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THE OFFICIAL BULLETIN OF THE INTERNATIONAL ACADEMY OF CARDIOVASCULAR SCIENCES VOL 9 NO 2 SUMMER 2010

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Seventieth Birthday of Professor Bohuslav Ošťádal

by Frantisek Kolar, Prague, Czech Republic



Professor Bohuslav Ošťádal, MD, PhD, DSc, a distinguished Czech cardiovascular physiologist, celebrated his seventieth birthday on January 28, 2010. He was born in Moravian town Zlín in a family of physicians, but he spent most of his life in Prague. His university education started in 1957 at the Faculty of Pediatric Medicine of the Charles University in Prague where he graduated in 1963. Already during undergraduate studies, he took part in research and teaching at the Department of Pathological Physiology where he continued his subsequent studies towards a PhD. His supervisor and admired mentor, Professor Otakar Poupa, greatly influenced his professional life and was an example to him not only of a scientist and also teacher. In 1966, he joined the Institute of Physiology, Czechoslovak Academy of Sciences (now Academy of Sciences of the Czech Republic), being appointed Chair of the Department of Developmental Cardiology two years later. Professor Ošťádal, familiar as Boja to his colleagues and friends, remained loyal to this institution during his entire scientific career.

Since the very beginning, Boja's main area of research has been focused on the ontogenetic development of heart structure and function.

Even his early experimental studies on developing coronary circulation belong to landmark papers in the field that achieved well-deserved attention. His laboratory was among the first to demonstrate the important ontogenetic differences in cardiac sensitivity to various pharmacological agents. In a series of papers he investigated developmental changes in myocardial responses to acute oxygen deprivation, mechanisms of increased ischemic tolerance of the immature heart, and protective effects of preconditioning and chronic hypoxia. He has also been deeply concerned with late cardiovascular consequences of risk factors acting during early phases of ontogenetic development, the phenomenon known as fetal programming. Recently, he became particularly interested in differences of ischemic tolerance between hearts of males and females, the topic which appears to gain increasing attention of both experimental and clinical cardiologists.

In addition to his long-life position in the Academy of Sciences as a research institution, Boja has been very active in teaching pathophysiology at the 2nd Medical Faculty of the Charles University in Prague for more than 40 years. As an excellent and popular lecturer, he influenced several generations of Czech physicians and researchers. In 1992, he was appointed Full Professor of Normal and Pathological Physiology.

Boja also became deeply involved in the organization of cardiovascular research and education on both national and international scale. He was among founding members of the Committee of Experimental Cardiology which has organized annual scientific meetings of Czech and Slovak researchers and clinicians continuously since 1972. In the

early period of transformation after 1989, he served for five years as a director of the Institute of Physiology, Academy of Sciences of the Czech Republic. In 2000, he created Centre for Cardiovascular Research based on a project involving more than 100 researchers from several theoretical and clinical institutions in Prague. He still works as a principal investigator of the Centre emphasizing the necessity of a tight collaboration between experimental research and clinical practice for the progress of cardiovascular medicine. In addition, he is the President of the Executive Committee of the Postgraduate Education in Biomedicine at the Charles University in Prague and a member of several scientific boards. He also served as a Council member of the International Society for Heart Research and President of the European Section of the International Academy of Cardiovascular Sciences. Boja was the main organizer of many local and international scientific conferences, the biggest one and the most successful being the World Congress of the International Society for Heart Research in 1995, which is still remembered with joy by its participants. For many years he served as the Editor-in-Chief of Physiological Research; currently he is the Editor-in-Chief of Experimental and Clinical Cardiology; and a member of Editorial Boards of another five journals.

Boja has published 190 full peer-reviewed papers, two books, more than 60 book chapters and edited another three books. He has delivered many invited lectures and seminars at national and international conferences, universities and institutes. He is a Fellow of the International Society for Heart Research and the International Academy of Cardiovascular Sciences and has received numerous awards and distinctions from scientific societies in recognition of his achievements and services.

I used the opportunity to join Boja's team shortly after completing my PhD. I have always considered it was a great privilege to have the possibility of working with him for almost three decades. He has taken particular care in maintaining a creative atmosphere, democratic attitude and friendly relationships among all members of his team. I firmly believe that we will profit from his wisdom and enjoy his friendship for many more years.



4th Congress of the International Academy of Cardiovascular Sciences



4th World Congress to be held in India in Vadodra on February 1-3 and Ahmedabad on February 4-6, 2011

We may have total participation of more than 1,500 delegates to the Conference.

FOR INFORMATION, PLEASE CONTACT:

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International Symposium on Scientific Basis for the Practice of Cardiology, Prague, April 8 - 11

by Frantisek Kolar, Prague, Czech Republic

The Vila Lanna in Prague, a neo-renaissance building from the 19th century, was the venue for the Symposium organized by the Centre for Cardiovascular Research, Institute of Physiology, Academy of Sciences of the Czech Republic, and the International Academy of Cardiovascular Sciences on the occasion of the 70th birthday of Dr. Bohuslav Ostadal as a tribute to his lifetime scientific achievements. The Canadian publishing company Pulsus Group, represented by Robert Kalina, was the main sponsor of the meeting.

The capacity of the venue limited the number of participants to 55 including 33 invited outstanding speakers and chairs from 12 countries. During the Opening Ceremony, welcomes were presented by Dr. Vaclav Hampl, rector of the Charles University in Prague, Dr. Naranjan S. Dhalla, founder of the International Academy of Cardiovascular Sciences, and Dr. Pavel Braveny who briefly listed some highlights of Dr. Ostadal's scientific carrier.

The special memorable lecture was given by Dr. Jim R. Parratt (Glasgow, UK), entitled "Decisions, directions, defects and disciples; a *Rückblick* of over 50 years of basic medical research". It opened the scientific program of 26 oral presentations in six sessions covering various important aspects of experimental and clinical cardiovascular research and chaired by distinguished scientists including Drs. Jutta Schaper (Bad Nauheim, Germany), Dennis McNamara (New Orleans, USA), Makoto Nagano (Tokyo, Japan), Jan Slezak and Attila Ziegelhofer (Bratislava, Slovak Rep.), and others. The first session on Angiogenesis, Cell Growth and Development started on a high note with Dr. Wolfgang Schaper's (Bad Nauheim, Germany) overview on the role of the innate immune system in arterial regeneration *via* development of collateral circulation. It was followed by an elegant presentation by Dr. Grant Pierce (Winnipeg, Canada) on nuclear protein import as a mechanism to alter cell growth. Dr. Karel Rakusan (Ottawa, Canada) then reviewed the cardiovascular risks of drug treatment in pregnancy, and Dr. Vaclav Hampl (Prague, Czech Rep.) reported about specific properties of placental circulation and its response to hypoxia.

The next session devoted to Heart Failure comprised interesting lectures by Dr. Naranjan S. Dhalla (Winnipeg, Canada) on gender dependent differences in the development of heart failure due to volume overload; Dr. Dipak Das (Farmington, USA) on regeneration of infarcted myocardium with nutritionally modified cardiac stem cells; Dr. Pawan Singal (Winnipeg, Canada) on cytokine interactions in heart failure; and Dr. Jane-Lise Samuel (Paris, France) who spoke about new biomarkers for pathological cardiac hypertrophy and heart failure.

At the session dealing with Cardiovascular Risk Factors, the audience was impressed by the opening lecture of Dr. Pavel Hamet (Montreal, Canada) entitled "Evidence for requirement of large number of genomic determinants for polygenic traits prediction: personalized medicine building". Dr. Josef Zicha (Prague, Czech Rep.) then emphasized the role of voltage-gated calcium channels and altered vascular contraction in systemic hypertension. Dr. Johanne Tremblay (Montreal Canada) discussed genomic determinants of cardiovascular complications in diabetes. Dr. Rudolf Poledne (Prague, Czech Rep.) presented the first clinical data on potential direct effect of perivascular fat on coronary atherosclerosis. Dr. Jan Herget (Prague, Czech Rep.) reviewed the mechanism of hypoxic pulmonary hypertension.

The five presenters of the session on Ischemia/Reperfusion Injury were Dr. Guy Vassort (Montpellier, France) speaking about TRP channels in cardiac arrhythmia, Dr. Tanya Ravingerova (Bratislava, Slovak Rep.) addressing subcellular mechanisms of adaptation to myocardial ischemia in healthy and diseased heart, Dr. Agnes Vegh (Szeged, Hungary) analyzing on the role of nitric oxide, superoxide and peroxynitrite in protection against arrhythmias, Dr. Keld Kjeldsen (Copenhagen, Denmark) focusing on the regulation of NA,K-ATPase and sudden cardiac death, and Dr. Peter Ostadal (Prague, Czech Rep.) presenting experimental and clinical data on statins in the therapy of acute coronary syndrome.

The last two sessions were composed of several lectures on a range of aspects of Cell Signaling. Intriguing data on the organization of cardiac cAMP signaling in subcellular microdomains were presented by Dr. Rodolphe Fischmeister (Paris, France), followed by Dr. Roland Vetter (Berlin, Germany) who spoke about modulation of cardiac sarcoplasmic reticulum calcium transport by SERCA2 overexpression and phospholamban silencing. Dr. Belma Turan (Ankara, Turkey) focused on the role of intracellular zinc in excitation-contraction coupling of cardiomyocytes, Dr. Peter Zahradka (Winnipeg, Canada) introduced atypical signaling pathways involved in a modulation of smooth muscle phenotype, and Dr. Enn Seppet (Tartu, Estonia) reviewed his data on compartmentalized systems of regulation of oxidative phosphorylation in cardiac cells.

The topic of acute and chronic effects of sigma receptor ligands in myocardium was covered by Dr. Marie Novakova (Brno, Czech Republic) and telomere biology in cardiovascular diseases was discussed by Dr. Naoki Makino (Beppu, Japan).

A Welcome Reception was organized at Vila Lanna. Following cultural program, Drs. Dhalla and Nagano presented Dr. Ostadal



Makoto Nagano (L), Boja Ostadal, Naranjan Dhalla (R)

the International Academy of Cardiovascular Sciences' "Distinguished Achievement Award in Cardiovascular Sciences". Drs. Singal and Pierce then conferred a plaque on Dr. Ostadal in honor of his leadership worldwide in the field of heart development biology and association with the Winnipeg family.

The Farewell Dinner took place at the historical Kaiserstein Palace located in the center of Prague Little Quarter that provided beautiful setting for discussions and entertainment. The organizers wish to thank all participants for their excellent contributions that enabled to create a high quality scientific program and to Pulsus group for a generous support, which made the meeting possible. Selected papers based on the Symposium presentations will be published in a special issue of the Experimental and Clinical Cardiology, an official journal of the International Academy of Cardiovascular Sciences.



Grant Pierce (L) Ivana Ostalova, Boja Ostadal, Pawan Singal (R)

To survive when the heart stops beating

by Petr Ostadal, Prague, Czech Republic



Petr Ostadal with his father Boja (L) and Ivan Berkowitz (R)

Cardiac arrest is probably the most serious health condition and survival is crucially dependent on the immediate initiation of cardiopulmonary resuscitation. However, even in cardiac arrest survivors the further prognosis is still poor despite current capabilities of intensive and resuscitation care including brain-protective procedures, such as hypothermia. Even in-hospital cardiac arrest is associated with unfavourable outcomes and not infrequently the resuscitation is terminated because spontaneous circulation cannot be restored despite having an advanced cardiopulmonary re-

suscitation team immediately available. It is, therefore, not surprising that extensive efforts have been put forth to improve chances to survive cardiac arrest. Among the possible ways to save lives when the heart stops beating are the minimally invasive systems for mechanical circulation support.

These systems usually comprise a blood pump that supports the failing left, right, or both ventricles or even by-passes the whole injured heart. The blood pump can be inserted into the heart chamber, mostly into the left ventricle, through a special catheter via one of the easily accessible arteries (usually femoral artery) or can be situated extra-corporally. Into the extra-corporal circuit can also be inserted a membrane oxygenator. This configuration is currently largely used as extra-corporeal membrane oxygenation – ECMO, enabling temporarily substitution of the functions of both heart and lungs. Even the extra-corporeal support systems can be introduced mini-invasively, mostly from femoral artery and femoral vein puncture. The short-term circulatory support systems are usually used as a “bridge to recovery”, “bridge to transplant”, “bridge to other intervention”, “bridge to decision”, or “bridge to bridge”. As a result of increasing experience with these systems during the last years, many hospitals worldwide have set up an ECMO-team as a group of experts responsible for the correct indication, appropriate system selection, introduction, settings, and continuous monitoring, all even in the urgent conditions.

In our Department of Cardiology, Cardiovascular Center, Na Homolce Hospital in Prague we have been deeply interested in the mini-invasive circulatory support systems for more than five years and up to the present time, more than forty of our patients benefited already from one of these systems. Up to now, we have experience with several different systems: TandemHeart (CardiacAssist, USA), Performer CPB and Bio-Console 560 (Medtronic, USA), Levitronix Centrimag (Levitronix, USA), Impella 2.5 (Abiomed, USA), and recently, we had the opportunity to use as a first, primarily non-surgical department in Europe, the system PulseCath iVAC 3I (PulseCath BV, The Netherlands). Most of the systems we tested also under the specific hemodynamic conditions experimentally in swine models. This invaluable experimental experience is very helpful not only for the better understanding of the systems but also for the development of new settings and applications.

The mini-invasive circulatory support systems currently became a powerful tool in the hands of healthcare specialists giving a new hope to patients with conservatively unmanageable cardiogenic shock and better chance to survive cardiac arrest even when the spontaneous circulation is unrestorable by standard techniques.

Nominations are requested for the following 2011 Awards of the Academy to be presented at the 4th World Congress to be held in India Feb 1 – 6:

Makoto Nagano Award for Achievements in Cardiovascular Education

Howard Morgan Award for Distinguished Achievements in Cardiovascular Research

Norman Alpert Award for Established Investigators in Cardiovascular Sciences

Naranjan Dhalla Award for Distinguished Investigators in Cardiovascular Sciences

Previous winners will be listed on the Academy web site: <http://www.heartacademy.org>

Please submit short CV and one page summary of contributions of the nominee by June 30, 2010 to Ivan Berkowitz, Heart Health Scholar – ivan@mts.net

ADVANCES IN CARDIOVASCULAR RESEARCH

Red Alert to Women's Heart

From genes and molecules to clinical applications

International symposium dedicated to 70th anniversary of Prof. Jan Slezak

June 6 - 9, 2010

Smolenice Castle - Congress center of the Slovak Academy of Sciences
Bratislava, Slovakia



Symposium is organized by



Slovak Academy of Sciences
Institute for Heart Research SAS
Slovak Society of Cardiology
Slovak Physiological Society
Slovak League Heart to Heart
Institut of Cardiovascular Sciences
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Sir Magdi Yacoub: Egyptians have the world's sickest hearts

online from translation from Arabic by Wael Ali almasryalyoum.com



Academy President Dr. Yacoub met his healthy, grown-up patient in Winnipeg
The interview is online at <http://www.heartacademy.org/yacoub.htm>

Because of air pollution, congenital diseases, shocking events, rheumatic fever, excessive eating, a lack of exercise, and feelings of deep sadness, persecution and oppression, Egyptians have some of the least healthy hearts in the world, says world-acclaimed Egyptian heart surgeon Magdi Yacoub. In an interview with Lamis el-Hadidy on Nile Life on Monday, Yacoub said taxi and micro-bus drivers are the most vulnerable to heart disease. Yacoub has returned to Egypt in order to achieve his lifetime dream of establishing a medical and scientific center in Aswan for Egyptians and Arabs, especially the poor and children. He expressed fears that his medical center might suffer the same challenges as projects by Ahmed Zewail and Farouk el-Baz, which failed to take shape, due to excessive red tape and a lack of interest, among other reasons. "One of the things that scares me most in Egypt is Egyptians' lack of interest in science," Yacoub said.

Commenting on sectarian tension in Egypt, Yacoub said he believes this represents a form of "ignorance."

Yacoub said he doesn't dream of receiving a Nobel prize, as he is happy to be able to relieve the pain of his patients. He mentioned that he has been honored by the British by his acceptance into the 350-year-old Royal Society, whose members included Albert Einstein and Isaac Newton. Yacoub said British Prime Minister Gordon Brown is a personal friend of his and that Brown wrote the foreword for Yacoub's book "Moral Courage."

Yacoub also said that the study of genetics is essential to treating heart disease properly.

Nominations are invited for the 2011 Award of the Academy's most prestigious Medal of Merit to be presented at the 4th World Congress to be held in India February 1–6, 2010:

Previous winners were:

- 2001 Michael DeBakey (Houston, USA) and Richard Bing (Pasadena, USA)
- 2002 Edwin Krebs (Seattle, USA) and Robert Furchgott (New York City, USA)
- 2003 Eugene Braunwald (Boston, USA) and Robert Lefkowitz (Durham, USA)
- 2004 Sir John Vane (London UK) and James Willerson (Houston USA)
- 2005 Sir Magdi Yacoub (London UK) and Robert B. Jennings (Durham, USA)
- 2006 Sir George Radda (Singapore) and Victor Dzau (Durham, USA)
- 2007 Louis Ignarro (Los Angeles, USA), Sen. Wilbert Keon (Ottawa, Canada) and Jutta Schaper (Bad Nauheim, Germany)
- 2008 Nirmal Ganguly (New Delhi, India), Sir Salvador Moncada (London, UK) and Wolfgang Schaper (Bad Nauheim, Germany), Howard Morgan (Lewisburg, USA)
- 2009 winners to be announced shortly

Please submit short CV, contributions and a one-page summary of consent of the candidate by June 30/10 to:
Dr. Naranjan S. Dhalla, Executive Director: nsdhalla@sbr.ca

Editor's Note: We have inadvertently missed the announcement of the appointment last year of three new Fellows: Dr. Shyam Agrawal, Dr. Louis Ignarro and Sir Salvador Moncado. A brief account of the achievements follows



Dr. L. Popescu (L) presented Dr Agrawal the (Hon.) Fellowship of the Romanian Medical Sciences

Dr. Shyam S. Agrawal

Prof. S. S. Agrawal, born on 1st September 1946, obtained his Masters and Ph.D in Pharmacology from prestigious All India Institute of Medical Science (AIIMS), New Delhi. He has been honored with D.Sc (Honoris Causa) by Rajiv Gandhi Technological University, Madhya Pradesh for his vast contribution in the field of pharmacy. Selected by Union Public Service Commission with five advance increments, Prof. Agrawal started his career as a lecturer in the year 1976, became Assistant Professor in 1984, and Professor in 1990. Since then there was no looking back, in April 1995 he became the Principal of College of Pharmacy (now DIPSAR), Director in 2005 and Project Director in 2009 of newly formed first Pharmaceutical University of India and perhaps in world (DPSAR-U).

Under his able leadership he transformed the College of Pharmacy to a research cum teaching institution in the name of Delhi Institute of Pharmaceutical Sciences and Research (DIPSAR) by creating and modernizing ten research laboratories and later into Delhi Pharmaceutical Sciences and Research University (DPSAR-U) enacted by Govt. of India. It is first Pharmaceutical University in India and perhaps in world to which he is serving as a Project Director.

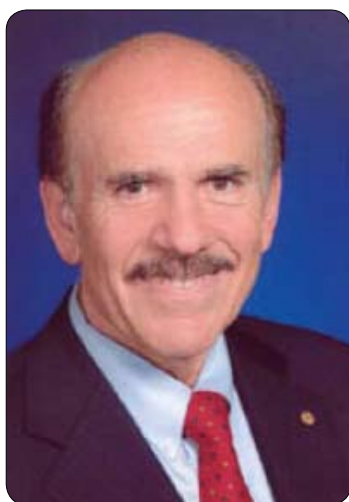
He is honoured as Fellow of International Academy of Cardiovascular Sciences (IACS), Honorary Foreign Fellow of Romanian Academy of Medical Sciences, Head of Department of Pharmacy in University of Delhi, Executive Member of High Power Committee for Delhi Health Authority to establish Health Policy for Delhi, Executive member of Delhi Pharmacy Council, National Co-coordinator for Quality Improvement Program AICTE (Pharmacy) for 10 centers all over India to improve quality of higher education of pharmacy Faculty, Nominated member for University Court, Sirsa University and Maharishi Dayanand University, Rohtak and Chairman of National Science Digital Library in Pharmacy.

Prof. Agrawal has served as Technical Consultant to Deolite for setting up of six new "National Institute of Pharmaceutical Education and Research" (NIPERs) in the country at Ahmedabad, Hyderabad, Kolkata, Bihar, Guwahati, Hazipur, Rai Bareilly. Dean, Faculty of Science (University of Delhi) from 1995-98, President of Indian Pharmacological Society in 2005, Member Editorial Board (Indian Journal of Pharmacology), Expert member of UGC, AICTE, ICMR, CSIR etc.

Prof. Agrawal is proud recipient of Distinguished Service Award by IACS, Gold Medal of Merit – 2001 World Congress on Heart Research, Winnipeg, Canada, Servier Young Investigator's award (FRANCE), Best Principal Award by Association of Pharmacy Teachers of India, Fellow of Indian Pharmacological Society, and CDRI Oration of Indian Pharmacology Society.

He has 7 patents to his credit and 26 more in pipe line. His major thrust areas of research include Antifertility and Infertility studies, Novel Drug Delivery System such as time specific release formulations and transdermal drug delivery system for cardiovascular diseases and, polyherbal formulations for Cataract and Hepatoprotective action, and cancer research at molecular level.

He has 101 research paper published in national and international journals of high repute. Prof. Agrawal has authored five books and standardization of five Polyherbal and three single Unani drug Monograph published in Unani Pharmacopeia, India. He has produced 18 Doctoral and 186 Masters Candidates. Currently he is guiding 9 Ph.D and 7 M. Pharm research projects. To promote research among the young scholars he initiated PhD programme at DIPSAR under stipendiary category (20 seats), where the Research Scholars are being paid a stipend of Rs 14000+ HRA by the Government of NCT, Delhi. He had created world class infrastructure in DIPSAR including a state of the art Gymnasium, One new Boys Hostel, Two Girls Hostels, Food Court, GLP compliant Animal house (with the concept of clean and dirty corridor), Medicinal & Poison- Antidote information center and swimming pool. Also a stunning Sports complex and an India International Hospitality centre (guest house) with all the state of art facilities were constructed under his apt supervision for National and International guests from all over the globe.



Louis J. Ignarro, Ph.D.

Dr. Louis Ignarro was born in 1941 in Brooklyn, New York of Italian immigrants, He grew up in Long Beach and had a predilection for science from an early age, which led to a bachelor's degree in pharmacy from Columbia University and a Ph.D. in pharmacology from the University of Minnesota. His university studies also concentrated in chemistry, enzymology and cardiovascular physiology, and resulted in several published papers. His work continued at the NIH in the fields he'd studied, collaborating with many other scientists to discover regulatory mechanisms of the cardiovascular system that would lead to his most famous work. Before relocating to California, he was a professor of pharmacology at Tulane University School of Medicine, New Orleans, for 12 years. Ignarro also worked as a staff scientist, research department, for the pharmaceutical division of CIBA-GEIGY Corporation in New York. His current endowed position is the Jerome J. Belzer, MD, Distinguished Professor of Pharmacology. at the UCLA School of Medicine's department of molecular and medical pharmacology in Los Angeles, which he joined in 1985. He is also Professor at King Saud University in Riyadh, Saudi Arabia

Dr. Ignarro has received many Awards but perhaps the most notable are: The Basic Research Prize of the American Heart Association, Medal of Merit from the I A C S, Election into the National Academy of Sciences, Election into the Academy of Arts and Sciences, and with Robert F. Furchgott and Ferid Murad

the 1998 Nobel Prize in Physiology and Medicine for their three major discoveries involving nitric oxide as a unique signaling molecule in the cardiovascular system. Experiments in 1990 led to the discovery that nitric oxide is the neurotransmitter responsible for penile erection. The discovery made it possible for a drug company to develop and market Viagra, the first oral medication for the effective treatment of erectile dysfunction.

His observations with nitric oxide have made it possible for medical professionals to understand what protects the cardiovascular system against pathological conditions such as hypertension, stroke, coronary artery disease and other forms of atherosclerosis, gastrointestinal ulcers and vascular complications of diabetes. He is the founder of the Nitric Oxide Society, and founder and editor-in-chief of Nitric Oxide Biology and Chemistry.

Dr. Ignarro's laboratory at the David Geffen School of Medicine at UCLA has never been larger than eight or nine people. Throughout his career, funding for the lab has come from the National Institutes of Health (NIH) and local heart associations. In 2000, Ignarro testified before Congress on the importance of NIH funding for basic science research. In his testimony, he said that only in America could the son of an uneducated carpenter receive the Nobel Prize in medicine.

Dr. Ignarro wrote in Les Prix Nobel 1998 "Another rewarding development has been my discovery that I also have a real knack for and love of teaching what I know to medical and graduate students. I have consequently made teaching a regular part of my schedule since I came to UCLA and I cherish the Golden Apple teaching awards I have won from my classes."

Dr. Ignarro is a Board Member of Operation USA. Operation USA helps communities alleviate the effects of disasters, disease and endemic poverty throughout the world by providing privately-funded relief, reconstruction and development aid.

Recently, he has become very serious about his own health. On his web site he says: "I walk, jog, run, and bike nearly every day and have never been in better shape. Running marathons has become a major hobby for me and it helps to ensure that I stay in great health." Ignarro worked with Herbalife to develop Niteworks, a dietary supplement designed to boost the body's own production of nitric oxide, and later became a member of the company's Scientific Advisory Board. He has written two best-sellers: "NO More Heart Disease: How Nitric Oxide Can Prevent - Even Reverse - Heart Disease and Strokes" and "Health Is Wealth: 10 Power Nutrients That Increase Your Odds Of Living To 100"



Sir Salvador Moncada

Sir Salvador Enrique Moncada (born in Tegucigalpa, Honduras on December 3, 1944) is a renowned pharmacologist. He is the director of the Wolfson Institute for Biomedical Research at the University College London. In El Salvador, he qualified to be a doctor because he was interested in cardiovascular science. His interest was triggered by working with the Peruvian pharmacologist, Augusto Campos who, at that time, was visiting the University of El Salvador. The 1970s was a time of political unrest in El Salvador due to social inequalities, a poor economy and the repressive measures of dictatorship. Civil war broke out between the government and left-wing parties. Prof. Moncada joined the throngs of protestors with the result that he was deported to Honduras, and forced to leave behind his first wife and child. Like all young investigators who are serious about building a career in research, he needed to gain experience working in an environment where the best intellects and equipment were on-hand. For many of his peers, that meant the US. But he "wanted to come to Europe for cultural reasons and for scientific reasons was particularly interested in research in the UK and I managed to get a fellowship to go to England in February, 1971." He secured a place in Sir John Vane's laboratory at the Royal College of Surgeons. "I was put in a project that was part of the discovery that aspirin-like drugs inhibit prostaglandin biosynthesis," he says of work for which Vane was later awarded the Nobel Prize.

However, a deep-seated belief that he owed something to the country of his birth compelled him to return to Honduras in 1974 "to see if it was possible to do research there." He was quickly disillusioned by the conditions. "There are more developed countries in Latin America such as Brazil, Argentina, Mexico, Chile, where research is possible. But Honduras is one of the most underdeveloped countries, so there's no infrastructure, no money and no connections with the outside world to do scientific research." He returned to the UK where he joined the Wellcome Research Laboratories, again under the leadership of Sir John Vane.

In 1986 Prof. Moncada developed a method for the biological detection of the so-called endothelium-derived relaxing factor (EDRF). Prof. Moncada and his colleagues demonstrated the release of nitric oxide (NO) from vascular endothelial cells and showed that this release occurred in quantities sufficient to account for the biological actions of EDRF. Most recently, Prof. Moncada and co-workers have investigated the role of endogenous NO in mitochondrial biogenesis; they have shown that NO promotes mitochondrial biogenesis (and hence oxidative metabolism) and that the inflammatory cytokine tumour necrosis factor (TNF- α) downregulates this process in obese animals. Furthermore, they have demonstrated that calorie restriction promotes mitochondrial biogenesis by inducing the expression of endothelial NO synthase. These findings have implications for novel treatment of diseases of metabolic origin, including type-2 diabetes mellitus and obesity-linked cardiovascular disorders. Since 1996 Prof. Moncada has established and directed The Wolfson Institute for Biomedical Research at University College London.

He married to Her Royal Highness Princess Maria-Esmeralda of Belgium, in London. They have a daughter, Alexandra Leopoldine (born in London in 4 August 1998), and a son, Leopoldo Daniel (born in London in 21 May 2001).

He is the author or co-author of almost 600 papers, including his work on aspirin, prostacyclin, and nitric oxide.

In 1990 he was awarded with the Spanish "Prince of Asturias Scientific and Technological Research Award" In 1992 the "Royal Netherlands Academy of Arts and Science" awarded him the "Dr A.H. Heineken Prize for Medicine" In 2008, he was honoured with the IACS' most prestigious Medal of Merit.

There is a Fundación Salvador Moncada para la Ciencia e Investigación (Salvador Moncada Foundation for Science and Research) in Honduras.

Dr. Moncada was knighted in the 2010 New Year Honours for services to science.

A Personal Plan to Prevent Heart Attacks!

by Ivan Berkowitz, Winnipeg, Canada

Don't worry, my vision of prevention of cardiovascular diseases (CVD) will not use 5-syllable words and explore such topics as the potential of genomics or choice of medical devices. I believe that my personal experience has been successful enough to be worth sharing.

Without having had my DNA analyzed, I know that my genes forecast substantial risk of CVD. My mother was only 56 and my father was 62 when they succumbed to sudden cardiac arrest.

Even before her death I realized that my mother had done an awesome job of bringing great joy to our lives, especially with the extraordinary food she loaded us with. Surprise ... when I was 17, I realized, on my own, that I needed to lose weight and stopped some things like sugar, cream and then even milk in coffee; butter and, without even starting, smoking. However, the importance of food taught by my mother has never left my being. Unless I had significant control, I have tended to eat too much and weight loss was followed, gradually, by gaining most of it back.

1978 was an important benchmark. My older daughter was planning for her Bat Mitzvah so we agreed to lose weight. More significant was an invitation to a talk by Dr. Kenneth Cooper who 'invented' the system of counting aerobic points at his Cooper Clinic in Dallas. His talk was the highlight of the opening of the Reh-Fit Centre in Winnipeg. Also, plans were underway for the first Marathon in Manitoba. All these influences attracted me to join the Reh-Fit, seriously pursue their running program, follow an extreme diet and even try the Manitoba Marathon. At that point, I was only able to walk and run 6 miles but I was smitten. The next year, I had a great base and was able to finish my first of 22 full (26.2 miles) marathons. The training affected my taste for heavy foods and I have not eaten red meat since. The serious lifestyle change really got me into the best shape of my life over the next 20 years; even started training others so over 100 students finished their first of many marathons; and, most importantly, brought into my life the love of my life.

The bottom line is that I feel I have enjoyed incredible health, vitality and ever-expanding interest in new ventures including my artistic spirit to create pottery.

Indeed I have followed a direction I read recently for Dr. Andrew Weil who gave 4 disciplines if living a long life is important: "You may want to adopt some of the habits that supercentenarians have in common. Supercentenarians - people who live to be 110 or older - share four lifestyle characteristics that may help explain their longevity. Throughout their lives, they have remained:

Physically active. Even as you get older, daily physical activity should be a priority. Modify your routine to incorporate small steps, such as daily walks, using the stairs instead of the elevator, or taking up hobbies that involve exercise, such as gardening, playing tennis or hiking.

Positive. Maintaining an optimistic outlook is important to managing stress and preventing related health issues such as heart disease. You can easily train yourself to start looking at the glass as half full. Begin with some simple self-reflection and meditation, and use humor for coping with negative thoughts.

Social. A network of family and close friends is vital to optimum health. You can enjoy the benefits of a well developed social life by spending time with people who make you happy, joining community groups or clubs, volunteering, and participating in support groups.

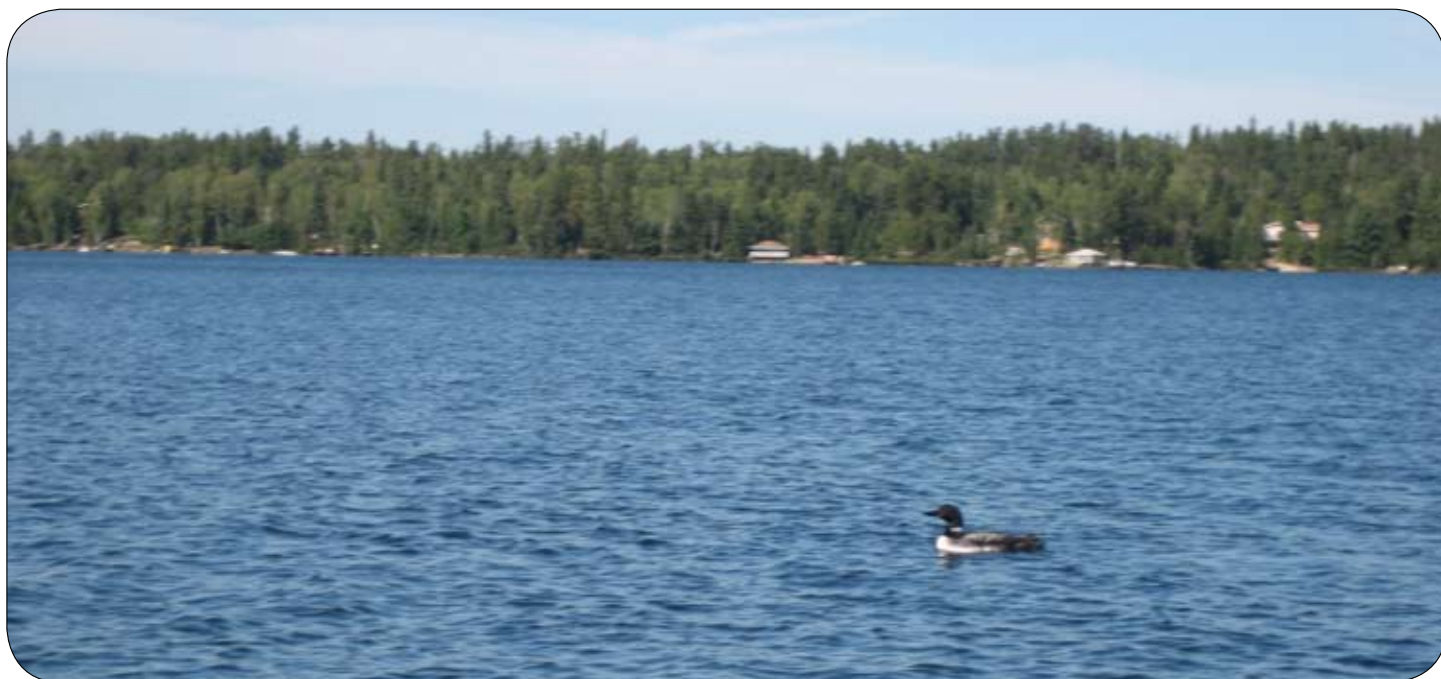
Spiritual. Regardless of your religious affiliation (if any), feeling a connection with nature, a higher being or purpose cultivates spirituality, and is an important part of graceful aging."

Two reports from the Centers for Disease Control and Prevention (CDC) published recently in the *Journal of the American Medical Association* provide an update to obesity prevalence in the United States. Based on data from 2007-2008, researchers report that 68 percent of U.S. adults and 32 percent of school-aged U.S. children and adolescents are overweight or obese. On a Blog posted on April 13, 2010, Dr. Regina Benjamin, U.S. Surgeon General reported: "Last week, I participated in a meeting on childhood obesity at the White House to discuss ways to combat the growing health epidemic. I joined the First Lady, Education Secretary Arne Duncan, Domestic Policy Council Director Melody Barnes, Office of Management and Budget Director Peter Orszag, Deputy Secretary of Agriculture Kathleen Merrigan and experts and practitioners from around the country to discuss the challenges. I have been traveling around the nation, taking the message around the country and talking to people about the challenges they're facing. I've traveled to Florida, where 43 percent of poor children and 45 percent of black children are either overweight or obese. I've met with Native American Tribal Councils, who are concerned about populations that have diabetes rates that are twice the national average. I've been to Durham, North Carolina, where the entire community is engaging in an effort to target obesity and other childhood health problems with unprecedented collaboration between public and private agencies. The problems are real, and so is the determination to solve them. I want to change the national conversation from a negative one that focuses on disease to a positive conversation about being healthy and being fit. But for people to act on these conversations, Americans need to live and work in environments that support their efforts. We need everyone's help to support common sense, innovative tools and solutions. The meeting at the White House was an important step in that direction." First Lady Michelle Obama has led the development of "**Let's Move!**" which has an ambitious but important goal: to solve the epidemic of childhood obesity within a generation. Let's Move will give parents the support they need, provide healthier food in schools, help our kids to be more physically active, and make healthy, affordable food available in every part of the United States.

Of great interest to me has been television coverage of “Jamie Oliver’s Food Revolution”, initially successful in the U K and now in the USA. The difficulty but amazing success is summarized online at: http://www.ted.com/talks/jamie_oliver.html

To be specific, I have not written a book like the “South Beach Diet” or the “Pritikin Program”. But I am delighted to share a simple one-page which I call the “Trout Lake Diet”, named after possibly the most important influence on my continuing good CVD prevention – since my father’s investigation located Trout Lake, Ontario in 1944, I found the greatest environment including water we can drink right from the lake, physical activity and the extraordinary peace found without electricity, indoor plumbing and such toys as cell phones! On CBC Radio, I recently heard Diana Beresford-Kroeger, author of “The Global Forest”. She is a gardener who likes to combine her medical training with her love of botany. Having studied classical botany, medical biochemistry, organic and radio nuclear chemistry, and experimental surgery, Diana believes that the cures for cancer and other ailments can be found in her garden located in Merrickville, Ontario. She referred to research proving that pine forests (like the woods around Trout Lake): “Trees are a living miracle,” Ms. Beresford-Kroeger said. “Leaves can take in carbon dioxide and create oxygen. And all creatures must have oxygen. Trees not only breathe and communicate; they also reproduce, provide shelter, medicine, and food, and connect disparate elements of the natural world.” She also talked about the Hawthorn trees whose berries are widely regarded in Europe to use to promote the health of the circulatory system and have been found useful in treating angina, high blood pressure, congestive heart failure and cardiac arrhythmia.

At Trout Lake, we have hosted friends from all over the world – will you join us and hear my favourite sound – the call of our loons?



Ivan’s “TROUT LAKE” Diet*

One page is all you get = my simple approach for people on the go.

My friend/doctor Jack Rusen has introduced me to:

2 glasses of ice water before every meal.

Forbidden products: (direct or as ingredients): salt, sugar, desserts, butter, white flour, red meat, cream, white potatoes, white flour pasta, skin, deep-fried food, white rice, soft / high fat cheese, liquor (except the odd glass of red wine), soft drinks other than diet, desserts with sugar and / or milk products and / or white flour

Encouraged products: fruits, salads, vegetables (especially dark coloured ones), pulse vegetables (garbanzo, chickpeas, lentils), oatmeal, soy products, tofu, fish, white meat of chicken / turkey, salmon, prunes, bran products, vinegars, Canola oil, flax oil or crushed, brown/wild rice, buckwheat, walnuts, almonds, skim milk, pepper, herbs, garlic, mushrooms, whole wheat flour products, green tea, chamomile tea (instead of coffee especially for an upset tummy).

Approaches to meals: Breakfast – soy/skim milk, oatmeal, shredded wheat/bran, egg beaters, fruit Lunch – salad, fruit Dinner – veggies / salad, meat or fish (not huge portions), fruit Exercise is strongly recommended. At least, walk 30 minutes every day. Weight workouts are good. Not necessary to train for and complete 22 full (26.2 miles) Marathons as I have done, but it helps!

And, NEVER, NEVER eat even a mouthful after 8:00 PM

**Based on personal experience over 50 years, losing probably a TON of weight (and recently another 20 pounds in 2 months concentrating on this approach!) but still fighting to lose the fat that creeps back, probably due to metabolism that attracts fat ... and an innate LOVE of food!*

With the assistance of the Myles Robinson Memorial Heart Trust, Ivan Berkowitz has been compiling information from around the world as the Academy’s Heart Health Scholar. A report on the economics of CVD was the first paper and now reporting on initiatives which can prevent the diseases.

"We can work hard and we can create exchanges and reform insurance and work on Medicare payments and things that need to get done, but true savings are going to come when we do the preventative measures that improve peoples' lives and that hit closer to home. That's how we're going to contain costs."

U. S. Congressman from Minnesota First District Tim Walz on the Heart of New Ulm project, as quoted in the New Ulm Journal



The Heart of New Ulm Project: Healthcare System Led, Community-level Primary Prevention of Myocardial Infarctions

by Jeffrey J. VanWormer and Gretchen A. Benson, Minneapolis MN

Coronary heart disease (CHD) continues to be the leading cause of death in the U.S. and in most countries around the world. The Heart of New Ulm (HONU) project aims to diminish this trend in one south central Minnesota postal district of about 13,000 adult residents. HONU is a 10-year, systems level demonstration project designed to apply evidence-informed practices that can improve the heart health of an entire community. New Ulm, Minnesota, located about 90 miles from the Twin Cities metropolitan area, was selected for this demonstration project in part because of its contained geographic area and high level of interest among community leaders to improve residents' health. Over 90 percent of New Ulm residents receive their medical care from one centralized facility, the New Ulm Medical Center. As such, the electronic medical record (EMR) can be reliably used as a surveillance tool to track the risk of the entire population, which is a rare luxury in the mainly private American healthcare system.

The HONU project's specific objective is to reduce the attack rate of acute myocardial infarctions (MI) over the next 10 years among residents age 40-79 years in the 56073 zip (postal) code. To meet this goal, efforts are focused on improving modifiable CHD risk factors (1) including blood lipids, blood pressure, blood glucose, obesity, tobacco use, physical inactivity, low fruit/vegetable consumption, stress, and medication (i.e., antithrombotic, anti-dyslipidemia, anti-hypertension) underutilization/non-adherence. Interventions will be delivered through worksite, community, and healthcare venues.

In regard to healthcare system interventions in particular, the main focus in 2010 is on delivering more frequent, ongoing primary prevention support outside of the traditional office visit. Recent population data in New Ulm indicated that about 2,500 residents age 40-79 years were identified at high risk without any known history of CHD or diabetes. This means they have an estimated 15% or greater risk for experiencing a major CHD event over the next 10-years per an indication of metabolic syndrome or multiple elevated risk factors (using a Reynolds or Framingham CHD risk score). When looking closer at this targeted group of high risk individuals, there are major gaps in their optimal care in that: 65% do not take daily aspirin, of those with high LDL cholesterol (≥ 100 mg/dL), 81% do not take a statin, and of those with hypertension ($\geq 140/90$ mm/Hg), 56% do not take an anti-hypertensive. In addition, 15% report current tobacco use and 40% are clinically obese.

This presents a major untapped opportunity to close the optimal care gap on a large segment of the New Ulm population that could benefit from more intense primary prevention efforts. This is important because 65-70% of all myocardial infarctions that occur in a given year in Minnesota are first-time events, meaning they occur among people who do not have existing CHD or a CHD equivalent such as diabetes (but many of whom are nonetheless high risk).

To support these individuals in heart disease prevention, a free telephone-based outreach program will be created to provide coaching, education, and medication guidance in between usual clinic visits. It's important to note that the program will be provided as a complement to usual clinical care, alleviating some of the current barriers of primary care providers' time constraints to practice more aggressive primary prevention of CHD. The average length of a physician office visit is as small as 10 minutes (2) — hardly enough time to address obesity, nutrition and smoking on top of addressing the main reason for the visit. The objectives of this outreach program are to:

- 1) Increase the proportion of participants taking a daily CHD preventive medication regimen that includes an antithrombotic medication, anti-dyslipidemia medication, and anti-hypertensive medication (if warranted)
- 2) Increase the proportion of participants with controlled biometric risk factors, including: LDL cholesterol ≤ 100 mg/dL and blood pressure $< 130/80$ mm/Hg
- 3) Increase the proportion of participants with controlled lifestyle risk factors, including: non-smoker, not obese, and 100% medication adherence.

Identified individuals are sent a packet of introductory program information including a letter from their primary care physician, a heart disease prevention handbook and goal setting guide, and information on eating for heart health. As part of the program, participants will receive up to six phone calls each year. Each call will last approximately 20 minutes with much of the conversation focused on optimal care components and lifestyle. Participants can opt-out of the program at any time. Physicians will be notified of their patients who are participating, including when medications are initiated/titrated. The program's health professionals (team includes a pharmacist, registered nurse, registered dietitian and is led by a nurse practitioner) will document telephonic coaching encounters in the participant's EMR for ease of communication and collaboration. In an effort to extend communications further, providers are invited to quarterly continuing medical education seminars facilitated by the HONU project, where they receive the latest project updates in addition to learning state-of-the-art CHD preventive strategies. Data will be continuously monitored to assess effectiveness of the program and prevention of MIs.

Ultimately, the goal of the HONU project is to create a model of preventive healthcare that can be translated and transferred throughout the United States and around the world in order to improve how prevention is delivered.

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- 1) Yusuf S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004 Sep 11-17; 364(9438):937-52.
- 2) Konrad TR, et al. It's about time: physicians' perceptions of time constraints in primary care medical practice in three national healthcare systems. *Med Care*. 2010 Feb; 48(2):95-100.









ISMC 2010

VI. INTERNATIONAL SYMPOSIUM ON MYOCARDIAL CYTOPROTECTION

From Basic Science to Clinical Perspectives



Pécs, Hungary, October 7-9, 2010

Congress President:
Elizabeth Róth, MD, PhD, DSc

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P R E L I M I N A R Y P R O G R A M

Wednesday, May 4

15:00 Registration
17:00 – 17:15 Opening and Welcome: Dr. Belma Turan (Dept. Biophysics, Ankara Univ. Fac. Medicine)
17:15 – 17:30 Opening address I: Dr. Serap Aykut Aka (Dept. Cardiovascular Surgery, Istanbul Univ. Faculty of Medicine)
17:30 – 17:45 Opening address II: Dr. Cetin Erol (Dept. Cardiology, Ankara Univ. Faculty of Medicine)
18:00 – 18:30 Opening lecture:
19:00 – 20:00 Reception

Thursday, May 5

9:00 – 10:30 Session I: 3 Talks
10:30 – 11:00 Coffee Break
11:00 – 13:00 Session II: 4 Talks
13:00 – 15:00 Lunch & Poster section
15:00 – 16:30 Session III: 3 Talks

Thursday, May 5 (cont'd)

16:30 – 17:00 Coffee break
17:00 – 18:30 Session IV: 3 Talks
19:00 Dinner

Friday, May 6

9:00 – 10:30 Session V: 3 Talks
10:30 – 11:00 Coffee Break
11:00 – 13:00 Session VI: 4 Talks
13:00 – 15:00 Lunch & Poster section
15:00 – 16:30 Session VII: 3 Talks
16:30 – 17:00 Coffee break
17:00 – 18:30 Session VIII: 3 Talks
20:00 Farewell Dinner

Saturday, May 7

8:00 Trip To Cappadocia (Full day)

Sunday, May 8

DEPARTURE

Medical education in cardiovascular sciences: accommodating a research-driven curriculum

By Paul Ganguly, Ali A. Khraibi and Bernhard H.J. Juurlink, Riyadh, Kingdom of Saudi Arabia



Prof. Paul Ganguly



Prof. Ali Khraibi



Prof. Bernie Juurlink

Why do we need changes?

Continual research-based revision and development of medical education processes is central to our core concept of the reform of the undergraduate medical education program. Therefore, to support this reform and to develop effective environment of teaching and learning in the cardiovascular sciences it is necessary that the researchers in this field should not shy away from creating an innovative undergraduate program suitable to our medical students. The present article will highlight a few concepts that we believe need to be included in the curriculum that extend beyond the text books. Generally in creating an effective curriculum, the medical schools have focused on: 1) providing students with competence based learning, core and general knowledge and skills, 2) promotion of student independent learning, 3) pedagogical training of teachers, and finally 4) quality assurance of undergraduate education. However, to strengthen the conceptual changes in medical studies we should not hesitate to include new data or concepts obtained through research in the basic and clinical cardiovascular sciences. Such new concepts will promote the viewing of the human body in an integrated manner. Although the obvious question that comes to mind is the validity of any research project/data that should be transmitted to the students, we strongly believe that the students should not be deprived of challenges, enthusiasm and innovation in education and exposure to new concepts that result from development of a research-based cardiovascular curriculum.

Over the past two decades, in order to link the cardiovascular theory to practice, many medical schools have adopted a problem-based learning (PBL) curriculum in which the integration of various subjects has been emphasized. But regardless of the learning style adopted, we still fail to bring new research-based concepts particularly to the overall content of the curriculum. For example, if we consider that the study of physiology should continue to play a central role in the development of cardiovascular curriculum, the past two decades certainly did not reflect the many changes obtained in our knowledge of the physiology of the cardiovascular system. We therefore believe that it is imperative to revisit the cardiovascular program. This has two benefits: 1) the twenty-first century medical students can then view the cardiovascular system in an effective and understandable way through various modalities available to them 2) the research-driven curriculum should also give them an opportunity to better understand the pathophysiology of disease processes. We believe that the following paragraphs should highlight areas that a medical school may consider in formulating a newer cardiovascular curriculum.

What are the most important concepts in Physiology?

The typical focus of most medical physiology textbooks is on the functional characteristics of the cardiovascular system which include transport of nutrients and hormones from their source of synthesis and release to the tissues and cells where they are utilized, and the transport of waste products away from tissues. Also, the participation of the cardiovascular system in homeostasis by maintaining an appropriate environment in tissue fluids for survival and proper function of the cells is emphasized. In order to achieve these functions, the cardiovascular system is generally subdivided in most medical physiology textbooks into three major components: (1) The heart, (2) The circulation and vascular system, and (3) Endothelial function and blood coagulation. Through these subdivisions, the students are exposed to normal and abnormal cardiovascular function, including heart function, heart muscle, the heart as a pump, the normal electrocardiogram, cardiac arrhythmias, vascular distensibility and functions of the arterial and venous system, capillary fluid exchange, lymphatic system, local and

humoral control of blood flow by the tissues, nervous regulation of the circulation and rapid control of arterial pressure, chronic control of arterial pressure, cardiac output and venous return, cardiac failure, heart valves and valvular heart defects, circulatory shock, blood types, and blood coagulation. In many textbooks the cardio-renal axis or the intimate relationship between the cardiovascular system and kidneys is not emphasized, especially in relation to blood pressure control. While the knowledge of the above cardiovascular goals appears to be adequate for students in the medical field, these goals certainly can be complemented with additional information that are clinically relevant and that have been the subject of research and data collection for many decades.

What newer areas can we target?

Race, socio-economic factor and stress: One of these areas that are not adequately included in medical physiology textbooks but that could benefit the students and further their knowledge is the role of race/ethnicity, and socio-economic status in cardiovascular disease and mortality. This is a subject that has been heavily researched in the United States. There are enough studies, data, and recommendations that have been published on this subject that warrant its inclusion in medical physiology textbooks. There are significant differences in the development of cardiovascular diseases between races and ethnicities. Furthermore, income and major risk factors appear to be associated with differences in cardiovascular mortality when race and ethnicity are taken into consideration. In fact some of the recommended effective treatment options for cardiovascular diseases vary amongst races. It should be noted that this deficiency could be dealt with by the inclusion of adequate PBLs in the curriculum to explain the ethnic differences and the risk factors in cardiovascular disease. However, we believe that this deficiency and others in the curriculum might be rectified by further exposure of students to journal club presentations early on which could have the effect of familiarizing them with the areas of research that are current and that are clinically relevant to their future practice of medicine.

Atherosclerosis and inflammation: Another area that is missing in medical curricula is inflammation as a central integrating motif to understand function and dysfunction of the body. The cardiovascular system is an ideal system to introduce inflammation since the major cardiovascular disease in the developed world is atherosclerosis, a disease that results in problems such as heart attack, stroke, vascular dementia and renal disease. Atherosclerosis is essentially inflammation of the arteries. Understanding the basic mechanisms that drive inflammation will reinforce the understanding of cellular signaling pathways and regulation of gene transcription and, as well, prepare students to better understand many other disease processes, such as factors that drive type II diabetes, osteoporosis or Alzheimer's disease. Inflammation, although a great integrating motif in the study of medicine, is not typically covered until relatively late in the curriculum, and then often covered poorly and usually mainly in the context of infectious disease. This is also a good time to introduce concept of preventative medicine since atherosclerosis is to a great extent a disease driven by changes in lifestyle, with lifestyle heavily influenced by socioeconomic status.

Atherosclerosis, signaling pathways and gene expression: Inflammation involves activation of the innate immune system. The innate immune system may be activated to initiate atherogenesis by a number of factors that include bacterial antigens, oxidized-lipoproteins or simply because of increased cellular oxidative stress due to a variety of factors generally influenced by lifestyle. The key is activation of monocytes and the expression of cell adhesion molecules on the endothelium that allow the activated monocytes/macrophages to infiltrate the intima. What should students know about inflammation, learned in the context of atherosclerosis? One is the pathways to pro-inflammatory gene expression. A primary driver of the activation of the innate immune system is the transcriptional factor complex known as nuclear factor kappa B (NFkB). Important players in activating NFkB are a family of receptors known as Toll-like receptors (TLRs). During an infection pathogen-associated molecular patterns (PAMPs) such as lipopolysaccharide activate TLRs. Activation of TLRs initiate a signaling cascade that results in the nuclear translocation of NFkB and promotion of transcription of genes that have kB elements in their promoter region, these generally are pro-inflammatory genes. In addition to PAMPs, free fatty acids and cell necrosis by-products can also activate TLRs.

Atherosclerosis and HDL/LDL : This is also an opportune moment in the curriculum to discuss the role of cholesterol in atherogenesis and the roles high density lipoproteins (HDL) and low density lipoproteins (LDL) play. LDL tends to promote inflammation since the polyunsaturated fatty acids bound in LDL tend to be located externally where they are readily oxidized whereas in HDL they are located internally. Oxidized LDL binds to scavenger receptors on monocytes and endothelial cells causing activation of NAD(P)H oxidase resulting in superoxide anion free radical production. This increased oxidative stress promotes activation of NFkB resulting ultimately in activation of monocytes to differentiate into activated macrophages and expression of cell adhesion molecules on the endothelium. The oxidized LDL is phagocytosed by the activated macrophages to form foam cells that now invade the intima, initiating atherogenesis.

This is also an opportune time in the curriculum to introduce students to mitogen-activated protein (MAP) kinase signaling. Activation of MAP kinases such as amino-terminal jun kinase (JNK) and p38 MAP kinase can also promote expression of pro-inflammatory genes. Like IKK, the kinase important in activating NFkB, the cascade of kinases that promote activation of JNK and p38 MAP kinase are countered by phosphatase activity. These phosphatases generally contain cysteine residues in their catalytic sites that are readily oxidized. Inactivation of phosphatases promotes the activated state of these MAP kinases (and NFkB), thereby promoting not only inflammation but also inappropriate gene expression that influence many disease processes. Thus, this is an opportune time to introduce students to the concept that many chronic diseases are associated with over-activation of MAP kinases.

Atherosclerosis and periodontal disease: One factor, only relatively recently recognized, is periodontal disease. Periodontal disease can cause systemic inflammation that promotes atherogenesis. Periodontitis can promote atherosclerosis both by increasing systemic inflammation as a consequence of periodontitis as well as by reactions of the endothelium to bacteria entering the circulation from diseased gums. Periodontal treatment has been shown to both decrease systemic blood inflammatory markers as well as the intimal thickness of the carotid arteries. It is incumbent on designers of the curriculum to include the importance of prevention of periodontal disease in preventing cardiovascular problems.

Atherosclerosis and nutrition. This is also an opportune time in the curriculum for students understand the roles of elevated cholesterol, fatty acids in atherogenesis and how diets influence lipid profiles. How foods rich in phytosterols (whole grains, nuts and cold-pressed plant cooking oils) can not only decrease dietary cholesterol uptake but also how these foods, rich in omega-3 fatty acids, raise HDL:LDL ratios. Omega-3 fatty acids also inhibit activation of TLR4 and, thus, decrease the probability of atherogenesis even in the presence of bacterial cell wall products. One can also introduce into the curriculum the role of cyclo-oxygenase (COX) in the production of eicosanoids that further drive the inflammatory process and how increasing the ratio of omega-3 to omega-6 fatty acids will decrease inflammation through alterations in the fatty acids composition at the SN2 position of phospholipid. With a higher proportion of omega-3 rather than omega-6 fatty acids in the SN2 position there is a decrease in production of pro-inflammatory eicosanoids by actions of COX1 or COX2 – this is a gentler form of ameliorating inflammation compared to COX inhibitors since COX1 activity is necessary for certain normal physiological functions (e.g., in stomach) as is COX2 activity (e.g., macula densa function).

Since there is an abundance of evidence that as we age there is a strong trend to have a more oxidizing environment that promote activation of NFκB and MAP kinases that in turn drives many aging-related problems, including atherosclerosis, there is much interest in the role of dietary anti-oxidants to counter such oxidative stress. Amongst the public there is great interest in nutraceuticals and functional foods. Should such topics be included in the modern medical curriculum? There is some skepticism about Hippocrates' dictum to "let food be your medicine and medicine your food". Especially since a number of clinical trials have indicated that increasing intake of specific anti-oxidants such as vitamin C or vitamin E have little effect on disease processes with an underlying inflammatory component. What is not appreciated by those running such clinical trials is that although vitamins E and C play important roles in the scavenging of oxidants, their roles are very limited. Thus, the essential role of vitamin E is to scavenge lipid peroxy radicals resulting in the formation of a lipid hydroperoxide and a vitamin E radical. The role of vitamin C is to reduce the vitamin E radical back to vitamin E. These are very important roles but the cell is left with a lipid hydroperoxide that will break down into strong oxidants that promote continued oxidant damage. It is critical for the cell to scavenge the lipid hydroperoxide. To do this it requires the selenoenzyme glutathione peroxidase and the electron donor glutathione (GSH). Any trial investigating the efficacy of anti-oxidants should ensure that the tissues have adequate GSH levels and adequate glutathione peroxidase levels. Thus, there should be adequate dietary intake of selenium for synthesis of selenoenzymes and adequate cysteine intake via proteins rich in cysteine residues. Thus, somewhere in the curriculum the essential pathways that enable cells to scavenge oxidants should be included. Also, somewhere in the curriculum should be provided some of the recent understanding how specific phytochemicals can affect cellular signaling and, thus, health. For example, how certain flavonoids may inhibit prolonged activation of MAP kinase pathways and, thus, potentially ameliorate inflammatory states. As well the relatively new findings that certain phytochemicals, e.g., metabolites of the principal lignan of flax seed, can increase the expression of phase 2 protein genes through the activation of the Nrf2 transcriptional factor pathway should be included in the curriculum. Phase 2 protein genes have protein products that either increase oxidant scavenging or decrease the probability of oxygen scavenging

Atherosclerosis and physical activity: It has been known for many years that physical activity promotes cardiovascular health. We are just beginning to determine some of the hormones that active muscle releases and still have a poor understanding how they influence cardiovascular health. One way appears to be through decreasing the expression of NAD(P)H oxidase in the endothelium making it more difficult to activate NFκB in these cells and, thus, decreases the probability of endothelial expression of cell adhesion molecules necessary for passage of activated leukocyte into the intima. Through unknown mechanisms physical activity also decreases blood LDL and increases HDL. Exercise has been demonstrated to increase release of a number of cytokines from muscle including interleukin-6 (IL6) IL8, IL15 as well as transforming growth factor-1. It is likely that many of the positive aspects of exercise on cardiovascular health are mediated by these hormones (cytokines). This brings the concept that the tissues of the body also communicate with each other in a number of ways that involve signaling molecules released into the blood, i.e., they communicate in an endocrine fashion. Here one can also discuss atrial natriuretic peptide and point out that hormones are not produced solely by the classical endocrine glands. The above discussion has provided some examples and certainly does not limit the areas that we may have to include in our curriculum.

Can we target important topics in Journal Clubs for assessment?

This is an open ended question which needs lot of thought. We leave the readers to judge if we are in a position to target Journal Clubs to accommodate a research-driven curriculum and to assess cardiovascular system beyond text book knowledge. We are using Journal Clubs at Alfaisal University and believe we are stimulating a great desire amongst our students for evidence-based medicine.

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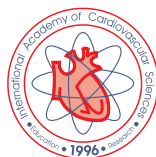
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