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Associate Professor Carlos Scheinkestel in the new state-of-the-art 45 bed ICU at The Alfred, opened in November 2008.

INTENSIVE CARE

Director: Associate Professor Carlos Scheinkestel MBBS, FRACP, FJFICM
Deputy Director & Head of Research: Professor Jamie Cooper BMBS, MD, FRACP, FJFICM

In 2008, the Intensive Care Unit continued its strong research program. The Alfred ICU is now regarded as one of the most successful research departments in critical care research in Australia. Research has continued on a number of themes built up over many years in collaboration with several important research organisations, including the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG), the National Trauma Research Institute (NTRI) and the Australian and New Zealand Intensive Care Research Centre (ANZIC-RC).

In 2008, Intensive Care Unit researchers were awarded NHMRC funding for two new studies in traumatic brain injury (POLAR and EPO) for $1.96 million and $1.85 million respectively. The POLAR study (led by Professor Cooper and Associate Professor Bernard in association with Dr Nichol and Professor Peter Cameron) will investigate the early use of induced hypothermia to improve outcomes, and the EPO study (led by Professor Cooper and Dr Nichol) will investigate the use of erythropoietin to improve outcomes in traumatic brain injury patients.

The enthusiastic and hard-working ICU research coordination team continued to successfully enrol patients into several clinical trials. This team included Lynne Murray, Shirley Vallance, Cindy Weatherburn, Siouxzy Morrison, Rachael Nevill and is supported by Lucinda Gabriel.

RESEARCH ACTIVITIES

Professor Jamie Cooper continued to lead (with Professor Jeffrey Rosenfeld) the DECRA trial, an international randomised trial of decompressive surgery for severe traumatic brain injury, which is within 12 months of completion. He also leads the SAFE-TBI II study, searching for mechanisms behind improved mortality with saline compared to albumin for resuscitation in traumatic brain injury (TBI) patients, and the Australian effort on the PROTECT study, which is comparing unfractionated and low molecular weight heparins in a large Canadian-led international study of critically ill patients.

With Ruwan Wijemunige, Professor Cooper is investigating BIS monitoring in TBI patients, and testing CO_2 titration to improve brain oxygen concentrations. He is also principal investigator on the national STATINS (investigation of statin therapy) and ARISE (investigation of early goal-directed therapy) randomised trials in patients with severe sepsis.

Associate Professor Carlos Scheinkestel was a Steering and Management Committee member of the highly successful RENAL study (completed in late 2008), which randomised over 1,500 patients.

Dr Andrew Davies continued to lead the multicentre ENTERIC randomised trial, testing small bowel feeding versus gastric feeding in ICU patients. He also ran a nationwide observational study on feeding strategies in patients with pancreatitis and is gradually developing a critical care nutrition research program in collaboration with the ANZIC-RC.

Associate Professor David Tuxen, Dr Alistair Nichol and Carol Hodgson have continued their randomised, controlled trial of an improved method of lung recruitment in patients with acute respiratory distress syndrome (ARDS), the PHARLAP study.

Associate Professor Stephen Bernard has continued his pre-hospital research program. Recently he completed studies on pre-hospital intubation in severe head injury (RSI trial) and on improved methods of cooling post-cardiac arrest patients pre-hospital (RICH trial) and has moved on to co-lead (with Professor Cooper) a significant study into hypothermia (both pre- and then in-hospital) for patients with traumatic brain injury.

Associate Professor Warwick Butt has continued to lead a prolific and diverse research program in both paediatric and adult critical care.

Dr Vincent Pellegrino has been analysing results of the multicentre NAVIGATOR trial testing an improved monitoring and haemodynamic management system for acute cardiothoracic ICU patients. He has continued to further establish the growing clinical extracorporeal membrane oxygenation (ECMO) program, which has included the establishment of an international symposium on the use of the ventricular assist device (VAD) and ECMO therapies.

Dr David Pilcher has continued to study ICU outcomes using the bi-national ICU database, particularly in regard to ICU discharge patterns and survival.

Dr Megan Robertson ran a pilot study in understanding whether heparin has an effect as an intervention in patients with septic shock, and has contributed to several other department research projects.

Dr Andrew Hilton has expanded the ICU echocardiography program and has continued investigating cardiac abnormalities in patients with brain injury and lecturing at meetings on echocardiography. Dr Tim Leong has continued his work in infection control and central line associated blood stream infections and Dr Deirdre Murphy has taken over from Associate Professor Bob Salamonsen in developing skills in artificial heart technology.

Dr Silvana Marasco (cardiothoracic surgeon) continues to lead a randomised trial of surgical rib fixation patients with Professor Cooper and Dr Davies.

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Medical Oncology research nurse Marisa Cikos conducts an interview with a trial patient.

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MEDICAL ONCOLOGY

Head: Professor Max Schwarz MBBS(Hons), FRACP, FACP, FAChPM

The Medical Oncology Unit provides coordinated multidisciplinary management for adult patients with malignancies. An important component of this care is the clinical trial and research activities, which enable the unit to offer forthcoming investigational treatments to patients.

The unit's research activities include Phase 1, 2 and 3 trials across a wide range of tumour types, incorporating both pharmaceutical industry sponsored and investigator-driven studies, with active participation in both national and international clinical trials.

A highlight of 2008 was the mandatory regulatory inspection by the US Food and Drug Administration (FDA) of a Phase 1 international clinical trial conducted by the unit, in collaboration with Nucleus Network. This was a rigorous, formal, five-day audit. No reportable findings were made by the senior FDA auditor, who highly commended the study conduct at The Alfred.

The unit was an active participant in an important international colorectal study. The results, which were published in the *New England Journal of Medicine* in October 2008, translate into a major paradigm shift in the prognosis and management of metastatic colorectal cancer. The veracity of the results has been verified by other worldwide research groups. Dr Jeremy Shapiro was the principal investigator of the study at The Alfred.

The unit plans to join the Cancer Trials Australia (CTA) group in early 2009, which will allow access to clinical trials and enhance research capabilities. It is expected that a central ethics committee review process, acceptable to all the major teaching hospitals ethics committees, will be introduced in 2009. Its implementation will be a major development for all researchers, with significant benefits in enhancing research capacity as well as streamlining governance.

CURRENT PROJECTS

- Suppression of ovarian function trial: a Phase 3 trial evaluating the role of ovarian function suppression and the role of exemestane as adjuvant therapies for premenopausal women with endocrine responsive breast cancer (Professor Max Schwarz)
- A Phase 3 randomized trial of chemotherapy with or without panitumumab in patients with metastatic and/or recurrent squamous cell carcinoma of the head and neck (Dr Andrew Haydon)
- Multicentre international study of capecitabine +/- bevacizumab as adjuvant treatment of colorectal cancer (Dr Andrew Haydon)
- A Phase 3 randomized study of brivanib alaninate (BMS-582664) in combination with cetuximab (Erbitux, C225) versus placebo in combination with cetuximab (Erbitux, C225) in patients previously treated with combination chemotherapy for metastatic colorectal carcinoma (Dr Andrew Haydon)
- A multinational, randomized, double-blind study comparing aflibercept versus placebo in patients treated with second-line docetaxel after failure of one platinum based therapy for locally advanced or metastatic non-small-cell lung cancer (Dr Andrew Haydon)
- Adjuvant immunotherapy with anti-CTLA-4 monoclonal antibody (ipilimumab) versus placebo after complete resection of high-risk stage III melanoma: a randomized, double-blind Phase 3 trial of the EORTC Melanoma Group (Dr Andrew Haydon)

PUBLICATIONS

9 Journal Articles

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Fourteen of the 15 consultant intensivists were invited to speak at international or national meetings in 2008. Of note, Professor Cooper gave a plenary lecture on traumatic brain injury at the Society of Critical Care Medicine (the largest annual American critical care meeting) and Dr Davies gave seven invited presentations at the Brussels ISICEM (the largest annual European critical care meeting). Several ICU registrars presented their work at the Australian and New Zealand Intensive Care Society Annual Scientific Meeting in 2008.

The end of 2008 saw the retirement from clinical service of Associate Professor Bob Salamonsen, who has pioneered many aspects of cardiothoracic intensive care in Australia, mostly through the use of life support machines such as VADs and ECMO. Bob's remarkable knowledge of cardiovascular physiology is legendary and assisted him to teach and guide generations of trainees and consultants in anaesthesia and intensive care.

MAJOR RESEARCH FINDINGS

- The VASST study found that low dose vasopressin improved survival in selected patients with septic shock (published in *New England Journal of Medicine*). The Alfred coordinated the Australian sites in a Canadian-Australian non-industry research collaboration.
- The LOVS study (also a Canadian-Australian research collaboration) reported that higher levels of PEEP did not improve outcomes in patients with ARDS (published in the *Journal of the American Medical Association*).
- The RENAL study found that high-flow continuous renal replacement therapy (CRRT) did not improve major clinical outcomes in ICU patients with renal failure compared to standard flow CRRT.

POSTGRADUATE STUDENTS

2 PhD Students

PUBLICATIONS

24 Journal Articles
4 Book Chapters