

香港大學心臟血管研究所

THE INSTITUTE OF CARDIOVASCULAR
SCIENCE AND MEDICINE



2002 Annual Report

Mission Statement of the Institute of Cardiovascular Science and Medicine

The Institute of Cardiovascular Science and Medicine (ICSM) commits itself to strive for excellence in research, teaching and training in cardiovascular sciences which contributes to the prevention and patient management of cardiovascular diseases in Hong Kong.

We shall offer the highest standards of teaching research and scholarship in an interactive environment conducive to creativity, to innovative learning and to freedom of thought, enquiry and expression in all aspects of cardiovascular sciences.

We shall continue to undertake research, teaching and other forms of service in clinical and basic cardiovascular sciences which will advance our quest for wisdom, truth and excellence in biomedical science at large.

We shall make known the mission of this Institute in Hong Kong and internationally

Governance

Council

The members of the Institute elect a Council, who are responsible for carrying out the work of the Institute according to its Mission, Objectives, By-Laws and Regulations. The Council consists of the Officers, the immediate Former Director (if available), and three to ten Council Members. The Officers of the Institute are the Director, Deputy Director, Honorary Secretary and Honorary Treasurer. Each Council serves the Institute for a period of two years.

The Officers and seven Members of the Third Council of the Institute were elected at the 5th Annual General Meeting on 1st December 2001: a further three Council Members were subsequently co-opted early in 2002. The members of the Third Council remained in office throughout 2002.

Third Council of the ICSM (December 2001 - December 2003)

Director:	Professor C.P. Lau	Council	Dr. A.K.T. Chau
		Members:	Dr. W.H. Chen
Deputy			Dr. B.M.Y. Cheung
Director:	Professor T.M. Wong		Dr. M.L. Fung
			Professor C.R. Kumana
Honorary			Dr. K.L.F. Lee
Secretary:	Dr. H.J. Ballard		Professor R.Y.K. Man
			Dr. Karmin O
Honorary			Dr. K.C.B. Tan
Treasurer:	Dr. Y.F. Cheung		Dr. H.F. Tse

Membership Sub-Committee of the Council

Dr. H.J. Ballard Professor C.R. Kumana Professor T.M. Wong

Fund-Raising Sub-Committee of the Council

Dr. K.L.F. Lee Dr. A.K.T. Chau

Membership

Membership of the Institute of Cardiovascular Science and Medicine continued to increase in the year 2002. At the end of the year, membership stood at 123, and consisted of 12 Founding Members, 50 Full Members, 19 Associate Members and 42 Affiliate Members.

Criteria for membership

Clinicians, scientists, researchers and students with an interest in the cardiovascular field are invited to become members of the Institute. The classes of membership open to applicants are Full, Associate or Affiliate Membership.

All applicants for admission shall

1. Be at least 18 years of age; and
2. Be of good character and repute; and
3. Undertake in writing to adhere to the By-Laws of the Institute, as amended from time to time.

Applicants for admission as a Full Member shall also

1. Be a full time or honorary teacher (Assistant Professor, Honorary Clinical Lecturer or above) of the University of Hong Kong or be deemed to be holding an equivalent position; and
2. Be engaged in research in cardiovascular science or cardiovascular medicine, as evidenced by his or her published works.

Applicants for admission as Associates shall also

1. Possess either a medical degree (MBBS or equivalent) plus a higher qualification (MRCP or equivalent), or a doctorate (PhD or equivalent) in science; and
2. Be engaged in research in cardiovascular science or cardiovascular medicine.

Applicants for admission as Affiliates shall also

1. Possess a University degree or equivalent in medicine, nursing or science; and
2. Be engaged in or have a strong interest in cardiovascular research.

Applications for membership, accompanied by the appropriate supporting documents (eg. resume, list of relevant publications, copies of certificates) should be submitted to the Honorary Secretary, to whom membership enquiries may also be addressed. The application form may be obtained by writing or e-mailing (icsm@hkucc.hku.hk) to the Honorary Secretary, or it may be downloaded from the membership section of our website (<http://www.icsm-hk.org>)

Research Activities Of The ICSM

Organisation of Research

Cardiovascular disease (heart attack and stroke) is the number 1 killer in Hong Kong and China. The **Institute of Cardiovascular Sciences and Medicine** aims to achieve academic/research excellence in cardiovascular sciences and medicine, international recognition and a reduction in the mortality and morbidity of cardiovascular disease through an integrated teamwork approach to research. The overall theme for our research remains the **Atherosclerosis Research Programme**, which is organised into 4 major projects, namely Epidemiology & Genetics, Atherosclerosis, Inflammation & Thrombosis, Novel Therapies, and Complications. The **Epidemiology & Genetics** group will evaluate cardiovascular risk factors in the Chinese population, predict trends in cardiovascular diseases, and identify genetic markers for susceptibility to cardiovascular diseases. The **Atherosclerosis, Inflammation & Thrombosis** group study the pathogenesis of vascular disease, particularly whether homocysteinaemia, inflammatory markers such as CRP or adrenomedullin are suitable targets for treatment and prevention of atherosclerosis. The **Novel Therapies** group are the only team in Hong Kong that is already developing stem cell transplantation for humans. Their focus is the regeneration of normal heart muscles, neurons and blood vessels in areas damaged as the result of atherosclerotic disease. The "**Complications**" team comprises two research groups: the **Hypoxia & Ischaemia** group are characterising the responses and adaptations of various organs to hypoxia or ischaemia, with the particular aim of exploiting preconditioning to induce some degree of protection against target organ damage in vascular disease, whilst the **Arrhythmia & Heart Failure** team are actively developing new treatments for these conditions, which commonly occur in patients with vascular disease, and which carry a very high mortality.

Epidemiology & Genetics: Cardiovascular Risk Factors

Co-ordinator Dr. Bernard Cheung

Key team members Stephen WK Cheng, Bernard MY Cheung, YF Cheung, TH Lam, Sidney CW Tam.

Outline: There is a shortage of prospective data on cardiovascular risk factors in Chinese populations. Our group are engaged in epidemiological studies involving thousands of subjects, which are representative, because of random sampling, and prospective, entailing a long open-ended follow up period. Clinical information will be obtained and DNA stored for future nested case control studies after 5-10 years of follow-up. Sub-samples of the subjects and the stored DNA and plasma will be used immediately for the investigation of genetic markers for diabetes and hypertension. Within the research team for this project, we have expertise in clinical, epidemiological, genetic, molecular, cellular and pharmacological research to facilitate the various aspects of the programme.

Epidemiology. We are examining the prevalence of risk factors in Hong Kong Chinese men and women, including hypertension, diabetes, hypercholesterolaemia, obesity and smoking, and how these change over time. The trends in the risk factors can be used to guide public health policy. Other projects include both retrospective and long-term prospective studies to investigate the effects of perinatal influences on cardiovascular risk factor development in adult life and the cardiovascular risk factors of peripheral vascular diseases, whilst a separate study focuses specifically on genes, lifestyle and diseases in Chinese elderly in Hong Kong.

Genetics: DNA collected in the large epidemiological studies can be used in the investigation of genetic markers for susceptibility to diseases such as diabetes and hypertension using the candidate gene approach and data from the prospective studies.

Pathogenesis: Atherosclerosis, Inflammation and Thrombosis

Co-ordinator Dr. Karmin O

Key team members JP Bourreau, WH Chen, B Cheung, RYK Man, K O, YL Siow, SCF Tam, F Tang.

Outline: There is mounting evidence that inflammation plays a role in the pathogenesis of atherosclerosis. Several large epidemiological studies have shown that even small increases in serum levels of C-reactive protein (CRP), a marker of systemic inflammation, are associated with increased risk of ischaemic heart disease, and serum CRP level is an independent risk factor for cardiovascular disease. Plasma CRP level is also increased in patients with diabetes and is related to endothelial dysfunction. The underlying mechanisms of the inflammatory responses in atherosclerosis and diabetic vascular complications are not clear. This is an important area of research as a better understanding of these mechanisms may help to design novel therapeutic approaches. Adrenomedullin is a peptide hormone that acts as a local autocrine and/or paracrine vasoactive hormone and it has vasodilator and blood pressure lowering properties. It may also play a role in mediating inflammatory responses. Plasma concentration of adrenomedullin has been shown to be elevated in patients with cardiovascular disease, in inflammatory states and septic shock, and in diabetic patients with complications. Platelet aggregation and thrombosis also play a crucial role in acute coronary syndromes, and studies are underway to evaluate the combination of anti-platelet and anti-thrombin therapy in these patients.

Novel therapies: Stem Cell Transplantation and Traditional Chinese Medicine

Co-ordinator Dr. H.F. Tse.

Key team members SWK Cheng, CP Lau, GR Li, JCL Zhang

Stem Cell Transplantation

Outline: Coronary atherosclerotic disease and stroke is a major cause of morbidity and mortality in industrialized nations. Sudden blockage of coronary and cerebral arteries can cause heart attack, which may be complicated by shock, chronic heart failure, strokes, and/or sudden death. Despite advances in drug therapy and catheter-based intervention, which are targeted toward opening of the blocked arteries and restoration of normal blood flow to the heart muscles and brain, a significant number of cases continue to result in loss of normal heart function and cerebral function. Loss of heart muscles results in heart failure, and in the most severe form, the patients have survival less than 1 year. Loss of brain function results in impairment of motor and sensory function. Drug treatment remains palliative, and heart transplantation is limited by the availability of donors. Regenerating normal myocardium, neurons and blood vessels is conceptually an attractive way to restore normal function to the damaged heart or brain. Our research group contains the only team in Hong Kong that is already developing stem cell transplantation for humans.

Traditional Chinese Medicine

Outline: There is an enormous, and presently under-exploited, potential for the use of Chinese medicinal drugs as an adjunct to, or replacement for, western medical approaches. These substances are very attractive to consumers, because of their natural origins, but a proper scientific approach to the investigation and validation of their properties is essential. Hong Kong, with its East-meets-West culture has a great advantage over both western and mainland Chinese Universities in this area, and the ICSM is excellently placed to carry out a research programme: our group includes cardiologists, cardiovascular physiologists and cardiovascular pharmacologists, who are already very active in this area, and who have long-standing research collaborations on the topic with groups in the mainland.

Complications

Pathogenesis of Complications: Hypoxia and Ischaemia

Co-ordinator Professor T.M. Wong.

Key team members HJ Ballard, JP Bourreau, YF Cheung, ML Fung , PCW Fung, GR Li, F Tang.

Outline: When an organ is subjected to hypoxia/ischaemia, it initiates a series of responses, some of which serve to protect the tissue against hypoxic/ischaemic damages, while others exacerbate the damages. Our goal is to identify the beneficial responses, and develop strategies to enhance them, and determine the deleterious responses so that we can develop means to negate them. We put particular emphasis on the heart and the brain as the incidence of ischemic heart diseases and stroke is increasing in Hong Kong and China. We are involved in characterising the responses and adaptations to acute or chronic hypoxia, and in the investigation of the phenomenon of the protection or pre-conditioning, which is particularly pronounced in the heart. Understanding of the compensatory responses and mechanisms of preconditioning will enable us to design better strategies in the prevention and treatment of diseases/disorders arising from hypoxia/ischaemia. The role of free radicals as intermediaries of hypoxic ischaemic injury is also under investigation.

Treatment of Complications: Arrhythmia and Heart Failure

Co-ordinator Professor C.P. Lau.

Key team members HW Chan, K Fan, CP Lau, KLF Lee, SK Leung, GR Li, HF Tse, CM Yu, J Zhang.

Outline: Coronary artery disease may result in a number of cardiac complications, including arrhythmia and heart failure. Heart failure is responsible for 20% of all mortality in Hong Kong, and the incidence of heart failure is increasing. Many cases of death from heart failure are sudden, usually related to the occurrence of cardiac arrhythmias. The Arrhythmia Service of the Cardiology Division of Queen Mary Hospital, the University of Hong Kong, is the most internationally recognized cardiac arrhythmia centre in Asia. We have an excellent track record of genetic, molecular, cellular, epidemiology and clinical research in heart failure and arrhythmias. Members of our research group are international authorities and pioneers in using pacing and ablation for atrial fibrillation, the use of catheter based cooling energy (cryoablation) for the ablation of focal atrial fibrillation, animal and cell model for anti-arrhythmic drug development, electronic cardiac signal processing during arrhythmia (patent pending), reverse cardiac remodelling after cardiac resynchronisation etc. Our group will develop new ablative device technology.

Patents awarded to ICSM members in 2002

A patent was awarded to W Xu, HF Tse, FH Chan, PC Fung, KL Lee and CP Lau for "A new Bayesian discriminator for detection of atrial tachyarrhythmias" (as described in their paper in *Circulation* 2002 Mar 26;105(12):1472-9).

Grants and Donations

External Research Grants awarded to ICSM members in 2002

<u>Investigator</u>	<u>Project Title</u>	<u>Amount (HK\$)</u>	<u>Awarding Body</u>
PI: H.F. Tse	Neovascularization of ischemic myocardium by autologous bone marrow cells transplantation	816,000	RGC
PI: Karmin O	Mechanisms of Enhanced Monocyte Binding to Vascular Endothelium in Hyperhomocysteinemia	1,216,175	RGC
PI: M.L. Fung	Molecular and cellular mechanisms underlying anatomical and physiological adaptation of the carotid body in chronic hypoxia: role of HIF-1 and its target genes.	876,000	RGC
PI: Y.W. Kwan	The Role of Nitric Oxide and Mitogen-Activated Protein Kinase in Mediating the Inhibition by β 3-Adrenoceptor Activation of Voltage-Dependent L-type Calcium Channels of Guinea-pig Single Ventricular Myocytes	1,262,000	RGC
CI: H.F. Tse	Establishment of a relationship between wrist pulses and cardiovascular conditions	2,948,000	Innovation & Technology Fund

Major Donations awarded to ICSM members in 2002

<u>Investigator</u>	<u>Purpose</u>	<u>Amount (HK\$)</u>	<u>Donor</u>
PI: C.P. Lau	Francis R Zimmern Centre for Cardiology	30,000,000	Mrs Helen Zimmern
PI: C.P. Lau	Support Coronary Care Unit	80,000	Mr Chung Siek Yung
PI: C.P. Lau	Support Cardiology Research	25,000	Mr Patrick Yuen
PI: C.P. Lau	Support Cardiology Research	179,400 (USD23,000)	Medtronic Inc

Scientific Meetings

The Institute of Cardiovascular Science and Medicine organised two Scientific Meetings in the year 2002:

The Sixth Annual Scientific Meeting: Atherosclerosis, Inflammation and Thrombosis From Bench to Bedside, From Prevention to Treatment

The Sixth Annual Scientific Meeting was held at the Convention and Exhibition Centre on October 5th and 6th 2002. Once again we returned to the "Bench-to-Bedside" theme, with a strong focus on the integration of basic science research with clinical medicine. The first Symposium was devoted to Inflammation and Atherosclerosis, and included excellent talks from our overseas visitors, Preston Mason from Harvard Medical School, Boston, USA, Philip Ding from National Yang Ming University, Taiwan, and Gregory Bondy from the University of British Columbia, Vancouver, USA, as well as our local speakers, Karmin O, KCB Tan and TM Wong. Symposium 2 was devoted to Advances in Antithrombotic Therapy, with presentations from Daniel Simon of Harvard Medical School, John Eikelboom from the University of Western Australia, Frans Van de Werf from Gasthuisberg University Hospital, Leuven, Belgium, and WH Chen from Hong Kong University. The Saturday section of the meeting concluded with a Dinner Symposium, in which Philip Ding from Taiwan and Lars Lindholm from Umea University Hospital Sweden addressed the topics of "The Heart Protection Study: What are the Implications for Practice" and "The Optimal Antihypertensive Regimen in Diabetes". The meeting continued on Sunday with a Symposium on Embolic Protection, including very informative presentations from Campbell Rogers of Harvard Medical School and Eberhard Gruber from the Siegburg Heart Centre, Germany, and concluded with an Interactive Interventional Case Discussion.

University Program 2002: Core Curriculum in Cardiology

The 2002 Core Curriculum was held directly after the Annual Scientific Meeting, also at the Hong Kong Convention and Exhibition Centre. It was a highly successful meeting, addressing such topics as "New directions in hypertension", "Who should be receiving an ICD in 2002", "Identifying viable myocardium" and "Electron beam CT to detect coronary artery calcification", as well as presenting highly relevant research data on "the effects of postmenopausal hormone replacement therapy on lipoprotein in Chinese women" and "vascular function in children and adolescents with a history of Kawasaki disease".

Collaboration with other Centres of Excellence

Many ICSM members have a long tradition of individual collaboration with other researchers. Early in 2002 a more formal collaborative arrangement was agreed between two Centres of Excellence, the Institute of Cardiovascular Science and Medicine and the Centre for Endocrinology and Diabetes at the University of Hong Kong. The work of our two Centres overlaps in many areas, so we decided to combine our efforts and expertise, and establish a "Research Centre in Atherosclerosis and Vascular Disease". This enhanced research effort will address a very important need in the Hong Kong community: Atherosclerotic diseases (heart attack and stroke) are the number 1 killer in Hong Kong and China, and their incidence is rising. Diabetes mellitus is another common cause of mortality among the elderly. Diabetes is associated with accelerated atherosclerosis: heart disease, peripheral vascular disease and stroke are the major causes of death in diabetic patients over the age of 50, whilst diabetes doubles the probability of stroke and increases the probability of myocardial infarction by 3-5 times.

Community Service

Hyperhomocysteinaemia is regarded as an independent risk factor for coronary heart disease. Homocysteine is an amino acid formed during the conversion of methionine to cysteine. Moderate elevation of homocysteine in the blood correlates to increased risk for cardiovascular disease, and susceptible individuals can be successfully treated with dietary folate.

During the year 2000, a homocysteine assay was set up by ICSM Council members Dr. Bernard Cheung and Dr. Karmin O, and reference levels for the Hong Kong Chinese population were established in a pilot study of 200 patients. Early in 2001, the assay was made available as an investigative service to cardiologists, and the uptake of the assay service has continued to increase steadily throughout 2001 and 2002.

Media Briefings

ICSM members continued to maintain a high profile in both print and electronic media throughout 2002. In March 2002, Professor C.P. Lau contributed interviews to two educational films on cardiac health produced by "Care for Your Heart", a cardiac patients' mutual support association. The first film was on the topic of coronary heart disease and the second was on cholesterol. These educational films are widely shown throughout Hong Kong, for example, on the TV systems of buses and minibuses. In April, Professor Lau was interviewed by the Hong Kong Economic Times on wrist-pulse research, and in May by the Medical Tribune on a new pacemaker to improve outcomes of heart failure. In June he held a press conference on the impact of drug-eluting stents, which was attended by several local newspapers, including Hong Kong Daily and Oriental Daily. This was followed up by a telephone interview with the Sun on the same topic in August. In September, Dr. Kathy Lee was interviewed on Commercial Radio on the subject of Heart Health, while Professor C.P. Lau was interviewed again by the Medical Tribune, this time on the subject of "new horizons in cardiac pacing". A very successful press conference was held in association with the Sixth Annual Scientific Meeting on October 5th 2002: Professor T.M. Wong reported on the use of morphine in treatment of heart attacks, while Dr. W.H. Chen reported on recent advancements in the treatment of acute heart attack. Dr. Kathy Lee was interviewed twice by the Hong Kong Economic Times during November, once on the topic of cardiac resynchronisation, and later on the subject of sudden death. She was also interviewed on the latter topic by other local media, including Sing Tao.

Fund Raising

The activities of the ICSM are funded through its commercial activities, such as advertising revenue associated with the Annual Scientific Meeting and assay services for cardiovascular risk factors, as well as donations, mainly from pharmaceutical companies. We aimed to increase our funding base, so as to be able to provide more funding to research projects. Our first advertising flyer was sent out to members of the general public in December 2001, to introduce our research work to the population of Hong Kong and to solicit donations for research funding. A number of donations were received from members of the public throughout 2002.

Meeting our Targets

Aims for 2002

Our principal aims for 2002 were to expand our collaborative links with other groups researching in areas related to cardiovascular science and medicine, and to secure funding to retain the ICSM Research Assistant Professor, Dr. G.R. Li, who was approaching the end of his first term of employment with us. Early in 2002 we joined with another Centre of Excellence, the Centre of Endocrinology and Diabetes, to form The Research Centre in Atherosclerosis and Vascular Disease. The major mortality and morbidity in an ageing population is attributable to cardiovascular disease, whilst diabetes is associated with accelerated atherosclerosis. The Research Centre in Atherosclerosis and Vascular Diseases therefore has the mission of "Targetting at Heart Disease and Diabetes". Many of the members of the two Centres of Excellence were already engaged in informal research collaboration. By formalising the links between the two groups, we have now paved the way for even more collaboration, and also increased our strength to bid for external funding sources. The ICSM was also successful, in an extremely competitive exercise, in securing the funds to renew the contract of Dr. G.R. Li.

Aims for 2003

Funding: The ICSM is mainly dependent on external donations for its funding base. Therefore, we undertook to review the distribution of our expenditure between administrative costs and research during 2003, and to improve efficiency, so that administrative costs could be reduced.

Research: We should continue to promote research collaboration, so far as our limited funding permits. We will also seek funding for another Post-doctoral Fellow or Research Assistant Professor.

Education: Education will be an important area of focus for the ICSM in the future. We would prepare separate educational materials for use by doctors and the general public. This would have the added benefit of raising our profile.

Community Service: Using the CRISPS2 data, a Framingham score can be calculated for a member of the local population. In the future, this service would be made available online, and educational materials could also be provided through this means. We would also promote increased use of the homocysteine assay, and move towards providing a commercial assay service for CRP in the future.

ICSM Publications in 2002

Selected manuscripts from the Third Annual Scientific Meeting of the ICSM were published in the August 2002 issue of *Clinical and Experimental Pharmacology and Physiology* (Volume 29, Issue 8), and manuscripts from the Fourth Annual Scientific Meeting of the ICSM were published in the September 2002 issue of the same journal (Volume 29, Issue 9). Abstracts from the Sixth Annual Scientific Meeting of the ICSM were published in the October 2002 issue of the *Journal of the Hong Kong College of Cardiology* (Volume 10, Number 4, pp. 205-248).

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