Promoting Cardiovascular Education, Research and Patient Care

CV network

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A Message from the President

Dr. Stephen Vatner

Uver the past decade the International Academy of Cardiovascular Sciences has grown from just a concept devised by its founder, Dr. Naranjan Dhalla, to a truly international organization. It will be difficult to equal the achievements accomplished by Dr. Dhalla, the past president, Dr. Howard Morgan and the Chairman Makoto Nagano. With that caveat in mind, I would like to propose a direction for the Academy under my presidency.

The first principle of the current leadership will be to maintain and advance the objectives of the Academy, which have already been established:

To promote cardiovascular education, research and patient care;

To promote the scientific basis for the practice of cardiology and cardiovascular surgery;

To foster the exchange of information among cardiovascular scientists, cardiologists and cardiac surgeons;

To increase public awareness with respect to cardiovascular health and disease;

To recognize the achievements of cardiovascular investigators.

The Academy already has sponsored meetings in North America, South America, Europe, India, Japan, Pakistan, Egypt, and West Indies . This commitment to communication of concepts and data is critical to continue and expand. An important next goal is to widen the involvement of post-doctoral fellows, graduate students and medical students. This will serve a triple purpose; first, it will enhance the educational mission of the Academy; secondly will help inculcate future generations of fellows and leaders; third, it will also help level the disparity in research between North America and many parts of the world, which have fewer resources to apply to cardiovascular research. An excellent model for this initiative is the highly successful National Research Forum for Young Investigators in Circulatory and Respiratory Health which has been organized primarily by Fellows of the Academy in Canada.

In honor of Dr. Dhalla's 70th Birthday, the Academy is organizing a unique Global Symposium on the "Future of Heart Health & Disease" in Winnipeg, Canada during October 12 – 15, 2006. Buoyed by the extremely positive initial reaction, there is a possibility this Symposium could be an annual opportunity to bring international focus to the Academy.

In addition, members of the Academy's leadership enjoyed a productive executive meeting during the recent Scientific Sessions of the American Heart Association in Dallas. I propose establishing the American Heart Association meeting site as an annual forum for the leadership of the Academy to meet and discuss policy.

Dr. Dhalla has proposed the concept of establishing "think tanks" of senior investigators and educators. There is probably no more important goal than to combine input from the various backgrounds of the Academy's leadership to establish new programs and directions. It will be important for the leadership from the different continents to meet each year at an international meeting.

If there is one deficiency in the Academy, it is the lack of financial support to further its educational mission. I propose an intensive effort on behalf of the leadership to solicit funds from philanthropic organizations as well as governmental agencies and corporate partners. This can only be achieved if we expand the educational mission of the Academy. One mechanism by which this can be jump-started is to provide short term research fellowships to permit students from countries with less research infrastructure to have a research and learning experience in well-funded laboratories of investigators from countries with relatively greater research funding. With travel funds supported by philanthropy, the remainder of the costs for this proposal can be borne by the host institutions. The trainees should be prepared to present their work at the next Academy meeting in their home country. In order to facilitate this program we plan to maintain a registry of well-funded laboratories to which the students may apply. We also plan to maintain a registry of the students to follow their growth and assess the impact of the Academy's influence on their careers. It would be most rewarding, if some of these students would follow an academic path and eventually become part of the leadership of the Academy.

After assuming the Presidency, I requested suggestions for future directions from other leaders of the Academy. The most frequently raised idea was to concentrate on endeavors relating to translational research. In this manner, state of the art concepts in cardiovascular research can be presented, which can be appreciated by clinical cardiologists (either in North America or in other countries). Whereas concentrating on the most basic aspects of research will be of benefit to others engaging in basic research, there are many more clinicians who would derive more benefit from lectures and workshops relating to translational research. This is particularly true in countries with less developed basic research programs.

Until this point the paths the Academy should follow have been stressed. At this juncture it might be useful to note paths that should not be followed. Other organizations designed to promote dissemination of scientific knowledge have become too inbred, which could be a potential concern for the Academy. Of course, we need to rely on the senior leadership to direct the progress of the Academy at this time. However, if three years from now the leadership remains constant and we have not developed and nurtured new and younger leadership, my tenure as President cannot be counted as successful.

In summary, the most important mechanism by which the Academy can grow is to provide increased communication among the leadership from the different countries. In the current age of electronic communication, this should be realistically achievable by expanding our web site. This mechanism can supplement the direct contact among the leadership at international meetings, and provide the impetus for further growth. We have a unique opportunity to promote use of our three Official Journals and especially "Experimental and Clinical Cardiology" in which we have published abstracts for our meetings and papers based on our NATO Workshop held earlier this year in Turkey. An additional possibility is to expand the dialogue through this newsletter, which already serves as an important forum for communication under the able leadership of Ivan Berkowitz.

However, none of the projected progress or direction can be achieved by a single individual; it will require a commitment of the worldwide leadership of the Academy to move it forward under the new administration.

CHALLENGES & OPPORTUNITIES

Chronic Disease - The Neglected Epidemic

by Richard Horton, Editor, The Lancet, London UK

THE LANCET

The reduction of chronic disease is not a Millennium Development Goal (MDG). While the political fashions have embraced some diseases - HIV-AIDS, malaria, and tuberculosis, in particular - many other common conditions remain marginal to the mainstream of global action on health. Chronic diseases are among these neglected conditions.

Chronic diseases represent a huge proportion of human illness. They include cardiovascular disease (30% of projected total worldwide deaths in 2005), cancer (13%), chronic respiratory diseases (7%), and diabetes (2%). Two risk factors underlying these conditions are key to any population-wide strategy of control - tobacco use and obesity. These risks and the diseasesthey engender are not the exclusive preserve of rich nations. Quite the contrary. Chronic diseases are a larger problem in low-income settings. Research into chronic diseases in resource- poor nations remains embryonic. But what evidence there is shows just how critical it will be to intervene early in the epidemic's course. There is an unusual opportunity before us to act now to prevent the needless deaths of millions. Do we have the insight and resolve to respond?

With a new series of articles, for which we thank the superb efforts of Robert Beaglehole, The Lancet aims to fill a gap in the global dialogue about disease. It is a surprising and important gap, one that health workers and policymakers can no longer afford to ignore. The

call by Kathleen Strong and colleagues for the world to set a target to reduce deaths fromchronic disease by 2% annually-to prevent 36 million deaths by 2015-deserves to be added to the existing eight MDGs.

Without concerted and coordinated political action, the gains achieved in reducing the burden of infectious disease will be washed away as a new wave of preventable illness engulfs those least able to protect themselves. Let this series be part of a new international commitment to deny that outcome.

To view the articles, please visit:

http://www.thelancet.com/collections/series/chronic_diseases

1. "Preventing chronic diseases: how many lives can we save?" Strong K, Mathers C, Leeder S, Beaglehole R ***Lancet 2005***; published online Oct 5

2. "Preventing chronic diseases: taking stepwise action" Epping-Jordan JE, Galea G, Tukuitonga C, Beaglehole R ***Lancet 2005***; published online Oct 5

3. "Responding to the threat of chronic diseases in India" Reddy KS, Shah B, Varghese C, Ramadoss A ***Lancet 2005***; published online Oct 5

4. "Preventing chronic diseases in China" Wang L, Kong L, Wu F, Bai Y, Burton R ***Lancet 2005***; published online Oct 5

PEOPLE AND PLACES

Sir George Radda recognized with Academy's most prestigious award

Sir George Radda was born in 1936 in Hungary. He began his career as a chemistry student in Budapest. In 1956 he left Hungary and arrived in England, where he finished his first class degree at Merton College before going on to complete his PhD. Sir George completed his postdoctoral work and a student fellowship with Melvin Calvin in Berkley, California, and then returned to England for a lectureship at Oxford in 1969, followed by a rapid rise to be Professorial Fellow. His main research interests center on the biochemical basis and cellular functions in heart disease. He became interested in using spectroscopic methods including Nuclear Magnetic Resonance (NMR) and in 1981, Sir George and his fellow colleagues published the first scientific report on the clinical application of his work. This resulted in the installation the first clinical magnetic resonance spectroscopy unit with a magnet large enough to accommodate the whole human body for NMR investigations in 1983 at the John Radcliffe Hospital in Oxford. In recognition of his pioneering research, which opened up the study of the workings of the living body, he was given a chair in 1984 by the British Heart Foundation. From 1996 to 2003 (on secondement) he was Chief Executive of the Medical Research Council. Also, he was Chairman National Cancer Research Institute (2001-2003). Sir George received numerous prestigious awards and honours for his pioneering efforts in using spectroscopic techniques for metabolic studies, including a CBE in June 1993 and a Knighthood in June 2000. He is a Fellow of Merton College, Oxford, a Fellow of the Royal Society and is the British Heart Foundation Professor of Molecular Cardiology. He is an Honorary Member of the American Heart Association and was awarded the Citation for International Achievement. From 1996 to 2003, Sir George was Chief Executive of the Medical Research Council in the UK. He is currently Emeritus Professor of Molecular Cardiology at the University Laboratory of Physiology Cardiac Science Centre, University of Oxford and Chairman of the Singapore Bioimaging Consortium.

In recognition of his lifetime of extraordinary achievement, Sir George Radda is honoured by the International Academy of Cardiovascular Sciences with the 2006 Medal of Merit.

XV International Congress of Cardiovascular Sciences makes successful move to Rio

by Ivan Berkowitz, Winnipeg, Canada

The dynamic energy of Prof. Dr. Otoni Gomes has driven his unique conference to new heights. After 14 years in Belo Horizonte, Dr. Gomes accepted the challenge of moving to one of the world's most extraordinary cities Rio de Janeiro for the XV International Congress of Cardiovascular Sciences on December 8 – 10, 2005. Held at the Rio Othon Palace Hotel on the fabulous Copacabana, more than 500 delegates gathered for the Scientific Forum; XXV ACCERJ Cardiovascular Surgery Congress; XXIII Brazilian Congress on Extracorporeal Circulation; IX South American Symposium of International Academy of Cardiovascular Sciences; VI International Forum on Applied Cardiovascular Physiology; I International Meeting of American Society of Angiology; and the new Symposium on Cardiology for the Family. As well, there were Forums named to honour E. J. Zerbini; Tomas A. Salerno; Tofy Mussivand; Domingos J. Moraes; and the initial Naranjan S. Dhalla Forum on Applied Cardiovascular Research.

A tradition of Dr. Gomes' Meeting is an Ecumenic Forum. This year's highlight was the Copacabana Baptist Church Chorus. International participants included Domingos Savio de Souza from Sweden and Canadians Tofy Mussivand and Ivan Berkowitz.

The IACS was well represented by Ricardo Gelpi, President for South America; Wagner Pádua Filho, Vice President S A; Otoni Gomes, Executive Secretary SA; Ivan Berkowitz, Director of Development; and Fellows Tomas A. Salerno, Miami USA; Tofy Mussivand, Ottawa Canada; Alfredo J. Fiorelli, Sao Paulo; Sérgio E. Kaiser, Rio de Janeiro; and David P. Brasil, Belo Horizonte.

Tentative dates for the 2006 Conference are November 30 – December 2, again in Rio. New initiatives will be 1st Rio International Summit on Therapeutic Advances in Cardiovascular Medicine being organized by David Brasil and a Public Heart Health Forum to be developed by Denoel M. Oliveira and Ivan Berkowitz. ❤

PEOPLE AND PLACES

Academy bestows its highest honour on **Dr. Victor J. Dzau**

Victor J. Dzau, MD, was appointed Chancellor for Health Affairs at Duke University and President and CEO of the Duke University Health System effective July 1, 2004. He is also James B. Duke Professor of Medicine and Director of Molecular and Genomic Vascular Biology at Duke.

Dr. Dzau served previously as Arthur Bloomfield Professor and Chairman of the Department of Medicine at Stanford. Most recently, he was the Hersey Professor of the Theory and Practice of Physics (Medicine) at Harvard Medical School, Chairman of the Department of Medicine at Brigham and Women's Hospital, and Physician-in-Chief and Director of Research at Brigham and Women's Hospital, Boston MA.

Dr. Dzau's academic interests are in cardiovascular translational research and mission-based education. His laboratory has studied the molecular and genetic mechanisms of cardiovascular disease and applied genomic and gene transfer technologies to develop novel therapeutic approaches. His work on the renin angiotensin system (RAS) paved the way for the contemporary understanding of RAS in cardiovascular disease and the development of RAS

inhibitors (e.g. ACE inhibitor) as therapeutics. He pioneered gene therapy for vascular disease, being the first to introduce DNA decoy molecules to block transcriptions as gene therapy in vivo. Two of his discoveries E2F decoy and nitric oxide synthase gene therapy are now being evaluated in clinical trials. He is currently advancing the novel concept of "preemptive gene therapy" using hypoxia regulated expression of heme oxygenase 1 transgene for coronary heart disease and recently has proposed the "Paracrine Hypothesis" for stem cell action in tissue repair and regeneration.

The recipient of many awards and honors, Dr. Dzau received the first Hatter Award from the Medical Research Council of South Africa in 2000. He was awarded the prestigious Gustav Nylin Medal by the Swedish Royal College of Medicine and the Swedish Cardiology Society, the Novartis Award for Hypertension Research by the American Heart Association (which also named him one of its Distinguished Scientists for 2004), the 2004 Max Delbruck Medal by the Max Delbruck Center for Molecular Medicine, Berlin, Germany, the 2005 Golden Door Award by the International Institute of Boston, and a 2005 Ellis Island Medal of Honor by the National Ethnic Coalition of Organizations.

Dr. Dzau has served on numerous committees and advisory boards, including, previously, the Executive Committee of The Academy at Harvard Medical School (of which he is a founding member) and the boards of Brigham and Women's Hospital, Partners Healthcare, and the Harvard Clinical Research Institute. Currently, he serves as a member of the Board of Directors for both Duke University Health System and Genzyme Corporation. He has been elected to the Institute of Medicine of the National Academy of Sciences (USA) and the European Academy of Sciences and Arts. Previous Chairman of the National Institutes of Health (NIH) Cardiovascular Disease Advisory Committee, he served on the Advisory Committee to the Director of the NIH. In 1999, he became Editor-in-Chief for the American Physiological Society's new journal, Physiological Genomics. A founding member of the Society of Vascular Medicine and Biology and the Council of Arteriosclerosis, Thrombosis, and Vascular Biology of the American Heart Association, Dr. Dzau was Editor-in-Chief of the Journal of Vascular Medicine and Biology.

Dr. Dzau received his MD from McGill University in Montreal and underwent postgraduate training at Harvard Medical School. He was born in Shanghai, China, raised in Hong Kong, and is a citizen of the United States. He and his wife Ruth have been married for 32 years and are the parents of two daughters.

The International Academy of Cardiovascular Sciences is delighted to present its prestigious Medal of Merit for 2006 to Dr. Victor Dzau.

PEOPLE AND PLACES

CardioGlobal in Brazil

by Dr. Wagner Padua Filho, Brazil

The 2nd Annual CardioGlobal 2005, an official meeting of IACS South American Section, was held in Porto Alegre in September with very positive results. There were many physicians from different parts of Brazil, from south to north and speakers from Brazil, Argentina, USA, Cuba and Canadá. Dr. Wagner Padua Filho (FIACS) and Raimundo Nascimento Neto (FIACS) from Brazil were the chairmen. "This meeting is one of the most important international meetings in our country and a place to meet physicians from all over the world. The scientific program covered different cardiovascular topics from laboratories to bedside", said Dr. Wagner Padua Filho.

In 2006, CardioGlobal will be held on October 20-21 in Recife - Pernambuco, a wonderful city in northeast of Brazil, with beautiful beaches and places to visit. The scientific program will be carefully prepared to provide an improvement in knowledge in cardiovascular sciences. The organizing committee members are Drs. Wagner Padua Filho, Raimundo Nascimento Neto and Domingos Melo from Brazil; Naranjan Dhalla and Pawan Singal from Canada; Ricardo Gelpi (Argentina) and Daniel Villarreal (USA).

We would like to invite everyone to participate in this meeting to enjoy the Brazilian beauty.

"even time to enjoy Brazilian football in the rain!"

European Section Executive Met in Prague

Bohuslav Ostadal, President (Centre), Karl Werdan, Vice President (Right) and Keld Kjeldsen, Executive Secretary (Left) held a successful meeting on November 27-28, 2005. Participants of the Prague meeting are convinced that there exists an open window for such activities of the IACS in Europe. Academy means teaching; while there are a lot of teaching seminars for young clinical cardiologists, organized predominantly by the European Society of Cardiology, substantially fewer possibilities are there for the young investigators (both clinical and experimental) interested in basic science. The main problem will be, however, to raise money. The European Section of IACS should, therefore, morally support the scientific meeting organized by the members of the IACS and simultaneously organize low-cost post-graduate teaching seminars on a given topic. Furthermore, IACS should promote the collaboration between clinical and experimental cardiologists in the individual countries. For such purposes it would be desirable to organize small workshops and round tables focused on "hot" and controversial issues. On request of the cardiology communities in individual European countries, IACS should help with the organization of scientific local events, including suggestions of appropriate international experts in the field etc.

Appropriate introduction of the Academy is necessary. The European Section should, therefore, open its website with all the necessary information concerning the IACS as soon as possible, including a link to www.heartacademy.org. The website will facilitate communication among individual countries which, particularly at the beginning of all activities, will be essential. Dr. Werdan kindly promised to establish the website before the end of March 2006; Dr. Ostadal will supply the necessary information by the end of 2005.

The Members of the Executive Committee have suggested to use the official logo of IACS with distinct indication "European Section". Dr. Ostadal will ask Ivan Berkowitz for professional help; the same is valid for the official letterhead.

Two official meetings will be organized under the auspices of IACS in 2006: V. International Symposium on Myocardial Cytoprotection in Pecs, Hungary, September 28 - 30, 2006, and Cardiovascular Ageing in Halle, Germany, October or November 2006.

Members of the Committee discussed the possible participation of the European Section in the Second World Congress in Sapporo in July 2006. Since the program seems to be already complete, the only possibility will be the official information about the activities of the European Section during a business meeting. The Committee suggests to organize symposia of the individual sections of IACS as a part of the scientific program of the next world congress.

Dr. Ostadal informed the Committee about the present status of the official journal of IACS, "Experimental and Clinical Cardiology". It was suggested to repeat the application for indexing as a necessary condition how to increase the scientific level of the Journal. Nevertheless, the Journal offers advantageous possibility for the organizers of international cardiological meetings to publish abstracts or full papers. Dr. Kjeldsen kindly offered the publication of a series of papers dealing with the methodology of medical research. The papers will be published during the next year.

It has been decided to organize regular meetings of the European Council at least once per year. The first will be organized in Prague in the second half of 2006.

International Symposium in Argentina

by Ricardo Gelpi, Buenos Aires, Argentina

From left to right: Daniel Villarreal, Naranjan Dhalla, Ricardo Gelpi, Stephen Vatner, Wagner Pádua, and Dorothy Vatner

During the XXXII Argentine Congress of Cardiology held in Buenos Aires, in October 2005, the Symposium of the Latin American Section of the International Academy of Cardiovascular Sciences was carried out. It took place on October 7th and included two round tables and a conference where the main subject was myocardial hypertrophy and cardiac failure.

Among the guest faculty were Drs. Naranjan Dhalla, Stephen Vatner (present president of the IACS), Dorothy Vatner, Daniel Villarreal, Otoni Morerira Gomes, Domingo Melo, and Wagner Padua Filo. Dr. Ricardo J. Gelpi, President of the Latin American section was in charge of the organization and among the local faculty were Drs. Carlos Bertolasi, Horacio Cingolani and Raul Oliveri.

The event developed in a friendly and informal atmosphere, where the different presentations presented an excellent scientific level. The presence of top leaders of the IACS worldwide helped to outline the future of the Latin American section, which will be based on the inclusion of other Latin American countries, particularly in the fields of research and teaching, both graduate and post graduate.

Fortunately, spring time temperatures of an average 20º C accompanied the event and all attendees welcomed the opportunity of tasting the remarkable Argentine "asado" (barbecue) with the best Malbec wine.

"A Glimpse of the 21st Century from Present Day Genetics"

edited oral presentation by Robert Roberts, Ottawa, Canada

Front; Garrett Gross, Dipak Das, Rudy Redekop, Robert Roberts and Pawan Singal (Awards Day Chairman); Centre: Ivor Benjamin, Arik Mahay and Naranjan Dhalla (ICS Director); Back: Rohit Singal, Raja Singh, Girma Asemu, Debbie Brown (Manitoba Heart & Stroke Foundation), and Harjot Saini

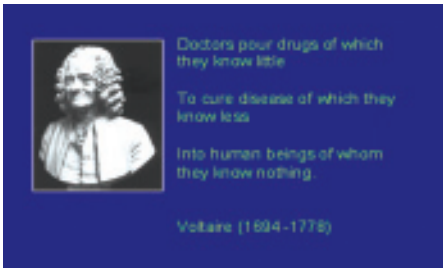
Editor's Note: This extraordinary talk originally was presented at the Institute of Cardiovascular Sciences Awards Day in Winnipeg on September 30, 2005. The award winners are shown above.

This talk is a superb preview of the IACS Global Symposium on "The Future of Heart Health and Disease" to be chaired by Dr. Alan Menkis, Medical Director of Winnipeg's Cardiac Sciences Program and Dr. Grant Pierce, recently appointed Executive Director of St. Boniface Hospital Research Centre. The one-day Symposium on October 14, 2006 will lead off with Dr. Roberts on "Can We Live for 150 Years?" See page 52 for details to honour Dr. Naranjan Dhalla on his 70th Birthday.

Good morning.

It's a great honour and a great pleasure to deliver the Beamish Lecture this year at the Institute of Cardiovascular Sciences in Winnipeg. I certainly knew Dr. Beamish and his pioneering work in forming the Canadian Journal of Cardiology. I think he always had his eye on the future and I think what I will say today is in keeping with his vision. Looking ahead rather than looking back.

Many of you will know I have a real enthusiasm for genetics and I'm going to use this opportunity today to look back and look forward in terms of what genetics is doing, could do and will do in this century. Molecular genetics is not a new thing. It had already made its mark in the world long before it came to medicine. In the sixties when I was an undergraduate, even though I did science, I also did philosophy and used to argue until two and three in the morning about what we should do with the exploding world population, we would not be able to feed. Women marched to Washington to bargain for birth control. What has happened in the mean time? A couple of things have happened and Canada has played a major role. One of the staples in terms of feeding the world is rice and the other is wheat. Canada took a major step forward to see what it would take to grow wheat in a country that can be as cold as the northern part of this Country. They crossed different types of wheat, and through genetics, bred different strains of this crop. Today, Canada can grow wheat, not inside of the Arctic Circle, but inside of thesemi-Arctic Circle. Canada can grow enough wheat to feed the whole world for about 10 years. Canada and the United States, together, can grow enough wheat to supply the whole world for about 23 years. Clearly genetics made this possible.



Looking back on what happened to the argument about not being able to feed the world's population? The world population has reached 6 billion and is increasing more per year than the world's population in 1500. The Economist carried an article a few months ago, pointing out that since that time in the sixties, we spend more money in one year, subsidizing our farmers so they will not grow crops, than we have spent in 44 years on birth control. It's a completely different picture. Today we pay hundreds of millions of dollars for

our farmers not to grow in part because genetics provided the power for them to grow too much food. So, there's no doubt, genetics is an indispensable tool to enable us to stay on this planet.

Before looking ahead, I would like to briefly look back at Voltaire, who was a great philosopher, and in many ways also a scientist. But he did not think much about physicians. Part of the reason is that his wife, at age 43, died during the birth of their first child, as did their child. Voltaire always attributed most of his thinking and his ideas to his wife and when she died, he felt he had lost a large part of his life. He blamed the physicians for not knowing much about medicine as indicated.

He probably was not far from the truth. Shown is a summary from Paul Dudley White textbook of 1939 showing much of what we do today in cardiology was not feasible at that time.

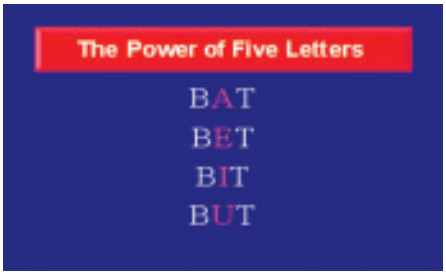
In 1937, chronic syphilis was a terrible disease of the aorta and heart. Just to marry the past with the future, the new treatment for chronic syphilis was arsenic. The genome of Treponema Pallidum, that causes syphilis, has been completely sequenced and it is expected to have a vaccine within the next 5 years which the World Health Organization hopes will wipe syphilis off the planet.

When you look at what has happened since the fifties, and include antibiotics, cardiology has advanced more in the past 50 years than the previous 2000, emphasizing technology, and the rate of change that technology has brought with it. In fact, today many of my colleagues spend most of their day working inside a coronary artery without ever having to open the chest. But I think in the future we will have the technology to implement prevention. This will be a quantum leap from simply treating the crisis.

My analogy for you is the impact of molecular genetics and the human genome on civilization will be what the alphabet did for democracy and western philosophy in the sixth century BC. Most historians agree the sixth century BC, was the greatest epoch of our time, certainly for the Western world. Given that we have a global world today that is simulating a lot of Western ideas, I think you can say it's probably the century for the world. It was in the sixth century BC the Greeks recorded the principles of democracy and Western Philosophy. Two millenniums later we're still defending that philosophy in many different parts of the world. And I think for most of us, we feel it's worth it.

The Industrial Revolution of the eighteenth century was the second greatest century. The twenty first century will be "the" third and perhaps the greatest of all.

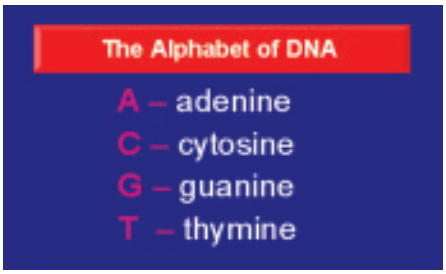
What was different about the sixth century B.C.? There were many languages before this time. The world was considered non-illiterate probably around 1200 to 1400 B.C. Most of those languages were picturesque languages. When you look at the symbol for "dog" in Chinese, it reminded you of a dog if you were Chinese. You didn't have to think much. Whereas today, when you look at D-O-G, in English, you have to do something quite different. You go from concrete thinking to conceptual thinking. When I see D-O-G, it's a huge massive program that is instantly turned on for me to say, that really stands for an animal with four legs and so on and so forth. And the concept, of course, grew into conceptual thinking and leads to philosophy and so forth. What made this all possible was the first symbolic language.



An alphabet is defined as something in which the language is confined to less than 30 symbols. The Phoenicians had an alphabet, but it wasn't really used. You couldn't go from the spoken to the written word. It was missing something. About 800 B.C., the Greeks came along and supplied the missing feature, the vowels. Without those vowels, it was not possible to go from the spoken to the written word. This is illustrated by the four words, each differing by only one letter, the vowel, yet totally different meanings.

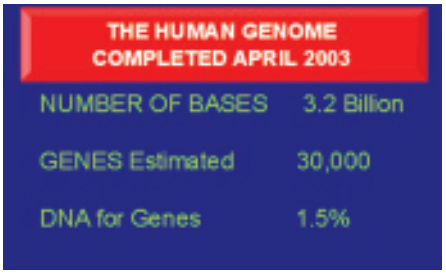
Those five letters changed the world forever. Before, when you had all these thousands of symbols most people did not attempt to become literate. It was now possible. Before the Greek era was over, they thought they had created an alphabet that was so simple, they could start teaching children to learn to read and write. They didn't really get started, but they had the idea. And it was about when the Romans came that they felt it would be possible that someday, even women could learn it.

The legacy that this brought was an alphabet, based on the simple 26 letters that made it possible to go from the spoken to the written language. So was born, the written philosophy and democracy we have today. Those five letters changed the world for the next 2000 years and will probably continue to do so. Thus, my analogy of the sequencing of the human genome. DNA has only four letters. It is made up of those four bases you see here, A, C, G and T, which stands for adenine, cytosine, guanine and thymine. They are joined together



and there are a little over 3 billion of them in the human genome. Everything you do, what you look like including your height and sex is based on the linear sequence of those four letters. The story that unfolds now is that the twenty first century, not just in the sciences, but in all aspects, will truly be touched by the human genome. Everyone recognizes the second greatest epoch was the industrial revolution and I would propose the 21st century will be the third if not the greatest in part because of the sequencing of the human genome.

There are 3.2 billion of those bases and we only have about 25 thousand genes, meaning that only about 1% of the DNA is used to make genes. The quest for us in the next 10 or 15 years is to identify those genes and determine what they do. What we as scientists and physicians will have will be equivalent to when the physicist got his alphabet, the periodic table of elements. We will have ours probably in about another 5 or 10 years which will truly give us the tools to really understand the inner workings of a human being.



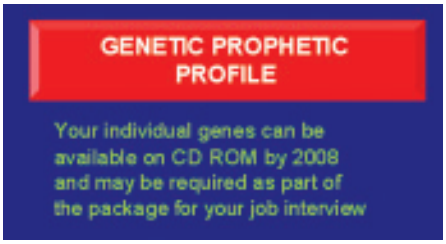
I might also point out to you, historically, that this is the first time ever in the history of mankind, major resources are dedicated to understand what makes us tick. If you stop and think about it, in the sixteenth and seventeenth century, the Europeans explored the whole world. In fact when Cook saw Australia, he wrote in his log, "I have not only travelled farther than any man, I have travelled as far as man can travel." Of course he didn't know about space then.

Exploring the earth by the Europeans was completed within 150 years. Then they turned to what makes up the Earth. The first things we got were coal, steam and subsequently, oil following by all the minerals and jewels. We spent the next 200 years exploring what is the composition of this Earth and how we can exploit it.

For the first time in the history of mankind, we have finally gotten interested in "US" - what is it that makes us tick, in terms of our biology? It is truly a new venture, a new era, in large part, accelerated by the human genome.

Like everything else, it has some bad moments. Freud said science had dealt a major blow to human esteem on two accounts: when Copernicus said we are no longer the centre of the universe, we go around the sun, he was put under house arrest. For the next 60 years many people were executed who tried to believe that and the other was when Darwin said we are related to animals. I think if Freud were alive today, he'd have a third one from the human genome. It is now recognized and well known that, of all the humans that have ever lived or will live, our DNA differs by only one tenth of one percent. Ninety nine point nine percent of our DNA is identical. And that would be a hard thing for some big egos to take, knowing they are different by only one tenth of one percent. One tenth of one percent is indeed what it's all about. One tenth of one percent of 3 billion is 3 million. Those 3 million bases is the key to what we are all about. Your predisposition to disease, your ability to resist it, your ability to be a marathon runner versus a couch-potato watching television is very much related to those 3 million bases. What we are looking at is another era, an era of prevention, rather than treating the crisis. We will have the tools within 5 to 15 years to really plan from day-one how to prevent heart disease, how to prevent cancer.

Many accept the fact that this is the last century for heart disease. The NCI, the National Cancer Institute, put on their web site a few months ago, that they expect to cure cancer by 2015, which is amazing given that there are over 200 different forms of cancer. But, you see the ball game that we are facing. We no longer want to accept the fact that we're only going to treat the crisis when it occurs.



Yes, its true, your genes will be on a chip. Chips are available at the moment with most of the genes for the mouse and certainly many of the human ones. As they become available they certainly will go on plastic, and there will be lots of entrepreneurial spirit, to do it. The person who got the Nobel Prize for sequencing DNA used to say that, "Your genomes would be available on a CD-ROM when you go for your employment interview by the year 2030." He has now sped that up and says, "Partial genomes will probably be available in the year 2008."

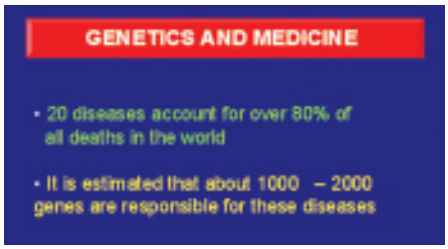
I would like to remind you that at the present time, there are many clinical trials ongoing in cancer, and all of them first test for a specific gene before they administer therapy. Several of the drugs, like Herceptin that has recently been FDA approved, is only given if you have a particular DNA variant.

If you look at what is happening in the world in terms of life span, you must again emphasize the rate of change. In 100 years, the life span of females doubled and males went about from 47 to 79. It is an incredible story to know that life span doubled in one century. In Science it is predicted that the life span will double again in the next 100 years. The average life span would then be about 160 years rather than 80 years.

We already know from human cells - HeLa cells, donated from a wonderful lady in 1944 with cancer of the breast - grown in culture, without disease, will do well for about 180 years. Then you start to see programmed cell death, another step to overcome if you want to live to be two or three hundred years. But, without disease, it is indeed expected to have a reasonable life span of 150 years.

If you look at what is happening in the world, it is getting older. It is a real concern that today, there are already 600 million people over the age of 60, and by 2050 there will be over 2 billion. An interesting tidbit is that when Queen Elizabeth was crowned in 1953, she sent 60 letters out to people who were over 100. Last year she sent out 6,000.

As you get older, your first response is going to be, "What about the quality of life?" I think all of us would agree that we will have to replace some of those organs, and some are more important than others, depending on your point of view. But the bottom line is that technologies are advancing. I personally expect it to be stem cells with the individual's nucleus. Nuclear transfer is now accepted in three countries in the world, Britain, and Finland and Russia. Certainly as time roles on, you'll see more of that in different forms. But, the ability to take the nucleus out of a biopsy of your liver, put it into a stem cell so you will make that organ identical to what you had without rejection, is going to be a quantum leap in terms of the quality of life. There is no question in my mind that within 5 to 10 years, that technology will be laid out at about the same time you will have about 20 thousand genes. With all of that technology coming together, I am very hopeful the quality of life will improve along with prolongation of life span.



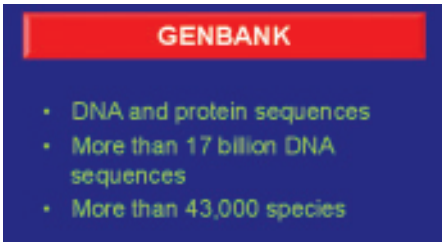
At the present time, 20 diseases account for 80% of all the deaths in the world. Number one is infection. Number two is cardiovascular disease, but will probably be number one by 2012. These diseases are probably controlled by about two or three thousand genes that predispose or make you resistant to these diseases. Stop and think what it would be like when all those genes and their sequence are available to us. Once we have the genome of bacteria, for example, it is much easier to develop a vaccine. And it is easy to see that in the next 10 years many infections will be treated with vaccines, rather than antibiotics. It will indeed be a brave new world. From a single fingertip blood sample, you will have 25 thousand diagnoses, available to you.

We're not really interested in cataloguing the genes, anymore than the physicist wanted to catalogue the elements of the periodic table. He wanted to know what he could do with them, what their features were, what their characteristics were, how to make an alloy so light that it could fly - like an airplane. And so the alloys that have evolved from these elements have made our society far better for mankind. In terms of genes, what we want to identify is what do they do, how can we use them to identify an early marker of disease, how can we design novel therapies to overcome those defects? And that is really where the quest is: determining the function of genes.

I had the opportunity in 1997 to be locked up for three days with Jim Watson at Cold Spring Harbour. There were about 30 of us and our quest was: "What can we do to identify all the phenotypes for those genes? How would they be manifested clinically?" At that time, if we wanted to determine the function of a gene, we had two options: First, we could find those rare diseases that are inherited, which make up for less than one tenth of 1% in our society. And second, put that gene into a mouse or knock it out of a mouse to see what it does without it.

We estimated at that time, if we set up 15 clinics in the United States, and knocked out one gene a week, we would determine the functions of those genes in 77 years. That was in 1997. Today, most of those genes will be identified; their function will be known within the next 10 to 15 years. The rate of change is because of several things. One of them is Bioinfomatics and I'll illustrate what it really does for us. In the nineties it was decided that every time you get a DNA sequence, you must record that sequence with one of the three gene banks in the world: Washington, Tokyo and London. You couldn't publish it unless you already deposited it with Genbank and had an accession number. Gene banks developed and made it possible to determine the functions of genes often without further experimentation.

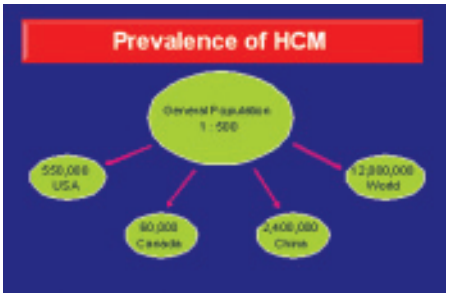
This is illustrated with the use of a little worm called C. Elegans. It's very tiny; you can't see it with the naked eye. You have to magnify it under the microscope. Sequencing of the genome of C. Elegans was a major break through in 2000 and got front cover of Science. C. Elegans has 19,000 genes versus our 25,000 genes but 36% of them are virtually identical. That may surprise and humble you. But, like us, this worm must ingest and digest food; it must absorb it and then convert it to energy. There is only one form of currency for energy: high-energy phosphorous. Everything must be reduced to high-energy phosphorous. It's not surprising then that the set of genes regulating this process is going to be the same in the worm as in the human. So when you put it in perspective, that's why you can determine the function much faster. There are 959 cells in each C. Elegans and the skin is transparent. With those cells labelled, and the genes labelled, one can determine where they're going and in many cases, their function. Remember, 36% of the genes in C. Elegans are virtually identical to that of humans. One thing we do know and have proven beyond a doubt is that if the function of a gene in any organism is determined it is also identical in humans. All calcium-binding proteins, bind calcium in C. Elegans, as they do in humans. They might add something here or there to localize it or to increase or decrease affinity, but it's still the same function. As a result we can identify rapidly the function of many genes through the process.



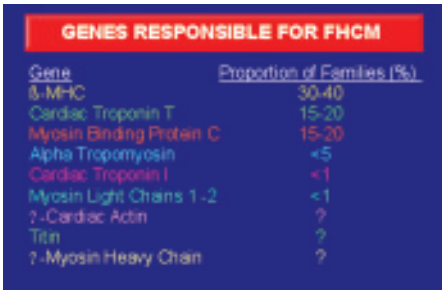
Gene banks today contain 322 organisms in which the genome is completely sequenced. Today, there are over 17 billion DNA sequences in gene banks. If you identify a human DNA sequence, you can go into gene bank and look for that sequence. If your sequence lines up with the fruit fly or C. Elegans, and you go to that little organism to determine the function, then you know this will be the function of the gene in humans. Within eight months, you may have a publication, as opposed to eight years. All of this again emphasizing the rate of change.

Our closest relative is the chimpanzee. The mouse broke away from us about 55 million years ago, and the chimpanzee only about 5 million years ago. The DNA sequence for the chimpanzee was just released and promises to be treasure trove.

I would like to illustrate how my laboratory has used the technology to go from bench to bedside as an example of what modern molecular genetics and recombinant DNA technologies has enabled us to do. Until recently, most of my research has been identifying genes for rare diseases. In the seventies, Brown and Goldstein had trouble getting funded because they were working on a rare disease called familial hypercholesterolemia. It accounts for probably less than 1/100th of 1% of all heart disease. What they identified, however, was the receptor for cholesterol. Subsequently they identified the gene and subsequently exposed the pathway for the synthesis of cholesterol. This lead to the first statin drug, which today is used by millions and millions people all over the world; not just for that rare disease, but for heart disease in general. In fact, I have often said that we should put statin in the water; (yes, Crestor is soluble in water) there's more justification for it than for fluoride. It would save many more lives.

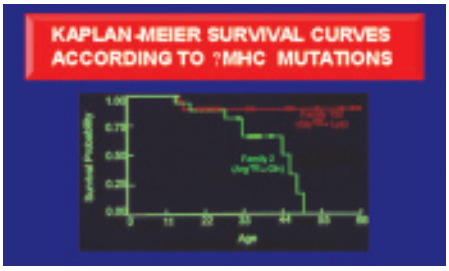


In familial hypertrophic cardiomyopathy the septum and the wall of the heart are very thick which is the typical pathological feature of this disease. Individuals with this condition are born with a gene that induces this condition. They usually don't get it until they reach puberty. It is a fairly common gene - by far the most common mutation for cardiovascular disease. One in every 500 people has it. It's the most common cause of sudden death in the young, particularly in athletes. With an incidence of 1 in 500, there are about 12 million people in the world with that gene who are at risk of developing the disease. In China alone, there is almost two and a half million people with this gene. In Canada and the US, it is 60 thousand and 550 thousand people, respectively.



Thirteen genes have been identified. The first was identified by Christine Seidman and from that time on, opened the field for all of us. Today, there are over 350 mutations in 13 genes. It is possible to screen for them today, but, no one will pay for it at the moment - it's really only done on a research basis. It is, however, just a matter of time before that will change. Moreover, there has always been an issue ethics in respect to screening for diseases. Many would say not to screen if there is no treatment. That probably would not be true in the case of hypertrophic cardiomyopathy since a defibrillator can be implanted to prevent sudden death.

Two different families with familial hypertrophic cardiomyopathy can serve as examples. In one family, nine people had died, most of them suddenly in their second or third decade of life. In a second family, on the other hand, only two had died. They had the same gene, but different mutations. If you have one of the mutations, you will have close to a normal life span. If you have the other mutation, lifespan is about 28 years.



Clearly, however, this illustrates the power and the ability to enable us to do personalized, individual medicine based on our genome, which is likely coming down the pipe in the next 10 to 15 years. We're certainly not ready for it in society and in terms of ethics, but I think that whether we want it or whether we're ready, it is going to happen. I think the benefits will out weigh all the bad things.

By means of another example, I would like to stress how important is it to screen for a disease in which we already know the gene even if we do not have a treatment. Tay-Sach's disease is a horrible disease. It occurs in children and most are dead by age three or four. They die a horrible slow death for about a year. Most of the afflicted are Ashkenazi Jews. In 1976, a decision was made in Canada and in Hong Kong that they could screen for Tay-Sachs. Knowing it was for Ashkenazi Jews primarily, the community agreed that in high school, if someone got interested in someone of the opposite sex, they would indeed be tested. If they both had the gene, they would be advised to break off the relationship - not the friendship. By 1996, Tay-Sachs disease in Montreal and Hong Kong had been decreased 85% - it is almost wiped out. Today, that program is in operation all over North America and many parts of Europe. There was no treatment - it was simply genetic counselling. And so we should not sell it short genetic screening just because we do not have a treatment.

The other part, if you look at hypertrophic cardiomyopathy is a review of a thousand cases that had a defibrillator put in to prevent sudden death. There is no genetic testing here. The reason you put in a defibrillator is either because:

- They have already died once or twice;
- They may have had an episode of uncosciousness;
- It has been documented that they have ventricular tachycardia;
- They have hypertrophic cardiomyopathy;
- They have a family history of sudden death.

Defibrillators have a little computer on it to record whether it fired or not and if it fired for the right reason. These people were prevented from dying with the defibrillator. So it shows that it does work. In North America, the average age of patients implanted with a

defibrillator is the 30's. We are waiting to get their family history; we are waiting for them to die at least once because that is the indication. Many don't survive, but those that do are appropriate candidates for a defibrillator. Most deaths from hypertrophic cardiomyopathy occur before the age of 35. Most patients are asymptomatic; their first symptom is sudden death and it is usually their last. If we screened for hypertrophic cardiomyopathy, we could put in a defibrillator.

What else you can do to identify appropriate treatment? Ideally, we would like to replace the defective gene with a normal gene. Since the heart renews itself about every three weeks, over the next five half lives, it could replace itself with the normal gene. However, this is not feasible currently and will have to be the holy grail of the future. In the meantime, having the human gene enables one to insert it into the egg of a mouse and generate transgenic animal models expressing the human gene with a phenotype virtually identical to that of the human. Several transgenic mouse models of Hypertrophic Cardiomyopathy were generated and utilized to explore the pathophysiology of HCM and to identify novel therapies. However, for the human myosin heavy chain gene, the mouse is somewhat questionable since it normally has alpha rather than the human beta form. The NIH was good to me in many different ways, but one of them was that they awarded me about 1 million dollars to develop a transgenic rabbit. The rabbits have a bigger heart, and, like humans hearts, express beta myosin. We had a hard time developing this model. I was not sure that I was going to appreciate the money we received because, after we had fiddled with the fallopian tubes to put that particular gene into the egg, the males would not mate with the females; they would just stay away from them. We did everything. We played classical music, we played rock and roll music, and we changed the chow. Fortunately for me, a guy came to work in my lab, by the name of Brugada - Ramon Brugada. His parents make a living raising rabbits and breeding them in Spain. He just would not believe it. We went through all this again and still could not get them pregnant. Eventually, we took them out of their cages and let them run around like they would on a farm. They became pregnant, and today we are breeding these animals all of which have hypertrophic cardiomyopathy identical to the human phenotype. We utilized both the transgenic rabbit and mouse models to evaluate new therapies.

"Just don't expect it to roar"

In the mouse, we did randomized placebo controlled trials and showed that after 6 weeks of blocking angiotensin II with Losartan, (Angiotensin II is the most potent growth stimulant of the heart) we completely reversed the fibrosis and improved cardiac function. In the rabbit model, we showed that a statin (Simvastatin) after 12 weeks of therapy completely reversed the fibrosis, hypertrophy and improved cardiac function. Statins are well known for inhibiting the synthesis of cholesterol. But they also do something else. By inhibiting the synthesis of cholesterol, they also inhibit formation of an intermediate - mevalonic acid - that is essential to perform farnesylation and geranylgeranylation. One or both of these processes involve the transfer of either a 15 or 25 carbon fatty acid molecule to signalling molecules essential for cardiac growth and hypertrophy such as Rho A and Rho C. By blocking this process with a statin we were able to reverse the hypertrophy and fibrosis. A similar result was observed with Spironolactone. Rabbits are like humans; they don't get the disease until they reach puberty. This afforded us the opportunity to perform a randomized placebo-controlled manner to access whether statins administered prior to puberty would prevent the development of the phenotype. The result of this study recently published showed that it was possible with Atorvastatin to prevent the development of the phenotype.

What we have is a model which enabled us to unravel the molecular pathogenesis of the disease and evaluate new therapies. We hope to start our first clinical trial in Canada and the US in the new year evaluating these therapies in patients with HCM.

The literature is filled with reports about drugs that work in animals, but do not work in humans. However, one thing we know about this therapy it is safe - millions of people have taken those drugs. We also know the side effects. It makes logical sense that something like blocking angiotensin II should reverse and or prevent the phenotype. These studies in HCM demonstrate the power of molecular genetics and recombinant DNA technologies. I really think the 21st century belongs to human biology and personalized medicine that is truly evidence based is around the corner. Thank you very much. ❤

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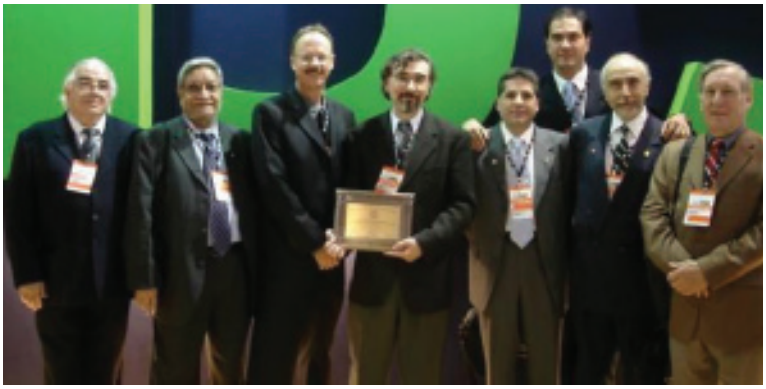
Academy's Award for Distinguished Service for **David Brasil**



From left to right: Otoni Gomes, Naranjan Dhalla, Grant Pierce, David Brasil, Domingos Melo, Wagner Pádua, Daniel Villarreal and William Weglicki

Dr. David P. Brasil, born in May 1961, was admitted into the Souza Marques Foundation School of Medicine (Rio de Janeiro) in February 1979 and simultaneously into the Faculty of Philosophy and Languages at Rio de Janeiro State University in January 1980. He received his M.D. in December 1984 and completed his postgraduate training in Cardiology in December 1988 in the acclaimed 6th Infirmary at Santa Casa de Misericordia Academic Hospital, Rio de Janeiro, Brazil.

He began his career in military service as a Medical Officer with the Brazilian Air Force, reporting for duty at the Air Force Hospital & Division of Health in Lagoa Santa. He transferred to the inactive reserve in January 1991. For about ten years he served the public health system as attending cardiologist at Odilon Behrens Municipal Hospital, one of the largest emergency hospitals in the State of Minas Gerais. At the beginning of the '90s he joined the teaching staff of his institution and actively devoted his career to the training of medical students and young physicians in the Residency in Internal Medicine. From 1990 to 1997 he had delivered 112 courses and lectures in meetings and symposia and participated in several clinical studies, dynamically contributing in the medical training of many resident doctors. He had also organized various scientific courses and symposia. Dr. Brasil effectively served on hospital committees as well as in positions in the Board of Directors of his State Society of Cardiology and the Heart Foundation of the Brazilian Society of Cardiology.

During 1998 and 1999 he undertook training in basic cardiovascular research as a postdoctoral fellow with the Institute of Cardiovascular Sciences at the University of Manitoba. Under Dr. Naranjan Dhalla's guidance he accomplished a project on vascular remodelling that generated a number of publications in peer-reviewed journals. In 1999 he also earned his Master of Medicine (Cardiology) and in 2000 he worked as a Clinical Research Scientist in preparing clinical trials in Canada.

In 2002 he joined the Cardiovascular Unit of the Center of Research and Post Graduation at Faculty of Medical Sciences of Minas Gerais, and also became a Fellow of the International Academy of Cardiovascular Sciences. During the latest 31 months he has delivered 117 lectures, full-length courses and presentations in programs of medical education in 43 cities, and produced three book chapters in Cardiovascular Medicine. Throughout his career he organized several international meetings in a variety of cardiovascular areas. Dr. Brasil also keeps a considerable record as a cardiovascular consultant for the pharmaceutical industry. His core fields of interest are Evidence-based Cardiovascular Medicine, Principles of Biostatistics, Atherosclerosis, Vascular Biology, Atherogenic Dyslipidemia, Metabolic Syndrome & Diabetes, and Peripheral Arterial Disease.

In 2004 he received an Award for Quality of Teaching from the postgraduate students in Cardiology and was designated Consultant Scientist to the Institute of Cardiovascular Sciences in Winnipeg. Dr. Brasil's solid record of medical teaching and research was acknowledged last September, when he was honored with the Academy's Distinguished Service Award in Cardiovascular Science and Medicine during a session of the Annual Congress of Brazilian Society of Cardiology. He has affectionately dedicated this Award to his devoted wife and their three sons. ❤

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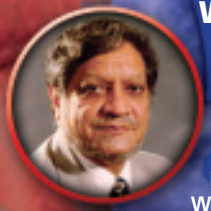

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DRAFT AGENDA

Saturday, October 14, 2006 · Co-chairs: Grant Pierce and Alan Menkis

8:00-8:30	Registration and Continental Breakfast
8:30-8:45	Opening Remarks - Stephen Vatner, President of International Academy of Cardiovascular Sciences, Newark Chair - Makoto Nagano, Chair of the Academy
	FOCUS OF RESEARCH - Chair - Grant Pierce
8:45-9:10	"Can we live for 150 years?" - Robert Roberts, Ottawa ON
9:10-9:35	"Can stem cell research change the face of cardiovascular disease?" – Piero Anversa, Valhalla NY
9:35-10:00	"Potential Stem Cell–Based Therapies: A Veritable Revolution" – Roberto Bolli, Louisville KY
10:00-10:30	Panel Discussion – Nagano, Vatner, Bolli, Anversa, Roberts, Pierce
10:30-10:45	Refreshment Break
	WHERE WILL SURGERY GO - Chair - Alan Menkis
10:45-11:10	"Will Cardiac Surgery Exist in 20 years?" - Randall Wolf, Cincinnati OH
11:10-11:35	"The Future of Mechanical Heart Assist Devices, Can They Be Permanent? Are They Ever Practical?" - Walter Dembitsky, San Diego CA
11:35-12:00	Panel Discussion- Menkis, Dembitsky, Wolf
12:00-1:10	Naranjan Dhalla's favourite Lunch
	HOW CAN WE IMPROVE QUALITY OF HEART PATIENTS' LIVES? Chair - James Tam
1:10-1:35	"Prevention will reduce heart disease more than any other factor" - Salim Yusuf, Hamilton ON
1:35-2:00	"Heart Disease in Women - Where it's going and the challenges ahead" - Noel Bairey Merz, Los Angeles CA
2:00-2:25	"The Medical and Public Health Impact of Cardiovascular Disease in Children: Globally under-appreciated and under-financed" - Edward Kaplan, Minneapolis, MN
2:25-2:55	"Cardiovascular Physiologic and Molecular Imaging" - Jamil Tajik, Scottsdale AZ
2:55-3:15	Panel Discussion - Bairey Merz, Tajik, Yusuf, Kaplan, Tam
3:15-3:30	Refreshment Break
	ROUND TABLE ON IMPLEMENTING FUTURE CHANGES Chair - Albert Friesen
3:30-3:45	"How Can We Afford Health Care in the Future?" - Roger Evans, Rochester MN
3:45-4:00	"The cost of disease management with drugs is justified and manageable in the future" - Terrance Montague, Montreal PQ
4:00-4:15	Private/Public Sectors Partnerships - Henry Friesen, Winnipeg
4:15-4:30	"The Role of Industry in Research & Development & Health Care. How will it Look 20 Years from Now?" - Calvin Stiller, London, ON
4:30-5:00	Panel Discussion -Stiller, Evans, Friesen, Montague, Friesen
5:00-5:30	"Keynote" Closing Address - Sir Magdi Yacoub, President-Elect of International Academy of Cardiovascular Sciences, London, England Chair: Alan Menkis
7:00 - 8:00	Reception
8:00	Dinner

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