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IN THESE COLUMNS, *Past Truth & Present Poetry*

I have told stories of the past, of the interplay of ideas which have become history. These columns were primarily devoted to the function of the heart and the circulation. Because of the universality of science, these columns could have discussed other subjects dealing with natural sciences; the same bell tolls for all the living sciences because of the universality of science, created by men and women who have helped to form it. Thus, it is not strange if I now venture further apart into a field concerned with both art and science, with the imagery and the perception of music by the brain. The exploration of this subject involves a variety of techniques used also in imaging of the heart, which permit us a glimpse into musical perception in the central nervous system. Progress has been dependent on the development of physics, on magnetic resonance imaging, and positron emission tomography. Knowledge acquired with these tests can never measure the resonance of emotion engendered by an auditory or visual stimulation, which is the essential of art.

The classical way to study the relationship between music perception and its localization is through a neurological deficit, resulting from brain lesions or from the surgeon's knife. A classical description to study impaired musical ability is the illness of the French composer Ravel. His disease is often mentioned as an example of the fact that aphasia, that is the lack of verbal ability, and amusia, the inability to recognize and create music, are independent. Ravel's first symptoms appeared in 1933. They consisted in difficulty in writing. But he was still in possession of his musical composition skills. However, by the end of 1933, he developed inability to sight-read music, to play his own compositions by heart, to name or write notes. His illness was a selective impairment of function underlying the translation of musical representation from one modality to another, such as from visual to motor or auditory; none of these



10. The Neurological Perception of Music

Newer methods have only amplified this conclusion. One of these methods is PET scanning. It is based on the use of positron emitters, that is positively charged electrons. It can measure metabolic activity of individual portions of the brain through the uptake of radioactive deoxyglucose and it can also determine cerebral blood flow in different localized areas with ^{15}O water. The images can then be localized by fitting them onto anatomical pictures by means of either stereotactic preobtained pictures or by superimposing them on magnetic resonance imaging pictures. Using this method, a multiplicity of locations for music perception has been found. For example, timbre and rhythm activate different neural networks, and so do sight-reading and keyboard performance. Sergant from Montreal found that the individual components, such as playing, listening to music and reading music engaged specific cortical areas. Tonal pitch was primarily located within the frontal and temporal cortices, while remembered melodies involve the right occipital cortex. Other workers at the Neurological Institute in Montreal found that listening to the first two notes of each melody resulted in right frontal lobe activation and that specialized neural systems in the right superior temporal

modalities were separately impaired. Another clinical example of the dichotomy between aphasia and amusia is the case of the Russian composer V.G. Shebalin, who lived in the early part of the 20th century and was a friend of Shostakovich. Shebalin had a series of strokes, the second one resulting in aphasia; he was unable to understand speech and could not speak, but he suffered no significant alterations in musical ability. He finished compositions which he had started to write before his illness.

The general information from these clinical observations is that music involves specific but different interconnected domains in the central nervous system and that music perception is not homogeneous.



cortex participate in central analysis of melodies, while pitch comparisons appear to be expressed via a neural network that includes the right prefrontal cortex.

Some musicians have always prided themselves of having absolute pitch. Of particular interest therefore, are the subtle differences in effective neuronal networks between musicians with absolute and relative pitch. It was found that the most remarkable characteristic of musicians with absolute pitch was an activation of the left posterior dorsolateral frontal cortex, the region which has been implicated in conditional associated with learning of sensory stimuli.

Functional magnetic resonance is another of the more recent tools in exploring musical perception. It is based on the paramagnetic effect of deoxyhemoglobin, which acts as an endogenous contrast agent. It is particularly useful for the non-invasive mapping of hemodynamic sequelae of neural activation, of blood/oxygenation measurements in clinical images, and in studies across a single area of the brain. The method makes possible the recognition of auditory regions of the brain stem. For instance, when music is delivered through a head phone, responses are localized in the classically-defined auditory projection, the cochlear nuclei, or the superior olivary complex. Remarkable differences in imaging between professional musicians and those who had never played an instrument were found: musical experience during childhood influences structural development of the auditory cortex. A particularly fascinating study furnished further evidence that afferent impulses can induce plastic reorganizational changes within the adult mammalian central nervous system. For example, the cortical representation of the fingering digits of the left hand in string players was larger than in controls. In string players who had begun to play at an early age, cortical reorganization appeared early.

The transition from the purely physi-

cal, biological domain as documented by measurable changes in the brain, to what we call "music", is a giant step. It is a step which transfigures the disembodied mind from the physical brain. Before that transition, the rules of biology apply. But once the step has been taken, we enter a purely spiritual territory. All the physiological measurements cannot explain what we feel when we listen to great music. Music is disembodied, and musical perception and its emotional impact belong to different worlds. One is measurable, the other indefinable.

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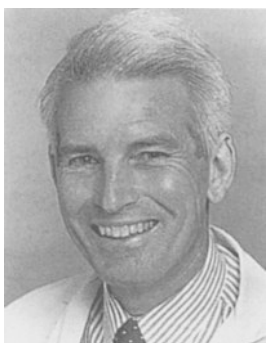
Richard J. Bing, M.D. ■

On 12 October 1999, Dr Richard J. Bing celebrated his ninetieth birthday. The editors of HEART NEWS AND VIEWS wish Dr Bing good health and much satisfaction from his scientific and musical activities.

On page 10, the **ISHR Fellowship Scheme** is announced (see also the President's Letter on page 3 and 4). ISHR members are encouraged to send proposals for candidates to Professor David J. Hearse, Cardiovascular Research, The Rayne Institute, St Thomas' Hospital, London SE1 7EH, UK (fax +44 171 922 8139).



PRESIDENT'S LETTER



The New Millennium

This will be the last issue of HEART NEWS AND VIEWS to be published in the 20th Century so let me use it as an excuse to wish every member of the ISHR a very successful and happy new millennium. The ISHR will enter the new era with great vigour - a healthy Journal, a growing membership and a splendid programme of Congresses planned well into the next century. In the spirit of academic co-operation, the ISHR and many of its Sections will continue to forge closer and closer relationships with other National and International Societies such as the American Heart Association, the European Society of Cardiology and the British Society for Cardiovascular Research. I would urge more such links since they often afford excellent opportunities for interaction between clinical and laboratory

scientists which are so essential for the advancement of our knowledge into the mechanisms and management of cardiovascular disease.

World Congresses into the Next Century

Planning for our Winnipeg World Congress (6-11 July 2001) is well in hand, a splendid scientific programme is evolving and full details will be distributed in the summer of 2000 - meanwhile, further information is available on the Congress web site (www.umanitoba.ca/heart2001). Outline plans for our Brisbane Congress are also developing well with a provisional Congress date of 7-11 August 2004. I'm particularly pleased that Dr Ed Lakatta, who helped give such a unique flavour to the scientific programme of Greece '98, has agreed to Chair the Scientific Programme Committee for Brisbane 2004. In addition, an exciting agreement has just been reached with the Cardiac Society of Australia and New Zealand such that we will hold the Brisbane ISHR Congress in tandem with the Cardiac Society meeting. The superb Brisbane Congress Centre will easily accommodate both Societies and there will be complimentary access to both meetings to members of both Societies. Adding even more value to a trip to Brisbane in 2004 is the fact that immediately before the ISHR Congress will be the World Congress of Clinical Pharmacology and Therapeutics, the theme of which will be: "Therapeutic Problems in Cardiovascular Medicine". The partnership between the ISHR and the Cardiac Society of Australia and New Zealand will provide a superb opportunity for our members to gain exposure to the cutting edge of cardiology and I have no doubt that the ISHR will offer our clinical friends a programme of world class laboratory research. In Brisbane, the ISHR will also be reaching out to the cardiac societies of South East Asia - an area of the world that, currently, is very under-represented in our Society. Beyond 2004, the Society is now inviting proposals for its World Congress in 2007 - already two exciting suggestions have come forward but additional proposals are always welcome. Those with ideas are asked to contact Jim Downey, our President-Elect, who will Chair the 2007 Selection Committee in Winnipeg in 2001.

Europe Joins the World!

In line with a long-standing tradition, the European Section of the ISHR has always magnanimously agreed to forego its Section Meeting in the year of a World Congress. This much appreciated gesture prevents attention and participation being diverted from our World Congress, it also provides an opportunity for the European Section to offer its help in organising the World Congress. Thus it will be in Winnipeg and in Brisbane where the Congresses will be designated as officially incorporating the European Section annual meeting.

Hail Fellow - Congratulations!

In previous issues of HEART NEWS AND VIEWS, I have announced a number of new initiatives, in particular, the establishment of an ISHR Fellowship. This scheme is intended to recognise the outstanding contribution made by our members to the advancement of knowledge in the field of cardiovascular biology and medicine. Fellowships will be conferred in very limited numbers and only after the deliberations of a distinguished international

(continued on page 4)



Credentials Committee chaired by Dr Howard Morgan. At no additional cost to the Society, Fellows will receive a number of benefits including free access to World Congresses and a complimentary subscription to the *Journal of Molecular and Cellular Cardiology*. Founding Fellows will be introduced at Winnipeg 2001 and the process of nomination and selection has just commenced. Although self nomination is prohibited, all members of the Society are encouraged to send to me (in confidence) proposals for deserving candidates. Full details of the Fellowship scheme are printed in this issue of HEART NEWS AND VIEWS.

Filling that gap!

Another new initiative that is coming on line in time for Winnipeg 2001 is the new Research Achievement Award. This award, which fills the age/experience vacuum between the Richard Bing Young Investigators Award and the Peter Harris Distinguished Research Award, is designed to recognise the achievements of active investigators who have already made, and will continue to make, a major contribution to cardiovascular research. Details of this prestigious and valuable award can be obtained from Roberto Bolli, our Secretary General.

As always, I would welcome any suggestions from our members as to ways of enhancing our Society.

David J. Hearse

Peroxynitrite is a Major Contributor to Cytokine-induced Myocardial Contractile Failure - 10,000 km Away from Home

What was my first thought about Edmonton, Canada? It would be really cold up there. Therefore, it would be a perfect place for me to do some experiments in a nice warm laboratory at the University of Alberta and to check sometimes if it was still snowing. Perhaps this was the magic ingredient of our study, which was rewarded at the XX European Section Meeting in Maastricht.

Getting Far from the Bench in Szeged

As a medical student I started to skip lectures and began instead to work as an undergraduate researcher in the laboratory of Dr Arpad Tosaki and Dr Matyas Koltai (now deceased) at the Pharmacology Department, Albert Szent-Györgyi University Medical School, Szeged, Hungary. Matyas taught me to love science and Arpad told me that cardiology was the only

“real science”. I believed them. Although they left the Department soon after I started to work for them, it was too late. I could only imagine becoming a cardiovascular scientist.

I worked a lot in the lab and won a couple of local and national young investigator awards. After getting my M.D. degree in 1991 (okay, I did not skip all the lectures at the medical school) I started my Ph.D. training at the Physiology Department and then at

the Biochemistry Department in Szeged. My major projects were studies on the role of free radicals¹ and K_{ATP} channels² in reperfusion injury and arrhythmias. I defended my Ph.D. thesis in 1995 and luckily I was immediately appointed at the Department of Biochemistry (thanks to the chairman, Dr László Dux), where I could start my own laboratory.

Closely collaborating with Dr Zoltán Szilvássy and with the help of two Ph.D. students, Tamás Csont and Csaba Csonka, we were working day and night. We used isolated working as well as Langendorff perfused hearts, measured cardiac cyclic nucleotides and oxygen free radicals. We established the direct detection of nitric oxide (NO) in the heart by using electron spin resonance. Preconditioning was the most exciting story for us, but we had also projects on cardiac effects of hyperlipidemia³, nitrates, and nitrate tolerance⁴. We found that NO is a trigger but not a mediator of classic preconditioning^{3,5}. We started to investigate the preconditioning phenomenon in diseased-animal models such as in hyperlipidemic/atheroscle-



rotic and nitrate-tolerant animals. We showed that the effectiveness of early preconditioning is largely diminished in hypercholesterolemic and nitrate tolerant animals, although hypercholesterolemia did not necessarily affect late preconditioning⁶.

In 1997, I suddenly realized that I was only 30 but had little chance to work any more at the bench. I was lost in writing grant applications, papers and reports, and the network of university and industrial collaborators kept me busy. I felt I had to escape somewhere, go back to the bench, and get some new scientific input. Even if I hadn't felt like this, my wife told me that we should go overseas for a year or two so that our kids would learn English. But where to go? I thought it should be a very good lab, something about the heart, something new about NO, good biochemical and pharmacological background, exciting scientific atmosphere, a project that would have sense and be aimed at a real clinical problem. One might think that a lab like this does not exist on planet earth. But my friend Csaba Szabo knew it did. He informed me that Dr Richard (Rick) Schulz from the Cardiovascular Research Group at the University of Alberta was looking for a postdoctoral fellow.

Getting Back to the Bench in Edmonton

With the support of fellowships from the Medical Research Council of Canada and the Alberta Heritage Foundation for Medical Research and with three connecting flights, my family moved to Edmonton - only 10,000 km away from home! The city is located on the bank of the North Saskatchewan River, not too far from the magnificent Rocky Mountains. The laboratory on the fourth floor of the Heritage Medical Research Center Building was my dream laboratory. The building (very close to the river valley) looks like the Pompidou Center in Paris, France. Rick Schulz, my new supervisor, is a recognized cardiovascular NO-peroxynitrite expert and turned out to be a very help-

ful supervisor and a good friend. There are other world-class scientists like Gary Lopaschuk, Marek Radomski, and Alex Rabinovich next door. The resources of the Cardiovascular Research Group are excellent.

So everything was more than perfect, but in the beginning it was quite hard for me to get back to the bench, start perfusing hearts again, pipetting all day, making up solutions, cleaning up my radioactive spills. But the project I got was very exciting.

We wanted to have clear cut evidence about the involvement of peroxynitrite in cytokine-induced cardiac depression and finally we succeeded. Previous studies had shown that pro-inflammatory cytokines depress myocardial contractile function by enhancing the expression of inducible NO synthase (iNOS), yet the mechanism of iNOS-mediated myocardial injury is not clear^{7,8}. As the reaction of NO with superoxide to form peroxynitrite mar-

See page 6: Award for Young Investigators

kedly enhances the toxicity of NO, we hypothesized that peroxynitrite itself is responsible for cytokine-induced cardiac depression.

So I started to perfuse isolated working rat hearts for 120 min with buffer containing interleukin-1 β , interferon- γ , and tumor necrosis factor- α . We measured cardiac mechanical function and myocardial iNOS, xanthine oxidoreductase (XOR), and NAD(P)H oxidase activities (sources of superoxide) during the perfusion protocol. Cytokines induced a marked decline in myocardial contractile function which was accompanied by enhanced activity of myocardial XOR, NADH oxidase and iNOS activities. Cardiac NO content, myocardial superoxide production and perfusate nitrotyrosine and di-tyrosine levels, markers of peroxynitrite, were increased in cytokine-treated hearts. The peroxynitrite decomposition catalyst FeTPPS con-



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centration-dependently inhibited the decline in myocardial function in cytokine-treated hearts and decreased perfusate nitrotyrosine levels. These results clearly showed that pro-inflammatory cytokines stimulate the concerted enhancement in both superoxide and NO generating activities in the heart, thereby enhancing peroxynitrite generation which causes myocardial contractile failure⁹.

In summary, I had a great time in Edmonton during my two years as a postdoctoral fellow; I got a lot of new scientific input, the number of my kids increased by one with a new Canadian-born baby boy and my two older kids speak great Canadian English. I am back in my lab in Szeged now and we have already planned a long term collaboration with Rick Schulz. We will probably compare the effects of the minimum and maximum temperatures in January and July in both Edmonton and Szeged on the effectiveness of cardiovascular research projects to find out finally why I got my award⁹!

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Award for Young Investigators

The first prize of the Young Investigators Award competition of the XX Meeting of the European Section (Maastricht, The Netherlands; June 23-26, 1999) was shared by two winners:

P. Ferdinandy (Szeged, Hungary): Peroxynitrite contributes to cytokine-induced myocardial contractile failure in rat hearts;

C.E. Zaugg (Basel, Switzerland): Postresuscitation stunning due to reduced myofilament Ca²⁺ responsiveness.

In this issue of HEART NEWS AND VIEWS, the winners introduce themselves to the membership of the ISHR.

A Stunning Experience

It is a great privilege to have been a finalist for the Young Investigators Award and to have the opportunity to introduce myself to the members of the ISHR. Winning this Award was as stunning to me as ischemia is to the myocardium. However, it is not only awards and ischemia that can be stunning. Ventricular fibrillation can lead to myocardial stunning too. This is what I have been studying.

Stunning After Ventricular Fibrillation

Ventricular fibrillation (VF) is a life-threatening arrhythmia. The only reliable way to terminate VF, and thus to save the life of a patient experiencing VF, is to administer high-energy defibrillation shocks. Although defibrillation shocks effectively terminate VF, they frequently leave behind depressed myocardial function (postresuscitation stunning), particularly after prolonged VF. In spite of hemodynamic support, this dysfunction may be responsible for deaths after initially successful defibrillation. It has been generally ac-

cepted that this postfibrillatory myocardial dysfunction is at least in part due to both ischemia occurring during VF and reperfusion occurring upon defibrillation. Thus, this dysfunction may be partially due to global post-ischemic myocardial stunning.

However, other factors related to VF and electrical defibrillation may also contribute to postfibrillatory myocardial dysfunction. Inspired by the work of Dr Marban¹ I tested the hypothesis that postfibrillatory dysfunction is related to the myocyte Ca²⁺ overload that progressively occurs during VF². Furthermore, I tested whether the severity

of the postfibrillatory dysfunction is related to the energy of the defibrillation shocks, as previously proposed³. Using the Ca²⁺ indicator indo-1 in whole rat heart preparations, I found that the postfibrillatory responsiveness of the myofilaments to Ca²⁺ was reduced (estimated as a ratio of left ventricular pressure to intracellular Ca²⁺ transients). In addition, this reduction was related to the duration of VF and to the degree of Ca²⁺ overload. However, the Ca²⁺ responsiveness was not related to the mode or the energy of defibrillation, whether pharmacological (using lidocaine), spontaneous, or electrical (up to 30 J per gram heart tissue, which is roughly 10 times the energy used in implantable defibrillators). Nevertheless, the Ca²⁺ antagonist diltiazem (1 μ M), when given before VF, attenuated both the Ca²⁺ overload during VF and the reduction of myofilament Ca²⁺ responsiveness after VF. In contrast to *in vivo* conditions, VF did not cause ischemia in our experiments (due to the constant perfusion pressure). This lack of ischemia was evidenced by unchanged levels of coronary flow and troponin I during and



after VF.

These results suggest that the myocyte Ca^{2+} overload that occurs during VF can lead to reduced myofilament Ca^{2+} responsiveness and consequently to postfibrillatory myocardial dysfunction. However, electrical defibrillation shocks appear not to contribute to this dysfunction, at least in the energy range tested. Further, since VF did not cause ischemia in our experiments (though most likely it does *in vivo*), our findings suggest that at least part of this dysfunction is due to VF-induced myocyte Ca^{2+} overload. This overload and probably also the reduction of myofilament Ca^{2+} responsiveness may be partially prevented by diltiazem, but only if given before VF. These findings support the view that myocyte Ca^{2+} overload is a key factor in the pathogenesis of myocardial stunning. Moreover, they may have implications for the prevention and treatment of (postresuscitation) stunning in patients.

The Road to Stunning

My academic road to postresuscitation stunning was shaped by various people. Attracted by the discipline of pharmacology, I studied at the school of pharmacy in Basel, the very building Paracelsus lived in a couple of centuries ago. After graduating in 1990, I enrolled in a Ph.D. program carried out at the Biocenter (Division of Biophysical Chemistry) and at the Hospital (Division of Cardiology) of the University of Basel. My Ph.D. thesis on endothelin-1 in myocardial ischemia^{4,5} was supervised by Prof. Peter Buser who became my mentor and has been a dear friend ever since.

Next I started a 3-year postdoctoral research fellowship at the Cardiovascular Research Institute of the University of California at San Francisco (UCSF) in 1993. During this fellowship, I was supervised by Prof. William Parmley whose wisdom inspired me far beyond medicine and science. Additionally, inside UCSF, I found wonderful opportunities for collaborations and training. Together with electrophys-

ologist Dr Randall Lee, I started studying the role of myocyte Ca^{2+} in arrhythmias, particularly in VF and defibrillation^{2,6-8}. Furthermore, in brilliant courses taught by Prof. Julien Hoffman and Mimi Zeiger, respectively, I acquired the essentials of biostatistics and signal processing as well as of scientific writing and lecturing. Finally, outside UCSF, I found great grounds for my favorite hobby, mountain biking. Once, however, I was stunned by a \$207-ticket for speeding on my bicycle down the hills of San Francisco.

Nevertheless, during this postdoctoral fellowship, I proverbially left my heart in San Francisco. It was then that I met my wife Vânia, a cardiologist from Brazil and also a fellow at UCSF. Fortunately, I could take my heart back to Switzerland; in 1996, I was offered a project leader position in the Department of Research and Vânia could work as a clinical cardiologist at the University Hospital Basel. This year, I was accepted for an academic career development program for assistant professors at the University of Basel. Accordingly, I started lecturing on cardiovascular pathophysiology and pharmacology as well as supervising Ph.D. students. Lecturing turned out to be a laborious but rewarding task that I truly enjoy.

In the future, I would like to continue experimental cardiology research and pursue an academic career. Winning the ISHR Young Investigators Award has certainly been a big step toward achieving this goal. It has both boosted my motivation and drawn attention to our research group. All in all, receiving this award has been a stunning experience, one that has been topped only by the recent birth of my baby girl.

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Report on the Symposium on Cardiovascular Physiology of Mice *in vivo* (Amsterdam, The Netherlands; December 4, 1998)

Last year, in December a one-day symposium entitled "Cardiovascular Physiology of Mice *in vivo*" was held at the Academic Medical Centre in Amsterdam. It can be considered as the predecessor of next year's three-day conference organised under the auspices of the ISHR and to be held in the same place.

During that time I was working as a post-doc at the department of Cardiology of the Rayne Institute at St. Thomas' Hospital in London. The main interest of this group headed by Dr Michael Marber is signal transduction pathways involved in protection of the heart after ischemic preconditioning. We were very lucky to benefit from the availability of one of the "creations" of modern molecular biology: a knockout mouse for a specific protein kinase C isoenzyme. Using Langendorff perfusion this model enabled us to study the role of this enzyme in protection of the intact heart after preconditioning without the use of rather unspecific inhibitors.

Mouse heart perfusion was carried out in the Department of Cardiovascular Research of the Rayne Institute headed by Prof. David Hearse. This lab has a long standing experience of perfusing hearts isolated from different species like rat, guinea pig and rabbit. Experience with the mouse was relatively limited at that time and soon it became clear that using this new model included some specific new difficulties. Especially temperature control, pacing rate, use of anaesthetics and susceptibility to ischaemia differed dramatically compared to the rat model. Likewise, in terms of physiologic behaviour of the heart, it was evident that the mouse is not just a small rat!

When a former colleague of mine e-mailed me the program for the mouse physiology symposium in Amsterdam I was im-

mediately enthusiastic as several titles of the talks on that day seem to have direct relevance for our research. The willingness of the organiser to hold the symposium in English meant that some interested colleagues could also join the meeting and I could also forward the program to a group in Oxford who had just organised an isolated rat heart perfusion meeting. Together with some participants from Belgium it was already a foretaste of next year's more international meeting.

Despite a relatively small advertising of the symposium, about 140 people showed up and not only from the Medical Centre in Amsterdam itself. The organiser of the symposium Prof. Can Ince opened the symposium by illustrating the new and fascinating possibilities of existing transgenic mice models in cardiovascular research. He also emphasised the purpose of this meeting: sharing of experiences with the mouse as new model in cardiovascular research. Up to now this model has not been as well characterised as traditional models. First Prof. P. Carmeliet, from the renown Centre for Transgene Technology and Gene Therapy in Leuven, discussed the availability of genetic models of cardiovascular disease in mice. He mentioned several VEGF isotypes knockouts and presented some results indicating that rupture in a mouse myocardial infarct model was prevented in mice lacking the urokinase-type plasminogen activator gene.

A small impression of the other presentations held that day will follow. The presentations dealt with varying subjects and covered a wide range of cardiovascular physiological research with direct relevance to the mouse model. Several talks concerning the functional aspect of mouse physiology discussed hemodynamic aspects, the isolated working mouse heart, microvascular endothelial function, and echographic assessment of heart function. All these are established techniques in the larger experimental animals, but some specific problems were encountered when an effort was made to adapt them for suitability in the much smaller mouse heart. Two reports from knockout mouse models with more and less expected results were presented. Electrophysiological studies of a connexin-

40 knockout mouse showed increased inducibility of atrial arrhythmias. Another study showed that in mice where the cytosolic isoform of creatine kinase (CK) was omitted, the flux through the forward CK reaction did not change with increasing workload as opposed to the wild type animals. Of the more general talks one commented on the use of different type of anaesthetics, their dose and possible drawbacks when used in cardiovascular studies in mice. Two others presentations with more indirect implications for cardiovascular research discussed cytokines and models of infectious disease as well as interorgan flux of NO. The afternoon was concluded with a poster session. To encourage the participation of young investigators, Ph.D. students and graduate students were invited to submit a poster about their findings and the best poster was awarded a prize of Dfl. 400.

So in conclusion my experience with the symposium was very positive, although it was clear that many of the participants were starting with mouse research. The latter may also explain the fact that there were not so many posters as hoped for. Therefore, I expect that next years conference will have more complete studies and I also hope that during the next symposium no one will feel inhibited to submit a poster due to preliminary results. In my experience a poster usually is a good starting point for further interesting discussions or even collaboration! In my case it was a good opportunity to establish some contacts for a future job when I would return to The Netherlands. And indeed this worked out very well since I recently joined Prof. Can Ince's lab in Amsterdam.

I hope to see you at next year's meeting in Amsterdam!

Harold Raat, Ph.D.
Amsterdam, The Netherlands ■



*The 2nd International
Amsterdam Mouse Symposium*

Cardiovascular Physiology of Mice

13-15 April 2000



THE PAST DECADE has seen a tremendous growth in insight into the molecular basis of cardiovascular disease due to the advances made in molecular biology. Complete information about the human and mouse genome is imminent and the challenge now is to investigate how gene structure is related to cardiovascular function. This is why functional genomics and an integrative approach to molecular biology and physiology are becoming increasingly important areas of cardiovascular research. Furthermore, developments in gene therapy are requiring detailed insights into the physiological consequences of gene manipulation in models of cardiovascular disease. Such molecular physiological investigations are being primarily focused on the mouse because of the availability of genetically modified mice, the large amount of knowledge of the mouse genome and the commercial availability of assays of the varied mediators and receptors involved in cardiovascular function. However, although knowledge and experience in molecular physiological investigations in mice is rapidly being gained, it is as yet thinly spread and there is a need to bring scientists interested in this area of cardiovascular research together.

THESE CONSIDERATIONS led us to organize a highly successful symposium last year and is the reason for us to organize this second more extensive symposium on the cardiovascular physiology of mice. The symposium will concern cardiovascular research directed at the molecular physiology of the mouse where the relation between gene and function is being investigated in conventional and genetically altered mice. Issues which will be covered include physiological methods and techniques in mouse research, cardiovascular physiology of mice, adaptive physiological mechanism in response to gene manipulation, mouse models of cardiovascular disease, and future directions in research into molecular cardiovascular physiology of the mouse.

LIST OF SPEAKERS: Introduction: D.J. Hearse (London, UK), H. Rockman (Durham, USA); **Physiological research in mice:** A.F.M. Moorman (Amsterdam, Netherlands), P.H. Reitsma (Amsterdam, Netherlands), F. Sutherland (London, UK), M. van Bilsen (Maastricht, Netherlands), C. Ince (Amsterdam, Netherlands), R. Remie (Groningen, Netherlands), C. Zuurbier (Amsterdam, Netherlands), K. Kramer (Amsterdam, Netherlands), A. Haas (Am Habland, Germany); **Functional genomics in knockout mice:** J. Schrader (Düsseldorf, Germany), N.E.P. Deutz (Maastricht, Netherlands), A. Gödecke (Düsseldorf, Germany), G. van der Vusse (Maastricht, Netherlands), L. Gustafson (Amsterdam, Netherlands), D. Duncker (Rotterdam, Netherlands); **Mouse models of cardiovascular disease:** G. Caligiuri (Paris, France), J.F. Smits (Maastricht, Netherlands), S. Demolombe (Nantes, France), D.D. Rees (Cambridge, UK), P. Carmeliet (Leuven, Belgium), C.W. Lowik (Leiden, Netherlands), M.M. Levi (Amsterdam, Netherlands), H. ten Cate (Amsterdam, Netherlands), L. Hofstra (Maastricht, Netherlands); **Future directions: Reporter genes, inducible genes and therapy:** D. Lefer (Shreveport USA), W. Franz (Lübeck, Germany), A.J. van Zonneveld (Leuven, Belgium), A. Kuivenhoven (Amsterdam, Netherlands), S. van Soest (Amsterdam, Netherlands), B. Mik (Amsterdam, Netherlands), L.A. Schwarte (Amsterdam, Netherlands), R. de Crom (Rotterdam, Netherlands).

PARTICIPANTS are encouraged to submit abstracts; poster sessions will be organized. The deadline for submission will be **February 1, 2000**. There is a limit of 300 participants. Fifty selected abstracts will be published in a special issue of *Basic Research in Cardiology* dedicated to this conference. There will be an industrial exhibition, as well as a section where (bio)technicians will be invited to present technical aspects of mouse research.

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ISHR Fellowship Scheme

An Invitation to the ISHR Members

THE COUNCIL of the ISHR (International) has decided to introduce a Fellowship scheme as a means of recognising those members who, through their research, have made a major contribution to our understanding of cardiovascular biology and medicine. Below are details of the scheme and all members are encouraged to send nominations for individuals they believe worthy of this honour. In the first instance, nominations should take the form of

the full name and address of each potential candidate together with the name of the nominating person. Please note that *self-nominations are not acceptable* and that nomination does not guarantee selection. The number of Fellows of the International Society for Heart Research will be strictly limited and therefore nominations should be sent in confidence without disclosure to the candidate.

The scheme will work as follows:

Fellowship benefits:

- Fellows will be entitled to add 'FISHR' to their degrees and distinctions.
- Fellows will receive a complimentary subscription (hard copy) to the *Journal of Molecular and Cellular Cardiology*.
- Fellows will be given free registration at World Congresses.
- The names of new Fellows will be published in the *Journal of Molecular and Cellular Cardiology*, they will receive a Fellowship certificate and a picture and biosketch of each Fellow will be published in HEART NEWS AND VIEWS.

Fellowship costs:

- Fellows will be asked to pay US\$ 45 per annum to the ISHR (International). This is additional to and separate to their Section membership fees.

Fellowship selection:

- *Fellows will be selected solely on the basis of scientific excellence* - this would normally be expected to be an established track record of publication (in peer reviewed, high impact, international journals) of independent research that has made a major contribution to advancing our understanding in cardiovascular biology and medicine. Political or service contributions to the ISHR will not be a factor in selection.
- Fellows must be fully paid up members of one of the Sections of the ISHR and their name must appear on the ISHR (International) membership database.
- Fellowship will be highly prestigious, there will be only 50 Founding Fellows and these will be introduced at the time of the 2001 World Congress in Winnipeg. Further Fellows will be appointed every three years, the numbers will be determined by Council but the eventual total number of Fellows would not exceed 5% of the membership of the Society.
- *Self-nominations will not be considered.*
- The final selection of Fellows will be made by an international Credentials Committee. This Committee will be appointed every three years by the Council of the ISHR (International). In the first instance, it will be Chaired by Dr Howard Morgan.
- Whilst Fellowships will be conferred solely on the basis of scientific merit, account will be taken of the very differing constraints, facilities and research opportunities available to members of different Sections of the ISHR.

ISHR MEETINGS CALENDAR

■ December 1-3, 1999. **XVI Annual Meeting of the Japanese Section.** Fukuoka, Japan. **Enquiries:** Dr K Hirano, Division of Molecular Cardiology, Research Institute of Angiocardiography, Kyushu University, Fukuoka 812-8582, Japan. Tel. +81 92 642 5550; Fax +81 92 642 5552; E-mail khirano@molcar.med.kyushu-u.ac.jp

■ April 13-15, 2000. **The 2nd International Amsterdam Mouse Symposium: Cardiovascular Physiology of Mice** (Under auspices of the ISHR). **Enquiries:** Dr C. Ince, Department of Anesthesiology, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. Tel. +31 20 566 5242; Fax +31 20 697 9004; E-mail c.ince@amc.uva.nl (Congress web site: <http://www.usouthal.edu/ishr/Amst-Mouse.htm>)

■ June 14-18, 2000. **XXII Meeting of the American Section.** Louisville, Kentucky, USA. **Enquiries:** Dr R. Bolli, Division of Cardiology, University of Louisville, ACB, Third Floor, 550 South Jackson Street, Louisville, KY 40292, USA. Tel. +1 502 852 1837; Fax +1 502 852 6474; E-mail rbolli@louisville.edu

■ July 1-4, 2000. **XXI Meeting of the European Section.** Stockholm, Sweden. **Enquiries:** Dr L. Kaijser, Karolinska Institute, Department of Clinical Physiology, Huddinge Hospital, SE-141 86 Stockholm, Sweden. Fax +46 8 774 8082; E-mail lennart.kaijser@labtek.ki.se **or** Congrex Sweden AB, Attn: ISHR 2000, Box 5619, SE-114 86, Stockholm, Sweden. Fax +46 8 661 9125; E-mail ishr2000@congrex.se (Congress web site: <http://www.congrex.se/ISHR2000>)

■ October 12-15, 2000. **XI Meeting of the Chinese Section.** Nanjing, China. **Enquiries:** Dr Q. Chen, Nanjing Medical University, Nanjing, China 210029. Tel. +86 25 6528 460; Fax +86 25 6508 960; E-mail qichen@njmu.edu.cn

■ July 6-11, 2001. **XVII World Congress of the International Society for Heart Research.** Winnipeg, Manitoba, Canada. **Enquiries:** XVII ISHR World Congress, c/o Institute of Cardiovascular Sciences, St. Boniface General Hospital Research Centre, University of Manitoba, Faculty of Medicine, 351 Taché Avenue, Winnipeg, Manitoba, Canada R2H 2A6. Tel. +1 204 235 3421; Fax +1 204 233 6723; E-mail ishr@cc.umanitoba.ca (Congress web site: <http://www.umanitoba.ca/heart2001>)

■ July 1-5, 2001. **International Muscle Energetics Conference.** Burlington, USA. **Enquiries:** Dr N.R. Alpert, c/o Department of Physiology & Biophysics, University of Vermont, College of Medicine, Given Medical Building, Burlington, VT, USA 05405-0068. Tel. +1 802 656 2540; Fax +1 802 656 0747; E-mail alpert@salus.med.uvm.edu

■ July 2-5, 2001. **Regulation of Energy Metabolism in the Heart and Vasculature.** Banff, Canada. **Enquiries:** Dr G.D. Lopaschuk, c/o Cardiovascular Disease Research Group, Department of Pediatrics, University of Alberta, 423 Heritage Medical Research Centre, Edmonton, AB, Canada T6G 2S2. Tel. +1 403 492 2170; Fax +1 403 492 9753; E-mail gary.lopaschuk@ualberta.ca

■ July 3-5, 2001. **Heart Failure Summit.** Toronto, Canada. **Enquiries:** Dr M.J. Sole, c/o The Centre for Cardiovascular Research, Eaton Wing 13 North - Suite 208, Toronto General Hospital, Toronto, ON, Canada M5G 2C4. Tel. +1 416 340 3471; Fax +1 416 340 5985; E-mail msole@torhosp.toronto.on.ca

■ July 12-15, 2001. **Diseases of the Cardiovascular System and Immunity: Interactions and Therapeutics.** Montreal, Canada. **Enquiries:** Dr G. Bkaily, c/o Department of Anatomy and Cell Biology, Faculty of Medicine, University of Sherbrooke, 3001 12E Avenue North, Sherbrooke, PQ, Canada J1H 5N4. Tel. +1 819 564 5303; Fax +1 819 564 5320; E-mail g.bkaily@courrier.usherb.ca

■ July 12-15, 2001. **Remodeling and Progression of Heart Failure.** Minneapolis, USA. **Enquiries:** Dr I. Anand, c/o Department of Cardiology, VA Medical Center 111C, 1 Veterans Drive, Minneapolis, MN, USA 55417. Tel. +1 612 725 2000, ext. 3723; Fax +1 612 725 2262; E-mail anand001@maroon.tc.umn.edu

In Blue: World Congress and Satellite Meetings



HEART NEWS AND VIEWS

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DIALOGUES
in cardiovascular medicine

Atheroma

Volume 4 Number 1

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The forthcoming issue, devoted to ATHEROMA, will feature articles by:

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D. Chew, M.R. Bennett

For further information on
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