The Future of Heart Health

At The Institute of Cardiovascular Sciences, St. Boniface Hospital Research Centre Annual Cardiovascular Awards Dinner on Friday, June 11th at the Winnipeg Convention Centre, the Chief Guest was Dr. James T. Willerson, possibly the world’s leading cardiologist, President of the University of Texas Health Science Center, Edward Randall III Chair in Internal Medicine and Alkek-Williams Distinguished Professor, from Houston, Texas. Lieutenant-Governor of Manitoba Peter Liba (Queen Elizabeth II’s representative in the Province) presented the Winnipeg-based International Academy of Cardiovascular Medal of Merit for his lifetime of exceptional accomplishments to Dr. Willerson whose response stimulated more than 400 guests with the following lecture.

Words don’t suffice to express my appreciation to the Academy, to Dr. Dhalla, and to members of the Selection Committee; to the Lieutenant Governor, and leaders of your Province and University – I am very grateful to receive your Medal.

Dr. Dhalla has asked me to speak of the “Future of Cardiovascular Medicine”. I want to provide you with an overview and a view from above.

The real revolution in medicine is now in progress. There was a revolution with the discovery of antibiotics. That will pale by what will occur in the next 15 years. Most diseases are caused by gene and protein abnormalities often interacting with the environment, but it is a genetic and proteomic risk that is dominant. You can run all day long, you can be as thin as a pencil, you can have the lowest possible...
cholsterol, but if you have a genetic risk for early heart attack, stroke or sudden death you will not outrun that risk. If you have a father who had a heart attack under the age of 50 years, some of your family members will have the same thing occur, and it will often occur in the same year and often in the same month. Therefore, the sequencing of the human genome is a great step forward. We have come to realize that we have many fewer genes that we thought we had; there is some disagreement about the exact number, but something between 26 and 30 thousand genes. For most of them, we do not know what they do. We can not assign a disease or an abnormality or a beneficial function to them. That will occur in the next decade. We will come to know the genes that cause cardiovascular problems, dementia, diabetes and most other diseases of our times. We will come to know genes and promoters, and repressors of those genes and to understand why some with the genetic abnormality have disease and others do not. However, more important than the gene discoveries will be the discoveries related to proteins, so-called proteomics. We don’t yet know how many proteins a single cell makes.

We will within the next 15 years predict the lifetime risk of medical disease in a small child as he or she is born, even in the mother’s womb. And we will predict what kinds of medicines patients respond to based on pharmacogenetic discoveries and understanding of how a patient with a certain genetic profile and proteomic production capability responds to certain medicines. All of you know medicines that have helped many people, but they don’t help another person. They cause many side effects. This will be predicted in advance and medicines will be chosen based on this understanding of individual patient’s pharmacogenetics.

In the next 10 to 15 years, we will be able to manipulate these genes. So one has a genetic risk, a proteomic risk, what can you do about it presently? You can follow a good lifestyle but as I’ve already explained, that won’t be enough to prevent that disease from being expressed if you are at maximal risk, but we’ll be able to manipulate these genes and we will be able to correct faulty genetic and proteomic systems for the prevention of disease in the future.

The second major advance that will occur is one you already heard alluded to - that is the use of stem cells to repair organs and I think even clone organs. I believe that in the next 15 to 20 years, maybe sooner, we will clone selected human organs. Your children or your grandchildren or maybe even one of you will have your heart cloned from stem cells. You will go to see a physician/scientist who will replace the heart, your own heart, in that manner, much like you might take a car to a garage right now and have the tire changed. Somewhat more complex, but the same result.

We have already treated in Brazil 18 patients with their own stem cells taken from their bone marrow. Stem cells here have to be considered in quotations because we’ve taken bone marrow cells and separated them into cells with a single nucleus, some of which are stem cells and some of which are not, and re-injected them directly into their heart muscle, using a special catheter to identify sites in their heart where the blood flow and the contractile function are reduced but the areas are alive, just dysfunctional.

We have been involved in stem cell research in animal models for 7 or 8 years. Once satisfied that stem cell methodology could at least partially repair experimental heart attacks in several different animal models and they were safe, we were willing to treat humans. We have come to feel that direct intraheart injections, intracardiac injections are the way to administer the cells. We have treated 18 patients in Brazil, and we have 7 controls. As early as 2 months later, those patients that were treated with their cells had better blood flow and better regional function where the cells were injected and that has been sustained for a year. Four of the 7 control patients have crossed over to be treated with their own stem cells as they continued to deteriorate.

About the time we submitted our work for publication, a German group had just published their work in Circulation. They treated patients with heart attacks and injected stem cells from the bone marrow directly into coronary arteries. This was work done by Bodo Strauer and his colleagues in Germany, and they found what we had found, improvement in cardiac function and blood flow. This was followed by another German group led by Andreas Zeier and Stephanie Demmler. They also treated patients with heart attacks, injecting cells directly into the artery. We treated patients with heart failure; the German groups treated patients with recent heart attacks without heart failure. We injected the cells directly into the heart muscle; they injected cells directly into the coronary arteries. Approximately 60 patients in total have been treated; the longest follow-up is a year. These were not really randomized double blind studies, but each study had temporal controls, but all three studies reached the same conclusion - better blood flow, better function.

In June of this past year, my colleagues and I at the Texas Heart Institute in Houston, Texas went to the FDA in the United States. We spent 8 months convincing them we could do this work in the United States and that it would be safe. In late February, or early March, of this year, they gave us permission to begin in the United States. Now, the Texas Heart Institute and St. Lukes Episcopal Hospital in Houston are conducting a randomized double blind study of patients with heart failure, taking their own 'stem cells from their bone marrow', and injecting them directly into their hearts. We are randomizing a patient a week. We have randomized three so far with no problems. Patients have been discharged the next day. Now it’s very early - one tends to get excited about this, but it’s very early and relatively few patients have been studied.

I think the future of this work is very bright. Please take this perspective with me. From your mother’s egg and your father’s sperm, from the union of those cells, everybody in this audience became what you are and what you aren’t. The way you look, your brain, your heart - that’s entirely stem cell development. Our Maker programmed us so that certain signals following the union of that sperm and egg result in the development of a human being. If you take that perspective, it’s impossible to doubt that stem cell therapies in some way, maybe not the way we are doing it now, but in some way will be very successful in repairing injured organs - brains (dementia), strokes, heart attacks, diabetes, liver disease. I believe one will ultimately clone organs from one’s own cells. The focus now and continuing even more vigorously will be disease prevention. It will be possible to prolong the useful lives of individuals with discoveries related to genetic and proteomic insights and stem cells. Diseases will be prevented well before they occur. Very large hospitals will be dinosaurs. Medicine will move increasingly rapidly into clinics. Treatment will be interventional treatment. It will be preventive treatment using some of the techniques I just mentioned. Big hospitals will be small hospitals, places where the sickest of the sick are cared for, people who need a place to stay.
There is a revolution in progress and it will have enormous impact. We need freedom to be able to use stem cells - not to clone human beings but to clone and repair organs. We need to embrace this genetic, proteonomic discovery because it will lead to insights ultimately preventing that we have no way to provide at the present time.

I am truly honoured to receive this Award. I am thrilled to be in Canada tonight, and I thank you for recognizing me in this way, Prof. Dhalla and your colleagues. In my final comments, I would just remind you that you have a jewel in Prof. Dhalla here. He has been a leader for many years, not just in Canada but in the world - treasure him and support him and his colleagues.

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**Stem Cell Research Map**

Countries with a permissive or flexible policy on human embryonic stem cell research are colored brown. These countries, listed below, represent more than 3 billion people, about half the world’s population. All have banned human reproductive cloning. (M = million)

<table>
<thead>
<tr>
<th>Country</th>
<th>Population (M)</th>
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<td>Australia</td>
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<td>Belgium</td>
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<td>Canada</td>
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<td>China</td>
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<td>Denmark</td>
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<td>United Kings</td>
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**Map Explanation**

By permissive is meant that various embryonic stem-cell derivation techniques can be legally pursued including somatic cell nuclear transfer (SCNT), also called research or therapeutic cloning. SCNT is the transfer of a cell nucleus from a somatic or body cell into an egg from which the nucleus has been removed. [Options 3 - 6 in Walters reference at end]

- By flexible is meant stem cells derived from fertility clinic embryo donations only, excluding SCNT. [Option 3 in Walters reference below: "Research is permitted only on remaining embryos no longer needed for reproduction."]

- Map is designed to reflect national policy and whether or not public funds may be used to pursue stem cell research using human embryos donated from fertility clinics.

- State & regional initiatives (eg. California and New Jersey in the U.S., Andalusia in Spain, etc.) are not indicated.

- The black dots show the locations of some of the leading genome sequencing research centers including those involved in the Human Genome Project. The dots are linked to center web sites.


Map is from William Hoffman: "Stem Cells: Human Health, Global Competition and National Security," St. John's University and the College of St. Benedict, Collegeville, Minnesota, November 19, 2003. [E-mail: hoffm003@umn.edu](mailto:hoffm003@umn.edu)
INTRODUCTION:
The influence of diet and specific dietary components within, such as fat, fiber, essential fatty acids and antioxidants, and their relationship with cardiovascular health continues to peak the interest of researchers around the globe. One class of compounds garnering recent attention is flavanols, a subgroup of flavonoids – which are polyphenolic compounds found in a wide variety of plant-based foods, including tea, red wine and purple grapes, apples, onions, cranberries, cocoa and chocolate. The research to date has focused on identifying, measuring and understanding flavonoids, especially flavanols, and their potential impact on cardiovascular health through recent epidemiological (1,2) mechanistic (3-8) and human intervention studies (6, 8-10, 11-13). Findings have shown that flavanols promote several beneficial effects in the cardiovascular system, including inhibition of LDL cholesterol oxidation, inhibition of platelet activation and modulation of the body's inflammatory immune response. Although tea and red wine are commonly accepted food sources of flavanols, certain cocoas and chocolates can contain additional flavonoids not found in relatively high abundance (14). Techniques in harvesting, handling and processing of flavanol-rich foods will dramatically affect their flavanol content (15). If properly harvested and processed, cocoa and chocolate can be relatively rich sources of specific types of flavanols (14, 16-19).

Molecular Structure:
As noted, flavonoids represent a large group of naturally occurring compounds that belong to the broader classification of plant compounds known as polyphenols. These compounds are naturally occurring, widely available, plant metabolites, some of which research have been shown to be bioavailable and bioactive following consumption. Flavanols, a specific sub-class of flavonoids, are commonly found in cocoa and chocolate, though the amount and type present are dependent on agricultural, post-harvest and processing practices.

Factors Influencing Flavanol Content:
Recent advances in analytic methods have led to a greater understanding of both content and factors affecting the flavanol levels of commonly consumed foods. The ability to assess and quantify content is an important step forward in evaluating and investigating clinical and therapeutic applications of flavanol-rich foods. This advance was largely enabled by the development of a quantitative high-performance liquid chromatography method by Hammerstone et al (19), and which now provides the foundation for the United States Department of Agriculture method of assessment of the type and amount of flavanols present in foods (18).

Variations in the flavanol content of flavanol-rich foods, particularly cocoa and chocolate products, can differ dramatically. With respect to chocolate, solid, dark chocolate products have the potential to be the richest sources of flavanols whereas milk chocolate contains a lesser amount due to the dilution of the cocoa solids and chocolate beverages are generally quite low (16, 18, 19). However, it must be emphasized that the content of flavanols in cocoa and chocolate products is dependent upon agricultural and post-harvest handling practices in the origin countries, and in the manufacturing processes used to make finished products. Data defining the extent to which the growing process affects the final product is limited. However, the common practices of fermentation, roasting and processing with alkali (commonly known as "dutching") are used to modify flavor and appearance, and can significantly reduce or virtually eliminate the flavanols present in finished products. Awareness of the highly variable nature of flavanol content in most cocoa and chocolate product is obviously a very important consideration with regard to the design of clinical studies and recommendations of optimal levels of flavanol intake for disease prevention and health promotion. Daily consumption of flavanols from all foods has recently been estimated at approximately 60 mg per day (18). However, single servings of chocolate or cocoa containing several fold more flavanols have been used in human intervention studies noting significant improvements in markers of cardiovascular health (6, 8, 9, 11,12, 20).

Flavonoids and Coronary Heart Disease:
Interest in the influence of dietary flavonoids and their potential health promoting effects upon coronary heart disease (CHD) risk reduction has been expanding within the last decade. Evaluative methods include dietary surveys, estimation of total flavonoid intake from all food sources, and assessment of specific food sources – such as tea, apples and onions. The use of tea has taken center stage in many of the research protocols, possibly due to the fact that in the earlier designs, cocoa and chocolate were not recognized as significant sources of flavanols and may have been overlooked as potential contributors.
Several studies have highlighted the potential benefits of flavanol-rich foods such as tea. For example, it was reported that men and women consuming more than 5 cups of tea per day had a lower total cholesterol and lower systolic blood pressure than those consuming less than 1 cup per day. A 12-year follow-up period identified a trend for a higher all-cause and CHD mortality rate in those drinking no tea at baseline, compared to the tea drinkers. For men, the relative risk of CHD death for those drinking more than 1 cup/day was of borderline significance (0.64, 95% CI 0.38-1.07) (21). Other studies have reported potential benefits in this context as well (22-24,27,28), and these have served to stimulate greater interest in understanding the true nature of the relationship between flavonoids and cardiovascular risk.

Cocoa Flavanols and its effect on Blood Pressure:

Flavonoids in general, and in particular, from soy, red clover, and wine suggest a blood pressure lowering effect (29-31), however clinical studies highlighting the benefits of flavanols from cocoa and chocolate are limited.

Data collected in studies involving the Kuna Indians residing in the San Blas Islands of Panama suggests that their relatively high intake of flavanols from cocoa might play a role in maintaining a healthy blood pressure (2, 32). The Kuna have a low prevalence of hypertension when living in the San Blas Islands and demonstrate little or no increase in blood pressure with age. However, once members of this group immigrate to urban areas in Panama, the apparent protective effects of the environment in the San Blas began to wane. One possible hypothesis, in light of the building evidence that cocoa flavanols can affect mechanisms related to vascular health, is the frequent consumption of flavanol-rich cocoa by the Kuna residing in the San Blas in contrast to those living in or near Panama City may be a contributory factor to these blood pressure observations.

A recent study looking at the effects of polyphenol-rich chocolate versus a flavanol-free white chocolate in hypertensive subjects provides additional evidence for supporting this hypothesis (33). In this study, 13 individuals aged between 55 and 64 years of age who had been recently diagnosed with isolated systolic hypertension and were not undergoing any pharmacological treatment were participants. A reduction in blood pressure was seen within 10 days of consuming the polyphenol-rich chocolate, while consumption of the polyphenol-free white chocolate did not elicit any change in blood pressure. Within 2 days of discontinuing the polyphenol-rich chocolate, participant’s blood pressure returned to pre-intervention levels. Unfortunately, the flavanol composition of the chocolate used in this interesting study was not characterized.

Further support for the hypothesis that flavanol-rich cocoa can favorably modulate blood pressure comes from in vitro and human studies investigating the effect this food can have on endothelial function and nitric oxide synthesis in the vascular endothelium. In 2000, Karim et al demonstrated that certain flavanols derived from cocoa could induce relaxation in aortic rings, and that this relaxation was nitric oxide dependent (4). Subsequent work in humans by Heiss et al demonstrated that the ingestion of flavanol-rich cocoa by human subjects with cardiovascular risk factors could transiently, but significantly, improve endothelial function in the brachial artery, and that this improvement correlated with an increase in the circulating nitric oxide pool (8). Most recently, Fisher et al demonstrated that flavanol-rich cocoa could improve blood in the finger of otherwise healthy human subjects, and that at least a significant portion of this effect is nitric oxide dependent (9). When considered in the context of the several important roles that endothelium-derived nitric oxide plays in vascular health, these studies offer the tempting possibility that flavanol-rich cocoa could play a useful role in many public health issues of great concern at the moment (35-37). These would include atherosclerosis, hypertension and Type 2 Diabetes most prominently. Clearly, further investigation is warranted to evaluate the effects of cocoa flavanols on blood pressure, as well as other vascular health complications.

Nutrition and Obesity

The obesity epidemic is gaining ground and the number of obese individuals is increasing at an alarming rate in many parts of the civilized world. In the United States alone, the number is fast approaching 30%. Parameters such as diet, lifestyle and physical activity are all important aspects to consider in getting this public health issue under control. Given this, we must consider whether or not flavanol-rich cocoa and chocolate products may be too calorically dense and contribute an unnecessary source of saturated fat. This issue has been addressed in part through clinical research in the past. Chocolate is a rich source of oleic and stearic acid, and several clinical studies have demonstrated a neutral effect on blood lipids following prolonged consumption of cocoa butter and/or chocolate (35). In addition, if the total fat intake does not exceed the individuals recommended dietary intake for calories, cocoa and chocolate should not pose any health threats beyond that of any other food unless consumed in excess. Indeed, the increasingly robust data suggesting flavanol-rich cocoa can have important cardiovascular health benefits offers the possibility that a food which many in the United States enjoy could also make a positive contribution to their health.
Conclusion:
As the science of nutrition, medicine and public health continues to evolve, a surprising and pleasant finding is that perhaps some foods that at one time were believed by many not to contribute to a healthy diet may in fact do so as a result of their previously unappreciated phytochemical content. Flavanol-rich cocoa certainly qualifies as one of these types of foods given the increasingly robust collection of positive research reported in the scientific literature. Unfortunately, it must be recognized that the majority of cocoa and chocolate products commercially available are relatively low in flavanol content due to common practices used in the processing and manufacture of cocoa and chocolate products. Due to the mounting research on cocoa flavanols, Masterfoods USA, A Mars Incorporated Company, has developed a patented process to retain a consistent quantity of cocoa flavanols in many chocolate products that they make. DOVE Dark Chocolate has in fact been used in several research studies as the flavanol-rich chocolate product. In addition, Masterfoods USA recently developed CocoaVia, a line of chocolate crunch bars specifically developed to contain a 100 mg concentrated dose of cocoa flavanols. This 80 calorie, heart healthy snack also contains polyphenols, which lower cholesterol and is a good source of vitamins and minerals that promote cardiovascular health. To learn more about the benefits and science behind this great tasting product, please visit www.cocoavia.com or for more information on the flavonal benefits of chocolate visit www.chocolateinfo.com.

Sweet Freedom!
Now you can help yourself and help take care of your heart.
Introducing new CocoaVia™ snacks that contain:

- Naturally occurring cocoa flavanols which promote healthy circulation and healthy blood vessels.
- Heart-healthy vitamins B6, B12 and folic acid.
- A good source of antioxidants, vitamins E and C, and an excellent source of calcium.
- 3 or less grams of fat and fewer than 90 calories per portion.
- Natural plant extracts which have been proven to maintain healthy cholesterol levels.

References:

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Endless skies meet rolling waves of grain. Vast prairie lands punctuated by cool clear lakes and lush green forests. A vibrant mix of urban excitement and rural charm. This is Manitoba.

Yet in sharp contrast to that simple and abundant beauty, is a pioneering spirit and a core of raw talent that together have propelled this province to the forefront of innovation and technology. The result is a world-class biotechnology industry that continues to raise the province's life sciences sector to new levels of excellence. This is also Manitoba.

Recent statistics support the high performance of Manitoba's biotechnology sector. The province currently represents 8% of Canada's total biotechnology activity (on a per company basis) -- twice its per capita figure of 4%.

Manitoba advantages

There are many factors that account for Manitoba's rapid advances in this industry. First and foremost, the provincial government has made life sciences a priority in its economic development strategy. This sector is seen as a major contributor to the province's future growth; as a result, the government has committed significant resources to the support, promotion and enhancement of this emerging industry.

Furthermore, a growing number of venture capital funds have been created to close the gap between research discoveries and their potential commercial applications. The funds encourage investment in companies involved in life sciences technologies, to assist in bringing a variety of beneficial products to market. The latest fund to target life sciences research is the $45 million Western Life Sciences Venture Fund, launched in January 2002.

Location, economy ideal for industry

Geographic location is also a factor in the ongoing advancement of Manitoba's biotechnology sector. Being situated in the centre of North America allows for easy access to Canadian and U.S. markets. As well, an unparalleled transportation infrastructure -- excellent rail links with Canada and the U.S., a strong trucking industry and an airport that stays open 24 hours a day, year-round and is rarely affected by inclement weather -- connects Manitoba to the world via rail, road, air and sea.

Add to that a dynamic and diversified economy, a skilled labour force, and easy access to low-cost, abundant and reliable hydroelectric power, and you soon understand why many multi-national biotechnology companies have established facilities and partnerships in this province.

Manitoba ideal test site

Investors in biotech enterprises also value Manitoba's capacity as a test site for new products. A culturally-diverse province, with a population of approximately one million, Manitoba has emerged as an ideal location for the testing of new drugs, new devices and new technologies for the international marketplace.

Manitoba is recognized as a leader in heart and vascular research and patient care. The St. Boniface General Hospital recently established a new clinical research institute dedicated to battling heart and vascular disease through clinical research trials. The I.H. Asper Clinical Research Institute serves as an innovative test site for the analysis of new cardiovascular therapies.
Studies confirm Manitoba’s strengths

Manitoba’s biotechnology sector is unique in that it represents a dedicated pool of expertise in biomedical and agricultural research. This robust life sciences community is anchored by a strong research base comprised of world-class scientists and facilities that specialize in leading-edge research in the life sciences industry.

KPMG studies from October 1997, March 1999 and January 2002 list Manitoba as one of the most attractive locations in the world for business investment in R&D ventures. These findings reflect the strength of the Manitoba economy, and the positive returns that can be achieved from investing in the province’s biotech expertise. The most recent KPMG study, released in February 2004, once again highlights Manitoba as one of the top ten locations in North America for R & D intensive industries.

Manitoba’s favourable R&D tax system is yet one more incentive for investors interested in biotechnology research. Furthermore, a 2000 Conference Board of Canada report noted that Manitoba’s R&D tax program is easily one of the most attractive in North America. In 2003, after considering both the federal SR&ED tax credit and Manitoba’s provincial R&D tax credit, the after-tax cost of one dollar of R&D expenditure in Manitoba for a non-manufacturing firm is between 41¢ and 46¢, depending on the size of the firm.

An Ernst and Young global biotechnology report released at the Biotechnology Industry Organization’s 2004 annual convention, BIO 2004, reported that Manitoba has the fastest growing biotechnology industry in Canada. This growth is reflective of the Province’s success in working with key industry stakeholders, such as universities, industry, business and research communities. In addition, the Province’s strategic investment in incubators and seed venture capital funds has served to stimulate this growth.

World-class infrastructure

A strong, knowledge-based infrastructure is critical to the growth and advancement of a biotechnology sector. Biotech companies in Manitoba are fortunate to be surrounded by state-of-the-art facilities that support the industry and supply the technologies that contribute to company growth and facilitate start-up enterprises.

The province’s educational facilities -- three universities and several colleges -- form an important part of that infrastructure. The University of Manitoba (U of M) is involved in diverse R&D programs encompassing a variety of internationally recognized biotechnology platforms, including genomics and proteomics. Furthermore, the U of M’s Smart Park provides opportunities for creating partnerships between the University and biotech companies, allowing for the transfer and commercialization of locally developed research and scientific technology.

A solid infrastructure of world-class hospitals, clinics and research facilities -- including two of the largest medical clinics in North America -- actively support Manitoba’s growth in the biomedical arena. This quality infrastructure, enhanced by world-class medical researchers like Dr. Naranjan Dhalla who has built the Institute of Cardiovascular Sciences, St. Boniface General Hospital Research Centre, University of Manitoba, has enabled Manitoba to earn international recognition for biomedical research.

Adding to this infrastructure is Canada’s new Public Health Agency to be located in Winnipeg. In May 2004, the federal government announced that Manitoba would be home to one of two pillars within the new Public Health Agency that will work with a group of specialized centres across the country. In addition it was also announced that Dr. Frank Plummer, internationally renowned scientist, would act as the interim Chief Public Health Officer (CPHO) in addition to his responsibilities as the scientific director of the National Microbiology Lab and Director General of Health Canada’s Centre for Infectious Disease Prevention and Control. The CPHO will be responsible for three functions within the new Agency: infectious diseases, emergency preparedness and chronic diseases.

Cardiovascular Therapeutics

Medicure, one of Manitoba’s leading biotechnology companies, has been focusing on the development of drugs that will treat cardiovascular diseases and stroke. Medicure was founded in 1997 by the renowned cardiovascular researcher, Naranjan S. Dhalla, Ph.D., Professor and Director, Institute of Cardiovascular Sciences, St. Boniface General Hospital Research Centre, University of Manitoba and by internationally recognized biotech entrepreneur, Albert D. Friesen, Ph.D. (President and CEO). Medicure became a public company in November 1999. It trades under the symbol MPH on the Toronto Stock Exchange (TSX) and MCU on the American Stock Exchange (Amex).

Medicure’s lead product initiative, of which Dr. Dhalla was principal inventor, MC-1, reduces ischemic injury caused by restrictions in blood flow and subsequent reperfusion following the removal of the restriction. As MC-1 continues its advancement towards the market, Medicure’s Drug Discovery Program is developing a pipeline of cardiovascular and cerebrovascular products.
Medicure's second drug candidate is MC-4232 for the treatment of diabetics with hypertension. MC-4232, a combination product incorporating MC-1 and an ACE inhibitor is being developed for the treatment of patients with diabetes and hypertension. According to Medicure, preliminary results from its Phase II study show a positive trend in diabetic hypertensive patients. The results from this trial support the Company's plans to proceed with additional Phase II clinical trials as a prelude to MC-4232's Phase III clinical study. The expanded program will include a broadening of the patient study group and an extension of the dose range.

Manitoba reaps success in nutraceuticals
Manitoba is poised to become a research and development leader in one of the most exciting emerging areas of scientific research worldwide – the nutraceutical and functional food industry. Winnipeg's National Centre for Agri-Food Research in Medicine, Grant N. Pierce PhD, Director, is currently making a name for itself through specialized research that examines the effects that nutraceuticals, functional foods and food components have on human health and well-being. Building on that technology is a new state-of-the-art integrated research and development centre, the newly established Richardson Centre for Functional Foods and Nutraceuticals at the University of Manitoba's Smart Park.

Researchers at the Richardson Centre will develop processes to identify, enhance and extract food components that promote good health, such as essential fatty acids and bioactive components, and help reduce the risk of chronic disease. Several crops in Manitoba, including oats, wheat, buckwheat, canola, flax and hemp have been identified as excellent candidates for value-added processing as functional foods. Manitoba is positioned to contribute in a significant way to the growing demand by consumers for nutraceutical and functional foods that are scientifically proven to be safe and effective.

Strong agricultural base
Manitoba's climate is ideal for growing a wide variety of crops. As a result, the province has developed into one of the world's most productive agricultural economies, boasting a product base that includes grains, oilseeds, pulses, livestock feed and specialty crops. Manitoba's strong agricultural production, coupled with a dynamic, cost-effective R&D environment, makes the province an ideal location for varietal development and field evaluations, centred around its world-renowned research in oilseeds and cereal grains.

Centres of excellence – Ag-biotechnology
Manitoba is home to a growing number of world-class centres of excellence, enhancing the province's reputation as a leader in biotechnology research. The Cereal Research Centre of Agriculture and Agri-Food Canada, based in the capital city of Winnipeg, is unique in that it works within the areas of cereal genomics, pathology and biotechnology to develop improved wheat and oat varieties. This facility has gained international attention for sharing plant material, publishing scientific articles and transferring new technologies to the farming public.

The U of M's Faculty of Agricultural and Food Sciences has also received international recognition for its work in the development of canola and high erucic acid rapeseed through the pioneering work of Dr. Baldur Stephanson.

Centres of excellence produce biomedical advances
Manitoba is home to a growing health biotechnology cluster supported by several internationally recognized companies that develop biopharmaceuticals and immunodiagnostics. This fast-growing biomedical community is anchored by some unique and equally renowned facilities in the province.

To begin with, the Canadian Science Centre for Human and Animal Health [include photo] is the first and only global centre with level-4 bio-containment capability for the study of both human and animal diseases. The $142 million facility works with a wide range of pathogens and diseases, and has a comprehensive training program that focuses on the diagnosis, investigation and control of the most lethal human and animal diseases.

In addition, the National Research Council Institute for Biodiagnostics (IBD) is the most state-of-the-art facility in Canada for studying and developing NMR (nuclear magnetic resonance) and MRI (magnetic resonance imaging) technologies. Its synergistic approach to research and development has helped this Winnipeg institute attract the attention of medical researchers and business partners from across the country and around the world. Construction is under way to double the size of the IBD.

On the verge
Winnipeg was recently named the site for the new International Centre for Infectious Diseases, a unique national microbiology and infectious diseases organization that will offer an enhanced environment for the training of scientists in microbiology and infectious diseases research. The Centre is expected to be a world leader in research, training, commercialization and innovation by addressing the threat and impacts of infectious disease.

Manitoba's Life Sciences Sector represents a proud culture of collaboration, built upon a strong foundation of scientific expertise, a skilled knowledge base, one of the lowest costs of living and doing business in Canada, and a growing network of businesses and technology commercialization facilities. Our biotechnology cluster includes: bio-pharmaceutical and contract manufacturing, infectious disease and cardiovascular research, Canada's new Public Health Agency, the largest concentration of MRIs and NMRs for research and development purposes in Canada, plant breeding (cereal and oil seed crops), nutraceutical research, cardiovascular diseases, oncology and child health. As our international reputation continues to grow, the province remains open to new investment and strategic partnerships that will ultimately benefit the biomedical industry, the stakeholders and the future health of individuals around the world.
Editor's note: Manitoba is the global headquarters of the International Academy of Cardiovascular Sciences. Various departments and agencies of the Government of Manitoba have been most supportive of such initiatives as the 2001 World Heart Congress which attracted 1,800 professionals from 72 countries; the initial infrastructure of the Academy; publications including six books based on the Congress, Journals and the Academy's CV Network; the CIHR Young Investigators Forum in May 2004; and recently, the enhancement of the Academy's web site and global communications from the base in Manitoba.

Healthy Heart Program In Iran

by Nizal Sarraf-Zadegan, Isfahan, Iran

The global burden of non-communicable disease (NCD) particularly cardiovascular disease (CVD) is escalating in Iran similar to many other developing countries. Rapid changes in dietary habits and diminished physical activity, as well as tobacco use are suggested as critical factors contributing to the acceleration of NCD epidemics. In this regard, epidemiologic transition mandates public health interventions at population level, and clinical interventions at individual level. Contrary to developed countries, the experience on effective intervention programs for prevention and control of NCD in developing countries is limited.

As a comprehensive public health response, an integrated comprehensive community-based national program entitled "Isfahan Healthy Heart Program" (IHHP) was launched in Iran in 1999 in order to integrate programs and policies that effectively impact on the major determinants of NCD mainly through lifestyle change. This program is conducted by Isfahan Cardiovascular Research Center (a WHO Collaborating Center for Research and Training in Cardiovascular Diseases Control, Prevention, and Rehabilitation for Cardiac Patients in the Eastern Mediterranean region), and Isfahan Provincial Health Office, both affiliated to Isfahan University of Medical Sciences. Two counties (Isfahan and Najaf-Abad) are considered for interventions in comparison to another one considered as reference (Arak). The population of the three counties is studied for major risk factors such as diabetes, hypertension, hyperlipidemia and smoking, as well as behaviour, attitude, skills and knowledge (BASK), along with continuous surveillance data collection in regard to disease registry (myocardial infarction, cancers), mortality, etc, in order to identify appropriate and feasible interventions to be implemented nationally at a later date.

IHHP Goals:
• To improve population behaviour, prevent and control risk factors and disease, delay the onset of disease, postpone death, reduce disabillities and disparities in treatment.
• To move the disease care system approach to a health care system basis.

IHHP Objectives:
1) To improve the public knowledge & awareness of causes and consequences of NCD’s with common risk factors (CVD, diabetes, hypertension, cancers) and skills to take action to control them
2) To improve life style behaviors associated with good health
3) To reduce the prevalence of modifiable risk factors namely smoking, hypertension, hypercholesterolemia, overweight & obesity, physical inactivity and stresses associated with NCD’s
4) To reduce mortality, disability due to NCD’s with common risk factors and its incidence rates
5) To improve knowledge & awareness and achieve early identification, treatment, control levels and rehabilitations of individuals at high risk or with clinical manifestations of the disease
6) To improve the health professional knowledge, skills of causes, consequences, screening, treatment of NCD’s and the importance of healthy lifestyle
To improve healthy social & physical environment (healthy policies, environments, legislations etc)

To evaluate the process & outcomes of interventions at the individual, public and environmental levels

To cooperate in planning, implementation & evaluation of the interventions at the national level (dissemination phase)

To maintain & sustain healthy lifestyle interventions at the provincial level (sustainability)

**Strategies**

The major strategies are based on:

Public policies; Cooperation and collaboration; Public information; Training and professional development; Research and evaluation

**Phases of the program:**

**Phase I:** Situation analysis, performed in 2000-2001 on a population of 20,000. In this phase, risk factors prevalence (using the MONICA questionnaire), serum lipids and glucose, CVD prevalence using the Rose questionnaire and electrocardiography analysis (by Minnesota coding), CVD and stroke mortality, knowledge, attitude and practice about NCDs were assessed in the general population (adults & children), health professionals as well as CVD patients and high risk groups using the WHO STEP wise approach to risk factors, morbidity and mortality. Monitoring is regularly implemented on small samples in order to assess the effect of different interventional strategies. Four annual cohort surveys are being conducted on all eligible persons aged ≥35 years (almost 6000 persons) who will be followed for the occurrence of fatal or non-fatal MI, stroke, sudden death, hospitalisation, physician referral, etc. Another four independent cross-sectional surveys of randomly selected small samples aged ≥19 years are being done. The samples are studied for demographic background, health knowledge and behaviour related to NCD risk factors. Two smaller studies were conducted on a sub sample of 1000 adults aged ≥19 years in each of the intervention and reference areas for determining the levels of new risk factors e.g. CRP, Lp(a), fibrinogen, small dense LDL cholesterol, homocysteine, ApoA, ApoB, etc, and to study the nutritional habits using a 24-hour dietary recall questionnaire and the Iranian Food Consumption Programme for two days and one holiday. The study will be repeated along with the post intervention survey in 2006. Cause-specific mortality rate data collection, MI and stroke registration according to the Monica protocol will be continued throughout the study in intervention and reference areas simultaneously.

**Phase II:** Besides health promotion and primary prevention activities, secondary preventive actions for cardiac, stroke, diabetic and hypertensive patients and their families are being performed. This phase began in late 2001 and will continue for 5 years. Integrated community-based interventions and high risk are done by both the population strategies for CVD patients and their families as well as diabetic, hypertensive and dyslipidemic persons focusing on:

- Improvement of dietary habits; Increasing physical activity; Anti-smoking activities; Dealing with stress and tensions
- The interventions are aimed at the whole population in the intervention areas using population and high-risk strategies for various target groups through 9 interventional projects called:
  - Healthy Food for Healthy Community; Isfahan Exercise Project; Heart Health Promotion from Childhood; Youth Intervention Project; Women Healthy Heart Project; Worksite intervention project; NGOs and Volunteers Intervention Project; Health professional education program; Healthy lifestyle for cardiac patients

Community Mobilization is performed by:

- Training of trainers from the community; Activities to improve BASK; Sport and physical activity; Education through social gatherings; Education in mosques, parks, gymnasiums, etc; Interventions in shops, restaurants, offices, etc; Involvement of community leaders (health, religious etc)

**Phase III:** The whole baseline survey will be repeated on an independent sample in both intervention and reference communities in the general population (based on age and sex), health professionals and high risk groups measuring behavioural, physical and biochemical variables at the end of the study in 2006.

For more information, please visit: [www.crc.mui.ac.ir](http://www.crc.mui.ac.ir) & [www.ihhp.mui.ac.ir](http://www.ihhp.mui.ac.ir)

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**Stress-Induced Biochanges in the Heart: From Genes to Bedside. Antalya, Turkey, February 2 - 7, 2005:**

The Nato Advanced Research Workshop, organized by the Academy, will focus on the effects of different stresses on:

- transport of signals through biological membranes and interpretation of such signals by cellular systems
- calcium signaling in animal cells
- mitochondria and their channels in pathological situation and apoptosis
Buoyed by the extraordinary success of the International Conference held in Lucknow, India, Jan. 9 - 11, 2004, the International Academy of Cardiovascular Sciences and the International Society for Heart Research (Indian Section) have announced plans for a second Joint International Conference - "BENCH to BEDSIDE in GANDHI's GUJARAT", December 31, 2004 - January 2, 2005. Grand Bhagwati, Grandhinagar - Sarkhej Highway, AHMEDABAD, INDIA. For details, please visit the web site: http://www.indianheart.com/conference/index.html Or contact the Conference Co-ordinator: Dr. Ramesh K. Goyal, Professor, Dept. of Pharmacology, L.M. College of Pharmacy. P.O.Box 4011 Navarangpura, Ahmedabad, 380 009, India. E-mail: goyalrk@hotmail.com

LIST OF KEY SPEAKERS
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Endogenous myocardial protection against ischemic stress
The role of plasmalemmal ATPases in signaling and termination of signals
Myocardial injury mediated by endocardium
Calcium handling in the diabetic heart
Endogenous cardioprotection operating in diabetic heart
Oxidative stress and antioxidants in myocardium
Nitric oxide signaling and effect of NOSs in cardiac protection
Catecholamine signaling in the heart

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Nominations for Fellows Invited!
Nominations are invited for the election of Fellows of the Academy for the year 2004.
Nominees should be individuals with outstanding achievements in cardiovascular research and education, who will be elected by the Fellows. The number of Fellows will not exceed 250 at any given time. Please submit a letter highlighting the distinguished accomplishments of the individual along with his/her curriculum vitae. It is understood that the nominee has given consent for letting his/her name stand for election.

PLEASE FORWARD: c/o Ivan Berkowitz, Director of Development International Academy of Cardiovascular Sciences 3006 – 351 Taché Ave.Winnipeg MB R2H 2A6 Canada or E-mail: ivan@mts.net
Special Announcements

1st Joint Symposium Society of Brazilian Cardiologists - Funcor, InterAmerican Heart Foundation & International Academy of Cardiovascular Sciences on Sunday Sept. 26 to Wednesday Sep 29, 2004. This part of SBC-Funcor program is intended for healthcare professionals and will be at the Convention Centre, Rio de Janeiro, Brazil. Also, there will be a CardioForum (Public Forum), which will take place on Sunday Sept. 26. For details, contact – Raimundo M. Nascimento, Brazilian Heart Federation, Telephone/Fax 0**11-3849-6438, E-mail: funcor@cardiol.br

XXXI ARGENTINE CONGRESS OF CARDIOLOGY Symposium of the basic science council "Prof. Dr. Bernardo A. Houssay" II ANNUAL MEETING OF THE INTERNATIONAL ACADEMY OF CARDIOVASCULAR SCIENCES – LATIN AMERICAN SECTION: Basic Principles in Ischemic Heart Disease and Arterial Hypertension. October 8, 2004. Directors: Celina Morales, PhD – Ricardo J. Gelpi MD, PhD. For details, please contact Ricardo J. Gelpi, Tel: 54 11 4962 4945, E-mail: rgelpi@fmed.uba.ar

CardioGlobal – International Intensive Seminar on Cardiovascular Diseases. Ouro Preto Federal University Center of Arts & Convention, Ouro Preto, Brazil. Wednesday, October 13 – Friday October 15. For details, contact – David Brasil, Co-ordinator for International Affairs, Telephone: +55-31-3281-2027, E-mail: davidb@pib.com.br

Teaching Course – "FAITH AND DISEASE" with the focus on the importance of faith in heart disease. The course is featured by the General County Counsel for Continuous Medical Education, Copenhagen, La Facolta di Medicin et Chirurgia, Universita degli Studi de Roma and the International Academy of Cardiovascular Sciences (IACS) in Rome, Italy, 1-5 December 2004. Lectures will be in English. Course fee is 1500 EURO. Accommodation and meals included. For further information contact Deputy Executive Secretary IACS Europe Thomas A Schmidt, MD, DSc: tas@dadlnet.dk. Enrolment on first come first serve basis.

IACS - South America will again be a sponsor of XV Scientific Forum and 1st World Congress on Cardiology for the Family. Dec. 2 - 5, 2004, Belo Horizonte, Brazil. For details, please contact Dr. Otoni M. Gomes, Rua Manoel Lopes Coelho, 365 - Itapoa - 31710-530 Belo Horizonte - MG, Brazil Tel: +55-31-3444-8807 / 3441-2254 (res.) E-mail: gomes@sevicor.com.br

The ACADEMY has been accepted as an "associate" of Amazon.com To make it easy (and even find bagains) to buy the six books recently published from the 2001 World Heart Congress or by many of our Fellows, people can click to Amazon.com from the logo on our home page - http://www.heartacademy.org/