The 2009 ISHR North American Section Meeting was held in the “Charm City”, Baltimore, Maryland from May 26th through May 29th at the Baltimore Marriot Waterfront Hotel. Baltimore is a city known for many things including being the home of the Major League Baseball’s Orioles, the National Football League’s Ravens, burial place for one of America’s most renowned poets, Edgar Allan Poe, and the location of the naval battle that inspired the lyrics to the “Star Spangled Banner”. A number of “firsts” also occurred in this: the first ice cream freezer in 1848, the first stomach antacid-seltzer was developed in 1891, the first surgery for treatment of Tetralogy of Fallot in 1944, and the home of the first African-American to serve on the US Supreme Court in 1967. So, it’s no surprise that Baltimore was chosen as the site for this year’s North American Section Meeting. The conference was jointly sponsored by the ISHR and the University of Maryland’s School of Medicine and was organized by Meredith Bond, William Stanley, Mandeep Mehra, Tish Murphy, Brian O’Rourke, and David Kass. The theme of this year’s meeting was “New Discoveries for Prevention and Treatment of Heart Disease” and this was clearly evident throughout all of the science presented.

The first day of the conference was action packed! It began with Interest Group Workshops, which focused on specific topics followed by discussion on the future direction and leadership of the Interest Groups. After your choice of 3 different workshops, the always-exciting Young Investigator Competition took place. This year the Young Investigator Competition was split into two categories with Early
Career Finalists, which consisted of graduate students through 3rd year post-docs, and Senior Fellows and Assistant Professor Finalists. The competitors of the Junior competition were Grant Budas (Stanford University), Dao-Fu Dai (University of Washington), and Asuka Ota (UCLA) and the finalists for the Senior competition were Julie Bossuyt (UC, Davis), Claudia Lagranha (NHLBI), Marcello Rota (Harvard Medical School), and Lina Shehadeh (University of Miami). The competition was intense with every participant doing an excellent job. Unfortunately, we would have to wait until Thursday evening’s Gala to find out the winners.

Following the Young Investigator Competition was the presentation of the Distinguished Leader Award, which was presented to Dr Robert Jennings of Duke University. As the first recipient of this prestigious award, Dr Jennings was honored for his leadership and outstanding contributions to accomplishing the mission and advancing the objectives of the ISHR.

The next two days were filled with stimulating and thought-provoking scientific presentations by leaders in the fields of proteomics, EC coupling, obesity and nutrition in heart failure, hypertrophy, and imaging. Some excellent new approaches to enhancing our understanding of the heart disease process were presented and led to great discussion and enthusiasm for the treatment of heart disease. These discussions continued on throughout the evening reception and poster sessions where scientists could mingle over a glass of wine. New this year, poster presentations were judged and six winners were chosen and announced at the Gala.

This year’s Gala Event was held at the American Visionary Art Museum across the scenic Inner Harbor from the hotel. If you had a chance to look around the museum before the Gala started, you would have noticed a number of unique and interesting works of art, including the 20-foot tall pink poodle, the 5-foot in diameter ball of brassieres, and an old-fashioned station wagon covered in colored glass bottles. The surroundings provided great ambiance for laid-back discussion and fun.

A number of awards were given out at the Gala event. The first award to be given out was for the JMCC Early Career Authors Prize. The winner was Dr Thomas J. Hund of Washington University in St. Louis. Two runners-up, Dr Suresh S. Palaniyandi of Stanford University and Dr John Fahrenbach of Loyola University, were also announced. The winners of the ISHR International Poster Awards were Samarjit Das (Johns Hopkins University), Alexey Glukhov (Washington University), Takeshi Aiba (Johns Hopkins University), Mariah Goodall (University of Maryland at Baltimore), Claudia Preston (Mayo Clinic), and Julio Ferreira (Stanford University). Finally, the winners of the Young Investigator Competition were revealed. Dr Grant Budas, who spoke about HSP90-mediated mitochondrial import of PKCε and how it is essential for cytoprotection, was the winner of the junior competition. Dr Lina Shehadeh was the winner of the senior competition. Her talk focused on regulation of compensatory angiogenesis during cardiac hypertrophy by a p300-miR-17-92 feedback loop.

The conference ended on a high note with the President’s Distinguished Lecture, given by Dr R. John Solaro of the University of Illinois at Chicago. This honor is bestowed upon an individual...
Litsa Kranias and the Recipient of the President’s Distinguished Lecture Award, Dr R. John Solaro (University of Illinois, Chicago) who has made significant contributions to the advancement of cardiovascular science in the fields of molecular biology, genetics, genomics or proteomics. Past winners of this award include Dr Mark Sussman of San Diego State University, Don Bers (President, North American Section) and runners-up for the JMCC Early Career Authors Prize, Suresh S. Palaniyandi (Mast cells and εPKC: A role in cardiac remodeling in hypertension-induced heart failure; JMCC 2008; 45: 779-786) and John Fahrenbach (Decreased intercellular coupling improves the function of cardiac pacemakers derived from mouse embryonic stem cells; JMCC 2008; 45: 642-649). Absent from the meeting was the winner, Thomas J. Hund (Role of activated CaMKII in abnormal calcium homeostasis and I_{Na} remodeling after myocardial infarction: Insights from mathematical modeling; JMCC 2008; 45: 420-428).

Dr Jeffrey Robbins of Cincinnati Children’s Hospital, and Dr Gerd Hasenfuss of the Georg August University Medical School, Goettingen, Germany. As the keynote speaker for the 2009 North American Section Meeting, Dr Solaro presented an elegant lecture entitled “Integration of Cardiac Sarcomeric Control Mechanisms with EC Coupling and Metabolism.” This lecture focused on the emerging role of protein phosphatases in the modulation of myocardial contractility. Dr Solaro described a novel signaling pathway whereby p21-activated kinase-1 (PAK-1) serves to regulate the activity of protein phosphatase 2a, which in turn is a critical regulator of sarcomere dynamics. Although much attention has been focused on protein kinases in the regulation of myocardial contraction, Dr Solaro emphasized a key role for protein phosphatase 2a.

And now we can say that we’ve added another “first” to Baltimore’s long list, as it played host for the first time to the ISHR North American Section Meeting, which focused on “New Discoveries for Prevention and Treatment of Heart Disease.” Next year, the 20th World Congress of ISHR will be held in the bustling city of Kyoto, Japan with the theme: Paradigm Shift to Integrated Cardiology - Gene, Function and Life (May 13-16, 2010). Deadline for abstract submission is November 30, 2009 and Travel Awards are available for young investigators, so get those pipettes pumping!
For many years, congenital malformations of the heart were of little interest to the medical profession because there was no treatment. As Osler wrote in 1892, “These [congenital affections of the heart] have only limited clinical interest, as in a large proportion of the cases the anomaly is not compatible with life, and in others nothing can be done to remedy the fact or even to relieve the symptoms.” This changed with the development of surgery to repair congenital cardiac malformations in the 20th century by Robert Gross, Alfred Blalock, Clarence Craaford, Russell Brock, and others. It was my good fortune to work with Blalock in Baltimore on the physiology of congenital heart diseases during the earlier phases of his surgical treatment of the Tetralogy of Fallot (1940s and 1950s). It was an exciting time when every study opened new prospects of diagnosis and treatment.

During the following years, introduction of the cardio-pulmonary bypass by John H. Gibbon, Jr., permitted complete corrections of some cardiac malformations by operating on the heart muscle directly. Yet some defects remained beyond the scope of cardiac surgery. The search for a cure for these malformations has challenged surgical skill and imagination. Restructuring of these hearts, in general, involves attempts to increase the effective pulmonary blood flow in order to correct the reduced oxygen tension in systemic blood with all its dire consequences.

The Blalock procedure, developed in the 1930s, is an anastomosis between the subclavican and a pulmonary artery. It was a singular achievement in the treatment of some cyanotic cardiac malformations such as the Tetralogy of Fallot (pulmonic stenosis, aorta which overrides both ventricles). Now, more than 50 years later, surgical procedures have been developed for the treatment of congenital heart diseases including tricuspid stenosis, Ebstein’s anomaly, and particularly hypoplastic left heart syndrome; some of these previously hopeless conditions are now amenable to palliative surgical treatment.

In 1951, we published an article on the circulatory dynamics in patients with tricuspid atresia. One of them was treated unsuccessfully with a Blalock shunt. Equally unsuccessful were surgical attempts to treat patients with hypoplastic left heart syndrome. This was particularly discouraging since this malformation can cause death soon after birth. Hypoplastic left heart syndrome is a spectrum of various degrees of hypoplasia of the left ventricle, leaving this chamber unable to maintain systemic perfusion. Some of these infants need surgical palliation in the first hours of life. Tricuspid atresia, a name given by Maude Abbott, belongs to the general category of univentricular hearts. In this malformation, the primary lesion is atresia of the tricuspid valve and as a result the right ventricle is poorly developed. Venous blood from the right atrium passes through a patent foramen ovale or an interatrial septal defect into the left atrium where it is mixed with blood returning from the lungs. Blood then passes through the mitral valve into the left ventricle and aorta. To reach the lungs for oxygenation, blood may course either through a defect in the ventricular septum into the small, right ventricle and from there into the pulmonary artery or, if the ventricular septum is intact, through a patent ductus into the pulmonary artery. In some cases in which the ventricular septum is intact and the ductus has closed, blood reaches the lungs only through dilated bronchial arteries.

The story of surgical treatment of some of these complicated cardiac malformations is one of imagination and persistence. Two surgeons played a major role: William L. Glenn and Francis Fontan. Glenn was born in 1914 in North Carolina, received his MD degree from Jefferson University Medical School and completed his residency at Massachusetts General Hospital in Boston. In 1948, he became chief of cardiovascular surgery at Yale University and, in 1954, he created the first cavopulmonary shunt in the treatment of cyanotic congenital malformations, an operation now referred to as “Bidirectional Glenn” or “bidirectional cavopulmonary shunt.” This operation creates an anastomosis between the superior vena cava and the right branch of the pulmonary artery, directing venous blood from the head and upper limbs to the lung, bypassing the right ventricle. This was a revolutionary approach and became an important palliative treatment of some cardiac malformations.

In 1971, the French physician, Francis Fontan published an article which extended Glenn’s procedure to open new approaches to the treatment of some cardiac malformations. As he expressed it, “The procedure is not an anatomical correction, which would require the creation of a right ventricle, but a procedure of physiological pulmonary blood flow restoration, with suppression of right and left blood mixing.” His purpose was to drain the vena caval blood into the pulmonary artery for oxygenation in the
lungs. The superior vena cava was anastomosed to the distal end of the pulmonary artery according to the Glenn procedure. The proximal end of the right pulmonary artery was then anastomosed to the right atrium. Thus blood from the inferior vena cava drained into the left pulmonary artery, bypassing the right ventricle. Since this operation, Fontan’s procedure has been modified to include a number of major variations, but the principle, that of redirecting systemic venous blood into the pulmonary artery via a conduit (preferably extracardiac), bypassing the right ventricle, has remained. Unfortunately, these procedures can be followed by complications such as protein losing enteropathy, thromboembolism, and myocardial failure. But the Fontan procedure has been life-saving, primarily in patients with univentricular heart.

Francis Fontan was born in 1929 in France in the foothills of the Pyrenees. His father was a well-known professional cyclist who successfully competed in the Tour de France. He attended medical school in Bordeaux, serving later as “Interne des Hôpitaux,” then commenced working in the newly created Department of Cardiac Surgery. In 1960, he became Chef de Clinique of the Department of Cardiac Surgery. It was at the Hopital Pellegrin-Tondu in Bordeaux that he developed his operation. At that time, he became aware of the work of Russian surgeons who had attempted a cavopulmonary shunt. But it was a specific patient’s history which motivated Fontan. In this patient, a woman with tricuspid atresia, Fontan fashioned an end-to-end anastomosis of the superior vena cava to the right pulmonary artery, connecting the right atrium directly to the remaining part of the bifurcation of the pulmonary trunk. In 1999, the patient was doing well. In 1970, Fontan operated on another patient with tricuspid atresia. The patient also improved. These 2 case histories were first published in 1971 by Fontan and Baudet.

Since then, the Fontan procedure or procedures have been used extensively all over the world to the benefit of children and adults with cardiac malformation which had been thought to be inoperable. While therapeutic advances achieved in the laboratory need long periods of testing and scrutiny, the surgeon has the advantage of seeing the results of his work almost immediately. The impossible has become possible, the difficult easier, all through the persistence, imagination, and courage of brilliant surgeons.

References


Richard J. Bing, M.D.
President’s Letter

William Harvey and the Discovery of the Circulation of the Blood
Part I

Dear Colleagues,

As I announced in my last column, I wish to write about the life and work of William Harvey – arguably the most important cardiovascular investigator of all times. That the average person has never heard of William Harvey is understandable (although appalling). That at least 10,000 more people know about Madonna and Britney Spears than about Harvey is scarcely surprising, given the deplorable state of our culture. What surprised me was the realization that even cardiovascular scientists, physicians, and physician-scientists either do not know Harvey or are only remotely familiar with his legacy, although his legacy is a gift of unimaginable value that he has given to each of us and that constitutes the basis for our daily work. Knowledge of history is as critical for physicians as it is for everybody else. As Cicero said, “to know nothing of what happened before you were born is to remain forever a child”. What a truism. So, I think it is very important to understand how the knowledge that we now take for granted – the circulation of the blood – came about. This is one of the few advances in medicine that can be single-handedly credited to one man, William Harvey.

Harvey not only made one of the most important discoveries in medicine, but also was one of the founders of modern science. Indeed, I believe that his greatest legacy is not the discovery of the circulation but the establishment of scientific experimentation as the method for biological research. With, perhaps, the exception of Louis Pasteur, Harvey is the most honored contributor to medical knowledge in history. There are Harvey societies, Harvey meetings, Harvey prizes, and there is the famous Harveian Lecture held by the Royal College of Physicians every year, which is the pinnacle of glory for a physician. Monetarily, if you are lucky enough to own a copy of his book, “De Motu Cordis”, you have a treasure, because 20 years ago a copy was worth $300,000 and now, no doubt, much more.

This is a portrait of Harvey at age 43. He was short, dark-haired, and very nervous. He was also full of energy – almost as if in perpetual motion. He awoke at night because of his energy, and had to walk until he got very, very active mind.

William Harvey was born on April 1, 1578, in Folkestone (in Kent). He was the first of seven children, and the son of a very wealthy man by trading with the Orient. William things as money because he was from a held him in such high regard that they took William was sent to a grammar school in were not allowed to speak any languages beginning of his classical education. In 1594 he entered Caius College, in Cambridge, where Kentians (people from Kent, like Harvey) were preferentially admitted at the time, and graduated four years later with a Bachelor’s degree. The graduates of Caius college were encouraged by the founder of the school, Dr John Caius, to pursue medical studies abroad. In the late 16th century, if you wanted to go abroad to have a good medical education, the place to go was Italy. It was like going to America in the 21st century. In particular, you would go to northern Italy, which offered some very prestigious universities such as Bologna, Padua, Pisa, and others. Among these, probably the most famous Medical School was the University of Padua, where William matriculated in 1598 at the age of 20. Padua had a great reputation for a number of reasons. Apart from the fact that Copernicus had studied there and that, at the time when Harvey was a student, Galileo was teaching mathematics (although the two of them apparently did not cross paths), Padua had a stellar cadre of very distinguished
Faculty members. Harvey’s favorite teacher was the anatomist Hieronymus Fabricius, also known as Fabricius ab Acquapendente (the successor of Gabriele Falloppio, after whom the Fallopian tubes were named). Fabricius became a very good mentor for Harvey. He described – amongst many things – the presence of valves in the veins, but had no idea what their function was. This discovery became a key turning point in Harvey’s life, because it inspired him to investigate the function of these valves, and in doing so, to discover the circulation.

At that time, Padua was a very cosmopolitan University, much like the American Universities are today. Going to Padua in the 16th century would be like going to Harvard nowadays (and probably just as expensive!). Students flocked there from all over Europe – from Germany, Belgium, France, England, Spain and so on. Each group of students was called a “Nation”, and each of them elected a Councilor to lead their Nation; the body of the Councilors, together with the Rectors, was the governing body of the University. Apparently, William had a charismatic personality, because he managed to be elected as the Councilor of the English Nation, a position of high distinction that gave him the privilege of having his own stemmata painted in the Great Hall of the University. You can still see them there.

Harvey received his diploma of Doctor of Physic from the University of Padua on April 25, 1602 (two years after Giordano Bruno was burned alive in Rome by the Catholic Church, his tongue having been cut before the fire). He went back to England and, two years later, married Elizabeth, the daughter of Dr Lancelot Browne, the personal physician of Queen Elizabeth and, subsequently, of King James. By becoming Browne’s relative, Harvey was catapulted into the “good society” of London and had access to many VIPs, which facilitated his career. We know very little about his marriage, except that he had no children (which left him plenty of time to do his anatomical studies), that Elizabeth (whose brother, ironically, was named Galen) had a pet parrot, and that she died before him. Three years after his marriage (1607), he became a Fellow of the Royal College of Physicians, and two years later (1609) he was appointed as physician at St. Bartholomew’s Hospital, where he developed a good practice. At the same time, he continued to study anatomy and do research (thereby being the precursor of what nowadays we refer to as the clinician-scientist).

In 1615, Harvey was given the prestigious title of Lumleian Lecturer at the College of Physicians. This was a major post in the college; he was required to give two lectures a week in six-year cycles (which he did until 1650). His meteoric ascent continued unabated. Two years later (1618), he became the Physician Extraordinary to King James I. When the king died, there were rumors that Harvey had plotted to kill him, and that he was part of a Catholic plot. He was investigated but fortunately for him, Charles I (the successor of James I) held him in high esteem, protected him, and appointed him as his own personal physician.

In 1628 Harvey published his immortal masterpiece, the De Motu Cordis. In 1651, he published his second book, De Generatione Animalium, which was not as groundbreaking as the first but, nevertheless, had some important intuitions. In 1654, he was offered the prestigious Presidency of the College of Physicians, but he refused for health reasons. He was suffering from gout, and his life was becoming increasingly miserable. In 1656, while he was living in Oxford and a year before his death, he donated money to Merton College to establish an endowment for the Harveian Lecture, which has been delivered yearly since 1658 – and has become, as I have mentioned, one of the highest recognitions for a physician.

On April 24, 1657, Harvey wrote to a colleague: “I am not only ripe in years, but also… a little weary. It seems to me indeed that I am entitled to an honorable discharge.” Less than two months later, on June 3rd, 1657, his wish was granted; he died of a stroke, at the age of 79.

(To be continued in the next issue)
The XXth World Congress of the ISHR will be held less than one year from now, on May 13-16, 2010 in Kyoto, Japan. It is my great honor to organize such an exciting meeting in Japan, and I look forward to hosting many delegates from all over the world.

The main theme of this Congress is “Paradigm Shift to Integrated Cardiology – Gene, Function and Life.” Recent research in the area of genomic science has elucidated many pathways involved in molecular signaling in cells and described dynamic changes in gene expression. Many functional and morphological responses of the cell to extracellular stressors, which determine the viability of the organelles, cells and individual, have also been clarified. Various diseases can now be defined as the result of abnormal responses of the gene, cellular function and individual behavior which restrict the life span of affected individuals and limit their ability to adapt to environmental changes. The Congress will cover a variety of important topics in cardiovascular research relevant to understanding the cardiovascular system in health and disease.

The Scientific Program will include:
- Approximately 45-50 Symposia, including around 20 symposia sponsored by ISHR International, 10 sponsored by ISHR Sections (Australasian, European, Japanese, Latin American, North American) and 15 symposia sponsored by industries.
- A Nobel Laureate Lecture by Oliver Smithies, Univ. of North Carolina at Chapel Hill, on embryonic stem cell and gene targeting technology.
- A Special Lecture by Shinya Yamanaka, Kyoto Univ., on induced pluripotent stem (IPS) cells.
- ISHR Award Lectures, including:
  1. Distinguished Lecture Awards:
     - Keith Reimer Distinguished Lecture;
     - Janice Pfeffer Distinguished Lecture;
     - President’s Distinguished Lecture.
  2. Outstanding Investigator Award
  3. Research Achievement Award
  4. Peter Harris Distinguished Scientist Award
  5. Distinguished Leader Award
  6. Free communications and moderated poster sessions
  7. The Richard J. Bing Young Investigator Award Competition
  8. Morning Tutorial Lectures
  9. Luncheon Seminars
  10. Evening Satellite Meetings

These programs will be held during the four-day Congress mainly in parallel sessions except for the Special and Award Lectures. The ISHR International symposia, planned by the ISHR International Scientific Program Committee, cover a broad range of topics including the genome, intracellular organelles, ion channels, membrane receptors, signal transduction, angiogenesis, cellular injury and protection, stem cells and regeneration, and will be complemented by the symposia planned either by Section Program Committees or by the Congress Scientific Program Committee, to provide an integrated and comprehensive scientific program. A unique feature of the coming World Congress is the incorporation of Section Meetings within the Congress.

Enjoy the Social Program
The social program will include the following events:
- An opening get-together (May 13)
- The FISHR dinner (May 14)
- A half-day excursion to “Aoi Festival” (May 15)
- A Japanese buffet-style banquet in the Conference Garden (May 15)
- Optional sight-seeing tours:
  - Kyoto one-day tour (May 13, 16)
  - Uji half-day tour (May 14)
  - Other optional tours (May 12-16)

ONLINE Registration will start on September 1st, 2009
Advanced registration is welcome until March 31, 2010.

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Hotel reservations can be made ONLINE when you register for the meeting. JTB
Western Japan Corporation is handling the accommodations for the Congress participants. You can select from a variety of hotels at a special Congress rate (see the website at www.ishr2010.com/travels/index.html).

Abstract Submission

Travel Grants are available
Travel grants will be provided to young investigators from abroad. Each Section will select the travel grant recipients from that Section, based on the submitted abstracts and subject to the relevant ISHR criteria.

Since the ISHR Sections will hold their 2010 meetings in conjunction with the ISHR World Congress, we are expecting around 2,000 participants from all over the world. You are cordially invited to share in the excitement and success of the World Congress 2010 in Kyoto.

Masatsugu Hori, M.D., Ph.D.
President, the ISHR XX World Congress; President, Osaka Medical Center for Cancer and Cardiovascular Diseases; Professor Emeritus of Osaka University

FELLOWSHIP OF THE ISHR

The International Society for Heart Research invites you to nominate candidates for membership in the Fellowship of the ISHR.

History of the Fellowship
The ISHR established the Fellowship of the ISHR as a means of recognizing those members who have distinguished themselves for outstanding contributions to cardiovascular research. Fellows are selected solely on the basis of scientific excellence, as evidenced by an established track record of publications in high-impact journals. The Society looks to its Fellows for leadership and guidance in its various activities; including the organization of topical meetings and selection of recipients for Society awards.

Fellowship Benefits
- Fellows will be entitled to add “FISHR” to their degrees and distinctions.
- Fellows will receive a complimentary subscription (hard copy) to JMCC.
- Fellows will be given free registration at World Congresses.
- The names of new Fellows will be published in JMCC and Heart News and Views.
- Fellows will receive a Fellowship certificate.

Nomination Procedure
The name and institute of each nominee and a brief (one page) letter of nomination outlining his/her major contributions to cardiovascular science should be sent by email (llobaugh@nc.rr.com) to Dr Leslie Anderson Lobaugh, Executive Secretary – ISHR.

details of the nomination and application procedures can be found at www.ishrworld.org. click on 2010 Fellows of the ISHR in the lefthand column.

The deadline for receipt of nominations is 30th September 2009. Nominations received after that date cannot be considered.
New Paradigm from a Historic Port – Report on the XXV Meeting of the Japanese Section (December 5-6, 2008: Yokohama, Japan)

The 25th Annual Scientific Meeting of the Japanese Section of the ISHR was held at the Yokohama City Port Opening Memorial Hall, Yokohama, Japan. Yokohama is known traditionally to be an international city, one of only a few ports of entry into modern Japan which was established 150 years ago. Prof. Tohru Izumi from Kitasato University, the president of this meeting, chose as the theme of the meeting “Reverse Remodeling in Cardiovascular Medicine”, with emphasis on the pathomechanisms and therapeutic interventions involved in remodeling. The concept of anti-remodeling or reverse remodeling is an engaging topic with clinical implications not only for heart failure but also for arrhythmia and vascular diseases.

With more than 400 participants, the conference was well attended and the level of science was outstanding: seamlessly combining basic cardiovascular science and clinical cardiology. The meeting included three symposia discussing cardiovascular remodeling as the main theme. The first symposium: ‘Cardiac Failure and Remodeling’ was preceded by the keynote lecture from Prof. Hideo Baba from Essen University concerning morphological and molecular alteration of the myocardium after LVAS implantation. In the second symposium, electrical remodeling, with regard to arrhythmia and conduction disturbances, was debated by 6 electrophysiologists after Prof. David Rosenbaum initially reviewed the pathomechanisms. Vascular remodeling was discussed at the last symposium from several viewpoints, including discussions of regeneration medicine and inflammatory processes presented by Dr Ricard Rocha from Novartis Pharma Co. and Prof. Gregg Semenza from John Hopkins University, respectively. Another focus on inflammatory pathomechanisms of not only myocardial diseases, as reviewed by Prof. Reinhard Kandolf from Tuebingen University, but also atherosclerosis and obesity.

The Young Investigator Awards session, always a point of interest, was especially emphasized this year. Fifteen candidates presented their distinguished work in three separate sessions. The standards were very high and the decision by the judges in choosing the winners was not easy. The winners were: Dr Kinya Seo from Tokyo University as the gold medal winner (‘Contribution of structural heterogeneity to stretch-induced arrhythmias examined in ventricular tissues and isolated myocytes’), Dr Yosuke Kayama from Chiba University as the silver medal winner (‘Arachidonic 12-lipoxygenase promotes the development of cardiac fibrosis and heart failure via induction of monocyte chemoattractant protein-1’), and Dr Fumiyuki Hattori from Keio University as the bronze medal winner (‘Novel methods for purifying and transplanting ES cell-derived cardiomyocytes with high cell survival rates and without inducing teratoma formation’).

While there were numerous presentations which were of great interest, including 75 poster presentations, one notable highlight was the President’s Distinguished Lecture by Prof. Gerd Hasenfuss from Georg-August University of Goettingen entitled, ‘Adult pluripotent cells for cardiac regeneration’. His speech described a novel approach to regeneration therapy for the failing infarcted heart using multipotent/pluripotent adult germline stem cells with characteristics of embryonic stem cells from the adult mouse/human testis. Another fascinating lecture by an invited speaker was provided by Prof. Metin Avkiran from King’s College London, the Secretary General of the ISHR International Council. Dr Avkiran delivered an outstanding report concerning protein kinase D as a novel regulator of cardiac function and remodeling.

The evening social event was held at a modern Italian restaurant near the meeting hall, accompanied by a mini-concert by a charming Japanese ladies quartet. All of the guests enjoyed appetizers, cocktails and conversation in this friendly atmosphere.

Yokohama is a historic city most Japanese are proud of, and its pioneer spirit has continuously encouraged us. The meeting hall, located in the center of Yokohama, is also a symbol as a venue of international communication. The historical relevance of this meeting encouraged us to enhance our scientific activities in the cardiovascular field in the beginning of the 21st century in order to construct a new paradigm for the future.

Prof. Izumi, the President of the meeting, enjoys a conversation with Prof. Reinhard Kandolf at the opening reception

Dr Takayuki Inomata  
Sagamihara, Japan
It is with great sadness that we report that Howard E. Morgan M.D. died on March 2, 2009 in Estero, Florida. As a former President of the International Society for Heart Research (1983-1986), Dr Morgan played a pivotal role in the development of the ISHR in its early formative years, leaving a legacy of excellence and scholarship that has greatly benefited the entire membership. His extraordinary scientific achievements have made him one of the giants in basic cardiovascular research of the 20th century, particularly in the area of cardiac metabolism, signaling, and hypertrophy. He also is well known for developing the isolated perfused working heart preparation that is used in metabolic studies worldwide.

Howard Morgan was born in Bloomington, Illinois on October 8, 1927 and attended school in Illinois during World War II. His education was accelerated by the war, and he graduated from Johns Hopkins Medical School with an M.D. in 1949 at the age of 21. Today, most 21 year old American students are juniors or seniors in college.

From Hopkins, he went to Vanderbilt where he specialized in Obstetrics and Gynecology. He became an instructor in this department in 1953, however, research work attracted him and, in 1954, he began studies of cardiac metabolism in the Hughes Institute and Physiology Department of Vanderbilt University Medical School under the tutelage of Prof. Charles R. Park. By 1966, he was a Professor of Physiology and, in 1967, he became the founding Chairman of the Department of Physiology of a new Medical School in Hershey PA., where he spent the next twenty years developing one of the best Physiology departments in the country.

In 1987, he became the first Director of the Weis Center for Research at the Geisinger Clinic in Lewisburg PA. He recruited excellent scientists into this Research Center and it became a very successful enterprise. At Weis, he was able to pursue his chief interest fulltime, which was applying molecular biological techniques to the study of heart disease. During the course of these experiments, he learned much about protein synthesis and degradation and the factors which control these processes in the heart.

Dr Morgan’s ability to emerge as a leader has been remarkable. He has held leadership positions in all major cardiovascular science organizations, including the American Physiological Society (where he was President in 1985-1986), the American Heart Association (where he served as President in 1987-1988), and the National Heart, Lung and Blood Institute, (where he served on the Advisory Council in 1979-1983). He served as Editor/Associate Editor of major journals such as the American Journal of Physiology, Physiological Reviews, and the Journal of Molecular and Cellular Cardiology.

During the course of his career, he received numerous awards and honors including election to the Institute of Medicine of the National Academy of Sciences in 1987. He received the Peter Harris Award for outstanding cardiovascular research from the ISHR, the Award of Merit, the Distinguished Achievement Award, and the Gold Heart Award of the American Heart Association, the Carl J. Wiggers and Ray G. Daggs Award of the American Physiological Society and the Medal of Merit for Outstanding Achievements in Cardiovascular Education and Research of the International Academy of Cardiovascular Sciences.

Our Society is honored to have such an exceptional scientist as one of its former presidents. Dr Morgan distinguished himself, not only as one of the preeminent cardiovascular investigators of the 20th century, but also as admirable and rare human being - an honest man who consistently adhered to principles of fairness in his dealings with people. His opinion was widely sought and freely given. The ISHR and the entire cardiovascular community has lost an icon.

Roberto Bolli, M.D.
Robert B. Jennings M.D.

Past-Presidents of the ISHR

Richard J. Bing 1967-1973
Albert Wollenberger 1973-1976
Lionel H. Opie 1976-1978
Robert B. Jennings 1978-1980
Peter Harris 1980-1983
Howard E. Morgan 1983-1986
Winifred G. Nayler 1986-1989
Yoshio Ito 1989-1992
Jutta Schaper 1995-1998
David J. Hearse 1998-2001
James M. Downey 2001-2004
Roberto Ferrari 2004-2007
Just as the last edition of *Heart News and Views* was going to press, the distressing news came of the death of Philip Poole-Wilson. There was little time for anything other than a simple announcement at that point, but we now have the opportunity to try to express more fully what Philip meant to the cardiovascular community and to the ISHR in particular. The respect and affection in which he was held has become evident since his death, in the tributes to him in the major newspapers and international journals, the dedicated session at the Nice ESC-HFA/ISHR meeting, the packed Memorial Service in London and the 500 or more letters received by his wife, Mary.

The honourable record of his life stands as its own monument to the doctor and scientist. At home, he was Simon Marks Professor of Cardiology, Head of the NHLI and finally on the Council of Imperial College. In the wider world, he became President of first the European Society of Cardiology and then the World Heart Federation. He won the Prix Europe et Médecine in 2001, awarded by the Institut des Sciences de la Santé in Paris, as well as the British Cardiovascular Society’s Mackenzie Medal, its most prestigious award. He published over 500 papers and trained at least 29 of the current world leaders in cardiology. With a sad irony, one of the fullest accounts of his accomplishments is to be found in an article published on March 4th, just a few days before his death. “Pioneer in Cardiology: Philip Poole-Wilson” took up 6 pages of the respected journal *Circulation*, which in itself must be a unique accolade.

Philip was heavily involved with the ISHR from the beginning, having followed its development during his time with Peter Harris. He was a council member from 1986-1994, treasurer from 1989-94 and became one of the Founding Fellows of the ISHR when those awards were instigated. He was very much in tune with the ideals of the ISHR, being a great supporter and advocate of basic science in public and within his own Institute.

Although the honours and achievements alone would justify the enormous reaction to his death, it is striking that the majority of the tributes are directed towards Philip the friend, helper and mentor.

**In Memoriam**

*PHILIP A. POOLE-WILSON* 1943 - 2009

Having known and worked with him for 28 years, I can see clearly why he was held in such great affection by so many. I would like to add a few personal memories which may strike a chord with others, and which illustrate his enthusiastic and endearing personality. I met Philip in 1980 when I came to the Cardiothoracic Institute in its first home in Wimpole Street. Cardiac Medicine was then still separate from the Thoracic Medicine section near the Royal Brompton Hospital, Winifred Nayler was just leaving, and Peter Harris was in charge. Philip had not long returned from a Fellowship with Glenn Langer at UCLA, and was still in the laboratory at the top of Wimpole St mixing the Ca⁺⁺ solutions with his hand over the open neck of the volumetric flask. His dissection technique for the septal preparation was notoriously rapid, involving removing much of the contents of the thoracic cavity as fast as possible, then running up 3 floors from the animal house to the laboratory. He was gathering the detailed information about Ca⁺⁺ and Na⁺ fluxes in ischaemia and during the Ca⁺⁺ paradox, summarised particularly in his 1984 review “Calcium out of Control”. I was working with Peter Harris at that time on G-protein biochemistry. When I became interested in isolating adult myocytes, Philip was extremely helpful. He introduced me to the surgeons who were to help me with tissue from cardiac operations, supported my first efforts to design a new method for measuring myocyte contractility and assisted me in my applications for funds. He became Head of Department as Peter Harris retired in 1988, and took over the reins as we moved to Dovehouse St, South Kensington to join the Thoracic Department and become the NHLI. During the next several years he retained a keen interest in the isolated myocyte work, and I remember particularly that he was instrumental in initiating the development of both the frequency responses and the nitric oxide sections of the work.

Philip was at the reins when we were taken over by Imperial College in 1995 and became a Division of their Medical School. Around this time there were very difficult financial circumstances both UK-wide and locally, as it was the time when Mrs Thatcher was squeezing higher education hard. Philip was the Head of Division for NHLI in Imperial College from 1997-2000, and had to deal with the loss of 12 out of 44 academic positions and the removal of large amounts of funding. Despite having attained high office in Imperial College, the ESC and the World Heart Federation, I don’t think Philip was at heart a political animal. He was too kind, too straightforward and too gentle. He was always keen to bring transparency to the finances and other dealings, even if it brought him more trouble. I cannot remember any occasions where he even raised his voice to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult. He never spoke badly to anyone, however provoked, or used any kind of insult.

Sian Harding, Ph.D.
London, UK
In June 2007, in the beautiful frame of the city of Padova, I was awarded the ISHR-ES/Servier fellowship. Each year, this prestigious fellowship provides a great opportunity for a young scientist to perform a year of basic research in the cardiovascular field. I joined the Laboratory of Experimental Cardiology at the University Medical Centre of Utrecht in The Netherlands as a postdoctoral researcher working under the supervision of Prof. Pieter Doevendans and Dr Marie-José Goumans in the spring of 2007. My research project focused on the characterization of human cardiac progenitor cells isolated from fetal and adult hearts and on the implementation of differentiation protocols towards the cardiomyocyte and vascular lineage. It is a great honor to be invited to summarize my project here.

Regenerative Medicine Approaches

Cell-based cardiac repair has the ambitious aim to replace the injured cardiac muscle developed after myocardial infarction with new contractile cardiomyocytes and vessels [1, 2] (Figure 1). Different stem cell populations have been intensively studied in the last decade as a potential source of new cardiomyocytes to ameliorate the damaged myocardium, compensate for the loss of ventricular mass and contractility and eventually restore cardiac function. An array of cell types has been explored in this respect, including skeletal muscle, bone marrow derived stem cells, embryonic stem cells, and more recently cardiac progenitor cells.

Cardiac Progenitor Cells from the Adult Heart

Our laboratory has successfully isolated and characterized a cardiac-resident population of cells that possesses the potential for being a suitable source for cell replacement therapy as well as an amenable cell system for drug screenings and toxicity tests [3, 4]. Human cardiac progenitor cells (hCPCs) can be readily isolated from enzymatically digested fetal and adult heart biopsies, either by single cell cloning or by purification with an anti mSca-1 antibody. These cells can be maintained and expanded in an undifferentiated state for several passages. They show expression of stem cell markers such as Isl-1 and cKit, and already express early cardiac transcription factors, namely: GATA4, NKX2.5 and MEF2C. None of the mature cardiomyocyte markers is expressed in the undifferentiated state (Figure 2a, b). hCPCs can be differentiated to mature cardiomyocytes by treatment with 5-azacytidine and TGFβ. hCPC-derived cardiomyocytes show expression of sarcomeric proteins, gap-junctional communication, action potentials of maturing cardiomyocytes and spontaneous beating activity in culture (Figure 2c, d).

Conversely, culturing these cells in pro-angiogenic conditions, in the presence of VEGF in a suitable extracellular matrix (Matrigel®), induces upregulation of angiogenic markers and organization of the cells in tubular structures, analogous to what endothelial cells can generate in such an in vitro system (Figure 3). More interestingly, when injected in the border zone of the infarcted region in a mouse model of MI as undifferentiated cells, they can improve cardiac function, and can be found as differentiated cardiomyocytes as well as CD31 positive cells organized in vessel like structures [5].

Histone Deacetylases Inhibitors to Improve Differentiation

Differentiation of hCPC towards the cardiac lineage requires the addition of a DNA demethylating agent (5 azacytidine), which causes profound epigenetic modification by erasing methylation...
marks, normally devoted to specific gene silencing in differentiated cells. Alternative epigenetic mechanisms controlling gene expression, besides DNA methylation, include histone acetylation and methylation. Histone acetylation, mediated by histone acetyl transferases (HATs), is generally associated with local chromatin expansion and increased accessibility to the DNA for the transcriptional machinery. Histone deacetylases (HDACs), on the other hand, perform the opposite job, leading to chromatin condensation. Methylation of histone tails, instead, exerts different regulatory functions depending on the residue and on its mono, bi or tri-methylated state. Many studies have focused on the role of HDACs in cardiac hyperthrophy [6]; however, an interesting role of these enzymes as inhibitors of differentiation has also been reported. HDACs inhibition by Trichostatin A (TSA) in embryonic carcinoma cells (P19-EC) was shown to induce differentiation of these cells towards the cardiac lineage by inducing the expression of GATA4, NKX2.5, MEF2c, BMP4 and cardiac actin. In contrast, inhibition of differentiation was observed upon overexpression of HDAC4 [7-9]. HDAC4 has been shown to negatively regulate skeletal myogenesis by associating with the myocyte enhancer factor 2 (MEF2c).

HDACs inhibitors are currently used in the clinic as anti-cancer drugs [10]. A possible alternative application of these compounds as tools to trigger CPC differentiation in vivo was obviously a very intriguing option to explore. I addressed the possibility that HDAC inhibition could induce differentiation of cardiac progenitor cells and assess the role of acetylation during induction of the cardiogenic lineage. Different HDAC inhibitors have been tested for this purpose on cultured cells; however, none of these was able to induce myogenic differentiation. In contrast, they modified the phenotype of the cells increasing their migratory behavior and inducing active remodeling of the extracellular matrix (manuscript in preparation).

In addition, an RNAi approach was undertaken to gain a better understanding of the role of epigenetic modifications as regulators of gene expression and differentiation. Different histone methylases and demethylases were knocked down in hCPCs using retroviral transduction. Candidate enzymes were selected based on their described function in mouse ES. This study, still ongoing, may lead to the identification of new key regulators of cell differentiation.

Future directions

Human cardiac progenitor cells harbor a great application potential in the contest of autologous cell replacement therapy. Encouraging animal studies show that they may have a positive role in restoring cardiac function after MI. Improvement
of the culture conditions and differentiation protocol as well as implementation of the delivery methods are now essential steps to face in order to bring the use of these cells to a clinical application.

Acknowledgements
This project was supported by an ISHR-ES/Servier fellowship and an ESC research grant. Special thanks to all the members of the Experimental Cardiology team.

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HEART NEWS AND VIEWS
is the official News Bulletin of the International Society for Heart Research and is published every fourth month.

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