In this issue:

- President’s Letter ........................................ 1
- Past Truth & Present Poetry by Richard J. Bing .............. 3
- Bridging the Gap, where clinical and basic sciences meet by Karl T. Weber ........................................ 4
- 2003 YIA Winner of the European Section .................... 6
- 2003 YIA Winner of the American Section ..................... 8
- Honorary Membership for Naranjan S. Dhalla ................. 10
- 2005 ISHR-ES / SERVIER Research Fellowship .......... 11
- Report on Dresden Meeting ................................ 12
- Report on Cancun Meeting ................................ 14
- Meetings Calendar ........................................ 15

President’s Letter

Among my all-too-many hobbies is boating. Most of my life I have primarily kept a boat as a tool for saltwater fishing, although I did go through a decade of sailing during the 1980s. There is an old saying among boat owners that the two happiest days of your life are when you buy your boat and then when you sell it. I would have to say that I have had a similar feeling about serving as the President of the International Society for Heart Research. I was thrilled when the membership selected me for this honor and I consider this to be the greatest achievement of my career. I have really enjoyed working these three years for the Society and hope that I have left it a little better than when I took over. Nevertheless this has been a working position and now it will be a relief to pass the torch on to Roberto Ferrari for the next three years. Perhaps I can use the extra time to go fishing a little more often. For those who aren’t familiar with Mobile Alabama, we are situated on the Gulf of Mexico and it is teeming with very co-operative fish. It is that and the warm winters that have kept me here for 30 years.

My tenure as President has overlapped an extraordinary period in history. It started with the September 11th attacks, the anthrax poisonings, a tough recession, and the “Bush” wars. These events, coupled with our president’s xenophobic and belligerent policies, were real threats to the ISHR’s international structure. For a while I thought that I would never be able to leave our borders

(continued on page 2)
President’s letter
(continued from page 1)

again. Despite those world-shaking events the ISHR has been able to maintain its cohesive world-wide structure and now remains strong as ever. My friend and colleague Roberto Bolli has been a very active and effective Secretary General and has made my job infinitely easier. Roberto must write 10 letters a day for the ISHR, as my mailbox is always full of copies of the letters that he has sent. To try to make life a little easier for both of us we recruited Dr Leslie Lobaugh to serve as an executive secretary for the Society. She is the ISHR’s one paid employee. In that capacity she has looked after membership services, the logistics of the many awards that we now give, and innumerable other details. We look for her to have an ever-expanding role in the administration of the Society and we encourage all of you to try to meet her at Brisbane.

Under the watchful eye of Rick Walsh the Journal of Molecular and Cellular Cardiology has flourished and the impact factor continues to rise. Industry takeovers have caused our publisher to change several times, which led to some obvious confusion, but we now seem to be in a stable period with Elsevier. I hope one of these days I will be able to produce a study of sufficient quality to actually get accepted in our Journal. At least I can always hope.

As President I have been invited to many of the Section Meetings and I have thoroughly enjoyed the interesting travel not to mention all of the frequent flyer miles. I am not sure how I will survive the trip to Brisbane, however. Mobile is served primarily by a big US airline called Delta. They actually go just about everywhere in the world so it has been worthwhile to accumulate my frequent flyer miles with them. I remember one time when I was waiting for a late-night British Air flight out of Bombay. I was dreading the grueling trip all the way home in economy when I noticed a small Delta sign on the wall. I followed the arrow and sure enough there was a Delta desk. Soon I was able to trade the British Air ticket and a few frequent flyer miles for a business seat to Atlanta on good old Delta. Delta may be a great airline but unfortunately they do not go down under. So that meant dealing with American Airlines with whom I have no leverage whatsoever. My itinerary is Atlanta to Los Angeles, Los Angeles to Brisbane, Brisbane to Johannesburg, Johannesburg to London and London to Atlanta. This Magellan-esque circumnavigation will all be in economy and I am sure that it will be a full week before I will be able to stand again. When you see me in Brisbane I will be only two legs into this odyssey so I should still be civil at that point. When my wife picks me up from the airport, well that will probably be a different matter.

I guess one thing that I can take credit for is the Society’s web services. Among my hobbies is computer tinkering and it has been a lot of fun to develop the ISHR’s web site and to personally maintain it and the server on which it runs. I hope to be able to continue this effort for the foreseeable future. Finally, some of you may be curious about the rather un-presidential picture of me that accompanies this article. Many of you already know that yet-another pastime of mine is antique motorcycles. Although the picture shows me on my one modern motorcycle, a Honda Valkyrie, I have a garage full of restored antiques. If you want to learn more about my motorcycle activities try typing - Jim Downey Motorcycle - into Google. At this point you are probably wondering what all this has to do with heart research. Actually nothing. It is just after having to fill this column on a regular basis for the past three years that I have absolutely run out of material. So on that note I will say adios amigos and Roberto Ferrari, sharpen your pen.

James M. Downey
As a child my parents took me to the source of the River Danube, a mere trickle of water destined to become a mighty river flowing past Vienna and Budapest to the Black Sea. I have chosen two examples, the discovery of p53, a tumor suppressor, and the discovery of insulin to show how great discoveries, like rivers, are insignificant and vulnerable at the beginning but develop into mighty streams of science and medicine. There is as yet no end to these rivers of discovery, and their impact will be felt for years to come.

**p53**

The earliest publications on p53 appeared in 1973. They described that after infection or transformation with a tumor virus, the simian virus SV40, an immunogenic protein could be precipitated. Further evidence showed that this protein is of cellular origin and is expressed in several murine carcinoma cell lines. The p53 protein is precipitated only by specific antibodies and is also found in tumors of non-viral etiology. At this point, like a meandering river, research on p53 took on a new course. It was the period in cancer research when oncogenes were the main and most fruitful topic. It was only natural to assume from these findings that p53 was an oncogene. Cloning of p53 furnished further evidence of its role in oncogenesis.

Now, the course of discovery changed again. It was found that the oncogenic effect of p53 was due to its mutations. Several mutants of p53 species were found, one containing two point mutation, the other a single different point mutation. It is the wild type of p53 which effectively interferes with the ability to elicit neoplastic transformation. Soon more evidence of the tumor inhibitory properties of p53 became available. Chromosomal changes in colon cancer had been known for a number of years, affecting primarily chromosome 17 where allelic deletions are expressed as mutations of the gene expressing p53. In colon cancer this deletion leads to tumor progression. Another evidence for the tumor inhibition by p53 was that mice lacking p53 are developmentally normal but are very susceptible to spontaneous tumor formation. P53 accomplishes suppression of tumors by the triggering of apoptosis, programmed cell death. Apparently there are a multitude of mediators of p53 induced apoptosis but in normal cells p53 is latent. A number of factors activate it, amongst them oncogenic activation, telomere attrition, nitric oxide and others. Like Moshe Oren writes in his Harvey Lecture, “all this extensive understanding will culminate in the development of new strategies to treat cancer.” We only can hope that he is right.

**Insulin**

The discovery of insulin occurred about 80 years before that of p53. At the time of the discovery of insulin, the nature of the gene and most of the biochemical processes were unknown. But the human drama of the discovery of insulin, with its small beginnings could have happened at any time in the history of science. The small brook of discovery was many times in danger of drying up.

It started with Frederick Banting who practiced surgery in London, Ontario at the beginning of the twentieth century. His practice was not lucrative and gave him time to think of advancing the cure of diseases, especially diabetes. One day he came across an article which described that ligation of the pancreatic duct leads to the digestion of the exocrine tissue while leaving the Islets of Langerhans intact. This became Banting’s idee fixe. Why not, he reasoned, tie the pancreatic duct in dogs and then extract the sugar lowering substance from the remaining tissue? With this idea he went to Professor Macleod, the head of the department of Physiology at the University of Toronto. On his way to his native Scotland for vacation, MacLeod gave Banting inadequate facilities in his department. He obviously expected little from a country surgeon. A young student, Charles Best, joined Banting during the summer and the two started to work on dogs by ligating their pancreatic ducts and extracting the remaining pancreatic tissue. The original idea of ligating the pancreatic duct was soon discarded in favor of using the whole pancreas. By the time Professor MacLeod returned from Scotland, Banting and Best were on the way to discovering insulin. When MacLeod saw the progress, he tried to take over the project which he previously had considered with scorn.

I cannot help but speculate how Banting and Best’s idea would play today. The animal rights committee would never have (continued on page 5)
A warm summer evening, June 25, 1965, and resident in medicine, Nick Pinheiro, was seated at his favorite tasca in Porto enjoying Portugal’s outstanding sea fare and a bottle of chilled vinho verdi. This had become Nick’s usual haunt on Friday evenings and he now knew most of the staff including Carlos, a waiter whose hoarse voice and slurred speech made deciphering the evening’s specials a challenge. Tonight, Carlos was quite troubled, mumbling that sharp, shooting pains in his feet and deep stabbing pains in his calves made tending tables difficult. Also troublesome was brother Juan, a chef in Lisbon. Earlier in the week Juan was dismissed because too much salt had been added to meals he prepared. Carlos explained this was not because Juan was careless or that he had overindulged in his favorite wine. Instead, this incident was more likely related to Juan’s recent unsteadiness and faltering vision. Nick offered assistance, but Carlos politely declined and departed in a rather wide-based, stumbling gait.

Friday next again found Nick dining at the tavern reflecting on several of his patients while gazing out at the River Douro. His reverie was interrupted by the clatter of fallen dishes. Not ten feet away stood an embarrassed, unsteady Carlos. Nick rushed to his aid. Carlos brushed the incident off as nothing more than a result of summer’s heat. Perhaps, too, he was weakened by diarrhea of several days’ duration, but his was an intermittent problem to which he had grown accustomed. Nick found Carlos’ pulse to be irregular and insisted he call an ambulance. A second episode of near syncope convinced Carlos that hospitalization was unavoidable. Nick wondered if this episode could be explained solely by fluid loss and subsequent orthostasis. Why arrhythmia? Perhaps there was hypokalemia.

At the hospital, Nick found Carlos normotensive but indeed orthostatic and began intravenous fluids. Bedside ECG demonstrated right bundle branch block, left axis deviation and sinus rhythm with premature atrial contractions. Runs of atrial fibrillation were seen on rhythm strip. Carlos’ right pupil was dilated with irregular outline and fringed edges; it did not react to light or accommodation. Thyroid nonpalpable; neck veins not distended; lungs clear. Cardiovascular examination did not reveal cardiomegaly, gallop, or murmur. Pain and temperature sensations in both lower extremities were blunted while position and vibration sensations were lost in feet and ankles. Given Carlos’ orthostasis, Romberg’s test would have to wait. Pertinent laboratory tests revealed: hemoglobin 10 g/dL with 3.9 million red blood cells/cm³; normal white cell count and differential, normal serum electrolytes and creatinine, albumin, and glucose; negative serology for syphilis; urine negative for porphyrins and Bence-Jones protein; cerebrospinal fluid protein 200 mg/dL, otherwise negative.

On rounds the following morning, Nick found Carlos sitting upright in bed with labored breathing and bilateral inspiratory rales on examination. A diuretic was given followed by sequential doses of oral digoxin over several hours. Why pulmonary congestion? Heart size and configuration on x-ray were normal. Since admission Carlos had received 3 liters of normal saline. Could he have occult constrictive pericardial disease? Perhaps intravascular volume was normal on admission and yet Carlos remained orthostatic. Ventricular extrasystoles presenting as parasystole on bedside ECG were evident later in the day. In 1965, a parasystolic focus was thought to represent a ventricular ectopic site with fixed rate impulse generation and therefore having common inter-ectopic intervals, and a fusion of ectopic and normal foci known as fusion beats.

Consuelo, Carlos’ 33-year-old frail and ill-appearing sister, came to visit him. Nick met with her in hopes of obtaining pertinent historical information and family history. Like Carlos and Juan, Consuelo too had become unsteady and walking was difficult, particularly at nights, when she often fell in attempting to reach the bathroom. And there was incontinence of urine and chronic constipation. She mused, “Doctor, all seems to be failing me.” Only this morning, in preparing for her visit, she scalded her right foot unable to gauge the temperature of her bath water. She also reported that their father had died suddenly at age 45. Prior to his demise he had complained of progressive
weakness of his legs, nausea, vomiting and constipation.

Nick had formed his differential diagnosis and was eager to discuss his thoughts on professor rounds.

What is the likely diagnosis?

In 1952 Corino Andrade reported on 74 patients belonging to 12 different families living in Povoa de Varzim, a fishing town in the Oporto region of Portugal. Patients presented with a puzzlesome constellation of symptoms and signs not unlike Carlos and his family. The illness had a long history in the region where it was known as “Mal dos pésinhos” or foot disease. Features included: insidious onset in young adults; peripheral neuropathy predominantly of lower extremities with impaired sensory and motor functions; and autonomic dysfunction (e.g., Adie’s pupil, sphincteric disturbance, orthostatic hypotension). Vitreous opacities blurred vision. Postmortem studies would demonstrate generalized amyloidosis.

Infiltration of the heart’s conduction tissue by amyloid fibrils and subsequent fibrosis (e.g., surrounding the AV node) leads to abnormalities of atrioventricular and intraventricular conduction and appear after the onset of progressive neuropathy. Amyloid deposition in atria can account for atrial arrhythmias while in perivascular and interstitial spaces of the ventricles and corresponding fibrosis account for a restrictive cardiomyopathy with diastolic dysfunction that can simulate constrictive pericarditis. In 1981, it was reported that digitalis selectively binds to amyloid fibrils leading to heterogenous concentrations of this sodium-potassium ATPase inhibitor within the myocardium. This perhaps provides substrate for abnormal automaticity, or spontaneous impulse formation, and parasystole—an ectopic, fixed rate, asynchronously discharging pacemaker tissue.

Today, it is recognized that familial amyloidotic polyneuropathy, a rare systemic disorder of the peripheral nervous system, involves a genetic variant of normal prealbumin, or transthyretin. Transthyretin transports thyroxine in the circulation. Its variant form causes autosomally dominant inherited forms of amyloidosis when it is deposited as amyloid fibrils accounting for peripheral neuropathy, cardiac amyloidosis, amyloid kidney and ocular disturbances. More than 30 amyloidogenic mutations in the transthyretin gene have been described. The mutated transthyretin in which valine has been replaced by methionine at position 30, the Met-30 variant, is most common. Most transthyretin is produced by the liver. In selected patients, liver transplantation has been effective in eliminating the source of variant transthyretin, reducing circulating concentration of transthyretin and ameliorating the disease.

Karl T. Weber, M.D.
After acquiring an interest in Biology at secondary school, I went to the University of Dundee in Scotland initially to study for a Life Sciences degree. Over the next couple of years, I realised that my main area of interest within the subject was Physiology, which led to me obtaining an honours degree in Anatomy and Physiology in 1995. Having decided that I would like to pursue a career in academic research, I moved to London where I studied for my PhD at the University’s Royal Veterinary College, focussing on the role of dietary lipoproteins in the initiation of atherosclerosis. My research led to several publications and the completion of my PhD thesis in 1998. This coincided with the establishment of a new Academic Cardiology Department at King’s College London by Professor Ajay Shah, in which I have been fortunate to be working as a post-doctoral scientist over the last 5 years. Since its conception, the department, which is predominantly funded by the British Heart Foundation has grown to 25 employees, who are mainly involved in investigating the potential role of oxidative stress in left ventricular hypertrophy (LVH), heart failure and endothelial dysfunction.

**Oxidative Stress and Heart Failure**

Despite major therapeutic advances, chronic heart failure continues to be a leading cause of mortality, the main initiating factors being ischaemic heart disease and hypertension. Both conditions are initially compensatory in nature as the heart adapts to increased load, through hypertrophy and remodelling. However a persistent insult can result in a progressive decline in contractile function and ultimately cardiac failure.

Oxidative stress, which refers to an imbalance between the production of reactive oxygen species (ROS – e.g. superoxide, hydrogen peroxide) and the endogenous antioxidant defence mechanisms, has been linked to the pathophysiology of heart disease. Elevated levels of ROS can have multiple actions such as direct damaging effects on cell membranes/proteins and inactivation of nitric oxide (NO) with the subsequent formation of peroxynitrite. ROS can also modulate redox-sensitive signalling pathways with the potential to induce specific acute and chronic effects, such as changes in cell phenotype and function.

It is important to determine the sources of ROS generation in the diseased heart and the factors responsible for their regulation. Potential sources of ROS include infiltrating inflammatory cells, mitochondria, xanthine oxidase and dysfunctional NO synthase. However, recent reports suggest that NADPH oxidase is an especially important source of ROS. Many studies have supported a role for NADPH oxidase-derived ROS in the vasculature; however, there have been relatively few studies which have specifically addressed its role in cardiac pathophysiology. The main focus of the research in which I have been involved over the past 5 years is to investigate the potential role of NADPH oxidase-derived ROS in the development of LVH and heart failure.

**Potential Role of NADPH Oxidase?**

NADPH oxidase is a multi-subunit enzyme complex which produces superoxide from molecular oxygen (Fig. 1). It comprises a membrane-bound cytochrome (consisting of one gp91phox and one p22phox subunit) and several cytosolic subunits (p47phox, p67phox, p40phox and Rac), which translocate to the cytochrome in the activated complex. NADPH oxidases are expressed in several cell types, including endothelium, fibroblasts, cardiomyocytes, vascular smooth muscle and neutrophils.

**Diagram of the activated NADPH oxidase**

*Figure 1. Diagram of the structure of the activated NADPH oxidase*

David J. Grieve (London, UK) was the winner of the Young Investigator Award at the XXIII European Section Meeting (Strasbourg, France; June 21-24, 2003).

Early studies from our laboratory suggested that a phagocyte-type NADPH oxidase may be an important source of cardiac superoxide production. In a guinea-pig model of pressure overload, we demonstrated that NADPH oxidase was a major source of ROS in cardiac hypertrophy and failure, and contributed acutely to LV diastolic dysfunction.

More recently, we have focussed our research on murine cardiovascular...
physiology in order to exploit the available transgenic models. Many of our studies have employed gene-modified mice which lack the gp91 phox subunit of NADPH oxidase, which is critical for enzyme activity. In our first series of experiments using these mice, we demonstrated that NADPH oxidase-derived ROS was pivotal in angiotensin II-induced cardiac hypertrophy and interstitial fibrosis. Subsequently, my work has focussed on the potential role of NADPH oxidase-derived ROS in cardiac hypertrophy induced by the more physiological stimulus of pressure overload. Firstly, we established a murine model of abdominal aortic constriction, which is similar to the previously employed guinea-pig model (albeit on a much smaller scale) and results in a progressive development of LVH; it is highly reproducible and carries a relatively low mortality. In contrast to the angiotensin II data, we found that a gp91 phox-containing NADPH oxidase was not critical for pressure overload LVH, although it was essential for the associated interstitial fibrosis. Pertinently, several different homologues of gp91 phox have recently been identified. Of these, we have found Nox2 (which is gp91 phox) and Nox4 to be expressed in the heart. Indeed, our further studies suggested that during pressure overload, an alternate Nox4-containing NADPH oxidase may be upregulated and mediate the hypertrophic response in the gp91 phox -/- animals.

Microconductance Analysis of Cardiac Function

It is important to know whether changes observed at the molecular level translate into functional alterations in the whole heart. We therefore set up the isolated ejecting mouse heart preparation in our laboratory, which enables the study of LV pressure-volume relations in an ex vivo situation (Fig. 2). Previously, microconductance technology had only been applied to measure LV pressure-volume relations in vivo. Whilst this is an excellent preparation, it does have a number of disadvantages, such as the confounding effects of anesthesia, autonomic tone and circulating neurohumoral factors and the difficulty in controlling cardiac loading. We believe that the isolated ejecting heart provides a useful complementary model for the assessment of cardiac function under controlled conditions, which is relatively free of potentially confounding factors. The application of microconductance technology allows a comprehensive analysis of cardiac function and the construction of pressure-volume loops, from which the end-systolic pressure volume relation (ESPVR) can be determined (Fig. 2). As far as we are aware, we are the first group to measure ex vivo LV pressure-volume relations in this technically-challenging preparation.

Further to our finding that a gp91 phox-containing NADPH oxidase was not essential for pressure overload-induced LVH, we used the isolated ejecting heart preparation to investigate a potential functional role of this enzyme. In contrast to the morphometric and molecular data, we found that ROS derived from this particular oxidase was critical for the development of the contractile dysfunction associated with pressure overload. Studies in isolated ventricular myocytes suggested that this was at least partly due to an intrinsic dysfunction of the myocyte. It therefore appears that a gp91 phox (=Nox2)-containing NADPH oxidase is involved in the development of contractile dysfunction and interstitial fibrosis, but is not essential for hypertrophy per se (which may be mediated by Nox4) during chronic pressure overload.

Future Perspectives

Our data suggest that the downstream effects of NADPH oxidase-derived ROS may depend both on the activating stimulus and the isoform responsible for ROS production. The relative contribution of the different intracellular sources of ROS and the downstream signalling pathways involved therefore require further study. Although current evidence suggests an important role for ROS in heart failure, much remains unanswered. Gaining an understanding of the role of different NADPH oxidases and their mechanisms of action may be beneficial in the quest for therapeutic intervention. So far, the relatively non-specific antioxidant treatments used in human studies have produced disappointing results. However, it is likely that the specific modulation of endogenous antioxidants will hold therapeutic potential for the treatment and prevention of human heart failure.

David J. Grieve, Ph.D.
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I was very fortunate to have been honored with the Young Investigator Award at the XXV Annual Meeting of the ISHR American Section. This study was featured as the cover article in the April 2004 issue of the *Journal of Molecular and Cellular Cardiology* (See Ref. and page 1 at the bottom of the first paragraph). I am originally from Boston, MA, and received my medical degree from Albany Medical College in 1998. I am currently finishing my final year of General Surgery residency at the Hospital of the University of Pennsylvania in Philadelphia, PA. I plan on completing a fellowship in cardiothoracic surgery, and pursuing a career in academic cardiac surgery. My research mentors are Drs Y. Joseph Woo, M.D. and Timothy Gardner, M.D., without whose expert guidance and advice I would not have been able to successfully complete this project. Our laboratory has been focused on devising novel and alternative treatments for heart failure, an increasingly common diagnosis in the industrialized world and a significant public health concern.

**Growth Hormone and Heart Failure**

Heart failure is predominantly caused by ischemic cardiac disease, with the majority secondary to previous myocardial infarctions (MIs). Pharmacologic treatment of heart failure includes beta-blockade and angiotensin-converting enzyme inhibition. Despite optimal medical management, however, 22% of men and 46% of women are disabled by congestive heart failure within six years of their initial MI. A central component of this ischemic heart failure is ventricular remodeling with wall thinning and chamber dilatation, a process that places the heart at increasing mechanical disadvantage and wall stress. Human growth hormone (GH) is a 191 amino acid polypeptide whose receptor is expressed on cardiomyocytes. Elevated serum levels of GH result in significant cardiac hypertrophy or wall thickening, and in animal models systemic treatment with GH following MI has been shown to attenuate or reverse ventricular remodeling and to provide a modest

![Figure 1](image-url)

*Figure 1. (A) Representative histologic sections 6 weeks following initial surgery. Hematoxylin and eosin staining has been performed, and arrows depict the diameter (D) and wall thickness (WT) measurement areas. Scale bar = 2mm. (B) Average left ventricular chamber diameter in each experimental group at the study endpoint. (C) Average left ventricular free wall thickness in each experimental group at the conclusion of the study. (Sham, n = 8; Null, n = 8; GH, n = 8). *p<0.001 GH vs Null, †p<0.05 GH vs Sham, **p<0.001 Null vs Sham, ††p<0.05 Null vs Sham.*
preservation of LV systolic function and geometry. To achieve this benefit, however, supraphysiologic serum levels of GH have been required which, if used in human clinical application, would put patients at risk for a diabetogenic state, hypertension, and several types of malignancies. We therefore hypothesized that localized overexpression of growth hormone restricted to the myocardium could provide functional benefits to the heart while limiting systemic exposure and subsequent morbidity.

Animal Model of Heart Failure and Experimental Design

To test this hypothesis we utilized a rat model of post-infarction heart failure and ischemic cardiomyopathy. We employed an adeno-viral vector containing the human growth hormone transgene driven by a cytomegalovirus promoter to provide high levels of localized myocardial expression. The viral vector was delivered by direct intramyocardial injection at the time of experimental MI, and the animals were subsequently analyzed and sacrificed after 6 weeks. A group of animals underwent surgery without creation of MI and served as an index of normal cardiac function and geometry (Sham group).

Results of Localized Myocardial Growth Hormone Overexpression

We found that there was significant preservation of left ventricular systolic function in the GH group. Importantly, we also observed that diastolic function (myocardial relaxation to allow ventricular filling) was also better preserved in the GH animals. In addition, the GH group had significant preservation of normal left ventricular geometry when compared to a control group of experimental MI animals treated with an empty virus (Null group) (Fig. 1). Borderzone myocyte fiber width was significantly increased in the GH group, confirming a hypertrophic effect of GH overexpression (Fig. 2). Our results demonstrated that growth hormone overexpression prevented the impaired myocardial function and ventricular remodeling associated with postinfarction heart failure.

Conclusions and Implications for Future Investigation

We propose that this treatment strategy may be useful in the immediate postinfarction clinical setting, or to treat evolving or established heart failure. The induction of regional hypertrophy is a novel approach to managing heart failure. The molecular pathways of myocardial hypertrophy may be fruitful targets for further investigation.

Reference


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Naranjan S. Dhalla joined the Council of the International Study Group for Research in Cardiac Metabolism in 1970 and was elected as Secretary General in 1972. He served in this capacity for six terms for a total duration of 17 years. During his tenure, he was instrumental in transforming the Study Group into the ISHR the way we know it today. He served as President of the ISHR during 1992-1995. Dr Dhalla also served concomitantly as Executive Secretary and President of the American Section of the ISHR during 1972-1991. Among many contributions in building the profile of the ISHR, he developed different Sections of the ISHR and instituted the Peter Harris Award as well as HEART NEWS AND VIEWS. His dedication and commitments have been appropriately captured by Dr David Hearse as given below:

An Appreciation of Naranjan S. Dhalla by David J. Hearse, July 1995

No single individual has served the ISHR for so long with such energy and such loyalty

Always seeking out new opportunities for the growth and development of the ISHR

Respected internationally for his productive, consistent and creative biomedical research

Amazing ability to create outstanding meetings attracting the most eminent of scientists

Never missing an opportunity to provide new opportunities for active young investigators

Justifiably proud of the many successes and respect that he has facilitated for the ISHR

Actively committed to supporting and encouraging disadvantaged scientists anywhere

Never too busy to listen and generously give his time and advice to colleagues everywhere

Sympathetic to the many needs and aspirations of science and scientists worldwide

Dedicated to promoting the international understanding and treatment of heart disease

Highly committed to the recognition of achievements of other major investigators

An inexhaustible supply of energy and creativity for pioneering new ideas and initiatives

Leader, scientist, humanitarian, ambassador, advisor, editor, speaker and visionary

Longstanding reputation for his lateral and resourceful approach to difficult problems

Author of numerous seminal papers, respected research director, teacher and good friend

Pawan K. Singal, Ph.D.
Winnipeg, Manitoba, Canada

During the XVII World Congress of the ISHR (Winnipeg, Canada; July 6-11, 2001) Honorary Membership was given to Dr Naranjan S. Dhalla (Winnipeg, Canada) in recognition of his exceptional merit and contributions to the International Society for Heart Research.

During the ISHR XVII World Congress, Honorary Membership was also given to Dr Jutta Schaper (Bad Nauheim, Germany). 'Jutta Schaper - an Appreciation' by Jim Parratt (Glasgow, UK) appeared in HEART NEWS AND VIEWS 2002; 10(1):8-9.
This fellowship is to foster European cardiovascular research integration

Who may apply?
Any ISHR member, aged under 35 years on July 1, 2005. The doctoral thesis will have to be completed before the ISHR-ES annual meeting in Tromsø, Norway, on June 23-25, 2005.

What is the ISHR–ES/SERVIER Research Fellowship?
A €20,000 grant is offered by SERVIER in partnership with the European section of the ISHR to support a cardiovascular research project within a European research group for a period of up to 1 year.

How to apply
Send 8 copies of the following:

► Curriculum vitae
► List of publications
► A description of your research program as a 1-page summary + no more than 6 pages of main text
► One letter of support from a supervisor
► Please refer to instructions on the ISHR Web site: www.ishr-europe.org

To: Prof Dr Gerd HEUSCH
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DEADLINE FOR APPLICATIONS
March 31, 2005
The XXIV European Section Meeting of the ISHR was held in Dresden, the “Florence on the Elbe River” on June 2-5, 2004. Interesting lectures, good weather and beautiful sights within the city combined to make this a successful conference. The meeting was held in the Dresden University of Technology, which over the three days became a forum of lively discussion between scientists and colleagues, while the three flights of stairs to the lecture theatres ensured that we stayed fit and active!

The meeting provided us with a broad range of interesting and stimulating talks relevant to the vast field of cardiovascular research. The conference began with the Gerrit-Isenberg Symposium, which consisted of eight presentations on topics relating to calcium handling and electrophysiology in health and disease. The following three days had a diverse scientific programme in which topics ranged from ion transport and electrical remodelling, preconditioning, ischemia and reperfusion to pharmacological interventions and stem cells and their potential in cardiovascular therapy. We were lucky to have two key note speakers, Eduardo Marban from Baltimore, Maryland, and Kai Simons from Dresden, Germany, both of whom gave excellent talks on “Biological Therapy for Cardiac Arrhythmias” and “Lipid Rafts: Structure and Function”, respectively.

Medals of merit were bestowed on Lionel Opie and David Hearse for their outstanding achievement and contributions to cardiovascular research. Seven young scientists aspiring to follow in their footsteps presented their research in the Young Investigators Award Competition. This was won by Dr W.-H. Zimmermann from Hamburg, Germany for his study “Structural and electrical integration of engineered heart...
tissue leads to improved regional function in infarcted rat hearts” while the 2004 ISHR-ES/SERVIER Research Fellowship was awarded to Dr K. Boengler from Essen, Germany. There were also approximately 100 posters on display throughout the meeting and the 2hr formal poster session, perhaps a little limiting in terms of time, gave presenters further opportunity to present and discuss their research. Prizes were awarded for the 10 best poster presentations and the top prize of Euro 500 was won by Dr Yaron Barac from Haifa, Israel for his poster entitled “FAS-mediated hypertrophy, and arrhythmias in neonatal rat ventricular myocytes are mediated by the 1,4,5-IP$_3$ cascade”. Congratulations to all winners. The penultimate day ended with the Gala Dinner at the Hilton, close by the Frauenkirche, with superb musical entertainment.

For those, like myself, who stayed an extra day to explore Dresden in the glorious sunshine, the beauty of the city and the stunning buildings and architecture on both sides of the river was a wonderful experience. And in the evening, from the Carola bridge, the view of the illuminated Hofkirche and Semperoper was just breathtaking.

Many thanks to Professor Ursula Ravens for organising this superb meeting and I am personally looking forward to more European Section meetings and particularly to Tromso, Norway with the northernmost University in the world, next year.

Jessica Sample, B.Sc.
Hull, UK
Science and Pleasure

"Where are you going?"
"I am going to Cancun."
"Oh, that will be a great vacation!"
"No, it will be a business tour."
"What, you are going to Cancun for business?"
A similar dialogue took place several times, and finally a lady at the check-in counter at the airport asked me about my fishing rods in the poster-case.

Yes, the place with the most beautiful beaches in the world was chosen for the XXVI Annual Meeting of the American Section and was organized in the finest traditions of the ISHR. Of course, each society has its own traditions but to my mind the ISHR has a very special, family style approach. The great scientist Dr Richard Bing not only founded our Society but also continues to support it and to help to make our life in science more productive and enjoyable. This is why it was a special pleasure to watch the video recording of Dr Bing’s touching lecture: “ISHR, Past, Present and Future”.

The lecture by Dr Benedict Lucchesi “Inflammation and the Loss of Myocardial Viability upon Reperfusion” was not only about heart disease but also revealed his personal role in promoting East-West relations in cardiovascular research. In 1988 he wrote a letter to Mikhail Gorbachev, President of the Soviet Union, asking him to help Russian scientists participate in the XIII ISHR World Congress in Ann Arbor. At that time it was still necessary for Russian scientists to get special permission from ministry officials to go abroad. The letter helped – not only to get the necessary permissions but also to tear down the wall that was separating Russian scientists from the rest of the world.

During three days and seventeen symposia the participants submitted their results, focused on different aspects of cardiovascular diseases. A poster session was organized along with a lunch break in the same hall. This smart idea allowed us to satisfy our appetite for science without starving.

The Young Investigator Award competition brought mixed feelings. The quality of the scientific presentations was very high. Mr Christopher L. Murriel from Stanford, CA, was the winner for his study “δPKC activation induces apoptosis in response to cardiac ischemia and reperfusion damage: a mechanism involving BAD and the mitochondria”. But we also felt sadness knowing that Dr Naranjan Dhalla was serving for the last time as Chairman of this competition after many years in this position.

The Landmark Lecture of Dr Michael DeBakey from Houston, TX, “The Development of Ventricular Assistance” showed us his long road from carotid artery replacement via aorto-coronary artery bypass to implantation of the artificial heart. What more can be done by a surgeon for a patient? Now it is time to bring the best of this new knowledge from the lab to the practice of medicine.

Tatyana S. Levchenko is discussing her poster "ATP-loaded liposomes protect mechanical functions of myocardium during and after global ischemia in isolated rat heart" with Drs Lindsay Brown (left) and Robert A. Haworth.
Dr Daniel Villarreal and the Organizing Committee did a great job to make this meeting an excellent opportunity to submit and discuss our research with colleagues and to discover the ancient culture and fantastic nature of Mexico.

Tatyana S. Levchenko, Ph.D.
Boston, MA, USA
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a private French pharmaceutical company committed to therapeutic advances in cardiovascular medicine as well as other key therapeutic areas. We have successfully developed products in the field of cardiovascular diseases (ischemic heart disease, hypertension, and heart failure), as well as in other major therapeutic fields. A number of landmark studies like PROGRESS, EUROPA, PREAMI, PEP, and HYVET are, or have been, conducted with our support.

The dynamism of our research is ensured by consistent allocation of as much as over 25% of the annual turnover of the Group to search for new molecules and develop their therapeutic applications.

Servier supports a number of important projects in the field of cardiology, such as the Education and Training Programs of the European Society of Cardiology.

Servier is also the founding father of The European Cardiologist Journal by Fax and Dialogues in Cardiovascular Medicine, a quarterly publication with a worldwide circulation edited by Roberto FERRARI and David J. HEARSE. Dialogues discusses in a comprehensive way issues from the cutting edge of basic research and clinical cardiology.

The forthcoming issue, devoted to METABOLIC SYNDROME will feature articles by:

B. M. Egan and S. Julius;
I. Zavaroni, D. Ardigò, S. Valtueña, and A. Dei Cas;
M. D. Esler, M. L. Correia, K. Rahmouni, and A. Mark

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