this meeting was exciting and optimistic, reflecting the interesting and important results that had been presented over the previous two days. The frequent breakout discussions on the various points raised created a stimulating feeling of openness and collaboration.

A social event marked the end of a rewarding conference. Barth Syndrome individuals, their families, physicians and scientists all gathered for an enjoyable evening of live music, food, and dancing.

In conclusion, Barth Syndrome remains a life-threatening rare disease. However, these conferences increase awareness, generate interest, advance what is known, and stimulate physicians and scientists to find a specific treatment for this condition. Notably, 2012 marked the first conference in which therapeutic ideas and studies were discussed in an open forum. The trajectory of scientific and medical advances, punctuated by these biennial conferences, is consistently upwards and reaches towards the vision of the BSF: "A world in which Barth Syndrome no longer causes suffering or loss of life." Slides of many of the speakers' presentations as well as the associated audio recordings will soon be available on the BSF website (www.barthsyndrome.org) for anyone to access and review.

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Image of the Month #2- October 2012 - Presented by The Archiving Working Group

Contributors: Robert Anderson, MD; Vera D. Aiello, MD; Diane E. Spicer, BS; Jeffrey P. Jacobs, MD; Jorge M. Giroud, MD

This is a special column that will be published bimonthly in *Congenital Cardiology Today* with contributors and images from the Archiving Working Group (AWG) of the International Society for Nomenclature of Paediatric and Congenital Heart Disease.

Please visit us at the AWG Web Portal at <http://ipccc-awg.net> and help in the efforts of the Archiving Working Group and the International Society for Nomenclature of Paediatric and Congenital Heart Disease.

The authors would like to acknowledge the Children's Heart Foundation (www.childrensheartfoundation.org) for financial support of the AWG Web Portal.

IPCCC: 09.29.33, 09.30.01, 09.29.31, 09.30.02, 07.10.01, 07.17.06

AEPC Derived Term:

- Interrupted aortic arch between subclavian & common carotid arteries (type B)(09.29.33)
- Perimembranous VSD (07.10.01)
- Infundibular septum posterior deviation (aortic arch obstruction type) (07.17.06)
- Aberrant origin right subclavian artery (09.30.02)

EACTS-STS Derived Term:

- Interrupted aortic arch (IAA), Type B2 (Interruption between the carotid and subclavian arteries with both subclavian arteries arising from the aorta distal to the interruption) (09.29.33, 09.30.01).
- Interrupted aortic arch (IAA)-modifier, with aberrant right subclavian artery from descending thoracic aorta (09.29.31, 09.30.02).
- VSD, Type 2 (Perimembranous) (Paramembranous) (Conoventricular), Outlet, Conal septal malalignment, IAA type (07.10.01, 07.17.06).

ICD10 Derived Term:

- Other congenital malformations of aorta (Q25.4).
- Other specified congenital malformations of peripheral vascular system (Q27.8).
- Ventricular septal defect (Q21.0).
- Congenital malformation of cardiac septum, unspecified (Q21.9).

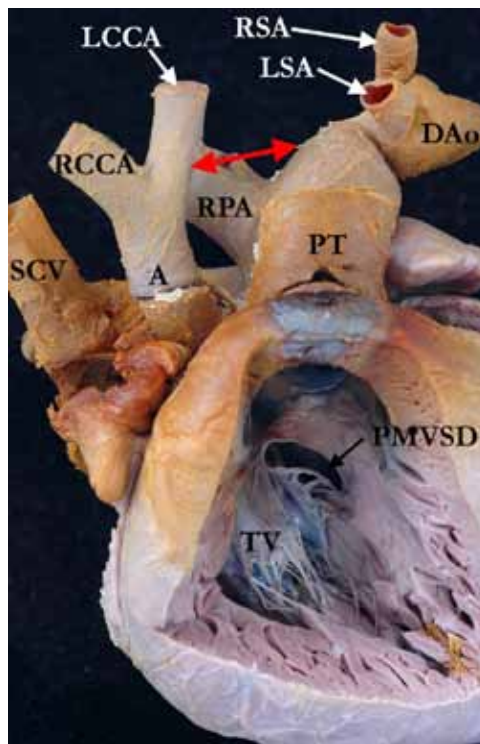


Figure 1. Description: This view shows the anterior, anatomic view of the right ventricle and great vessels, the free wall of the right ventricle has been dissected away. The tricuspid valve (TV) can be seen in the inlet. A perimembranous ventricular septal defect (PMVSD) extends into the outlet portion of the right ventricle, an alternative term is a malalignment ventricular septal defect. There are concordant ventriculo-arterial connections, the aorta (A) and pulmonary trunk (PT) normally related, with a hypoplastic ascending aorta. The aorta is interrupted (red arrow) between the left common carotid (LCCA) and the left subclavian (LSA) arteries. There is distal retroesophageal origin of the right subclavian artery (RSA). (DAo-descending aorta, RCCA-right common carotid artery, RPA-right pulmonary artery, SCV-superior caval vein).

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Comments: Interruption of the aortic arch is known to occur at three specific sites, namely: at the isthmus, which is between the left subclavian artery and the descending aorta, between the left common carotid and the left subclavian arteries, or between the right and left common carotid arteries. The first two variants are much more common than the third option, with the variants also known as Types A through C, using the classification produced

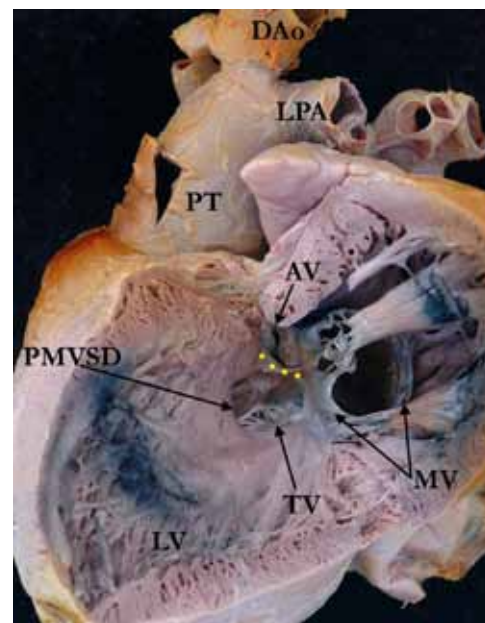


Figure 2. Description: This view shows the septal surface of the left ventricle (LV), revealing the posterior malalignment of the muscular outlet or infundibular septum (yellow dotted line), which indicates that the perimembranous defect (PMVSD) is of the posterior malalignment type. The malalignment also encroaches markedly on the subaortic outflow tract, and almost certainly produces obstruction. The tricuspid valve (TV) can be seen through the ventricular septal defect and is in fibrous continuity with the mitral valve (MV). (AV-aortic valve, DAo-descending aorta, LPA-left pulmonary artery, PT-pulmonary trunk).

Contributor: Diane E. Spicer, BS

by Celoria and Patton. The lesion is also known, however, to co-exist with anomalies of the subclavian arteries, and these additional malformations can make the situation more difficult to correctly interpret. In the images shown, it might seem that the interruption is between the right and left common carotid arteries, with the ascending aorta supplying the right brachiocephalic artery. In reality, the interruption is between the left common carotid and left subclavian arteries, and there is additional retroesophageal origin of the right subclavian artery. Even more rarely, it is possible to find this type of interruption with isolation of the right subclavian artery, in other words with the subclavian artery arising from a pulmonary artery via a patent arterial duct, so the diagnostician needs to be aware of all these potential pitfalls. In addition, the

AWG Web Portal link for this series of images:

http://ipccc-awg.net/Ao_Arch_Interruption/Int_AO_Arch_B_VSD_09_29_33/Int_AO_Arch_B_VSD_09_29_33.html



Figure 3. Images for the next column: 'Identify the malformation' – Dec 2012

branching pattern typical for the right aortic arch can be seen with either a left brachiocephalic artery, a retrosophageal left subclavian artery, or an isolated left subclavian artery. All known cases with the branching pattern typical for the right-sided aortic arch have DiGeorge Syndrome. The case is also of interest because of the morphology of the associated ventricular septal defect. Interruption itself is often associated with lesions that reduce the flow through the ascending aorta. When found with a ventricular septal defect, then the defect is

usually of the malalignment type, described by some as a conoventricular defect. Such defects, as in this case, can be perimembranous. Their main feature is the posterior deviation of the muscular outlet, or infundibular, septum, which then obstructs the subaortic outlet from the left ventricle. On occasion, the septum can be fibrous rather than muscular, and the defect then becomes doubly committed and juxtaarterial. Perimembranous defects, of course, are not always associated with malalignment of the muscular outlet septum, nor

are conoventricular, or malalignment, defects always perimembranous. In this particular case, the defect becomes perimembranous because there is fibrous continuity between the leaflets of the mitral and tricuspid valve, so the atrioventricular conduction axis will be at potential risk in the postero-inferior margin of the defect. (Reference: Celoria GC, Patton RB. Congenital absence of the aortic arch. *Am Heart J.* 1959 Sep;58:407-13).

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Medical News, Products and Information

6th World Congress Paediatric Cardiology & Cardiac Surgery 2013 - Highlights from Track One: Surgery, Anaesthesia and Intensive Care

This is one of the five “Tracks” – or focus areas – of the Congress. With this meeting being held in Africa for the first time, the Congress hopes to present a truly global view which will include a focus on developing and poor communities. At the same time the programme is wide-ranging, covering issues from fetal to adult life, as well as numerous allied disciplines. Abstracts will be presented by E-poster and oral sessions.

At the Congress website one can find full detail of the International Faculty as well as the Scientific Programme. However, here are some highlights that might have wide appeal:

1. BASIC SCIENCE

Although there will be aspects of basic science throughout the program, a full session will be dedicated to an update on the dramatic growth in embryology and stem cell research. Long-held embryological concepts are being discarded in the light of new evidence, and exciting ground is being explored in the area of growing “spare parts” from stem cells.

This session will be headlined by world leaders such as Roger Markwald, Robert Anderson and Simon Hoerstrup. Subjects of note include:

- New concepts in cardiac embryology and how these relate to clinical practice
- The future of autologous tissue replacement
- Molecular mechanisms that regulate cardiac morphogenesis
- Lineage as a driver of morphogenesis

2. SURGERY OF THE LEFT VENTRICULAR OUTFLOW TRACT

Over the first two congress days we will focus on congenital lesions involving the left ventricular outflow tract, with the exclusion of Hypoplastic Left Heart Syndrome. Thus we will look in detail at subaortic, supra-aortic, and valvular issues of the left ventricle from before birth to adulthood. Included will be lectures by world leaders on all aspects, from embryology and morphology to examining the various surgical options in management. There will be one full session on coronary surgery in children. Subjects of note include:

- Contemporary techniques to repair the incompetent aortic valve
- Surgery for malposition of the great arteries: the REV procedure
- The Small LV: how small is too small for biventricular repair?
- Comparing surgical aortic valvuloplasty with balloon dilatation
- Valve-sparing root reconstruction
- Anomalous origin / course of the coronary arteries
- The aortic translocation (Nikaidoh) procedure, and the double-root variant

3. SURGERY FOR RHEUMATIC HEART DISEASE with the WSPCCS

Rheumatic Heart Disease, whilst almost eradicated in the developed world, remains the most common cardiovascular disease of children and young people in developing countries. It affects over 15 million people around the world and kills hundreds of thousands every year. The need for surgery for rheumatic heart disease is greater than the need for correction of congenital defects in many countries. With this continuing high burden of disease in mind, we will have a special symposium together with the World Society for Pediatric and Congenital Heart Surgery focussed on surgery in rheumatic disease. Subjects of note include:

- Repair options for rheumatic valves
- Dealing with multiple valve disease
- Potential for valve replacement without anticoagulation
- The rationale and design of a Global Rheumatic Heart Disease Registry

4. ANAESTHESIA, INTENSIVE AND PERI-OPERATIVE CARE

With leading cardiac intensivists and anaesthetists on the faculty, we will have a number of sessions targeting peri-operative and intra-operative care. Some of the highlights:

- ANAESTHESIA
 - The anaesthetist as intraoperative intensivist
 - Management of the difficult airway in congenital cardiac surgery
 - Techniques to reduce blood loss
 - The use of intraoperative transesophageal echocardiography
- PHARMACOLOGY & FLUID THERAPY
 - The importance of tight glucose control
 - Evidence-based fluid management: crystalloids versus colloids
- HOW TO ELIMINATE SEPSIS
 - The science of recognizing sepsis
 - Infection control as a cost-saving investment
- SAFETY AND QUALITY
 - Multidisciplinary collaboration in the ICU: strengths and pitfalls
 - An ICU designed for safety
- THE FIRST 24 HOURS IN PICU
 - Ventilation matched to the post-operative heart's needs
 - Peri-operative renal protection
 - Fast tracking in the 21st Century: what have we learnt?
- NEUROLOGICAL ISSUES
 - Preoperative evaluation of cerebral injury and the risks
 - Neurocognitive outcomes: minimising brain injury during surgery

For more information on the meeting, visit: www.pccs213.co.za.

World Congress Legacy Project - Congenital Heart Disease Information System

The World Congress 2013 is a registered public benefit organisation whose objective is to organise this important global congress, but



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whose mission is to facilitate improvements in cardiac care for all South Africans.

As part of that humanitarian objective, an agreement with Scientific Software Solutions has enabled a web based platform for patients, parents and professionals to access information on heart disease. The platform is accessed through the home page of the Paediatric Cardiac Society of South Africa (PCSSA) www.saheart.org/pcssa.

The information site was developed by Scientific Software Solutions with the assistance of our colleague Dr Allen Everett.

There is an open access, community site providing information on congenital heart disease for parents and patients which can also be accessed directly at www.africa.congenital.org. "Community web" is patient-oriented, fully illustrated and covers all major congenital heart defects.

You can access useful information on tests, procedures, adult concerns, nutrition, health, exercise and pregnancy. Complex procedures are made clear with hundreds of illustrations and vivid animations. As a further manifestation of this "legacy project," this site will shortly be translated by PCSSA from English into a number of African languages.

In addition, PCSSA members now have access to "PedHeart Resource." This programme is the result of 2 decades of development by Scientific Software Solutions with a focus on congenital heart disease education for health professionals. There is detailed information on heart defects, surgery and interventions with full-colour diagrams and animations. There are tutorials on echo, electrophysiology and other investigations. There is a vast image library with downloadable PDF hand-outs containing advice for patients. Further aids include 1200 teaching slides. Access to the medical practitioner site is limited to paid-up members of the PCSSA who have to register with the site administrator. Members of PCSSA will also be working with Scientific Software Solutions to add information on acquired heart diseases, Rheumatic Heart Disease in particular.

This is the first heart health information service in South Africa, and is a legacy project of the PCSSA and the 6th World Congress of Paediatric Cardiology and Cardiac Surgery.

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