

# **CONCORD HOSPITAL**

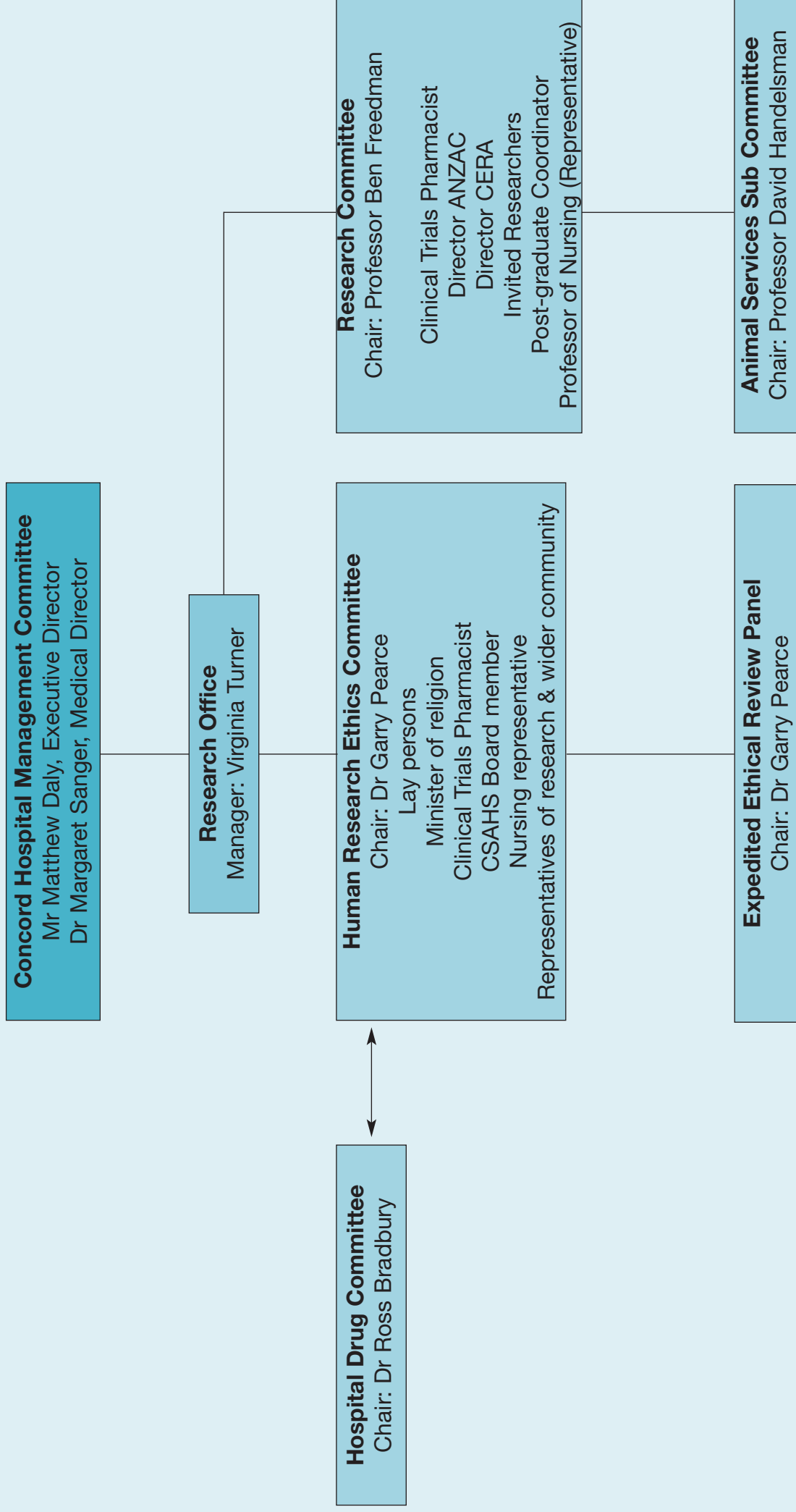
## RESEARCH REPORT

2002/2003



Concord Repatriation General Hospital  
Hospital Road, Concord 2139 Australia

# Organisational Chart: Research at Concord Repatriation General Hospital



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## Overview of research

Research at Concord Hospital is diverse, spanning the spectrum from basic, laboratory-based research through applied clinical research to population-based studies. This reflects the enormous breadth of talent and expertise at Concord and our close links with The University of Sydney and the ANZAC Research Institute. Furthermore, specialist services, such as the Burns Unit, provide the opportunity for ground breaking studies in areas of need.

The establishment of the ANZAC Research Institute has been a major factor in promoting laboratory-based research on this campus. The Institute has provided state-of-the-art laboratories to facilitate quality research and promote an environment which fosters scientific excellence. This, together with the recruitment over recent years of a number of world class senior staff with experience in a variety of research techniques, has strengthened and expanded the repertoire of conditions and diseases investigated.

An important feature of the research at Concord Hospital, and one which sets us apart from many centres, is the multidisciplinary nature of many of the studies. By drawing on the expertise of all facets of professional health care the relevance and calibre of the research is ensured.

Furthermore, research is performed while maintaining the highest standards of clinical medicine and patient care. The combination of talented, dedicated staff and the improved physical environment brought about by the redevelopment of the hospital suggests that the future of research at Concord Hospital will be bright.

Jillian Kril  
Associate Professor (Geriatric Medicine)  
Editor, Research Report



## Message from the Chair of the Concord Hospital Research Committee

It is a great pleasure to see the production of this Research Report come to fruition. In some ways it marks the coming of age of research at Concord Repatriation General Hospital, which for many years has been a teaching hospital of the University of Sydney. The new millennium has seen the commissioning of the ANZAC Research Institute – a purpose-built modern research facility – right here on the Concord campus.

The ANZAC Research Institute or ARI, headed by the inaugural Director Professor David Handelsman, commemorates in a very tangible way the Hospital's links with the veteran community, and has a primary theme of ageing. The ARI has initiated new directions of research excellence in men's health and in bone disease, as well as capitalising on previously established research in ageing through CERA (Centre for Education and Research on Ageing) and genetic aspects of neurodegenerative disorders. The ARI has already established itself as a major focus of research activities at Concord.

This publication illustrates the broad depth of research at Concord on many fronts, ranging from direct patient care to the molecular and genetic

basis of disease. It is obvious that this research is multidisciplinary in nature, with contributions from nurses, physiotherapists, dieticians, speech therapists and pharmacists in addition to those from physicians and surgeons and basic science researchers. We have chosen not to be exhaustive, but to showcase the highlights. We have also featured biographies of our two newest Professors, Markus Seibel and Robert Cumming, Rosemary Burke the director of Pharmacy, and Biao Zeng, one of our many PhD students - our researchers in training.

This research report would not have been possible without the hard work of Associate Professor Jillian Kril and Virginia Turner who collected, collated and edited the material. We owe them both a debt of gratitude for a job well done.

Research in a teaching hospital has a fundamental place not only in improving our understanding of disease but in improving healthcare. It deserves recognition and support from the community. This can best be achieved by fostering an understanding of what is happening here at Concord. We hope this publication will go some way towards facilitating this goal.

Professor Ben Freedman  
Chair, Concord Hospital Research Committee



## A message from the Chair of the Ethics Committee

The Human Research Ethics Committee (HREC) is central to the governance of good research in the hospital. As a result of the recommendations of the Review of Research at Concord Hospital in 2000, much has occurred to improve the running of Research and Ethics at our hospital.

Central to this has been the reorganisation of the Research Office with the appointment of Virginia Turner, who has worked extremely hard to bring real professionalism to the office and who is ably supported by Rodger Lomberg.

The Concord HREC has 20 members, including lay people, a Minister of Religion, two lawyers and a group of professionals with a diverse range of expertise in research and clinical care.

In 2002, the HREC was fortunate to have the addition of two more lay representatives (making a total of five), Mr Rob Neurath and Mrs Elizabeth Buckpitt. Dr Matt Rickard (colorectal surgeon) and Mr Leo Turner (Clinical Nurse Consultant) also took up positions on the Committee in 2002. In 2003, Professor Robert Cumming (Professor of Epidemiology and Geriatric Medicine) and Dr George Lau (Department of Cardiology), joined the HREC. In 2003, the Committee welcomed Rev Paul Weaver, and was pleased to retain the services of retiring Minister of Religion, Rev Paul Watkins as one its lay representatives. Two other long-standing members have retired. Dr Sue Liew retired in 2000 after 15 years as Chairperson and Mrs Ethel (Stalky) Lane retired as Veterans' Representative after

serving almost the same length of time. The hospital owes a debt of gratitude to both these dedicated people.

The Concord HREC has struggled with many issues over the last twelve months. Many of these issues arise from the new Information Privacy laws which have been introduced at both State and Commonwealth levels. In the light of this new legislation, the Ethics Committee has had to look at the need to provide more stringent ethical oversight of medical records research and the issue of identifiable information kept on databases within the hospital.

The Committee has also developed new policies for meeting the increasingly frequent demands for genetic testing as part of large multi-centre, pharmaceutical company-sponsored drug trials.

The issue of healthy volunteers taking part in research has also been a contentious one and the Committee has developed guidelines for providing sufficient information to healthy participants about any risks involved in the research for which they are volunteering.

In 2001, the HREC agreed to a process involving a new committee called the Expedited Ethical Review Panel (EERP) to assist with some of the more managerial/administrative aspects of the ethical review process.

Finally, I would like to thank my colleague Dr Ross Bradbury, who chairs the Concord Hospital Drug Committee, and all the clinicians who assist Ross in the process of assessing and reviewing Clinical Drug Trials before they are seen by the Ethics Committee. My thanks also go to the Pharmacy Department and the Clinical Drug Trials Pharmacists who have worked so hard to make clinical trials of new drugs possible at Concord Hospital.

Dr Garry Pearce  
Chairman  
Concord Human Research Ethics Committee



## Markus J Seibel

In late 2001, Professor Markus Seibel joined Concord Hospital as Professor of Endocrinology and Head of the Bone Research Program at the ANZAC Research Institute.

Markus, a native of Germany and France, graduated from the Universities of Mainz, Germany, and Pennsylvania, USA. He then trained in Anatomical Pathology (University of Freiburg and WHO Centre Mainz, Germany), Rheumatology, Gerontology and Rehabilitation Medicine (University of Basel, Switzerland), Immunobiochemistry and Endocrinology (Columbia University, USA) and Internal Medicine (University of Heidelberg, Germany). Markus completed his PhD on the *"Biochemical Assessment of Bone Turnover and Remodelling"* in 1997 (University of Heidelberg, Germany) and became an Associate Professor at the University's Department of Medicine and the Director of the Department's Endocrine Diagnostic Laboratories.

Markus is an advisor to national and international research foundations and a member of the scientific advisory board of the International Osteoporosis Foundation. He is also a member of the editorial boards of several international journals.

Several of the current areas of research which are part of the Bone Research Program at the ANZAC Research Institute are described below.

### Preventing The Spread Of Malignant Tumours To Bone

Dr Colin Dunstan, a world-recognised bone researcher, was awarded the prestigious BioFirst Award to support his work on the mechanisms that govern the spread of malignant tumours, such as breast and prostate cancer, to bone. This work uses a novel animal model of metastatic bone disease developed by Markus Seibel's team in Germany.

Understanding the mechanisms of malignant spread to bone will help to develop more efficient strategies for the prevention and treatment of these painful and often fatal complications of many cancers.

### Genetic Influences on bone mass and bone turnover in healthy and osteoporotic men

Dr Christian Meier from the University of Basel, Switzerland joined the laboratory to undertake research on genetic factors in bone metabolism. This project is carried out in collaboration with Professor John Eisman and the Dubbo Epidemiological Study. The project is expected to shed light on the presently ill understood mechanisms causing osteoporosis in men, and is expected to provide opportunities for new and better prevention and treatment.

### Bone metabolism

Research is also underway into the mechanisms governing normal and abnormal bone metabolism. Using transgenic mouse models, the effects of cortisone on bone will be evaluated. A frequent adverse outcome of this widely used drug is severe bone disease. A better understanding of why cortisone is so damaging to bone will point the way to strategies for the reversal or prevention of its detrimental effects on the skeleton.

### Bone markers

All bone diseases are characterised by changes in bone formation and in bone resorption, the two major processes that keep bone alive, healthy and strong. Measurement of specific 'bone markers' in serum and urine determines the activity of these processes and can help the clinician assess the severity, and monitor the treatment of bone diseases such as osteoporosis. In collaboration with Clinical Associate Professor Michael Hooper, research is underway into the development and clinical validation of novel or improved markers of bone turnover. Present studies focus on the evaluation of bone turnover rates in the very elderly, the significance of androgens on bone health, the effect of anti-osteoporotic drugs on bone remodelling fracture rates in patients with osteoporosis, and the novel use of bisphosphonates on the healing of prostheses used for total hip replacements.





## Robert Cumming

Professor Robert Cumming has recently been appointed Professor of Epidemiology and Geriatric Medicine at Concord Hospital. This newly created Chair is the first of its kind in Australia and one of the few in the world to formally recognise the important contribution that epidemiology can make to improving the health of older people.

Robert graduated in medicine from the University of New South Wales in 1979. Following several years at Prince of Wales Hospital he worked in general practice in England and Australia before spending a year in Geriatric Medicine at War Memorial Hospital in Sydney. In 1986, Robert enrolled in the Master of Public Health Degree at the University of Sydney. He subsequently won a scholarship to study at Columbia University in New York, where his research work on health problems of older people began. Since returning to Sydney in 1990, he has worked in the School of Public Health at the University of Sydney.

Most of Robert's research has been in two areas: falls and fractures in older people and age-related eye diseases, particularly cataract. He has more than 150 publications and is well known for his work on the role of calcium in prevention of fractures and the importance of psychotropic drugs as causes of falls in older people. He also has an international reputation for his expertise in the design and conduct of randomized trials of non-pharmacological interventions for prevention of falls and fractures. Robert's research on cataract resulted in the first paper to report an association between use of inhaled corticosteroids and risk of cataract.

One of the research projects he is currently doing is a randomised trial of improving vision to prevent falls.

This project is based at Concord Hospital and will involve more than 1,000 people aged 70 years and over, recruited mainly from aged care services. He is also involved in randomised trials of hip protectors and of the use of Tai Chi to prevent falls. Another project is the Blue Mountains Eye Study, one of the world's largest epidemiological studies of eye diseases.

Future plans include a randomized trial of falls prevention in hospitals and a large observational study of the health of older men.

Professor Cumming is a member of the Centre for Education and Research on Ageing, as well as being a member of the University of Sydney's School of Public Health.



## Rosemary Burke

Rosemary Burke commenced as Director of Pharmacy at Concord Hospital in 2001 after seven years as Director of Pharmacy at the Wollongong and Port Kembla Hospitals. She has also worked at Prince Henry and St George Hospitals. Rosemary holds a Diploma of Education and is a fellow of The Society of Hospital Pharmacists of Australia (SHPA). She has been involved for many years in this society and was NSW Chairman for five years. Rosemary has also chaired the national committee of Specialty Practice in Hospital Pharmacy Management and is the current chairman of SHPA's Committee of Specialty Practice in Medication Safety. She is also a reviewer for the Pharmacy Board's graduate review panel.

Rosemary's major professional interests include education of health professionals and patients, and the quality use of medicines and medication safety. She has also been involved in a number of projects aimed at improving the continuum of care and developing communication networks with General Practitioners. She has been an invited speaker at many meetings and has presented on her areas of interest at a number of conferences.

In 2001 Rosemary received the SHPA Neil Naismith Baxter grant which is awarded to a hospital pharmacy manager who is considered to have contributed to the profession. With this support she undertook a study

tour of the United States focusing on the area of medication safety. The report of this visit has recently been published in the Journal of Pharmacy Practice and Research.

The pharmacy department at Concord has been involved in a number of practice research projects often in collaboration with other hospitals through groups such as the NSW Therapeutic Assessment Group. These include drug utilisation review and collaborative programs for quality improvement. The hospital joined the 2001 International Round-table Adverse Drug Events Improvement Collaborative (ADEIC). There were numerous projects involving the pharmacy department including work designed to ensure safer use of anticoagulants in the hospital.

The pharmacy department plays an important role in the review of clinical trials at Concord Hospital. The Hospital's Drug Committee acts as the scientific review committee and the department is involved in the management of suspected adverse drug reactions related to clinical trials. Apart from stock management and the institutional review process, the department is involved in literature searches and the importation of investigational drug material. Pharmacists are often called on to provide advice on the design of investigator initiated trials or randomisation methods. The department is able to offer aseptic reconstitution facilities for clinical trials based at the hospital. This service can cover a number of aspects including aseptic reconstitution, blinding of the investigator and the design and formulation of placebos.

Recently, Rosemary has been successful in obtaining a \$100 000 grant from the Australian Council for Quality and Safety in Health Care to carry out a study which aims to identify the reasons for adverse events from high risk drugs in elderly hospitalised patients. The study also aims to design strategies for preventing similar recurrences.

Rosemary hopes to facilitate more pharmacy practice based research programs at Concord. The department is well placed to both initiate and assist with a wide range of research activities centred around medication use.



## Biao Zeng

Dr Biao Zeng obtained his MBBS in 1984 and Master's degree in Cardiology from Tongji Medical University, China. From 1984 to 1993 he trained in Cardiology and worked in the Research Institute of Cardiovascular Disease, Union Hospital. From 1994 to 1997 he was funded by the Victor Chang Foundation to work in the Department of Cardiology, Royal North Shore Hospital.

In 1998 Biao enrolled as a PhD candidate, under the supervision of Dr David Brieger and Professor Ben Freedman in the Department of Cardiology, Concord Hospital. He was awarded an NHMRC Postgraduate Research Scholarship in 2000. In 2002 Biao was awarded the poster prize by the Cardiac Society of Australia & New Zealand (CSANZ) for his presentation at the XIVth World Congress of Cardiology in Sydney.

Biao's research interests include the investigation of neutrophil mediators of fibrinolysis in plasminogen knockout mice. This research, which is described in detail on page 16, was published as a paper titled "*Influence of plasminogen deficiency on the contribution of polymorphonuclear leucocytes to fibrinogenolysis*" in the *Journal of Thrombosis and Haemostasis* in 2002.

Biao has also been involved in research on the role of matrix metalloproteinases (MMPs) in patients with coronary artery disease (described on page 15). Results from this study indicated that circulating plasma levels of the gelatinolytic MMP-2 and MMP-9 were elevated in patients with symptomatic coronary disease. The strong correlation of MMP-9 levels with circulating levels of high sensitivity C-reactive protein (hs-CRP), suggests MMP-9 is a more sensitive marker of the systemic inflammatory process that underlies the pathophysiology of acute coronary syndrome.

Biao's research and clinical experience have given him broad insights into cardiovascular disease. He hopes to continue his research in areas that lead to the discovery and understanding of the mechanisms underlying cardiac disorders.



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## ANZAC Research Institute

### The ANZAC Research Institute

The ANZAC Research Institute was established in 2000 on the Concord Hospital campus in conjunction with the University of Sydney. The establishment of the Institute ensured dedicated research infrastructure so as to promote basic and applied medical research on the Concord Hospital campus.

The main research theme of the ANZAC Research Institute is ageing, with the long-term goal of prolonging enjoyable, independent living for the ageing population. As the only major independent biomedical research institute with a primary focus on ageing, the ANZAC Research Institute aims to co-ordinate the highest quality innovative research at all levels - from public and population health, to clinical research, molecular physiology (animal models) as well as cell and molecular biology.

Under the overall leadership of its Director, Professor David Handelsman, the major research groups of the ANZAC Research Institute are:

**The Andrology group** (leader: Professor David Handelsman) is conducting research into male reproductive health, medicine and biology.

**The Biogerontology group** (leader: Professor David Le Couteur) is studying age-related changes in the liver. It is proposed that these changes accelerate many of the major diseases (such as cardiovascular disease and osteoporosis) that accompany ageing.

**The Bone Biology group** (leader: Professor Markus Seibel) is studying bone disorders, especially osteoporosis and bone cancers.

**The Neurobiology group** (leader: Professor Garth Nicholson) has as its major research focus the identification of genes that cause neurodegenerative diseases.

**The Respiratory group** (leader: Dr Sam Lim) has been studying lung function and the effects of steroid treatment in major respiratory diseases such as asthma and chronic obstructive pulmonary disease. Following Dr Lim's recruitment by GlaxoSmithKline (UK) to head their respiratory clinical Research & Development, **the Vascular Biology group** (leader: Associate Professor Len Kritharides) has commenced research in a new laboratory. This group is studying the role of inflammatory factors in cardiac and vascular injury and ischemia, with the aim of improving early detection and developing better treatments for heart disease.





## The Centre for Education and Research on Ageing (CERA)

CERA is a multidisciplinary centre that aims to improve the health and quality of life of older people through research into ageing, diseases of old age and service delivery. CERA is a joint facility of the Aged and Extended Care Department of Concord Hospital and The Department of Medicine of The University of Sydney and is involved in education of aged care workers and students in many professional areas.

CERA is staffed by geriatricians, nurses, psychologists, scientists and other professionals who work together in health care delivery and research. CERA's director, Professor David Le Couteur, is a leading figure in geriatric pharmacology and he serves on a number of national committees including the Australian Drug Evaluation Committee.

In addition to the provision of in-patient and ambulatory care for Geriatric Medicine, CERA maintains a high profile in geriatric and gerontological research. The centre's research utilises laboratory, clinical and population methodologies and covers a broad spectrum of issues of significance to ageing. Research at CERA occurs in four main areas:

**The ageing liver** – Professor Le Couteur's team, at its laboratory in the ANZAC Research Institute, is studying age-related changes in the blood vessels of the liver, as these are thought to underlie a number of diseases which increase in prevalence with age (see also p32).

In particular, the team is examining how structural changes in the ageing liver can predispose to atherosclerosis, heart disease and stroke, all common diseases of the elderly. The ultimate aim of this research is the development of therapeutic strategies which prevent blood vessel changes in the liver and consequently prevent many of these debilitating diseases.

**Neurodegenerative disease** – The prevalence of dementia rises steeply with age, yet Alzheimer's disease and other causes of cognitive decline remain poorly understood. Dr Helen Creasey, Associate Professor Jillian Kril, Dr William Brooks and colleagues at CERA are studying the clinical, psychological, genetic and pathological aspects of brain ageing and dementia in communities and clinic based populations. A major outcome of this research is improved understanding of the risk factors for dementia and improved diagnosis of dementia. Another major recent discovery was the particular genetic defect that causes a dementia syndrome in a family that has been studied for decades at CERA.

**Population studies** - The recent appointment of Professor Cumming as the Chair of Epidemiology and Geriatric Medicine has brought internationally renowned expertise in research into falls, osteoporosis and medication usage in older people. This work has shown the importance of calcium in preventing osteoporosis, and the role of medications and visual impairment in falls in older people. In addition, the major epidemiological study of ageing, the Sydney Older Person Study (SOPS), has continued in collaboration with Professor Broe and Dr Creasey. This study has identified risk factors for neurodegeneration and clarified health service delivery needs of older people in the community.



**Residential and Community Care** - This area has been developed by Chris Shanley, (Assistant Director, Education and Information Services) to address the health care needs of older people in the community and residential care. In particular, the work has focused on the prevention of falls in residential care, advanced care directives in older people (similar to “living wills”), and the organisational strategies for establishing best practices in residential care facilities.



PhD candidate Sarah Hilmer at work in the laboratory

## Cardiology

The Cardiology Department has a strong and varied research profile. The Department undertakes clinical, laboratory-based and basic research into many aspects of cardiovascular disease.

### The GRACE Registry

Acute coronary syndromes, including the full spectrum from unstable angina to myocardial infarction (“heart attack”), represent a major cause of morbidity and mortality throughout the world. GRACE – the Global Registry of Acute Coronary Events – is a large, multinational, observational study of patients hospitalised with acute coronary syndromes (ACS). The aim of GRACE is to improve the quality of care for patients with ACS. The registry gathers information on the relationships between patient characteristics, treatment practices, and in-hospital and post-discharge outcomes at hospitals around the world. A total of 94 hospitals in 14 countries in North America, South America, Europe, and Australia/New Zealand are currently collaborating in GRACE. In Australia and New Zealand, the study is being coordinated by Dr David Brieger.

Information on patient demographics, medical history, acute symptoms, clinical characteristics, electrocardiographic (ECG) findings, treatment approaches, and in-hospital outcomes is collected. Patients are followed up by telephone at 6 months after hospital discharge. The information collected from the GRACE project has provided important and extensive insights into patient characteristics, current practice patterns, and outcomes for patients with acute coronary syndromes. Given the pressures of practicing evidence-based medicine in a cost-effective manner, the results of GRACE provide a multinational perspective into these important outcomes, and identify areas requiring improved patient care.

### The SPORTIF 3 Study

Atrial fibrillation is a common condition affecting 5% of the population over the age of 65. The danger of this condition is that people with it are at a greater risk of stroke, which can only be prevented by thinning their blood with anticoagulants. The only orally active anticoagulant available at present is warfarin. This is a difficult drug to use as it increases the risk of bleeding significantly. Furthermore the levels of warfarin in the blood are very sensitive to both diet and other medications so the blood levels must be constantly monitored, a major inconvenience for patients and doctors alike. Recently a new anticoagulant, Exanta, has been developed which appears to be safer and can therefore be used without monitoring. The SPORTIF 3 study is an international trial in 4,000 patients which compares treatment with warfarin versus Exanta. In Australia, this study is being conducted out of Concord Hospital under the direction of Dr David Brieger. Promising preliminary results suggest that this new therapy should be available in the near future.

### Echocardiography

Dr Kevin Fung, under the supervision of Associate Professor Len Kritharides, has investigated whether new ultrasound techniques can detect very mild and previously undetectable degrees of heart muscle damage. He found that reversible and irreversible weakness of the heart muscle can be detected using the technique of *Tissue Doppler*, and applied this technique to study patients undergoing electrical shock to revert abnormal heart rhythm. In addition, in a collaborative study with Clinical Associate Professor Alastair Corbett from the Department of Neurology, he investigated patients with myotonic dystrophy, a disease which causes widespread weakness of the muscles. It was found that *Tissue Doppler* could detect a reduction in heart muscle function well before weakness could be detected by conventional techniques.

### Liver Dysfunction in Heart Failure

In this study, Dr George Lau and Associate Professor Len Kritharides are investigating the build up of fluid in the liver which occurs in patients with heart failure. The ability to diagnose such build up would be improved by knowing the patterns of damage which are typical of



fluid build up, and the cardiac factors which contribute to it. This study to date has shown that the pattern of biochemical damage is the same as the pattern seen in patients with blockage of bile flow. Furthermore the biochemical changes are directly related to the severity of leakage across one of the heart valves, the tricuspid valve. This result may allow doctors to use liver imaging tests more sparingly and save patients inconvenience and time.

### Investigation of matrix metalloproteinases in patients with coronary disease.

Matrix metalloproteinases (MMPs) are enzymes involved in the breakdown of extracellular matrix components and have been implicated in both the development of atherosclerosis and in plaque rupture in acute coronary syndromes. However, few studies have examined the association between circulating MMPs and symptomatic coronary artery disease.

Dr David Brieger and colleagues measured plasma activities of MMP-9 and MMP-2 in healthy controls, and in patients with unstable and stable angina. In patients with stable angina, MMP-9 levels were significantly elevated relative to controls. In unstable angina patients, levels of both MMPs were significantly elevated relative to controls and patients with stable angina. This incremental elevation in patients with unstable angina may be of diagnostic utility and supports the role of MMPs in the pathogenesis of unstable coronary syndromes. Further studies investigating the mechanism and clinical significance of these findings are planned.

### Minimally-Invasive Detection of Coronary Artery Disease

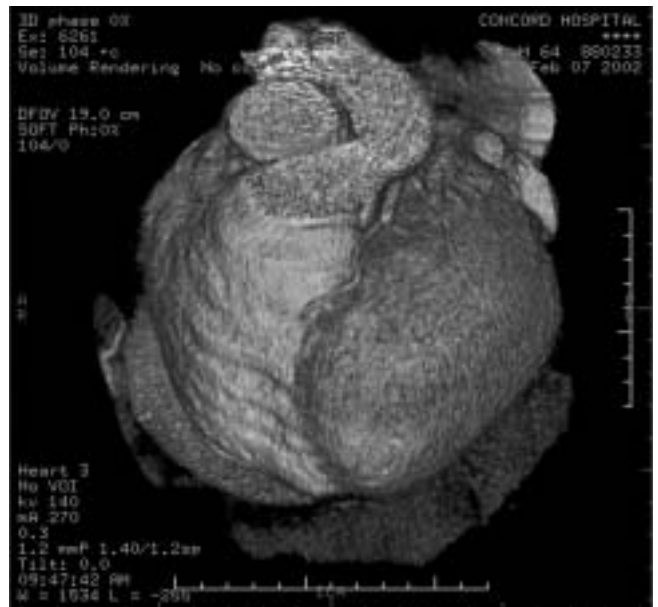
Computer tomography (CT) is a minimally-invasive technique to image coronary arteries. Recent refinements in image acquisition and analysis are currently being evaluated by the research team of Associate Professor Len Kritharides, Dr George Lau and Dr Lloyd Ridley from the Department of Radiology.

In this study patients underwent conventional coronary angiography followed by CT coronary angiography. The conventional angiographs and the CT angiographs were assessed to identify coronary vessels which have blockages (*stenoses*). Using the new CT method, stenoses were identified with 88% accuracy, with lower risk and inconvenience to the patients than

conventional angiography. This technique will allow the accurate assessment and classification of coronary artery disease in the majority of patients.



A study patient having a cardiac CT scan



Three-dimensional image of the heart by computer tomography (CT)



### Investigation of neutrophil mediated fibrinolysis in plasminogen knock out mice.

When blood clots (thrombi) form they are broken down by a process called fibrinolysis which most commonly occurs due to a protein called plasminogen. If no plasminogen is present then clots cannot be lysed. In order to study alternative, non-plasminogen dependent mechanisms of fibrinolysis, mice were bred which do not make any plasminogen (*Plasminogen knock-out mice*). In these mice it has been found that white blood cells contain non-plasmin fibrinolytic proteases, however the degree to which these cells contribute to clot degradation in these animals is not known.

Thrombi were generated in carotid arteries and jugular veins of *knock-out* and normal (*wild type*) mice by the application of a ferric chloride solution. White blood cells quickly accumulated in the thrombus and a greater number were retained within the thrombi of *knock-out* mice compared to the *wild type* mice providing the potential for more fibrinolytic enzymes to be present. In addition the researchers, PhD student Biao Zeng and Dr David Brieger, showed that white blood cells extracted from *knock-out* mice were able to break down fibrinogen to a greater extent than cells from *wild type* mice and that the fibrinogen breakdown products were distinct in the *knock outs*. These results suggest that a relatively greater role for white blood cell-initiated fibrinolysis exists in the setting of plasminogen deficiency.

## The Burns Unit

The Burns Unit at Concord Hospital was established as a statewide referral centre for burns injuries by the NSW Department of Health in the late 1980's. The Unit provides specialised treatment to complex burns cases under the directorship of Dr Peter Maitz in collaboration with Dr Peter Haertsch, Head of Plastic and Reconstructive Surgery. The Unit will soon move into a new location on the seventh floor of the Multi building. Here it will have a 17-bed treatment centre, dedicated Operating Theatre and a new skin laboratory. A multi-disciplinary team of researchers carries out its work in the Burns Unit

### The Skin Culture Laboratory

The Burns Unit tissue culture laboratory was established in 2001 to provide tissue for skin regeneration in severe burns patients. The laboratory has developed procedures for skin cell replacement (*keratinocyte grafting*), for the treatment of existing scars and the late resurfacing of burn wounds.

*Keratinocyte grafts* are prepared from healthy cells taken from an unaffected area of the patient and grown in the laboratory under specialised conditions (*cell culturing*). These are used to form skin sheets, or put into a liquid to spray over the surface of the wound, providing rapid healing with little scarring. Work in this laboratory has shown that the cultured skin sheets needed to resurface 20-25% of the body area can be produced in 16-18 days, and sheets to cover 90% of the body area can be made in 23-25 days. When cell sprays are used, it takes less than 2 weeks to culture cells to cover 25% of the body surface.

The laboratory has also prepared suspensions of cells, harvested from the patient, and sprayed them immediately onto the patient, without culture. These sprays are suitable for small area injury such as harvest sites, and have the advantage of also containing other types of skin cells including those which produce the pigment in skin (*melanocytes*), so that the natural skin colour is preserved.

As well as providing this clinical service for patients in Concord Hospital, the laboratory is working at improving both the clinical outcome of using cultured skin and the skin culture process. For the best cosmetic outcome, the cells should be applied to the wound as soon as possible after injury and the laboratory is working towards speeding up cell production time by growing islands of healthy cells on membranes or dressings which can be applied directly to the patient soon after injury. In this way the wound is closed whilst new skin is developing.

Other uses for *keratinocyte grafts* to be explored in the future include their use as biological dressings for the treatment of chronic skin disorders, such as vascular and diabetic ulcers, congenital naevi and small epidermal injuries.

**Investigations into skin graft infection and graft survival**  
Another focus of research interest in the Burns Unit has been in the area of skin graft infection.

Currently, the key surgical intervention in severely burned patients is the replacement of burned skin with skin grafts taken from healthy skin elsewhere on the same patient. Early excision of deep burns and immediate skin grafting have been shown to reduce fatality rates in severely burned patients, and improve functional outcomes by reducing scarring. Skin graft survival is important for good functional and cosmetic results and, in severely burned patients, for patient survival.

It is well recognised that infection is an important cause of graft failure in burn wounds. A study was undertaken to examine whether there is a clinically important association between biopsy evidence of infection in tissues underneath burned skin that has just been surgically removed, and subsequent skin graft survival.

Biopsies were examined histologically and were submitted for microbiological cultures. Subsequently, percent skin graft survival, graft infection, episodes of bacteraemia, and length of hospital stay were recorded for each subject.

Only a small proportion of patients' biopsies grew any organisms at all. The remainder of the biopsies showed no organisms, and only mild inflammation, consistent with a burn injury. The culture results did not correlate with skin grafting outcome. Of those with a positive culture only one (which grew *S.aureus*) required repeat skin grafting. Meanwhile, several patients who did require repeat grafting had biopsies which were negative on culture. The biopsies, therefore, do not appear to predict the risk of graft failure. Clearly there are other factors that have more influence on graft outcome. These may include general factors such as patient age, and local factors such as size and location of wounds.

### Physiotherapy research in the Burns Unit

Over the past five years, a number of projects have been conducted by the Senior Burns Physiotherapist, Dr Frank Li, to improve patient care.

It was observed that many burns patients with skin grafts to their hands showed a significant decrease in range of hand motion and strength when reviewed in the out-patient clinic 6 weeks after discharge. A study was conducted to test grip strength using a hand held dynamometer. All patients with skin grafts to their hand(s) were tested at regular intervals for 3 months. It was found that their grip strength improved steadily after surgery until about 2 weeks after discharge, then a decline occurred. Unless the patient had regular hand therapy treatment, the decline would continue for 4 to 6 weeks. The results demonstrated that this group of patients requires regular follow-up for at least the first three months following their discharge.

Burns patients experience a great deal of pain throughout their recovery phase and are reluctant to exercise because movement aggravates the pain. Physiotherapy treatment targets this problem by a program of daily stretching exercises. In order to walk properly, a range of movement of the knee of about 120 degrees is required. A Continuous Passive Motion

machine, which is used by patients with Total Knee Replacement to improve knee range, was trialled on burn patients. Patients with lower limb burns, who required skin grafts to both legs, were invited to participate in the study. The Continuous Passive Motion machine was used on one leg while the other leg received passive stretches only. The results indicated that there was no difference in terms of range achieved. However, the patients felt less pain with the use of the Continuous Passive Motion machine. This positive result supports the proposal to purchase Continuous Passive Motion machines in the development of the burns service in New South Wales.

### Occupational Therapy in the Burns Unit

Scar management is one of the major tasks in the long-term management of burn patients. The therapeutic value of customised pressure garments in the management of scarring after burn injury is well documented. However, most patients find pressure garments uncomfortable to wear. Researchers, Michelle Carne and Cheree Walker, are undertaking a study to identify the most appropriate and cost effective pressure garment manufacturer from 3 major Australian suppliers. Participants in the study compare two different brands of pressure garment by wearing them on alternate days and completing satisfaction questionnaires after 2 weeks and 3 months. The occupational therapist also makes an evaluation of the effectiveness of the garment, and results on the outcome will be available in 2003.



## Breast Cancer

Last year in NSW, over 4000 new cases of breast cancer were diagnosed. Concord Hospital researchers are involved in research studies which look at promising new approaches to improve breast cancer treatment and quality of life.

### Treating Cancer with Chemotherapy

Sydney Cancer Centre at Concord Hospital is an active participant in international breast cancer research trials, accruing patients from both Concord Hospital and Strathfield Private Hospital. These trials are called 'adjuvant' therapy trials, which means that they are testing the value of additional treatment after surgery for breast cancer. Giving treatment at this time can improve the chance of cure.



Appearing from left to right: Ms Lili Truong (Clinical Trials Data Manager), Mrs Sumitra Nidagal (receiving Herceptin treatment), Dr Anne Sullivan (Oncologist), Ms Chantal Gebbie (Clinical Trials Nurse)

In 2000-2001, 17 women were recruited to International Breast Cancer Study Group trial 20, which compared a standard adjuvant chemotherapy to adjuvant chemotherapy including the new drug docetaxel, in women with breast cancer that had spread to lymph nodes in the axilla (armpit). The trial is

now closed and the first results should be available in May 2004.

Currently, Concord Hospital is involved in two Breast Cancer International Research Group (BCIRG) trials. Trial 6 is examining the addition of Herceptin® to chemotherapy for women with breast cancer which is positive for the HER2 oncogene (15 – 20% of all breast cancers). It is known that breast cancers positive for HER2 are more aggressive, and have a worse prognosis. Herceptin® is an antibody which binds with and inhibits HER2. It has been shown to be of significant benefit to women with metastatic breast cancer, and the current research is examining its role in addition to adjuvant chemotherapy in an international randomized trial. Internationally, 700 women are already participating and accrual will be complete in about 12 months when just over 3000 women will be enrolled.

In 80% of women breast cancer is negative for HER2. These patients are offered participation in BCIRG trial 5, which is testing sequences of giving chemotherapy drugs. Internationally, 1,800 women are already participating and accrual will be complete by the middle of 2003 when just over 3000 women will be enrolled.

### Research into Surgery for Breast Cancer: The "SNAC" TRIAL

The major morbidity from surgery for breast cancer is related to removal of the lymph glands in the armpit (or axilla).

The SNAC (Sentinel Node biopsy vs Axillary Clearance) trial has been set up with a view to minimising the extent of surgery in this area. The trial is being carried out in hospitals around Australia under the auspices of the Royal Australasian College of Surgeons and the National Health and Medical Research Council Clinical Trials Centre. At Concord, the trial is being carried out by Professor David Gillett and his colleagues from the Department of Surgery. Approximately 5 percent of the patients involved in the study have come from the breast service at Concord Hospital and Strathfield Private Hospital.

In 60 to 70 percent of breast cancer patients the axillary nodes are not affected by metastatic cancer and, therefore, do not require removal. It is essential,

however, to know if these glands contain cancer or not and in the past, it has been practice to remove at least two thirds of them to determine the likelihood of their involvement.

The SNAC trial has been set up using a technique to define the pathways along which cancer cells will travel from the tumour to the lymph glands and to define the most significant lymph gland or *sentinel node*. It is believed that if this gland is free of tumour all the other glands will be free of tumour and that removing only this gland will adequately determine the status of the axillary nodes in general. It is proposed that removing one gland will produce much less morbidity than removing two thirds of the glands. Preliminary studies have indicated this to be the case and the SNAC trial is a randomised prospective trial to conclusively prove that the patients are not disadvantaged by having only this gland removed (if it is free of tumour) and not having any treatment to the other glands in the axilla.

To date some 600 patients have been randomised into this trial. It is expected that accrual of 1000 women will be complete towards the end of 2003. The initial data analysis has been done and shows that the sentinel node can be identified in 100 percent of cases and that cancer has been detected in 30 percent of patients as expected.

The success of this trial is dependant on cooperation between the surgeons, the radiologists and the Nuclear Medicine personnel who inject radioactive material next to the tumour to define and mark the sentinel node.

#### Quality of Life for patients with Breast Cancer

Research into treatments for breast cancer involves not only measures which improve patient's length of life but also their quality of life.

Minh Arvin, Clinical Nurse Consultant for Breast Surgery at Concord Hospital has been looking at the quality of life for women receiving Tamoxifen adjuvant therapy following surgical management of breast cancer.

Patients were surveyed for sociodemographic information (age, marital status, level of education, employment status, number and age of children,

menopausal status) and information relating to their breast cancer history. At the same time, patients were asked about their quality of life, physical symptoms, general and psychosocial well-being and daily functioning. Information was collected from patients regarding their Tamoxifen treatment (eg side effects), how they adjusted to their breast cancer diagnosis and treatment, and the effect of both on family and friends. A majority of women with breast cancer who were prescribed Tamoxifen did well following the completion of their surgery and chemotherapy. This information may be helpful for newly diagnosed women, and for women facing the end of treatment. However health carers should be alert for continuing symptoms of distress in follow-up care, such as symptoms of depression or social dysfunction. Early intervention may help to reduce subsequent problems. Interventions, such as stress management, relaxation, counseling and support for the family can improve mood, physical functioning and quality of life in breast cancer patients.

Many women complained of menopausal symptoms with Tamoxifen. These included fatigue, hot flushes, sleep disturbance and depression. Although most women tolerate these symptoms and are able to remain active, others find it can have an impact on their quality of life or functional ability. Some women have considered discontinuing therapy, or have been less compliant with their daily Tamoxifen regimen.

Many women experienced positive effects from breast cancer. Coming to some understanding of and finding a new sense of meaning in their illness experience may be an important aspect of the recovery process. These women have developed personal resources and skills, and their positive attitudes greatly enhance their coping and adjustment. Many women reported improved outlook on life and stronger interpersonal relationships.

It is hoped that the results of this study can be used to inform clinicians, researchers and breast cancer survivors about the longer-term impact of Tamoxifen on health and related quality of life.

## Brain Diseases

Researchers from the Department of Neurology, Molecular Medicine and the Centre for Education and Research on Ageing (CERA) are investigating diseases of the brain which occur more frequently as we age.

### Parkinson's Disease

The Parkinson's Disease Clinic in the Department of Neurology offers a comprehensive multi-disciplinary service to patients and their carers, and provides a focus for clinical research into the disease.

The clinic's director, Dr Michael Hayes, in collaboration with researchers from both within the hospital and outside, is looking at ways of measuring neuronal (nerve cell) damage in patients with Parkinson's Disease. These studies include blood tests, magnetic resonance imaging (MRI) and a smell test, since the loss of smell is an early finding in many patients with Parkinson's Disease. Early diagnosis of Parkinson's Disease will become very important once more effective treatment is available.

The Parkinson's Disease clinic is also involved in two international, multi-centre, Phase III, randomised, placebo-controlled trials of new drugs. Both of these drugs act to stimulate chemicals in the brain which are depleted in Parkinson's Disease (the dopamine system). One of the studies involves patients whose response to standard therapy has become less predictable and requires supplementation. The other is aimed at people with early Parkinson's Disease who have had little drug exposure and are being tested with a medication in the form of a patch that is only changed once daily. Both studies are funded by major pharmaceutical companies and offer valuable opportunities for Parkinson's Disease research. Patients have access to drugs that are not otherwise available in this country and they usually learn more about their condition; doctors get first-hand experience in assessing new medications and if the drugs prove to be useful this local experience is likely to

assist in getting PBS approval.

The pathogenesis of Parkinson's Disease is also being studied by the Molecular Medicine Laboratory, under the direction of Professor Garth Nicholson, who is researching the genetics of the disease. Only a few causative mutations for Parkinson's Disease have been identified, including one in the so-called *parkin* gene. Researchers are screening the parkin gene for deletions, which may cause a sporadic (or the recessive) form of Parkinson's Disease. To date they have found some undescribed mutations which may be a cause of isolated cases of Parkinson's Disease.

### Stroke

The Stroke Unit and Stroke Service at Concord Hospital were established in 1996, the second of their kind in NSW. The Stroke Unit, directed by Clinical Associate Professor Alastair Corbett, has facilitated the study of patients with stroke and has participated in a number of national and international trials for the management and prevention of stroke. Currently the unit is participating in two international, multi-centre drug trials. One study is assessing the potential benefits of the antihypertensive drug Ramipril (a drug which lowers blood pressure) by itself, or in combination with another antihypertensive drug Telmisartan. Another study is investigating the usefulness of Telmisartan alone in preventing stroke and other vascular complications in patients who have already experienced stroke or myocardial infarction (*heart attack*).

The Stroke Service is also assessing improved methods for patient management and looking at some of the outcomes of stroke, including vascular dementia.

### Vascular Dementia

Associate Professor Jillian Kril from the Centre for Education and Research on Ageing (CERA) in collaboration with Associate Professor Corbett and other neurologists and geriatricians across NSW, is studying brain pathology in patients with vascular dementia. Professor Kril and colleagues run a brain donor program where interested individuals consent to the use of their brain for research following their death. This program, which has been running for over ten years, studies patients with a variety of

neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease as well as those with stroke. The program also looks at the brains of normal, aged subjects.

Recently, Professor Kril and colleagues have shown that one of the primary memory areas of the brain, the *hippocampus*, undergoes substantial degeneration in vascular dementia. It was previously thought that this region, which is markedly damaged in Alzheimer's disease, is spared in vascular dementia. However, the results of this study suggest that memory impairment is a feature of vascular dementia and that significant overlap in clinical symptoms between Alzheimer's disease and vascular dementia might be expected.



A computer tomography (CT) scan of the brain of a patient who has had a number of strokes.



## Respiratory Diseases

Chronic Obstructive Pulmonary Disease (COPD) is a lifelong inflammatory disorder of the lungs that is ranked third behind heart disease and stroke as a major cause of disability and early death in Australia. The prevalence, morbidity and mortality of COPD are increasing in many western countries. COPD results in the deaths of over 5000 patients per year in Australia and serious disability occurs in many more. Chronic cigarette smoking is the main cause of COPD. Currently, there is no cure for COPD nor is there any treatment available to reverse the lung damage or the decline in lung function. COPD is one of the major focuses of research carried out in Respiratory Medicine at Concord Hospital.

Cell culture experimentation: The Expression of Matrix Metalloproteinases (MMPs), Tissue Inhibitors of Metalloproteinases (TIMPs) and Cytokines from Alveolar Macrophages in COPD.

Inflammatory cells in the lung called alveolar macrophages are increased in number in the lungs of those who smoke. These cells can produce substances called cytokines and matrix metalloproteinases (MMPs), which can destroy the lung tissue and thus may be important in the development of COPD. Tissue inhibitors of metalloproteinases (TIMPs), also produced by alveolar macrophages, inhibit the action of MMPs and thus may be protective against lung damage.

Dr Linda Seeto is investigating whether there is an

overproduction of pro-inflammatory cytokines and MMPs and/or an imbalance between the pro- and anti-inflammatory substances produced in the lung in cigarette smokers who develop this disease (see Figures 1 and 2).

Alveolar macrophages are harvested from two sources: lung specimens removed during surgery and lung washings performed via fiberoptic bronchoscopy. The cells are cultured in the laboratory and stimulated with various drugs including steroids, bronchodilators, and beta-blockers which inhibit the effect of bronchodilators. Levels and activity of MMPs and TIMPs are measured by two techniques: enzyme linked immunosorbent assay and zymography. Cytokine levels are measured by the former.

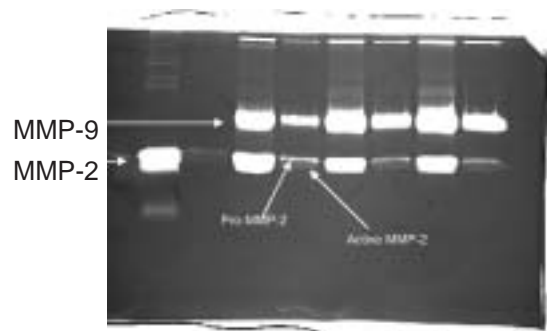


Figure 1: MATRIX METALLOPROTEINASES (MMPs) IN COPD SUBJECT Zymogram showing areas of enzymatic digestion by MMPs (white bands) from lung macrophages from a patient with COPD. The band size reflects the amount of enzymatic activity. Pro-MMP in vivo is the inactive form of MMP-2.

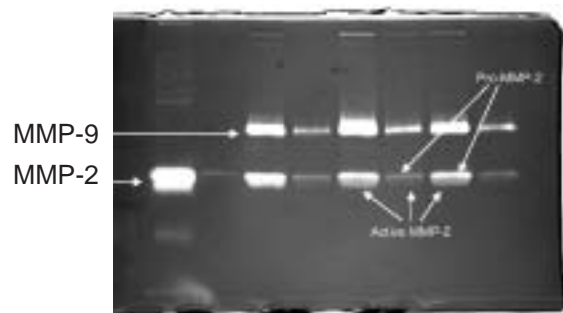


Figure 2: MATRIX METALLOPROTEINASES (MMPs) IN CONTROL SUBJECT Zymogram showing MMP activity from lung macrophages from a subject without COPD. Smaller band size reflects lower levels of enzymatic activity.

## A clinical study of theophylline as treatment for COPD

Theophylline has been shown to be effective in dilating the airways in people with asthma. Although an inexpensive and effective drug, theophylline can be associated with side effects such as gastrointestinal upset and abnormal heart rhythms. In cell culture studies, theophylline has been shown to be anti-inflammatory at doses below that required for airway dilatation in people with asthma.

Dr Seeto's study, the first of its kind, seeks to define changes in lung function, quality of life, and airway inflammation due to theophylline treatment versus placebo in subjects with COPD. If theophylline is shown to be anti-inflammatory in people with COPD, this will be the first evidence in clinical trials that it can be useful in the management of patients with COPD for its anti-inflammatory effect.

## Laryngopharyngeal Sensitivity in COPD

Members of the Concord Hospital Respiratory Investigation Unit have been using a multi-disciplinary approach to investigating the relationship between swallowing function and COPD. This research is being carried out by Nicola Clayton (Speech Pathology) and respiratory physicians, Clinical Associate Professor Matthew Peters and Dr Alvin Ing.

Preliminary studies have shown that swallowing function is impaired in patients with COPD, and this may lead to increased pulmonary infection through aspiration and inhalation of food and gastric contents. Pulmonary infection is regarded as a major cause of COPD exacerbation, and a major factor in the decline of lung function and increased morbidity in these patients.



A volunteer undergoing the FEELSS test

The aims of this study were to use a newly developed technique to assess the degree of swallowing impairment in patients with COPD as well as to assess laryngeal sensitivity. The ultimate aim is to establish a simple method of assessing swallowing function and aspiration risk at the bedside.

Patients with COPD underwent the new technique known as Fiberoptic Endoscopic Evaluation of Laryngeal Sensitivity and Swallowing (FEELSS). This procedure involves the delivery of a quantifiable pulse of air to the larynx via a fiberoptic nasoendoscope, which then induces the Laryngeal Adductor Reflex (LAR). The LAR is an airway protective mechanism and is assessed by the visualization of the vocal cords adducting (drawing together). In normal subjects an air pulse of 2.5 to 4.5 mmHg is sufficient to induce the LAR. In patients with COPD, air pulses of 9.9 mmHg were required to induce the LAR. This implies COPD patients have impaired laryngeal sensitivity and are at risk of aspiration and recurrent pulmonary infection.

The second part of the study involves assessment of swallowing. Under direct visualisation of the larynx via the nasoendoscope, COPD patients swallowed fluid and solids of varying consistency. The passage of food and fluid into the oesophagus was directly observed. Evidence of laryngeal penetration (material entering the laryngeal vestibule above the level of the vocal cords) and aspiration was observed and recorded. COPD patients were found to have a higher incidence of aspiration and swallowing difficulties than control subjects.

This study found that COPD patients have impaired laryngeal sensitivity and impaired swallowing function, which places them at risk of recurrent pulmonary infection. The researchers also found that this new technique is reliable and easy to use in the ward situation. By applying this technique to a larger group of COPD patients, they hope to predict which patients are at risk of recurrent infection and COPD exacerbations, and prevent this with diet modifications and swallowing therapy.

## Asthma

Asthma is a major focus of respiratory research at Concord Hospital. Associate Professor Matthew Peters from the Department of Thoracic Medicine is co-ordinating a series of clinical trials looking at new treatments which may lead to improvements in the management of this complex disease.

One such trial is investigating a new drug which acts by blocking a specific enzyme involved in the inflammatory process of asthma (called phosphodiesterase 4). In a second trial another new type of anti-inflammatory medication (aimed at blocking specific inflammatory cells and their proteins) will be tested in people with mild to moderate asthma. Both trials will use medication in tablet-form, and not the traditional inhaler or "puffer" form.

In a third clinical trial, also commenced in 2003, a new inhaled preventer medication will be assessed to determine its effectiveness in asthma management. A second aim of this study is to examine the frequency and occurrence of side effects from the medication in comparison to other inhaled steroids currently available on prescription.

## A nurse initiated discharge plan in the Emergency Department to improve the management of patients with asthma

Asthma is a significant problem in the community, with one in ten adults affected by the disorder. Over 20,000 asthma admissions to hospital are recorded nationally every year. Of these, 9% will be readmitted within 28 days and 34% within one year, resulting in considerable economic costs.

A team of researchers led by Julie Munro and Margo Richardson have undertaken a study to try and reduce hospital re-presentations due to asthma, following the implementation of a nurse-initiated discharge plan in the Emergency Department. The discharge plan consists of an education program for staff and patients, the provision of an individualised Asthma Action Plan, education on correct use of medication devices and peak flow meters, a follow up medical appointment and a nurse follow up phone call 2-3 days post discharge.

A retrospective medical record audit will establish past

management practices and re-presentation rates to the emergency department, and these will be compared with data from those patients who have received the specialised discharge plan. It is hoped that this will a) increase the number of patients with asthma who have an Asthma Action Plan and regular medical follow up, and b) decrease the number of patients with asthma who re-present to the emergency department. Findings from this study could also be used to influence policy and practice related to discharge planning in the Emergency Department.

## Andrology

The Department of Andrology at Concord Hospital is the first Department of its type in Australia catering specifically to men's reproductive health.

### Therapeutic use of androgen in the older man

The Department has performed a number of novel studies examining the therapeutic use of androgen (male hormone) in older men as a way to potentially reduce frailty and disability. These studies aim to determine whether androgen therapy can improve quality of life for community-living, healthy older men by improving physical functioning (including enhanced muscle strength) or by improving balance and walking endurance. Importantly the safety of such treatment was also of prime importance in these studies.

In a series of clinical trials of 3 months duration, two novel hormone preparations were studied: (1) the most powerful naturally occurring androgen (dihydrotestosterone) made into a gel to allow daily administration on the skin and (2) a new, genetically engineered, hormone (hCG), not yet available for routine treatment, which can be conveniently self-administered twice weekly. These studies used a special design, called *randomised placebo controlled* design. This guarantees that they are of the highest quality and most persuasive to the peer scientific community. In both studies, an increase in muscle and a reduction in fat were found. But the improvement in muscle strength was only modest and there was no detectable change in physical function. The studies showed that in the short term, these treatments caused no adverse effects on either the cardiovascular system or the prostate.

In another important study (also a *randomised placebo controlled* study) the Andrology group examined in greater detail the potential safety of high dose standard testosterone injections on sleep and breathing in older men. They showed for the first time that high dose therapy could shorten sleep and worsen breathing in

community-living, healthy older men thereby raising safety concerns regarding high dose standard testosterone injection therapy. This study was honored by an invitation for presentation as the first of only 4 oral presentations, at the prestigious Clinical Trials Symposium of the US Endocrine Society Annual Scientific Meeting in San Francisco, California.

### Male Hormonal Contraception

The staff of the Department of Andrology have been involved in groundbreaking studies to develop a hormonal male contraceptive over the last 15 years. Currently the only male contraceptive methods are condoms, vasectomy, abstinence and the withdrawal method. None are ideal: vasectomy is reliable but not readily reversible; condom use and withdrawal are often unreliable and not popular among couples in stable relationships. For these reasons, there is a pressing need to develop a male contraceptive method which is reversible, reliable and safe. Such a method would allow couples to share more equally in family planning responsibilities. Landmark studies performed under the auspices of the World Health Organisation (WHO), with the Department of Andrology as its largest centre, proved during the 1980's and 1990's that a safe and reversible male hormonal contraceptive was feasible. Although successful, this early study required weekly injections of testosterone, and was therefore impractical for community use.

Since then, the researchers have pursued the idea of using depot combination hormonal preparations. These preparations are combinations of 2 or more hormones and are long acting. (Instead of weekly injections, only a single visit to a clinic every 4 months for treatment is required).

A two-centre Australian study, led by the Department of Andrology, has recently completed a study of the combination hormonal preparation and established clearly that the approach is feasible. This new treatment proved much more effective than condom use, and at least as reliable as female hormonal contraception. This research is a major contribution to the development of a practical male contraceptive. Future practical developments of contraceptive products will require pharmaceutical company involvement, now that academic researchers have proved that a safe, depot hormonal male contraceptive is feasible and effective.

## Urology Research

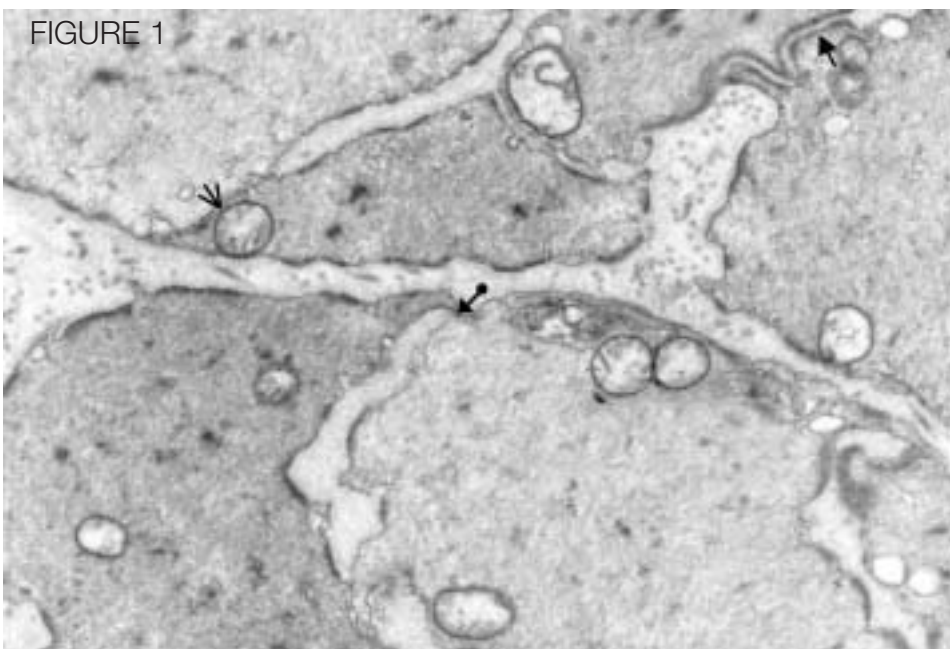
One in five people over 40 may suffer from urinary frequency, urgency or incontinence, a condition termed the ‘overactive’ or ‘unstable’ bladder. Although medical disorders such as stroke, Parkinson’s Disease or spinal cord injury may cause symptoms of the overactive bladder, in the majority of people the cause is unknown.

**The ultrastructural basis of voiding dysfunction**  
 The Detrusor Ultrastructure Group, led by Dr Lewis Chan and comprising members of the Urology Department, the Electron Microscopy Unit, and scientists from the University of Sydney, has been investigating the cause of this common and often debilitating disease.

The project “Ultrastructural Basis of Voiding Dysfunction” has been focusing on the structure of the bladder muscle in normal and overactive bladders. Using the electron microscope, this group has demonstrated the presence of abnormal connections between bladder muscle cells in patients with overactive bladder (see Figure 1).

It is postulated that these abnormal ‘gap junctions’ may act as short circuits and allow electrical activity in a muscle to spread to its neighbours and cause an involuntary bladder contraction resulting in urgency or urge incontinence.

The group’s recent study using a molecular biology technique has demonstrated that there are higher levels of gap junctional proteins (called *connexins*) in these unstable bladders. The researchers are currently trying to identify the exact type of connexin protein present at these abnormal gap junctions. In future, drugs targeting these proteins may offer a novel treatment for patients with overactive bladder.



Types of Junctions  
 Protrusion (●→)  
 Ultraclose abutment (—→)  
 Normal intercellular (—→)

A view of the bladder under the electron microscope. Protrusion and Ultraclose abutment junctions are postulated to act as low resistance electrical pathways which may play a role in the pathophysiology of detrusor instability. (x 29900)

## Research into Pain Relief

Several teams of investigators at Concord Hospital, from a number of disciplines, are undertaking research into pain and pain relief.

### Prevalence of pain in a teaching hospital (Department of Palliative Care)

A number of studies in the past have suggested that many patients in hospital experience pain. Dr Ghauri Aggarwal and colleagues from the Department of Palliative Care are investigating this finding to establish how common pain is at Concord Hospital. They are interested in whether patients report pain to nursing or medical staff, and if so, whether adequate pain relief (*analgesia*) is used.

In addition, the researchers are using an interview-style questionnaire called *the brief pain inventory* as well as a self-administered questionnaire to look at the impact of pain on the functional ability of the patient. Medical students are involved in administering part of the questionnaire, including recording patient characteristics.

Early results of the study indicate that about 60% of patients in hospital experience pain. This pain is mild to moderate in intensity and interferes with quality of life to a moderate degree. However, under-treatment with analgesics or under-reporting of pain to medical staff is not common. Studies of this type allow researchers to assess the adequacy of pain management in the hospital setting.

### Continuous wound infusion with ropivacaine using the OnQ/Painbuster system following thoracotomy (Department of Anaesthetics and Pain Management)

In 2001 Dr Janet Smith, from the Department of Anaesthetics led a team of investigators which trialled a new pain management procedure following thoracotomy.

Thoracotomy (an incision to the chest wall made during surgery) is a very painful procedure, and it is often necessary to use several different types of analgesia to make patients as comfortable as possible (*multimodal analgesia*). The mainstay of analgesia is morphine, or another similar opioid, usually delivered by a patient-controlled analgesia machine, but in addition local anaesthetics (intercostal nerve blocks) are also used which anaesthetise the wound for several hours postoperatively. Once the blocks wear off, opioid drugs used alone in sufficient doses to control the pain often produce unpleasant side effects such as nausea, vomiting, or drowsiness.



Mr Arthur Darnley of Auburn received both patient-controlled analgesia (opioid) and local anaesthetic delivered by the Painbuster device to optimise analgesia after his operation.

This study aimed to see whether the continuous infusion of ropivacaine (a long-acting local anaesthetic) into the wound for 2-3 days would increase patient comfort, and decrease the amount of morphine needed. The investigators used a simple, commercially available infusion device, the OnQ™ device (which is now marketed as Painbuster™). The device consists of a distensible elastomeric balloon, which infuses drug at a constant rate through a simple restrictor tubing (Figure 1).

The investigators studied a total of 40 patients who had catheters placed in the posterior part of their wounds, near the intercostal nerve, before the wound was closed. Half the patients received ropivacaine, and half received normal saline at a rate of 5mls/hour via the catheter for 2-3 days after their operation. All patients were able to use as much morphine as needed from their patient-controlled analgesia machine. The investigators collected information on how much pain the patients had (using pain scores at rest and on coughing), how much morphine was used on each of the first two days, and what side effects occurred.

Physiotherapists assessed how well the patients performed physiotherapy, and patients were also asked to rate how easily they could do their physiotherapy, which is an important part of recovery from the procedure.

The study found that a much higher proportion of patients receiving ropivacaine were able to use very low amounts of morphine, and had far fewer side effects (Figure 2). The physiotherapists did not detect any difference in actual performance of physiotherapy, but a higher proportion of patients receiving ropivacaine

reported finding physiotherapy easy or very easy to perform. There were no complications or side effects attributed to the infusions.

This study has demonstrated a safe, simple and effective way to improve patient comfort after thoracotomy

### Pain relief following back surgery (Department of Neurosurgery)

The success rate for the surgical treatment of ruptured lumbar discs is directly related to the early mobilisation of the patient after surgery. This in turn is related to the effectiveness of post-surgical analgesia. Current methods of pain control are generally effective, but have less desirable side effects such as making the recipient drowsy.

It has long been known that morphine applied directly to the spinal region (epidural space) is an effective analgesic, but it is rapidly absorbed and has a short duration of action. One of the risks of this type of delivery is suppression of respiration. Morphine may instead be delivered by a tube into the region, but this method introduces the risk of infection.

The present study being conducted by Clinical Associate Professor Noel Dan and colleagues from the Department of Neurosurgery, is testing a morphine paste applied directly to the epidural space. This study, which is being conducted in collaboration with the paste's manufacturer, The Bard Corporation, is examining whether the morphine paste will provide satisfactory pain relief with a lower risk of complications. The success of the technique is assessed by carefully monitoring the quantity of other analgesics used during the six weeks immediately following surgery.

Preliminary results indicate that the use of other painkillers is reduced following surgery. Furthermore, an assessment of the cost effectiveness of delivering the analgesia by the epidural route indicates that it is competitive with other methods.

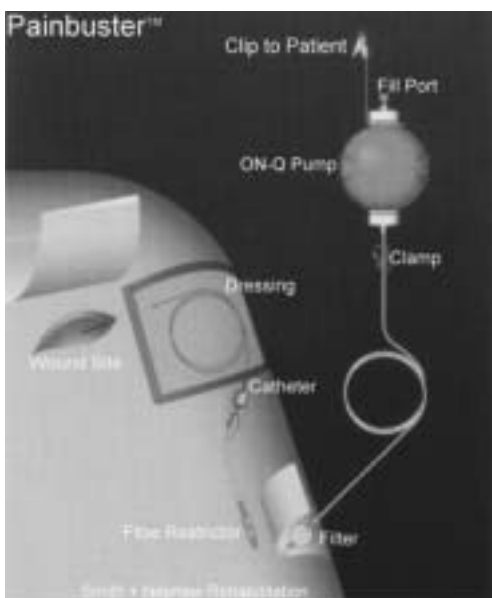
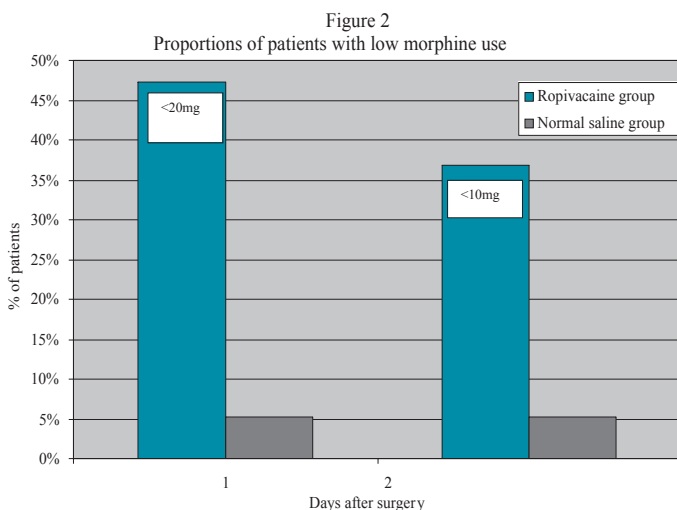


Figure 1 The Painbuster™ continuous infusion device (courtesy of Smith+ Nephew)





## Orthopaedic Research

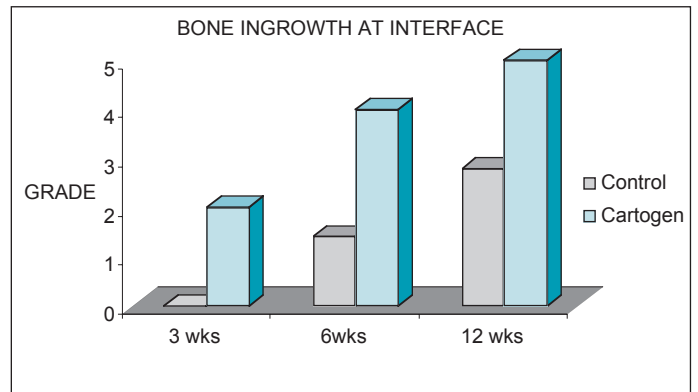
Dr Warwick Bruce, an orthopaedic surgeon, has major research interests in the areas of Sports Medicine and Joint Replacement.

### Sports Medicine Research – anterior cruciate ligament reconstruction

A large part of Dr Bruce's research has looked at improving anterior cruciate ligament reconstructions of the knee, particularly where the tendon is in contact with the bone. The aim of this research is to use different methods to improve bony ingrowth into the tendon. If bone grows more rapidly into the tendon, then the patient is able to rehabilitate more quickly and get back to sport more quickly.

An initial study was to assess the improvement of anterior cruciate ligament grafting in sheep by adding growth factors. Whole blood was taken from the sheep and concentrated using a special filter which gave a concentrate of growth factors. An anterior cruciate ligament reconstruction was then performed on the sheep and growth factors were injected into the bony tunnels. The growth factors had a positive effect on the healing tendon bone interface with improved strength of the graft and improvement in the radiographic appearance of the tunnel.

The next stage of the study was to use low dose ultrasound (Cartogen) on sheep after cruciate reconstruction. The sheep had a standard cruciate ligament reconstruction and then had an ultrasound device strapped to their knee for approximately 20 minutes each day. There was rapid improvement in bone ingrowth into the tendon in both the femur and the tibia. The benefit of this research is that people who have anterior cruciate ligament reconstruction can shorten their rehabilitation time and their return to sport by attaching an ultrasound to their leg in the recovery period.



Twenty minutes ultrasound treatment per day rapidly improved bone ingrowth into the tendon after surgery to the knee in sheep.

### Testing new joint replacements

Dr Bruce also researches new joint replacements that are put on the market, to assess their performance before they are used in a patient. This involves using pressure measurement devices to see that there are not areas of high pressure which may lead to premature wear of a knee or hip replacement.

The investigators also carry out computer modelling to see how the hip and knee replacements will affect bone over a long period of time. Some joint replacements are so rigid that they do not stress the patient's bone evenly and can lead to loss of bone over many years.

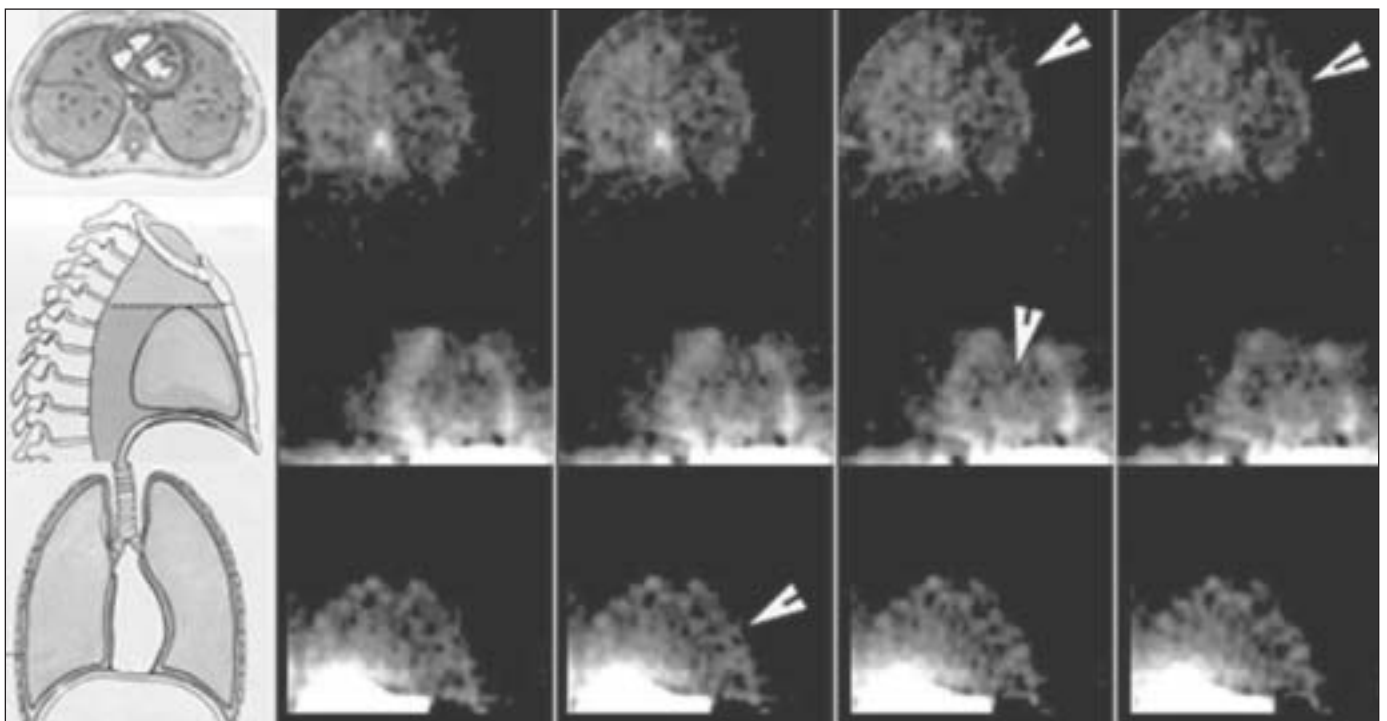


## Distinguishing fat emboli from pulmonary emboli after joint replacement surgery

Another major study has examined the incidence of fat emboli and pulmonary emboli after joint replacement surgery. After a joint replacement, fat can be released into the blood vessels of the leg and travel to the lungs and cause respiratory distress to the patient (*embolisation*). Another possibility is that blood clots can be released into the vessels and travel to the lungs. Until now, it has not been possible to tell the difference between emboli of blood or fat.

complication rate after joint replacement surgery is significantly decreased. This has major implications for joint replacements in the future.

In collaboration with Dr Hans Van Der Wall, Department of Nuclear Medicine, the investigators have developed a test that can be performed postoperatively if patients have respiratory complications. This test will tell doctors whether a patient has a fat embolus or a blood clot. The advantage of knowing this is that a fat embolus does not need to be treated with blood thinning agents, whereas the blood clot does. Doctors therefore do not have to use blood thinning agents on patients who have fat emboli, which means that the



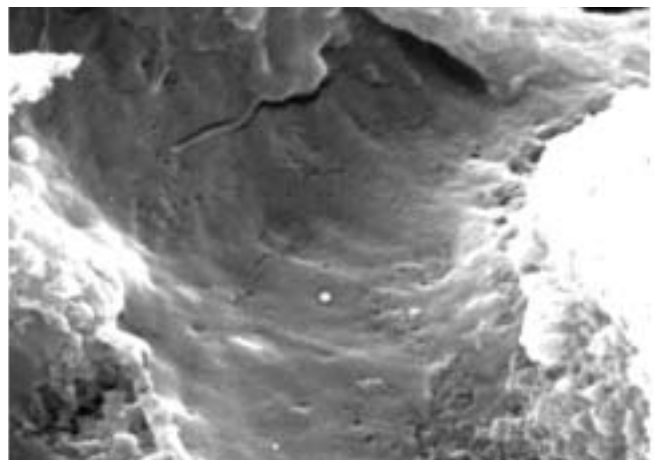
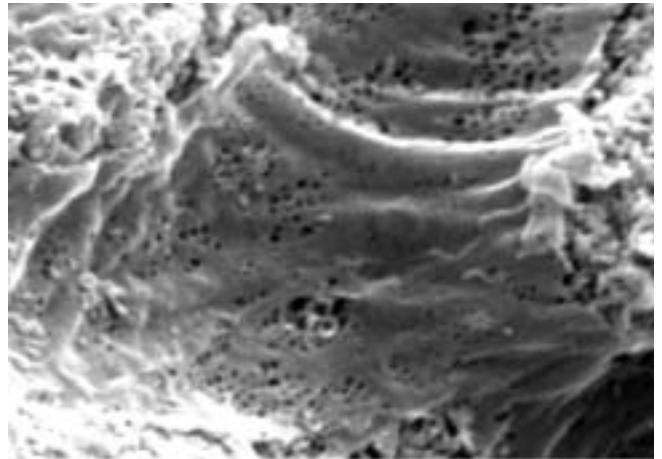
Diffuse mottling is seen in both lung fields (arrows) at sites of fat embolism. The lungs would normally show no uptake and would be a uniform black colour in a patient without fat embolism.

## The Ageing Process and the Liver

This research is led by CERA Director Professor Le Couteur and Dr Muller in the ANZAC Research Institute. The team are interested in why ageing increases the susceptibility to disease. Their main interest has focused on an age-related change in the blood vessels of the liver which they recently discovered and called *pseudocapillarisation*.

Pseudocapillarisation involves thickening of the blood vessels with loss of pores and these changes prevent the passage of toxins and nutrients from the blood to the liver for processing. These changes in the liver, particularly the loss of pores, impair the ability to break down dietary fats and predispose to atherosclerosis, heart disease and stroke. Professor Le Couteur and colleagues have also shown that ageing is associated with impaired capacity of the liver to handle neurotoxins, including pesticides. This may explain why ageing is the main risk factor for Parkinson's disease.

Pseudocapillarisation of the ageing liver is associated with impaired oxygenation of the liver cells, which provides an explanation for the age-related impairment of liver medication metabolism, contributing to the increased prevalence of adverse drug reactions in older people. These studies are now focusing on therapeutic strategies to reverse or prevent age-related pseudocapillarisation, as a way of preventing and treating diseases of older age. The researchers are utilising cultured liver endothelial cells to improve understanding of the basic biology of the pores in the liver blood cells and to screen for novel therapeutic agents.



Scanning electron micrographs of the liver endothelium. In the blood vessel from a young liver (top), there are numerous pores called fenestrations that allow the passage of fat and possibly other large molecules. With old age (bottom), the fenestrations are reduced, thereby impeding the ability of the liver to break down fat. This may explain why hyperlipidaemia and atherosclerosis are more common in old age.

## Palliative Care

Palliative care is the total care of patients whose disease is not responsive to curative treatment.

Palliative care encompasses control of pain and other symptoms, as well as the psychological well-being and quality of life of the patient.

### End of life decision-making in the care of the patient.

The aim of this study is to assess the care of the dying patient and how health care professionals' decisions may play a role in this last phase of life. This will be assessed by collecting information from the medical records of 150 patients who have died at Concord Hospital. Dr Ghauri Aggarwal and colleagues have developed a survey form to document a number of factors believed to be of importance in the decision-making process. These factors include the use of medication in the last phase of life; any procedures or interventions in that phase; the documentation of a 'Not For Resuscitation' (NFR) order and how well this is explained in the medical records.

Other background information about the patient's last illness, diagnosis and reason for admission will also be collected. Patients' charts, nursing and physician notes will be examined to provide further information about decision-making and changes of care in the last phases of life. It is hoped that the data will be collected over a period of 8 months. The patient's terminal phase will be looked at in a critical manner, documenting the appropriateness of decisions, medical and nursing care and changes to interventions and medications during that time.

This study will provide valuable information on the needs of dying patients by recording the adequacy of care in this important phase of life. It will be used to help develop strategies to improve the care of the dying. It is also hoped that the results will be used to provide educational tools to better equip our medical and nursing staff to react appropriately to changing

conditions in this last phase, and in particular, to provide adequate palliative care and comfort measures when it is apparent that a patient is dying.

## Cognitive Behavioural Treatment of Panic Disorder

Fiona Kemp & Fiona Wilkinson, clinical psychologists at Concord Hospital, have undertaken research into treatments for Panic Disorder. The investigators analysed the components of Cognitive Behavioural Therapy (CBT) which were most successful in the treatment of Panic Disorder.

Cognitive Behaviour Therapy (CBT) is a psychological therapy that focuses on irrational thoughts (cognitions), and how these thoughts effect subsequent emotions and behaviours. Therapy includes 'cognitive restructuring' which involves identifying these thoughts, challenging them and developing a different set of attributions. The behavioural component of CBT includes changing behaviours so that these thoughts and emotions may further be challenged. For example, a person who is anxious may be required to go into a fearful situation that they would normally avoid in order to challenge the thoughts and emotions that have previously been associated with the situation. This type of behavioural exercise is known as exposure therapy and may be done in the situation itself, in the imagination, or interoceptively (behaviours that induce feared bodily sensations). CBT for people who are anxious may also include 'breathing retraining', a technique that rectifies the shallow breathing and ensuing hyperventilation often associated with panic.

A person who experiences Panic Disorder will typically experience the following symptoms: a brief episode of intense fear with physical sensations such as heart palpitations, dizziness, and shallow breathing. In addition the person will be concerned about future panic 'attacks'. For example they may fear losing control or 'going crazy'. They may also modify their behaviour to avoid future panic attacks.

Substantial evidence supports the efficacy of CBT in the treatment of panic disorder. Controversy exists as to which components of CBT are essential for change. Standard cognitive behaviour treatment of panic disorder usually includes the following components: cognitive restructuring, "in situation" exposure, breathing retraining, relaxation training and psychoeducation. Researchers have suggested an increasing trend towards omitting the breathing retraining component in panic control, and including interoceptive exposure. To investigate this issue, the current study examined the relative efficacy of two standard components of CBT for panic disorder, namely interoceptive exposure and breathing retraining. Subjects meeting the criteria for panic disorder were recruited and allocated to one of two treatment groups: - interoceptive exposure and breathing retraining. Each group received six one hour CBT sessions which differed only by the inclusion / exclusion of breathing retraining and interoceptive exposure.

Findings to date suggest that, contrary to expectations and previous research, it would appear that the group that received breathing retraining has attained greater treatment benefits than the group that received interoceptive exposure. This finding suggests that breathing retraining is an essential component in the effective treatment of panic disorder, while the importance of interoceptive exposure requires further investigation.



CONCORD

HOSPITAL

RESEARCH

REPORT

Researchers	Project	Origin of Funding
Anesthesiology		
J Smith, A Spralia and P Hendel	A study to investigate the effects of continuous infiltration with ropivacaine using a commercially available infusion device on postoperative opioid requirements, pain scores and patient mobility	Astra Zeneca Johnson & Johnson
Anatomical Pathology/Electron Microscope Unit		
B Lin, R L Sutherland et al.	Molecular pathology of pancreatic cancer	
B Lin, C Chan, E L Bokey et al.	Molecular genetics and immunohistochemical analysis of Stage B colonic carcinomas	
L Hughes and L Chan	Analysis of p53 expression in transitional cell carcinoma	
L Hughes, S Lim et al.	Assessment of disease control in chronic airways limitation by sputum eosinophil count	
S Brammah, L Wright, E Delikatny et al.	Ultrastructural changes induced by TTP-based cationic lipophilic phosphonium salts (CLPS) and chlorpromazine (CPZ)	NHMRC Leo & Jenny Leukaemia and Cancer Foundation
C Hawke, P Kirwa, R van Driel and A Baxter	Mycobacterium as an environmental enhancer of SLE in a mouse model of SLE	
Burns Unit		
T Heath, P Maitz and T Gottlieb	Invasive burn wound infection: its relationship to skin graft outcome and sepsis	
P Maitz and J Sharp	The application of cultured epithelial cells to grafts on burns wounds	
P Maitz and R Johnson	A Phase Iia clinical evaluation of a topically applied, biologically active, milk-derived extract (B6011A) in the treatment of skin graft donor site wounds	GroPep Limited
M Carne	Pressure garment comparison	
F Li and M Carne	Does splinting effect the incidence of heterotopic ossification at the elbow in burns?	
Cardiology		
A Sindone	CHARM (Candesartan in patients with heart failure)	AstraZeneca
A Sindone	EPHESUS (Eplerenone in the survival from heart failure after heart attack)	Searle
A Sindone	OVERTURE (Omapatrilat vs Enalapril in prolonging survival and delaying the progression of heart failure) ENABLE (Bosentan in heart failure patients)	Bristol-Myers Squibb Actelion Ltd.
A Sindone	CHAT (Quality of life of patients with heart failure)	
A Sindone	I-PRESERVE (Irbesartan in heart failure patients with preserved systolic function)	Bristol-Myers Squibb & Sanofi-synthelabo
A Sindone	PERINDOPRIL (Perindopril in heart failure patients with preserved systolic function)	Servier

G Lau, L Kritharides, L Ridley and D Brieger	Accuracy of Coronary CT angiography	
G Lau, L Kritharides, D Sullivan, L Ridley, P Bannon and D Brieger	CABG-Risk Study (Risk factors for coronary vein graft disease)	
G Lau, H Tan and L Kritharides	Liver Dysfunction in Heart Failure	
S Chandar, R Walls and S B Freedman	C-Reactive Protein (CRP) and thrombus in unstable angina	
G Lau, S Riminton and S B Freedman	C-Reactive Protein (CRP) and vascular injury	
D Brieger and M Hayes	SPORTIF (Study of a new anticoagulant in patients with atrial fibrillation)	Astra Zeneca
D Brieger	GRACE (A registry to define characteristics, management and outcomes of patients with Acute Coronary Events ACE)	Aventis
D Brieger	Synergy (Enoxaprin in high-risk patients with acute coronary syndromes)	Aventis
D Brieger, D Bruce, B Zeng and S B Freedman	Alternate mediators of fibrinolysis in plasminogen knock-out mice	NHMRC
<b>CERA (Centre for Education and Research on Ageing)</b>		
D Le Couteur, A McLean and A Ansellin	Hepatic oxygenation and ageing	NHMRC (project grant)
D Le Couteur	Pathogenesis and functional significance of age-related pseudocapillarisation	SESQUI, University of Sydney NHMRC
D Le Couteur, Z Khalil, G Andrews, J Kril et al	Scoping study on ageing research	
D Le Couteur, C Shanley, et al.	Falls prevention in residential care	Dept of Health and Aged Care
D Le Couteur	Purchase of HPLC	NHMRC Equipment grant,
K Double, G Halliday, D Le Couteur et al	A potential new test for diagnosing early dopamine cell loss	Australian Brain Foundation
A McLean and D Le Couteur	Ageing and the liver	NHMRC/DVA
J Kril, P Waley, S Patel and F Png	Correlates of brain atrophy in Alzheimer's disease (AD)	Medical Foundation of The University of Sydney NHMRC
J Kril, H Creasey, G Halliday and M Broe	Non-Alzheimer dementias: Pathogenesis and clinicopathological correlations	
G Halliday, G A Broe, A Harding and W S Brooks	Genetic factors and regional brain atrophy in the diagnosis of dementia with Lewy bodies.	NHMRC (grant held by POW Medical Research Institute)
C Masters, P R Schofield, G A Broe, H Creasey and W S Brooks	NHMRC Network of Brain Research into Mental Disorders (Genetic Linkage Consortium, Diagnostic Assessment Consortium)	NHMRC (grant held by the University of Melbourne)
J Kwok, P R Schofield and W S Brooks	Cloning and biochemical characterisation of a new gene that causes Alzheimer's disease.	DVA (grant held by the Garvan Institute of Medical Research)

Clinical Andrology	
D Handelsman, S Kelleher and A Conway	A study of the prostatic contribution of circulating DHT (dihydrotestosterone)
D Handelsman, S Kelleher and A Conway	Long-term pharmacokinetics and clinical efficacy of Andromen Forte 5% Cream for androgen replacement in hypogonadal men
D Handelsman, S Kelleher and A Conway	Pharmacokinetics of Andromen Forte 5% cream: A dose-finding study
D Handelsman and P Anderson	Development of a serum panel to develop normal laboratory ranges when testing for reproductive health in men
D Handelsman, L Turner and A Conway	Efficacy, safety and service feasibility of an androgen/progestin depot regimen for hormonal male contraception.
D Handelsman and M Cousins	The effects of Nandrolone Decanoate on rehabilitation and quality of life in men with chronic pain and opioid-induced androgen deficiency: a randomized, placebo-controlled cross-over clinical trial.
P Liu, D Handelsman and R Grunstein	A double-blind, placebo controlled randomised crossover study of testosterone on physical activity, sleep and cognition in men over 60 years of age.
D Handelsman	Prenatal Factors in Male Reproductive Health
Colorectal Unit	
L Inwig, L Bokey, P Chapui et al.	Population screening for colorectal cancer
L Bokey, P Chapuis et al.	Maintenance of the Colorectal Cancer (CRC) Hospital Registry
Dermatology	
E Collins, M Piggan, J Fegon and C Ong	An open-label study to evaluate the safety and long-term clinical efficacy of Imiquimod cream applied once daily, seven days per week for 6 weeks on the treatment of superficial basal cell carcinoma
Endocrinology	
M Hooper	CORE (Raloxifene in lowering risk of breast cancer in postmenopausal women with osteoporosis)
M Hooper	GHBQ-PTH (New combination treatment for osteoporosis in women)
M Hooper	Alendronate in Paget's disease
M Hooper	Rio-Lipids study (a new drug for weight loss in obese patients with dyslipidaemias)
M Hooper	PEARL (Lasofoxifene for postmenopausal women with osteoporosis)
M Hooper	Lasofoxifene in sexual dysfunction
R Chen	HMR 1964 (fast-acting insulin) in Type1 diabetes
M Hooper	Extension study: Risedronate in osteoporosis
M Hooper	Zoledronic acid in osteoporosis extension 2
M Hooper	Zoledronic Acid in Paget's Disease
M Hooper	Risedronate for osteoporosis in men
	Lawley Pharmaceuticals
	Lawley Pharmaceuticals
	Andrology Australia
	CONRAD
	Serono
	NHMRC
	Commonwealth project grant
	3M Pharmaceuticals
	Eli Lilly
	Eli Lilly
	Merk, Sharp & Dohme
	Sanofi
	Pfizer
	Pfizer
	Aventis
	Proctor and Gamble
	Novartis
	Novartis
	Aventis/Proctor Gamble



R Chen, M Hooper, T Cromer, C Ting, N Kormas and C Shankley	HMR1964 VS regular human insulin in type 2 diabetes mellitus	Aventis
Gastroenterology		
G Park, M Ngu, B Jones, P Katelaris and D Le Couteur	The Caffeine Breath test	NHMRC
Hypertension Unit		
R Wyndham	FIELD study (Fenofibrate in preventing vascular disease in patients with non-insulin dependent diabetes)	NHMRC
Immunology		
R Walls and G Hu	Traditional Chinese medicine in treatment of allergic diseases	Taiji-University of Sydney Research Fund for Traditional Chinese Medicine
Microbiology		
T Gottlieb and G Funnell	Australian Group for Antimicrobial Resistance (AGAR) – Staph aureus study	
T Gottlieb and G Funnell	Australian Group for Antimicrobial Resistance (AGAR) – Gram Negative study	
T Gottlieb and G Funnell	Australian Group for Antimicrobial Resistance (AGAR) – Pneumococcal study	
T Gottlieb	Community acquired bacteraemia	
S Siarakas, T Gottlieb et al.	Multi-Centre Evaluation of Rapid Commercial Tests for the Diagnosis of Clostridium difficile	Multiple company sponsorship
S Siarakas, J Santos and H Agus	The Role of Clostridium perfringens in Nosocomial and Community diarrhoea (Supervised Honors Project)	Company sponsorship University of Sydney
S Siarakas, A. Kewley, P Lorentzos and H Agus	Clostridium difficile: Living in the Variant Era (Supervised Honors Project)	University of Sydney.
M Leroi, S Siarakas and T Gottlieb	Role of Novel Antibiotics against Clostridium difficile	Pharmacia Bayer
T Gottlieb and M Peters	Linezolid vs. Vancomycin/ Oxacillin in Gram Positive Cannula related sepsis	Pharmacia
T Gottlieb	Australian Candidemia study	
J Merlino, R Bradbury, T Gottlieb et al	Phenotypic and Genotypic studies of Staphylococcus aureus (non-multidrug and multidrug resistance MRSA) isolates in CSAHS	University of Sydney
J Merlino, R Bradbury, T Gottlieb et al	Surveillance and Evaluation of New Detection and Isolation Methods for Staphylococcus aureus (non-multidrug and multidrug resistance MRSA) in CSAH	University of Sydney Company sponsorship
M Poyten, J Merlino and T Gottlieb	Detection of Extended Spectrum Beta-Lactamases in Gram-negative Bacilli at CRGH	Company sponsorship
T Gottlieb, M Leroi Concord Animal Hospital	Coxiella burnetii in cats in Sydney – a serological survey	
T Gottlieb and G Funnell	Moxifloxacin susceptibility in respiratory isolates – Multicentre study	Bayer

Molecular Medicine		
G Nicholson and M Kennerson	Genetic Basis for Charcot-Marie-Tooth and Hereditary Sensory Neuropathy type I	NH&MRC
G Nicholson and M Kennerson	Finding the gene for hereditary sensory neuropathy	Rebecca L. Cooper
G Nicholson and M Kennerson	Functional studies on the gene causing hereditary sensory neuropathy	Clive and Vera Ramaciotti Foundation
G Nicholson	Mapping the mutation for hereditary sensory neuropathy	USA Muscular Dystrophy Association
G Nicholson and M Kennerson	Gene mutation analysis in Parkinson's disease using real time PCR	Clive and Vera Ramaciotti Foundation
G Nicholson	Identifying new gene mutations for motor neurone disease	The Amyotrophic Lateral Sclerosis Association USA
G Nicholson and M Kennerson	Molecular genetics of spinal cord neuropathies	Department of Medicine University of Sydney
Neurology		
A Corbett	PROGRESS (Perindopril and Indapamide for secondary stroke prevention)	Servier and MRC New Zealand
A Corbett	TRANSCEND and ON TARGET (Ramipril and Telmisartan for secondary prevention of complications in stroke, coronary artery disease, diabetes and peripheral vascular disease)	Boehringer Ingelheim/Canadian Cardiovascular Collaboration Project Office
M Hayes	A multi-centre, multinational, Phase 3, randomized, double blind, double-dummy, 3-arm parallel group, placebo- and ropinirole-controlled trial of the efficacy and safety of rotigotine CDS patch in subjects with early stage, idiopathic Parkinson disease	Schwarz Pharma
M Hayes	A phase 3, double blind, placebo controlled, randomized study comparing the efficacy, safety and tolerability of sumanirole versus placebo or ropinirole, as an adjuvant to levodopa, in patients with advanced Parkinsons Disease	Pharmacia
M Hayes	Botulinum toxin and lower limb spasticity following stroke	Allergon
A Corbett, J Watson, J Cullen and S Allen	Priority Health Care Program – Stroke	Department of Health
Neurosurgery		
N Dan and N Kazemi	A prospective, randomized, double-blind trial to evaluate the efficacy of analgesic epidural paste in lumbar disc surgery	
Nursing		
J Randall, L Chenoweth, C Luck, C Smith and C Fennell	Discharge Planning from the perspective of patients and their family/carer.	The Association of Discharge Planning Nurses
V Sutherland and D Lear	Extraventricular drains – sterile versus aseptic technique	Research Centre for Adaptation in Health and Illness, University of Sydney
G Glynn	The implementation of the Family needs Protocol to assist nurses in addressing the needs of the family members of critically ill patients	Research Centre for Adaptation in Health and Illness, University of Sydney
J Munro, M Richardson, J O'Connell and R Hawley	Evaluation of a nurse-initiated discharge plan to improve the management of patients with asthma in the Emergency Department	Research Centre for Adaptation in Health and Illness, University of Sydney

Nutrition and Dietetics		
P MacLennan, K Jukkola, A Thornnton, N Czinner and J Ravens	Investigation of the effects of charting High Protein, High Energy Nutritional Supplements on the Outcomes of Elderly Hospitalised patients at risk of Malnutrition.	Research Centre for Adaptation in Health & Illness, University of Sydney
N Crockett, P Beale, J Jacquet and P MacLennan	Investigation into the effect of Nutrition Intervention in Long-term Chemotherapy Patients.	Research Centre for Adaptation in Health & Illness, University of Sydney
L Bayfieh, R Johnson and P Maitz	Diarrhoea incidence in burns patients in the Burns Unit at Concord Hospital – possible aetiological mechanisms and intervention.	Research Centre for Adaptation in Health and Illness, University of Sydney
Oncology		
P Beale, S Clarke and A Sullivan	NSABP C-07 trial (Clinical Trial of chemotherapy following surgery for bowel cancer)	National Surgical Adjuvant Breast and Bowel Project (NSABP)
P Beale and S Clarke	Celecoxib/CPT11 (Clinical trial of celebrex with chemotherapy for patients with advanced colon or rectal cancer).	Pharmacia
M Stockler, A Sullivan and P Beale	ANZ0001 trial(Clinical trial of chemotherapy for women with advanced or metastatic breast cancer)	Australia New Zealand Breast Cancer Trial Group (ANZBCTG)
A Sullivan and P Beale	BCIRG trials 005 & 006 (Clinical trials of chemotherapy and antibody treatments for women following surgery for breast cancer).	Breast Cancer International Research Group (BCIRG)
M Stockler, M Boyer, S Clarke and P Beale	YM 598 prostate trial (Clinical trial of a new drug with chemotherapy for advanced prostate cancer)	Yamanouchi
P Beale and S Clarke	Chrysin/CPT11 study (Clinical trial of a drug to prevent diarrhoea with chemotherapy for bowel cancer)	
M Stockler	ZEST study (Clinical trial of antidepressant drug in advanced cancer patients)	NHMRC-CTC
S Clarke, M Millward and P Beale	JMAT NSCLC (Clinical trial of chemotherapy for patients with advanced lung cancer)	Eli Lilly
S Clarke, M Millward, P Beale and M Boyer	AG3340 NSCLC (Clinical trial of a new drug to prevent tumour spread in lung cancer patients)	Agouron
A Sullivan and M Stockler	IBCSG Study 20 (Clinical trials of chemotherapy for women following surgery for breast cancer).	Australia New Zealand Breast Cancer Trial Group (ANZBCTG)
S Clarke, M Millward and P Beale	IRESSA NSCLC (Clinical trial of a new drug with chemotherapy to prevent tumour growth in lung cancer patients)	Astra Zeneca
M Stockler, M Boyer and P Beale	TAX 327 (Clinical Trial of chemotherapy for men with advanced prostate cancer)	Aventis
S Clarke and P Beale	Capecitabine TS study (Predicting toxicity from treatment for advanced bowel cancer)	
M Stockler and P Beale	Cisplatin inpatient/outpatient study	
Orthopaedics		
W Bruce and H Van der Wall	Early Prospective Detection of Bone Marrow/Fat Embolism after Joint Arthroplasty	

<b>Ophthalmology</b>		Evaluation of dry eye tests in normal asymptomatic population	
F Booth, J George and A Lee			
<b>Palliative Care</b>		Documentation of the Incidence of Malignant Ascites and the Use of Paracentesis and Diuretics in Current Management of Malignant Ascites (Pilot Study)	
G Aggarwal and M Agar			
G Aggarwal, N Sathasivam and C Wong		End of life decision-making in the care of the patient	
G Aggarwal		Double-blind, Double-dummy, Randomised, parallel-arm equivalence study comparing Hydromorphone Hydrochloride extended-release capsules (HHER) with MS Contin Tablets, at a dose ratio of 1:7.5, in Cancer or Non-Cancer patient with a history of moderate to severe pain	Mundipharma
P Glare and G Aggarwal		Database of patients using strong opioids for non-cancer pain	
G Aggarwal and A Koutantos		Prevalence of pain in a teaching hospital	
J Clayton, P Butow, M Tattersall R Chye and G Aggarwal		Communication of prognostic information in palliative medicine – an analysis of audiotaped doctor/patient consultations	NHMRC Medical/Dental Research Scholarship
P Glare, J Yip and G Aggarwal		Pain in hospitalised patients with cancer: prevalence, clinical characteristics, impact on quality of life and barriers to treatment.	
J Clayton, M Tattersall, P Butow and G Aggarwal		Piloting a question prompt sheet for palliative care patients and subsequently conducting a randomised controlled trial of the question prompt sheet.	NHMRC medical postgraduate scholarship
<b>Physiotherapy</b>		Quality Improvement Project to review outcome measures post upper and lower abdominal surgery	
Y Silva and F Li			
P van den Dolder and M Kwan		A Trial into the Effectiveness of soft tissue massage in the treatment of Shoulder Pain	
K Refshauge, C Maher, L Barnsley and L Pengel		Exercise or Advice for subacute Low Back Pain?	NHMRC Australasian Physiotherapy low back trial consortium
F Li and Y Silva		Forces and Frequencies used in percussion and vibration techniques	
Y Silva, F Li and M Peters		The effectiveness of pulmonary rehabilitation on patients post lung resection.	
F Li, V Graham, N Buckle, D Delaney and A. Karkovic		Multi-centre trial of a revised version of the Elderly Mobility Scale; a retrospective study.	
<b>Psychological Medicine</b>		The behavioural and neurotoxic effects of MDMA (“Ecstasy”)	NH&MRC
I McGregor and G Hunt			
<b>Psychology</b>		Cognitive behavioural treatment of panic disorder	Research Centre for Adaptation in Health and Illness, University of Sydney
F Kemp and F Wilkinson			
P Mangioni		Comparison of patients’ psychological state attending cardiac rehabilitation with those patients receiving “normal” discharge care	Research Centre for Adaptation in Health and Illness, University of Sydney

Rheumatology		
R Chow and L Bamsley	Low Level Laser for Neck Pain	
L Bamsley	Outcomes of radiofrequency denervation for chronic neck pain	
L Bamsley	Remicade for Rheumatoid arthritis	
Speech Pathology		
N Clayton, A Ing, M Peters and G Mann	The effect of chronic obstructive pulmonary disease (COPD) on laryngo-pharyngeal sensitivity (LPS) and dysphagia	
Thoracic Medicine		
L Seeto	The role of AKT in the molecular pathogenesis of Chronic Obstructive Pulmonary Disease (COPD).	
L Seeto	Alveolar macrophage expression of p21 in Chronic Obstructive Pulmonary Disease (COPD).	
L Seeto	The expression of matrix metalloproteinases (MMPs) and cytokines from alveolar macrophages in Chronic Obstructive Pulmonary Disease (COPD): The effect of oral theophylline in COPD, a randomised double blind placebo controlled study in patients with COPD.	Mitsubishi
L Seecombe	Risk factors for developing hypoxia during air travel in passengers with lung disease.	
M Comsa	Study on the etiology of community-acquired pneumonia in patients admitted to Concord Hospital.	
G Cossa	A study to examine the effects of environment (aeroallergens) on nocturnal asthma using an automated wheeze quantification device (PulmoTrack)	
K Wade and L Plowman	Metered dose inhaler (MDI) assessment in subjects with chronic obstructive pulmonary disease (COPD) or asthma.	
A Ing and B Rost	The Role of Neurotrophins in Chronic Idiopathic Cough	
Urology		
V Tse, L Chan, J Yin, C McLachlan E Wills and S Brammah	Ultrastructural Basis of Voiding Dysfunction (Correlation of Gap Junctional Protein Expression and Ultrastructural Features in the Unstable Human Detrusor	Abbot Australasia Institute of Urology, CSAHS
A Lalak, L Chan, A Mitterdorfer, D Vasilareas and N Hanly	GUOG – A Phase II Study to Assess the Effect of Intermittent Androgen Blockade in the Treatment of Advanced Prostate Cancer	Schering Plough
L Chan, D Eisinger, A Mitterdorfer J Rogers, D Vasilareas and N Hanly	A Randomised, Double-blind, Parallel Group, Placebo and Active Controlled, Multi-Centre Study of YM905 5 mg and 10 mg in Patients with Overactive Bladder	Yamanouchi
L Chan, D Eisinger, A Mitterdorfer J Rogers. D Vasilareas and N Hanly	An Open-label, Long-term Safety and Efficacy Follow-up Study of YM905 5mg and 10mg in Patients with Overactive Bladder	Yamanouchi
L Chan, D Vasilareas and N Hanly	UK-338,003 (Study of a new drug for treating symptoms of benign prostatic obstruction).	Pfizer
A Lalak, A Mitterdorfer, P Maher and N Hanly	TRIUMPH Study (Study of the management of patients with benign prostatic hyperplasia)	Yamanouchi
J Medd, A Lalak, L Chan, P Maher and M Stockler	Patients Experience of Urodynamics and Prostate Biopsy	



## Funding:

The research described in this publication was supported by funding from the following sources:

- Altana Pharma
- Amgen Inc.
- Astra-Zeneca
- Australian Brain Foundation
- Aventis Pharma
- Bard Corporation
- BioFirst Award (NSW Government)
- CONRAD
- Department of Veterans' Affairs
- Eli Lilly
- Federal Department of Health and Ageing
- International Osteoporosis Foundation
- Johnson and Johnson
- Mitsubishi (Japan)
- National Health and Medical Research Council
- National Health and Medical Research Council Postgraduate Scholarship
- NSW Health Department Infrastructure Grant
- Pfizer Cardiovascular Lipid Research Grant
- Pharmacia Australia
- RACP McCaughey Research Scholarship
- Research Centre for Adaptation in Health and Illness, University of Sydney
- Roche Pharmaceuticals
- RM Gibson Foundation of Australian Association of Gerontology
- Royal Australian College of Surgeons
- SchwarzBiosciences
- Serono
- Singapore College of Physicians
- Swiss National Research Fund
- The University of Heidelberg Research Foundation
- The Medical Foundation of The University of Sydney
- The University of Sydney
- Vingmed GE Australia

