

## President's Message

By Michael A Gatzoulis

**Education, Education, Education.** The adult congenital heart disease (ACHD) field has reached a point where education is the key to translating past and recent advances into improved patient care, inclusive of the large number of ACHD patients lost to cardiac follow-up.

**We need to reach out and educate a broader professional audience on the principles and challenges regarding the care of the patient with CHD.** This broader audience includes general cardiologists and physicians, obstetricians, other hospital specialists, family doctors and health allied professionals. While we (the congenital heart disease [CHD] aficionados) constantly need to educate ourselves -and there are endless continuing medical educational opportunities- we also need to expand our educational portfolio and efforts. A change in emphasis is now required from the high-level, sophisticated, somewhat esoteric material which has been the main academic drive for many of us, material which remains essential for maintaining and improving tertiary practice towards educational material at a more basic level, accessible to and understandable by this broader target audience. Widely available guidelines, more basic textbooks and more publications in general cardiology and

general medical journals are a few tools in achieving this goal. In other words, we need to bring the main issues and basic principles of managing ACHD into a larger professional body. And why is it so? Because we can't do the whole job ourselves. We can't provide comprehensive, total health care for an ACHD patient in a tertiary centre for reasons such as geography, lack of capacity and need for local emergency care to mention only a few. It is essential, therefore, that we engage and support these broader professional groups in the management of our patients to achieve our common goals. Furthermore, we need a stronger representation of ACHD in medical school curricula. This is not only because of its rich clinical material that students cherish, but also because of the pressing need to encourage people to join the ACHD field early in their career development by alerting them of the wonderful clinical and academic ACHD opportunities that exist.

**We need to support CHD patient education on medical and surgical aspects of their condition. More so, we need to discuss early with our patients lifestyle issues, such as exercise, pregnancy (and contraception), career planning and insurability.** We need to provide more educational material for them and

encourage them to create their own health files and become proactive about their health. Copying clinic letters and discharge summaries to patients may be a sensible way to start. We need to extend our deliberate discussions with them in what can be complex areas, such as moderate to high risk pregnancy or moderate to high risk "elective" operations/reoperations, allow them time, and ultimately support them in their decision. Most of these challenge areas are covered better and carry a lower risk when these discussions take place early and a clear plan of action has been formulated and agreed. And yes, all this requires more of our time and more of the limited resources available. But I don't think there are good alternatives or any place for compromise. In brief, we need to strengthen further our relationship with our patients and patient support groups in a proactive - not reactive - advisory model establishing a life-long "partnership" with them.

Last but not least, we need to educate the "public". By that, I mean a) the general public, b) the 80% or more of patients with CHD who are lost to specialist follow-up (and thus, are subjected to poorer outcomes) and c) government and other funding bodies whose support is crucial for

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## Mission Statement

*The purpose of the International Society for Adult Congenital Cardiac Disease is to promote, maintain and pursue excellence in the care of adults with congenital cardiac disease.*

*The Society is dedicated to the advancement of knowledge and training in medical disciplines pertinent to congenital heart disease in adults.*

# Executive Committee

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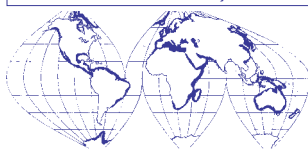
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International Society for



Adult Congenital Cardiac Disease

# From the Grown up Congenital Heart Patients Association (GUCH), UK

*Michael Cumper, Chairman of Trustees, GUCH, UK*

It is shortly the first anniversary of me having been elected as Chairman of Trustees of the Grown-Up Congenital Heart Patients Association (GUCH), the UK patient support charity. It is a great privilege to hold the position having taken over from its founder, Prof Jane Somerville who was Chairman for the charity's first 10 years. I believe the change has been particularly noteworthy as I am a GUCH.

The charity has been incredibly successful in the first 10 years and I am determined to build upon that success to ensure that we increase the support that we provide for GUCH patients in the UK and at the same time assist where we can in the international arena of GUCH patient support groups.

I learned a lot as a trustee and more since becoming Chairman. There is much to be done.

I see the work of the charity falling into three separate, although obviously overlapping, categories:

- patient services – providing direct support to the patient group;
- medical profession liaison – raising our profile with the profession and completing the process of us being accepted as having our part to play in the well-being of the patient;
- political – trying to get the NHS to provide the services necessary so the patients have access to the expertise their condition demands.

And of course all this takes money so perhaps there should be a fourth category of fundraising.

I have been both delighted and surprised at the relationship that I have encountered in representing the patient charity with the profession. Delighted by the incredibly warm and helpful responses that so many have given us, their support is excellent. Surprised, or should I say disappointed at the lack of inclusiveness from a few quarters ranging from indifference to even hostile.

Having a background in both business and politics, these reactions are no strangers to me, but I did not expect to find them when in an organisation to support patients from people whose interests must surely be the same. I believe it is important to share these thoughts as it gives everyone, including us, the opportunity to re-evaluate their own outlook to make sure that we are all pulling in the same direction, ultimately to ensure that patients get the best all round care that we can achieve for them during the time while we are in a position to influence this.

So what are we as the patient support charity doing?

In terms of patient services we are updating and compiling information leaflets on subjects affecting GUCHs such as insurance, pregnancy etc. We have responded to requests from patients for a booklet to contain information

on their condition to allow them to both better understand it themselves and also communicate it to others, especially dentists and other medical professionals by producing the Personal Health Passport. This is now freely available to all patients and we hope all units caring for GUCHs will issue them to all their patients.

We have produced both leaflets and posters to be available and displayed at all in and out patient areas to spread the message that we are here to help.

Our website ([www.guch.org.uk](http://www.guch.org.uk)) contains a well used message board allowing patients to chat about things worrying them, we have a help-line for advice too and an excellent newsletter called "GUCH News".

On the political front, we are very happy that the Department of Health has put so much emphasis on the patient's views during the ongoing discussions about what services should be provided. I feel that there is a real hope that something might happen to move the GUCH service provision forward in a sensible and planned way rather than the somewhat haphazard way as it seems to have been done in the past. Maybe this can be used as an example by others trying to get services organised in other countries where they are also having difficulties.

One of my next tasks is to look at how we might be able to

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# The Zurich Centre Experience

from the AHA Scientific Session in November 2004

At the Semi-Annual ISACCD Meeting on Sunday 06 November 2004 (held jointly with the AHA meeting) in New Orleans, Dr. Erwin Oechslin shared the Zurich centre's experience. He is an adult cardiologist fully trained in adult congenital heart disease (a 1 year fellowship in pediatric cardiology, Hospital for Sick Children, Zurich, and a 2 year fellowship at the Toronto Congenital Cardiac Centre for Adults).

There has been a tradition of congenital heart disease in Zurich since 1961 when Prof. Ake Senning (1915-2000), a pioneer and a historical personality in congenital heart disease surgery, was appointed as head of the division of cardiovascular surgery (1961-1985). He had a very close collaboration with Prof. Martin Rothlin, Emeritus Professor of Cardiology, who established the first follow-up program for congenital heart disease patients. Both, Ake Senning and Martin Rothlin grew-up with the problems of their patients operated on their congenital heart defects.

In Switzerland, there is an estimate of approximately 15,000 to 20,000 adults with congenital heart disease between 20 and 45 years of age requiring expertise care. The organization of the health care may be even more complex in Switzerland (population: 7.3 million; size: 41,000 km<sup>2</sup>) than in other countries. Switzerland is a federation consisting of 26 cantons (provinces). Each of them does have a ministry of health and its own health care system. Out of the five university hospitals (Basel, Berne, Geneva, Lausanne, Zurich), Zurich has been the largest centre for decades for many reasons: historical aspects, home of many famous researchers and physicians, largest population in the Zurich area, vicinity to the Swiss Federal Institute of Technology, financial centre, etc.

There was a revival of the adult congenital heart disease program in Zurich after Dr. Erwin Oechslin's return from Toronto in 1998. Three staff physicians with expertise in adult congenital heart disease, one congenital heart surgeon and other cardiovascular subspecialists belong to the team. Prof. René Prêtre, a congenital heart disease surgeon, has been appointed who is covering the whole spectrum of congenital heart disease surgery from childhood until adulthood. Today, more than 50% of congenital heart disease surgeries in children and adolescents are performed in Zurich, the others occur in the other hospitals (Berne, Geneva, Lausanne). An adult cardiologist with a one year training in pediatric cardiology joined the team in 2004.

Erwin Oechslin has established a very close collaboration not only with cardiovascular subspecialists, but also with representatives of other disciplines (e.g. obstetrics, respirology, intensive care medicine, psychosocial and social support, etc.). This multidisciplinary approach is the key to address the complex needs of this population! There is also a very close collaboration with the pediatric cardiologists. In 1998, a transition clinic was established and there has been a smooth transition from the pediatric to the adult care system since then. Diagnostic and therapeutic

strategies are discussed at the congenital heart disease conference.

## Outpatient Workload in Zurich

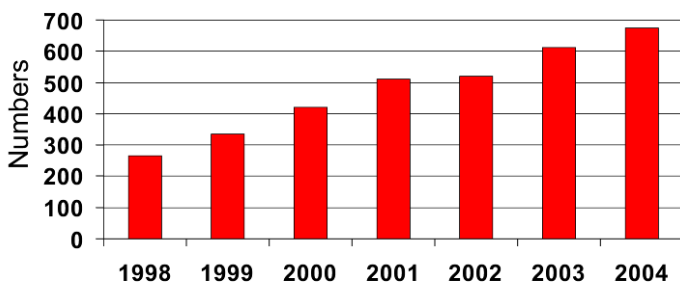
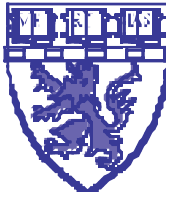


Figure 1

The workload of the outpatient clinic has been increasing continuously (Figure 1; there are no statistics until 1997). The number of patients has doubled more than twice and all patients have been entered prospectively into a database since 1998 (more than 1300 patients in the Zurich

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# Pulmonary Hypertension and Adult Congenital Heart Disease

*Michael N. Singh, MD and Boston Adult Congenital Heart/Pulmonary Hypertension Group*

The 3<sup>rd</sup> World Symposium on Pulmonary Hypertension in Venice, Italy, in June 2003, began to look at pulmonary hypertension (PH) in a different way. The Evian classification from the 1998 symposium was examined, which led to an updated classification. Some of the modifications included: replacement of the term “primary pulmonary hypertension” with “idiopathic pulmonary arterial hypertension” (IPAH); the reassessment of risk factors and triggers for PH; and re-classification of pulmonary veno-occlusive disease (PVOD) and pulmonary capillary hemangiomatosis (PCH) into a single group under the category of PAH. There was also an emphasis on congenital heart disease (CHD) as it relates to PH.

We have learned CHD is not an isolated trigger for PH, but rather CHD patients exist in a “sea” of other factors that act as triggers for PH. We have learned PH in CHD is not just within the category of PAH, but there are other factors involved. We looked for these other factors and found CHD patients do indeed have associated triggers or risk factors for developing PH. Some of these triggers/factors include: pulmonary venous hypertension, chronic obstructive lung disease, hypoxia, restrictive lung disease, hypoventilation syndromes, anti-phospholipid antibody (APA), lupus anticoagulant, chronic thrombo-embolic PH (CTEPH), portal hypertension, toxins (anorexigens, amphetamines), infections

(HIV), as well as, excessive pulmonary flow.

Looking within our own group at patients who underwent cardiac catheterization to evaluate PH, we found only a small group of patients (~12%) had simple lesion such as atrial septal defects (ASD) or ventricular septal defects (VSD). A much larger group of patients (~88%) had more complex lesions (single ventricle, double outlet right ventricle, truncus, or Ebstein anomaly). What we also found was only a small group had PAH alone and a larger group had other triggers (left atrial hypertension, pulmonary artery or venous stenosis, CTEPH, APA, and paravalvular leaks.) One example is to look at the tetralogy of Fallot (TOF) patient with unilateral pulmonary artery (PA) stenosis and otherwise normal appearing PA vasculature. They typically present with elevated right ventricular (RV) pressures, as compared to “normals” with unilateral PA stenosis that don't develop elevated RV pressures.

We are beginning to understand relationships in PH on the mechanical, biochemical, and cellular levels. We have learned about role of ventricular interdependence. The relationship between the LV and RV has been demonstrated, such that, even if you have a right-side heart lesion, the other ventricle is affected in adverse ways. We have seen that elevated atrial level pressures in patients with ASD aren't always normalized after closing the defect. In our own

group we have seen that a good majority of patients with Eisenmenger physiology have high left atrial pressures, which also suggests RV/LV differences and interactions. It has been shown there is neurohormonal activation in right ventricular outflow tract obstruction. We have seen that CHD patients also have restrictive and obstructive lung disease related to scoliosis or obesity, and that some of these patients have an increase in O<sub>2</sub> saturation with supplemental O<sub>2</sub>. There has been progress in understanding the growth and development of the pulmonary vasculature, the different pulmonary vascular lesions, and the role of dysregulated endothelial-smooth muscle cell interaction. Studies from the late 1980s and early 1990s showed us that pulmonary vascular responsiveness with nifedipine and treatment with warfarin were factors for survival. We also saw that only ~10-15% of patients with PH were “responders” to nifedipine and in our patients it may be even lower. On the pulmonary vascular molecular level we have seen abnormalities in the regulation of K<sup>+</sup> channels with a decreased efflux of K<sup>+</sup> out of the cells leading to membrane depolarization and an increased influx of Ca<sup>++</sup> leading to pulmonary vasoconstriction. Within the last 10 years there have been new discoveries, which would lead us to view the endothelium as an organ itself because of the various substances it produces and metabolizes, as well as, its interaction with thrombolysis,

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## Letter from the Chair

Dear Colleagues,

I will finish 5 years as Chair of the American College of Cardiology Committee on Congenital Heart Disease and Pediatric Cardiology- during which I have served as a Liaison to the Leadership of CVDY and worked closely with many of you. I am proud that together we have founded the Joint Council for Congenital Heart Disease as a Coordinating forum for group dialog in our field and that it is now Chaired by Tom Klitzner. The new Chair of our ACC committee will be Dr. Gerard Martin- and he will succeed me in March. In my last Communication for the CVDY Newsletter I have **Really Big News**.

The ACC is exploring the formation of member sections as a means to bring together small groups of ACC members with similar interests in a cohesive manner. A member Section would provide a framework for us to work together to achieve objectives of high interest to our community but which may not be a priority for the ACC membership as a whole. We would also have the opportunity, through the collection of modest Section dues, to fund small projects of our own choosing. The ACC Women in Cardiology Committee has also agreed to participate in this pilot. 500 members have already joined their Section on payment of \$25 annual dues, and projects are planned for 2005.

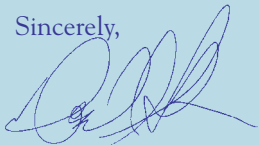
The CHDPC Committee met in a special session on November 9, 2004 in New Orleans in order to explore the proposal in depth. A number of distinguished leaders (see attached listing) were invited to join our discussion. **All present unanimously agreed that the ACC Trustee's invitation provides our specialty with a unique and groundbreaking opportunity.** Section objectives include fulfilling training needs for those working with children and adults with congenital heart disease, advocating for access to care for adult patients, and ensuring that our members have a voice at all levels of the ACC governance structure. Our discussion resulted in a listing of potential objectives which we then narrowed to a list of five short term and five long term priorities that the Section might address during the pilot period including: fellowship training awards, traveling grants for fellows, a trainees forum, visiting professorships, and the development of advocacy materials for patients- especially Adult CHD patients.

We hope you will attend the inaugural Section meeting in March, Sunday, March 6, 2005, Noon – 2:00 p.m. to help us celebrate the formation of our Section, and also to share your ideas with us and contribute your suggestions for immediate goals and projects. A complimentary brown bag lunch will be available.

We also invite you to join the Congenital Heart Disease Section right away by completing the attached enrollment form and returning it with your check for annual dues in the envelope provided. Annual dues have been set at \$35 (\$25 for fellows and Cardiac Care Associate members) to enable the Section to fund projects outside of the ACC budget.

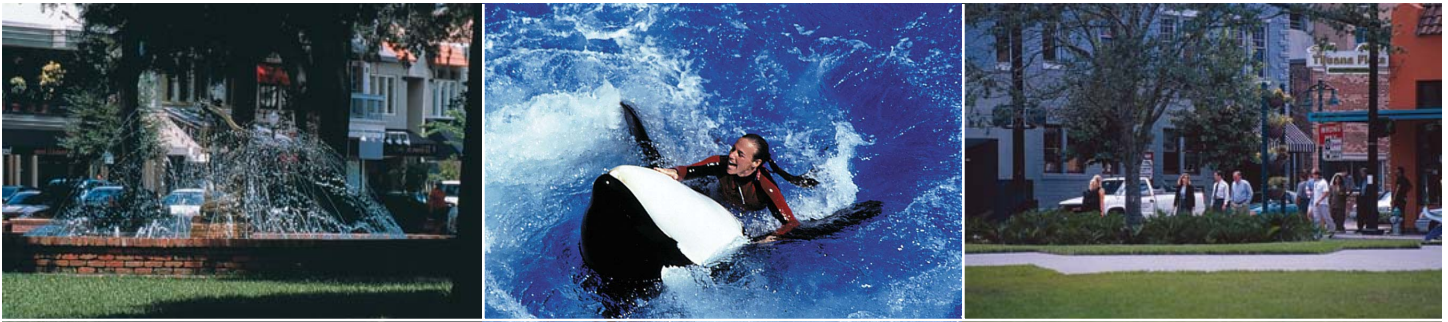
I am both grateful to the Leadership of the ACC and thrilled that we have been given this opportunity to strengthen and empower the voice of the Congenital Heart Disease Community and to develop a Section of Congenital Heart Disease and Pediatric Cardiology. Please join with us to celebrate this opportunity and work with us to make sure our Section has major input on CHD issues and to make it an ongoing dynamic entity in cardiology.

Sincerely,



David J. Sahn, MD, MACC  
Chair, Congenital Heart Disease and Pediatric Cardiology Committee

*If you are not receiving this newsletter via e-mail, please contact the society at [info@isaccd.org](mailto:info@isaccd.org) or (919) 861-5578, so that we can update our records with your current e-mail address.*



## ISACCD to Meet in Orlando!

**Sunday, March 6, 2005 • 7:00-9:00 am • Salon 14**  
**Rosen Centre Hotel • 9840 International Drive • Orlando, FL 32819-8122**  
**(800) 800-9840 • [www.rosencentre.com](http://www.rosencentre.com)**

The semi-annual meeting of the International Society for Adult Congenital Cardiac Disease (ISACCD) is scheduled to be held during the Annual Scientific Sessions of the American College of Cardiology.

The ISACCD meeting will take place Sunday, March 6, 2005, 7:00-9:00 am, at the Rosen Centre Hotel.

### Lectures will include:

"Ross Procedure: The Treatment of Choice for Aortic Valve Replacement"  
—Mr. Darryl F. Shore, Royal Brompton, London, England

"ACHD Centers Experience: The Edmonton and Western Canada ACHD Group"  
—Drs. Isabelle Vonder-Muhll and Dylan Taylor

**All are encouraged to attend! We look forward to seeing you in Orlando.**

**If you will be attending the meeting, return this form by February 25, 2005 by mail, fax or e-mail.**

Yes, I will attend the semi-annual meeting of the ISACCD March 6, 2005, 7:00-9:00 am, in Orlando, FL.

Name \_\_\_\_\_

Affiliation \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ Zip \_\_\_\_\_

Phone \_\_\_\_\_

Fax \_\_\_\_\_

Email \_\_\_\_\_

### Send registration to:

ISACCD, 1500 Sunday Dr., Suite 102, Raleigh, NC 27607; Fax: (919) 787-4916; Email: [info@isaccd.org](mailto:info@isaccd.org)

**Please RSVP by Friday, February 25, 2005!**

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**International Symposium  
On Congenital Heart  
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visit: [www.acc.org](http://www.acc.org)**

**May 26-28, 2005  
Toronto**

**Program Co-Directors:**

**Peter P. Liu,  
MD, FRCP(C), FACC**

**David J. Sahn,  
MD, FACC**

**Gary Webb,  
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**5th Advanced Symposium on  
Congenital Heart Disease in the Adult**  
25<sup>th</sup> to 27<sup>th</sup> September 2006

Venue:

Royal College of Surgeons of England, London, England

Host Institution:

Royal Brompton Hospital

Programme Directors:

Dr Michael A Gatzoulis  
Mr Darryl F Shore

For more information Visit: [www.rbh.nthames.nhs.uk](http://www.rbh.nthames.nhs.uk)

## President's Message

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resource allocation. **There should be more public support and additional sources of funding for such an area concerned with the most common inborn defect, with a worldwide distribution inflicting young individuals (and their families) who strive to have a full life despite variable levels of physical disability.** If congenital heart disease patients who are lost to follow-up were aware of the issues involved and the need for life-long follow-up they would seek expert advice. This would put enormous pressure on any ACHD centre, operating already at maximum capacity. But with time, it will create the conditions and bring in the resources for staged expansion of ACHD services, both tertiary and secondary which is long due. Patients after all have (or should have) a stronger voice and more lobbying power than professionals. Persistent representation of the ACHD issues (and the enormous need) to government and other funding bodies, including philanthropy and industry, will remain essential in securing resources to improve clinical infrastructure, promote education and research.

It is only through educated professionals, educated ACHD patients and educated "public" that we can truly extend the outstanding results of pediatric cardiology and cardiac surgery into adulthood and enable every patient with CHD to reach and enjoy their full life potential.

### Program Outline

## AAP National Conference and Exhibition

### Joint ISACCD/AAP

Friday, October 7, 2005

10:15 am - 12:15 pm

Washington, DC

#### Symposium 1: The Transition to Adulthood for Children with Congenital Heart Disease, a Joint Session with the International Society for Adult Congenital Heart Disease

- Moderator:* Michael A, Gatzoulis, MD, PhD and Tom Graham, MD
- Session 1: Demographics and Scope of the Problem**  
Michelle Gurvitz, MD, UCLA/Mattel Children's Hospital, Los Angeles, CA
- Session 2: Heart Failure and Arrhythmias in Adult CHD**  
Douglas Moodie, MD, Ochsner Clinic Foundation, New Orleans, LA
- Session 3: Pregnancy and CHD**  
Karen Stout, MD, University of Washington Medical Center, Seattle, WA
- Session 4: Optimizing Outcomes in Adulthood**  
Michael Gatzoulis, MD, PhD, Royal Brompton Hospital, London, UK



## From the Grown up Congenital Heart Patients Association

*continued from page 2*

widen the scope of the work of the charity in raising funds to enable the provision of direct resources toward such things as training, research etc and the trustees will be considering what we might be able to include in a three year plan to be drawn up shortly.

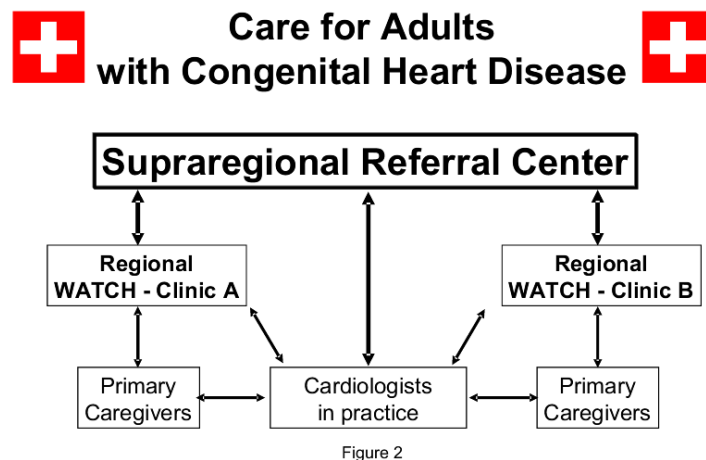
In my first year however there have been two feelings upper most in my mind. Firstly what a great bunch of patients the GUCHs are, with an amazing outlook on life, positive, determined and uplifting and secondly the level of interest and dedication shown by those who we are fortunate to have caring for us. There may be much to achieve, but with these two factors the outlook must be good.

## The Zurich Centre Experience

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database). The success of the Zurich program is based on a structured follow-up care, the multidisciplinary approach and its mission to serve as partner for all physicians and patients.

The Swiss WATCH (Working Group for Adults and Teenagers with Congenital Heart Disease) of the Swiss Society of Cardiology developed a national care plan for adults with congenital heart disease based on three levels of care (Figure 2). Cardiologists with some expertise in congenital heart disease run regional WATCH-clinics in collaboration and interaction with the supraregional referral centre. Several regional WATCH clinics are established across the country. The communication and interaction among



the different levels of care are the key for optimal care! Based on the population in Switzerland, only one supraregional referral centre would be required. However, two supraregional centres may be established for political reasons: one in the German and one in the French speaking area of Switzerland. The Zurich centre is serving and acting as an established supraregional referral centre: there are referrals not only from the whole German and Italian speaking area, but also from the French speaking area in Switzerland.

Care of adults with congenital heart disease has improved: there is a national network of caregivers, as well as a structured follow-up program, a multidisciplinary team of care, a close collaboration with the pediatric cardiologists and a transition clinic in Zurich. However, there are political obstacles and there is still a gap in the quality of care between adults with acquired and congenital heart disease which has to be closed! The awareness of the politicians as well as of the leaders of the cardiovascular community and of the academic centres has to be improved. They have not taken an appropriate interest in the care and have not addressed the increasing needs of this new population, yet: the need for financial, structural and personal resources, and – last but not least – the establishment of appropriate positions in the academic centres. Congenital heart disease is continuity from childhood until adulthood and there must be a commitment to a life-long specialised care!

# Pulmonary Hypertension and Adult Congenital Heart Disease

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coagulation, inflammation, and immune processes. We have learned from the vascular injury/inflammation model and its role in PH. We have learned the role of adhesion molecules, matrix metallo-proteins, and extracellular matrix, and their interaction with proliferation, apoptosis, gene expression, and cell migration. There have been studies on bone-morphogenic growth factor beta, and their role in cell-to-cell signaling. It has been found that endothelium-smooth muscle cell-to-cell signaling errors occur in nearly all cases of PH. There are two models for endothelial cell proliferation consisting of endothelial cell mutations and shear stress/inflammation processes. There have been new discoveries in an infectious etiology and the role of Human Herpes Virus (HHV) in clonal endothelial cell expansion. The thought is that Kaposi's sarcoma herpes virus (KSHV) HHV 8 may be a new paradigm in PH.

In clinical practice, the first real parenteral medication for the treatment of PH was epoprostenol (Flolan), a type of prostacycline. Prior to this medication the available treatments were digoxin, anticoagulation, supplemental O<sub>2</sub>, diuretics, and oral vasodilators (calcium channel blockers). An early randomized trial with epoprostenol showed reduced clinical events with PH patient in functional class III-IV. From hemodynamic data we learned right atrial pressure was the most powerful baseline

hemodynamic predictor of outcome and cardiac index was the hemodynamic change most predictive of successful therapy. For many years, epoprostenol was the only medication on the horizon, but now there are several new medications with different mechanisms of action.

Treprostinil (Remodulin), a prostacyclin analogue, is delivered by continuous subcutaneous infusion. In a 12 week double-blind, placebo controlled randomized trial with PH patients (~20% with CHD) in functional class II-IV, there was a mean increase of 10 meters in the 6 minute walk test for the whole group. Although, not a great improvement in walk distance, it was enough to gain Food & Drug Administration (FDA) approval. The main adverse reaction of the medication was infusion site pain in 85% of patients causing 8% to withdraw from the study. With higher doses there was a greater increase (36 meters) in the 6-minute walk test. The medication is expensive costing ~\$93,000/year.

Beraprost is an oral PGI<sub>2</sub> analog, which was studied in a double-blind, placebo controlled randomized trial with PH patients (~18% with CHD) in functional class II-III. There was a 25 meter increase in the 6-minute walk test. Any clinical benefit was lost over the first year of treatment; making it the first PH medication shown to have a loss of efficacy.

Iloprost is an inhaled PGI<sub>2</sub> analog with effects lasting 30-90 minutes. In a 12-week double blind, placebo controlled randomized trial with PH patients (none with CHD) in functional class III-IV; there was an increase of 36 meters in the 6-minute walk test. The clinical end point of 10% increase in 6-minute walk plus improvement in functional class was met in 17% of the treatment group versus 4% of the control group.

Bosentan (Tracleer) is an oral endothelin A & B receptor antagonist. In a 16-week double blind, placebo controlled randomized trial with PH patients (none with CHD) in functional class III-IV; there was an increase of 44 meters in the 6-minute walk test with the highest dose. The medication is expensive costing ~\$36,000/year.

The results of the sildenafil (Viagra), a phosphodiesterase-5 inhibitor, trial in PH were recently presented at the American College of Chest Physicians. In a 12-week double blind, placebo controlled randomized trial with 3 drug doses; there was a 50 meter increase in the 6-minute walk at the highest dose with 35% of patients in the treatment group having an improvement in functional class versus 7% in the placebo group. The cost of the medication is ~\$10,000/year. There are three pediatric CHD trials underway studying peri-operative and chronic use, as well as, dosing with sildenafil.

BREATHE-5 is a multi-center, double blind, placebo controlled randomized trial using bosentan in patients with Eisenmenger physiology. Due to the very tight exclusion criteria there is difficulty in enrolling patients. The main reason for the tight exclusion criteria is to maintain control over all non-tested variables and to ensure resistance is at the pulmonary arteriolar level. There are two primary end points: 1) change in O<sub>2</sub> saturation and pulmonary vascular resistance; and 2) hemodynamics, 6-minute walk test, WHO functional class, adversities, dyspnea, and quality of life. It is designed as a 16 week "safety"/non-inferiority trial with a 6 month extension period.

The future prospects of ACHD and PH includes more multi-center trials in CHD with PAH and non-PAH anatomic disease to evaluate abnormal pulmonary architecture and elevated systemic ventricular end-diastolic pressure. Treatment of non-hypertensive pulmonary arteries such as in Fontan physiology needs to be evaluated, along with, combination therapies such as those used in treating heart failure and asthma. Other future prospects include surgeries for flow and oxygen restriction to the pulmonary arteries. On the horizon are targeted drug, cell, and gene therapies. The future and existence of adult congenital heart disease (ACHD) as a subspecialty academic cardiovascular field is acutely and ultimately dependent on the quality of its research, therefore, more multi-center and randomized controlled trials are needed.