

Global cardiology comes to Australia: 14th World Congress of Cardiology, Sydney, 5–9 May 2002

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THE 14TH WORLD CONGRESS OF CARDIOLOGY, held in Sydney 5–9 May 2002 (the first time ever in the antipodes), was a joint meeting with the 50th anniversary meeting of the Cardiac Society of Australia and New Zealand (CSANZ). The Congress is the principal meeting of the World Heart Federation, a body comprising all of the world's cardiac societies and heart foundations. Delegates came from 115 countries, and there was a total registration of just over 9000. More than 3000 abstracts were received from investigators in 82 countries.

In addition to focusing on developments at the cutting edge of cardiovascular disease, the Congress explored themes such as the world burden of cardiovascular disease and the likely rise of this burden in the 21st century, particularly in developing countries — a prospect of particular concern to the World Heart Federation.

Worldwide issues

Ischaemic heart disease is the leading cause of death in developed countries. While age-adjusted mortality from the disease is gradually falling in developed countries, including Australia, it is set to become an epidemic in developing countries, and over the next 20 years will probably become the most important global health problem. This was put into perspective by Salim Yusuf (*Director of Cardiology, McMaster University, Hamilton, Canada*). George Mensah (*Head, Car-*

diovascular Division, Centers for Disease Control and Prevention, Atlanta, USA) highlighted the fact that the epidemic of ischaemic heart disease is driven by tobacco use, particularly in Asian and former Eastern European countries, while Stephen Colagiuri (*Director of Endocrinology, Prince of Wales Hospital, Sydney*) emphasised the rapid increase in diabetes that is occurring with population aging and increasing overweight and obesity.

David Wood (*Professor of Preventive Cardiology, National Heart and Lung Institute, London, UK*) made the point that both prevention and treatment must translate into practice the large scientific and clinical evidence base of effective measures, but that we should also focus on developing tools to assess future absolute risk of cardiovascular disease rather than concentrating only on individual risk factors. These measures should support compliance with therapeutic regimens (Martha Hill, *Dean of Nursing, Johns Hopkins University, Baltimore, USA*) and, very importantly, consider the underlying psychosocial and socioeconomic determinants of disease (Michael Marmot, *Professor of Epidemiology and Public Health, University College, London, UK*), particularly in the vastly populated poor regions of Asia (Sania Nishtar, *Director, Heartfile, Pakistan*).

Atherosclerosis

Inflammation is now regarded as a key process in the development of atherosclerosis and the destabilisation and rupture of plaques in acute coronary syndromes and cardiac death. The role of activated macrophages and T lymphocytes in secreting matrix metalloproteinases and tissue factor during plaque rupture was highlighted.¹ This information has almost immediate practical application: diagnostic assays for inflammatory markers such as C-reactive protein are predictive of risk of myocardial infarction, stroke and death in population studies. Valentin Fuster (*Director, Weiner Cardiovascular Institute, Mount Sinai School of Medicine, New York, USA*) also emphasised the need to find a systemic solution to atherosclerosis, possibly through novel approaches to reducing the effects of inflammation.

In a plenary session on presymptomatic detection of atherosclerosis, the importance of defining high-risk populations was emphasised (Sidney Smith, *Chief Scientific Officer, American Heart Association, Dallas, USA*), as the first manifestation of vascular disease is often a catastrophe — myocardial infarction, stroke or sudden cardiac death. Techniques reviewed included global risk factor algorithms such as those based on the Framingham study (Sidney Smith, *Chief Scientific Officer, American Heart Association, Dallas, USA*), the use of ultrasound to estimate arterial-wall thickness (Olli Raitakari, *Senior Lecturer, University of Turku,*

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Turku, Finland), the use of computed tomography scanning with and without contrast to detect coronary calcification and/or define coronary stenoses, and the use of magnetic resonance imaging to outline areas of myocardial damage and even plaque characteristics.

Steven Nissen (*Vice Chairman, Cardiovascular Division, Cleveland Clinic, Cleveland, USA*) presented exciting new data on the reversibility of atherosclerosis with aggressive cholesterol lowering. New intravascular ultrasound studies have shown that coronary plaques can undergo regression and stabilisation, potentially translating into clinical benefit for people with coronary artery disease.

Intervention

A major focus of interventional cardiology was the exciting results of trials using drug-eluting stent technology. Substudies from the RAVEL trial² and smaller pilot registries suggest that sirolimus, a macrolide antibiotic with powerful antiproliferative properties, effectively prevents restenosis *de novo* not only in coronary lesions and femoral artery lesions but also with in-stent restenosis. Patients with diabetes seem to benefit to the same extent as those without diabetes. Promising data were also reported for stents eluting paclitaxel, while ongoing clinical trials are evaluating other drugs.

Arrhythmias

The highlight of the sessions on arrhythmias was the presentation by Bernard Gersh (*Professor of Medicine, Mayo Clinic, Rochester, USA*) of data from the AFFIRM study, in which 4060 patients with recent paroxysmal or chronic atrial fibrillation were randomly allocated to either a "rate control" arm (with emphasis on obtaining an acceptable ventricular response rate) or a "rhythm control" arm (with antiarrhythmic drugs and elective cardioversion to attain and maintain sinus rhythm).

The primary outcome measure of the study was total mortality: there were 306 deaths in the rate control group, compared with 356 deaths in the rhythm control group ($P = 0.056$). For other endpoints, such as hospitalisation, ischaemic stroke and arrhythmia attributable to antiarrhythmic drugs, the rate control group also tended to do better. Nearly all strokes occurred in patients who had an international normalised ratio of less than 2.0 or who were not taking warfarin, emphasising the importance of anticoagulation therapy regardless of the treatment strategy.

The general conclusion of this landmark study is that decisions on returning patients to sinus rhythm with aggressive antiarrhythmic therapies can be based largely on symptoms and patient preferences rather than the (incorrect) assumption that this approach will improve prognosis.

Heart failure

Heart failure remains the leading cause of medical admission in people over 65 years, and its prevalence is increasing as the population ages. The high level of morbidity associ-

ated with heart failure was illustrated by Duc and colleagues,³ who found that major depression is present in 18% of patients who have heart failure, and depressive symptoms in another 26%. These conditions are often unrecognised and untreated.

The emerging role of B-type natriuretic peptide (BNP) in heart failure management was highlighted in the sessions. Post and colleagues⁴ reported that measuring BNP can help to distinguish cardiac causes of dyspnoea from non-cardiac causes in the emergency department. Mean levels of BNP were 83 pg/mL in patients with non-cardiac-related dyspnoea and 905 pg/mL in patients with heart failure. Aronson et al⁵ showed that administration of BNP increased heart rate variability, a surrogate for improved prognosis (heart rate variability is an indicator of autonomic function, low variability being associated with dysfunction and adverse prognosis).

Carvedilol can be successfully initiated and titrated, and withdrawal rates have been low, even in high-risk groups such as elderly people⁶ and those with severe heart failure.⁷ Krum et al (in the COPERNICUS study)⁷ showed that within the first eight weeks of therapy there was no excess of clinical events, and death in high-risk groups was less for carvedilol than placebo (3 v 15 deaths; $P = 0.005$). The efficacy of biventricular pacing to achieve ventricular resynchronisation also received attention: the MIRACLE study⁸ of patients with moderately severe heart failure and wide QRS interval (> 130 msec) showed improved functional status, quality of life and exercise tolerance after this treatment.

While "high tech" approaches to heart failure were featured in some presentations, a Spanish study showed that patient education through home visits, telephone contact and clinic review could halve the number of readmissions for heart failure.⁹ Other studies of home-based education also reinforced this finding, with Stewart et al, in a four-year follow-up study,¹⁰ demonstrating benefits in terms of reduced mortality and cost savings from reduced readmission.

Acute coronary syndromes

Lars Wallentin (*Director of Cardiology, Uppsala University Hospital, Uppsala, Sweden*) presented late results from the FRISC2 study, which had shown the benefit of early revascularisation (by either angioplasty or bypass surgery) in patients with unstable angina or a small infarction. Benefit was maintained at two years, with death or infarction reduced from 16.3% to 12.1%. He speculated that these results will lead to increased intervention for acute coronary syndromes, but noted that the cost-benefit ratio could be maximised by selecting patients at increased risk based on clinical predictors.

Despite the recent development of more powerful thrombolytic drugs than tissue plasminogen activator (tPA), initial studies showed no clinical benefit and possibly increased haemorrhage. It appears the thrombolytic ceiling has been reached, and this is probably also true of combinations of tPA with antithrombotic drugs.

Highlights of the 14th World Congress of Cardiology*

Worldwide issues

- Epidemic of cardiovascular disease in developing countries
- Tobacco, diabetes and obesity
- Global cardiovascular risk assessment

Atherosclerosis

- Inflammation
- Presymptomatic detection of coronary artery disease
- Reversibility with aggressive cholesterol reduction

Intervention

- Drug-eluting stents

Arrhythmia

- Rate or rhythm control for atrial fibrillation

Heart failure

- B-type natriuretic peptide
- Beta-blockers
- Outpatient management

Acute coronary syndromes

- Acute intervention
- New fibrinolytics and antithrombotics

Molecular biology

- Gene and cell therapy
- Genes and cardiomyopathy

* Some of the highlights are available as a webcast on <<http://www.prous.com/wcc2002/program.asp#>> (accessed 8 September 2002).

promote angiogenesis have been used in early clinical trials of patients with severe coronary and peripheral vascular disease, with some promising results summarised by Elizabeth Nabel (*Director, Clinical Research Program, National Heart, Lung, and Blood Institute, Bethesda, USA*). The next phase was to use endothelial progenitor cells to assist in the cellular component of the response. Early data on the possible benefit of muscle stem-cell therapy for severe heart failure were presented by French¹¹ and Dutch¹² investigators. There was some concern that skeletal myoblasts may contribute to arrhythmogenesis.

The winner of the International and CSANZ Young Investigator Basic Science Award, Thomas Yeoh (*Research Fellow, Victor Chang Institute, Sydney*), presented data on the control mechanisms of proliferation of skeletal muscle stem cells. This area of research is receiving intense interest internationally. In a provocative presentation entitled "Bench to bedside", Claude Lenfant (*Director, National Heart, Lung, and Blood Institute, Bethesda, USA*) stressed the need for translating the discoveries in the basic sciences into clinical care. In other sessions, Christine Seidman (*Professor of Medicine and Genetics, Harvard Medical School, Boston, USA*) showed how understanding gene defects and the changes they produce in myocardial proteins is unlocking the mechanism of an increasing number of cardiomyopathies underlying heart failure.

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The one-year results of the GUSTO V study of abciximab plus tPA treatment for patients with ST-elevation infarction showed no reduction in mortality. This was similar to the 30-day findings in the same study (Michael Lincoff, *Associate Professor of Medicine, Cleveland Clinic Foundation, Cleveland, USA*). Thus, the significant early reduction in recurrent infarction and rescue angioplasty with abciximab did not translate into reduced late mortality. The most promising strategies for ST-elevation infarction involve pre-hospital fibrinolysis and early direct angioplasty. The latter strategy was investigated in a national study in Denmark (DANAMI-II), whose one-year results were presented by Henning Andersen (*Professor of Cardiology, Skejby University Hospital, Aarhus, Denmark*). There was reduced death and reinfarction in patients having angioplasty compared with those treated with thrombolytic agents, even though many were transported long distances by ambulance to the hospital performing the angioplasty. Most of the benefit was in reduced reinfarction, a result that may also be achievable with lytic therapy plus low molecular weight heparin, together with elective revascularisation in the first few days after infarction.

Molecular biology

In a plenary session on gene and cell therapy, speakers highlighted the potential and possible limitations of a molecular biology approach for end-stage heart disease. Genes to