Cardiovascular Medicine

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Research activities in the Department of Cardiovascular Medicine span the continuum from prevention and early disease detection to the management of end-stage cardiac disease. A particular feature in recent years has been the growth in research in the cardiac catheterisation laboratory particularly in relation to the evaluation of devices of which some have originated through work at AMREP. In addition, there has been expansion in research into novel cardiac imaging, particularly cardiac MRI and CT angiography.

Effects of Good Cholesterol

In relation to prevention and risk factor management, work has continued on the effects of HDL (good) cholesterol and the metabolic and inflammatory changes which accompany obesity. Collaborative studies between Professor Anthony Dart and Professor Jaye Chin-Dusting at Baker IDI have examined some of the inflammatory and endothelial changes which accompany severe obesity and their amelioration by treatment. These studies have focused on novel findings with endothelial microparticles and have demonstrated that obese individuals have higher levels of these particles in the blood than do their lean counterparts, indicating the presence of damaged vascular endothelium.

Professor Bronwyn Kingwell and colleagues have demonstrated that reconstituted HDL infusion inhibits fasting-induced fat breakdown and oxidation in patients with Type 2 diabetes, potentially through both AMPK activation in adipose tissue and elevation of plasma insulin.

New Hypertension Treatment

Research into hypertension has concentrated on the management of patients who remain substantially hypertensive despite the use of multiple medications. A major finding in this area has been in relation to percutaneous renal denervation, with a first in man clinical trial led by Professor Henry Krum, Professor Murray Esler and Dr Tony Walton demonstrating this as a promising new approach to an intractable clinical condition. The procedure requires percutaneous placement of a catheter in the renal nerves, with subsequent radiofrequency induced interruption of the renal sympathetic nerves. The recent trial with the ARDIAN innovation device in such patients has been important and has indicated that blood pressure control may be achievable through this procedure.

In addition to clinical evaluation, this research has further examined the basic physiological mechanisms underlying the benefit from this procedure with evidence suggesting that both efferent and afferent renal sympathetic nerves may be contributing to the elevated pressures. This work has featured in publications in *The Lancet* and *New England Journal of Medicine*. Expansion into other fields where exaggerated renal sympathetic function is a likely factor is currently under way. In particular, it will include a major study into the effects of renal denervation as a possible treatment for heart failure, led by Professor David Kaye.

Coronary Artery Disease

Work in relation to coronary disease has concentrated on acute coronary syndromes and the management of acute myocardial infarction. Dr Stephen Duffy and Dr William Chan have completed a major trial into the effect of iron chelation on outcomes after primary angioplasty in patients presenting with an ST elevation acute myocardial infarction. The project has utilised cardiac MRI to estimate myocardial infarct size and to measure cardiac remodelling over the subsequent three months.

Using a lipidomic approach, eight plasma lipids have been identified from over 300 candidates which accurately distinguish unstable from stable coronary artery disease presentation in a study in collaboration with Associate Professor Peter Meikle at Baker IDI. In the next phase of these studies it is planned to examine prospectively the ability of this lipid subset to predict which patients with coronary disease are likely to present with myocardial infarction or unstable angina.

In other studies, Dr Karen Lu Fang and Professor Anthony Dart have demonstrated differences in circulating fibrocytes between patients with stable and unstable coronary disease. These may not only then serve as potential biomarkers but may also contribute mechanistically to the explanation of why some atherosclerotic plaques become unstable.

The department continues to be a major contributor to the Melbourne Interventional Group. Research from this group has identified peri-procedural atrial fibrillation as a poor prognostic sign in patients undergoing angioplasty. In addition, current studies are evaluating the outcome of patients treated with an intra-aortic balloon pump during emergency angioplasty. The ability of novel biomarkers to predict peri-procedural myocardial infarction in patients undergoing major vascular procedures has also been undertaken in a collaborative project with the Department of Vascular Surgery.

Cardiologist Dr James Hare investigates novel tissue characterisation techniques using cardiac MRI.

Antiplatelet Therapy

Research has also continued into evaluation of antiplatelet therapy, in particular its potential interactions with concomitant medications such as proton pump inhibitors. The problem of contrast-induced nephropathy has been studied with preliminary results from a newly developed device to effectively remove contrast from the circulation. Again, this resulted from an original development at AMREP from the work of Professor David Kaye.

Percutaneous Aortic Valve Replacement

In other work originating from the cardiac catheterisation laboratory, Dr Tony Walton and Dr Stephen Duffy have continued to evaluate the benefits of percutaneous aortic valve replacement contributing substantially to local and international research in this area. The catheter laboratory at The Alfred was the first in Victoria to undertake this procedure, which looks a promising alternative to cardiac surgery for aortic valve replacement in the elderly.

Cardiac Imaging

Research into cardiac imaging has continued particularly in cardiac MRI with the more recent initiation of research into coronary CT angiography. A particular finding in relation to cardiac MRI is the demonstration in subjects with heart failure that the likelihood of significant ventricular arrhythmias in patients considered for implantable defibrillators can be predicted from the extent of cardiac fibrosis detected by MRI. Multisequential cardiac MRI was used to detect acute and chronic rejection in heart transplant recipients, and also to predict response to cardiac resynchronisation therapy in heart failure patients. Given both clinical and research application for cardiac MRI, the department is fortunate to have recruited Dr James Hare, a second cardiologist with extensive experience and training in this modality, to complement the work of the head of this service, Dr Andrew Taylor.

Atrial Fibrillation

Associate Professor Peter Kistler continues to lead research in clinical arrhythmia development particularly atrial fibrillation and its relation to the development of heart failure and its management. An intriguing study completed during the year demonstrated that atrial fibrillation is rare in patients who had undergone double as opposed to single lung transplantation, reinforcing the need for complete pulmonary vein isolation when pulmonary vein isolation is used as a therapeutic modality.

Extensive collaboration between Professor Anthony Dart, Dr Silvana Marasco from the Department of Cardiothoracic Surgery and the laboratory of Associate Professor Liz Woodcock at Baker IDI has been evaluating the role of signalling molecules in the inositol pathway to the development of atrial fibrillation. Current studies in this translational research are concentrating on microRNAs – important regulators of gene function.

Cardiovascular Disease and HIV Infection

A particular feature of research in the department is close links with neighbouring AMREP partners, particularly the basic laboratories at Baker IDI and the Burnet Institute. A number of projects have evolved as collaborations with HIV researchers on the campus, reflecting the growing importance of cardiovascular disease to the natural history of HIV infection. The enhanced cardiovascular risk in this particular cohort likely reflects an enhanced inflammatory state. Collaborative studies with Professor Jennifer Hoy and colleagues in the Infectious Diseases Unit have been addressing this.

Professor David Kaye and Research Assistant Ouda Khammy.

Clinical Trials

The department continues to contribute to a large number of externally originating clinical trials, including both commercial and non-commercial, and is fortunate to have a number of experienced and committed clinical trial nurses. Current trials include the exciting new approach of alternatives to warfarin in patients requiring anticoagulation, novel anti-inflammatory drugs in patients with unstable coronary disease, heart rate lowering medications in patients with stable coronary disease and new lipid lowering drugs. In addition the department contributes data to a number of studies involving new devices.

Major Achievements

In addition to the major findings already presented, researchers in the department have also achieved a number of noteworthy research related outcomes. Professor Dart and colleagues have been awarded a further NHMRC Centre of Research Excellence for five years for Training in Translational Cardiology. This is the third consecutive quinquennium in which investigators from the department have received this or a similar award.

Professor Dart is also an investigator with Associate Professor Dmitri Sviridov from Baker IDI on a new NIH grant in relation to atherosclerosis and HIV. Dr Jonathon Habersberger won the prestigious Ralph Reader Prize at the annual meeting of the Cardiac Society of Australia and New Zealand for his work under the supervision of Professor Karlheinz Peter. Dr Dani Michel's work on the effect of high blood pressure on the adhesion of leukocytes to the vascular endothelium won first prize at the High Blood Pressure Council of Australia annual meeting. Dr James Hare has been the recipient of a CSANZ fellowship. Dr Peter Kistler has been appointed as an Associate Professor by the University of Melbourne. Himawan Fernando (BMedSc student) was awarded an H1 for his year's work under the supervision of Dr James Shaw.

Postgraduate Students
19 PhD Students
1 MD Student

Publications
75 Journal Articles