

Intensive Care and Hyperbaric Medicine

The Department of Intensive Care and Hyperbaric Medicine is one of the largest clinical departments at The Alfred, comprising the Intensive Care Unit and the Hyperbaric Unit. Among the many recent developments have been the installation of a new and enlarged hyperbaric chamber in the Hyperbaric Unit in 1999 and the opening of a new state-of-the-art 35 bed Intensive Care Unit in 2000, making the entire department one of the most modern in the world, and certainly the largest in Australia.

The Intensive Care Unit at The Alfred has expanded considerably over the last 15 years allowing more complex multidisciplinary management of the most severely ill patients in the Hospital. Trauma, heart and lung transplantation and burns patients, along with patients with many other serious illnesses, are cared for in a highly specialised environment and have been shown to have outcomes as good as anywhere in the world.

Clinical research projects predominate, and the majority are in the areas of trauma (particularly severe brain injury), acute respiratory distress syndrome, septic shock, fluid therapies, nutrition, support of the patient following cardiac surgery and the use of hyperbaric oxygen as therapy in various conditions.

Previously published research on asthma, mechanical ventilation, trauma, burns, and renal failure has been recognised at an international level. In the last few years, the focus of research has changed as a swing towards large multi-centre research projects has occurred, with the objective that therapies which might affect major patient outcomes (such as overall mortality) can be studied and subsequently applied to clinical practice.

2001 was another exciting year for research in the Department with the completion, publication and commencement of a number of important research studies as well as the receipt of a number of important grants.

The most notable research study publication was a multi-centre, prospective, randomised, controlled trial of a recombinant form of activated protein C in patients with severe sepsis. In this landmark trial, published in the *New England Journal of Medicine*, drotrecogin alfa activated (activated protein C) led to a substantial 19.4% reduction in mortality (figure 1).

This drug, which has both anticoagulant and anti-inflammatory properties, and is about to be licensed for use in Australia, is likely to be an important addition to the therapy of septic shock around the world. Its development is exciting as it follows a number of other anti-inflammatory agents, all of which have not been shown to be beneficial in studies of septic shock over the last 20 years.

A large multi-centre study on hypertonic saline in head injured patients continues under the direction of Associate Professor Jamie Cooper. Patient recruitment was completed in early 2002 and results should soon be available.

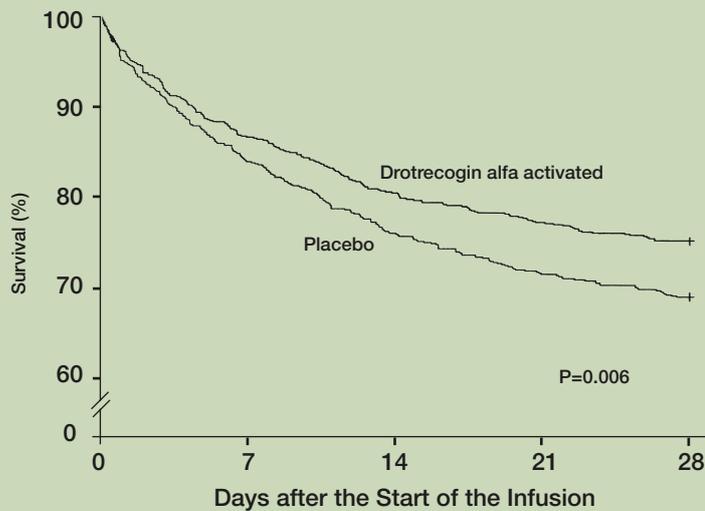
A number of important studies were commenced in the Intensive Care Unit during 2001. The most important of these is the SAFE (Saline versus Albumin Fluid Evaluation) study, which will compare the effects of albumin and saline in 7000 patients admitted to 16 intensive care units in Australia and New Zealand.

This is a multi-centre initiative of the Australian and New Zealand Intensive Care Society Clinical Trials Group, in partnership with the Institute for International Health of the University of Sydney and the Australian Red Cross Blood Service. It is one of the largest research studies ever attempted in Intensive Care. Principal investigators for the study at The Alfred hospital are Associate Professor Cooper and Dr Andrew Davies. The pilot phase of this study commenced in November 2001 and the main study will begin in March 2002.

In the Hyperbaric Unit, a trial of hyperbaric oxygen therapy as an adjunct in the early management of severe lower leg injury has commenced under the direction of Dr Ian Millar.

2001 has also been successful for the receipt of grants, with several large funding bodies awarding significant funding for research in a number of areas. In addition, Associate Professor Cooper was awarded a five year NHMRC Practitioner Fellowship for Clinical Research.

Obtaining funding for intensive care research in Australia has traditionally been difficult, perhaps due to the short history of the speciality, the high clinical workload of intensivists, and the fact that many research areas are not considered mainstream because they cross surgical and medical boundaries. The Department's recent ability to attract substantial funding is due almost entirely to the tireless efforts and enthusiasm of Associate Professor Cooper. It is hoped that the research which comes out of this funding, will demonstrate major benefits of various



No. AT Risk					
Drotrecogin alfa activated	850	737	684	657	640
Placebo	840	705	639	602	581

Figure 1. Kaplan - Meier Estimates of Survival among 850 Patients with Severe Sepsis in the Drotrecogin Alfa Activated group and 840 Patients with Severe Sepsis in the Placebo Group. Treatment with drotrecogin alfa activated was associated with a significantly higher rate of survival (P=0.006 by the stratified log-rank test).

established and novel therapeutic strategies, so that significantly improved patient outcomes will ensue.

Current Projects

Hypertonic saline in head injured patients: a prospective randomised pre-hospital clinical trial

Cost benefit analysis of prehospital hypertonic saline in resuscitation of hypotensive patients with traumatic brain injury

Effects of low dose aminophylline on renal function in critically ill patients

SAFE: A multi-centre double blind randomised controlled trial of the effects of intravenous volume replacement with albumin compared to saline in critically ill patients

VASST: Randomised controlled trial of vasopressin versus noradrenaline in septic shock

The efficacy of enteral naloxone to treat opiate-induced constipation in critically ill patients

Hyperbaric oxygen as an adjunct in the early management of severe lower leg trauma

Sedation in critically ill patients

Prevention of AF in cardiac surgery

EXPEDITION: Cariporide in CABG patients

STRIVE: A phase 2 study to determine the efficacy and safety of sivelestat in subjects with acute lung injury

Anterior pituitary dysfunction in traumatic brain injury

Glucose, insulin and potassium for complex cardiac surgery

Publications

Journal articles

Bernard GR, Vincent J-L, Laterre P-F, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med.* 2001 344:699-709.

Cooper DJ. Albumin usage declining in UK intensive care. *Crit Care Resusc* 2001;3:7.

Davies AR, Bellomo R, Raman JS, Gutteridge GA, Buxton BF. High lactate predicts the failure of intra-aortic balloon pumping after cardiac surgery. *Ann Thorac Surg* 2001;71:1415-20.

Henzler D, Cooper DJ, Mason K. Factors contributing to fatal outcome of traumatic brain injury patients in Victoria: a pilot case control study. *Crit Care Resusc* 2001;3:153-157.

Scheinkestel CD, Davies AR, Bristow PJ. Evidence-based medicine in intensive care. *Med J Aust* 2001;174:526-7.

Book chapters

Cooper DJ, Murray L. 2001. Hypertonic saline in acute brain injury. In: Vincent JL (Ed.). Yearbook of Intensive Care and Emergency Medicine. Springer Verlag. pp 342-9.



Julie Charlton

Julie Charlton is a Clinical Trials Coordinator in the Department of Intensive Care at The Alfred. She is a trained nurse who has gained postgraduate critical care nursing qualifications and has worked in a number of ICUs in Australia. In 1999, she began her research career as a Clinical Research Coordinator in the highly regarded Heart/Lung Transplant Unit at St Vincent's Hospital in Sydney. After moving with her husband to Melbourne, she briefly flirted with research in the pharmaceutical industry before arriving at The Alfred in early 2001.

Julie has taken on the coordination of a number of projects, including the SAFE, VASST study and STRIVE studies. She has had a major administrative role in these projects, including assistance with the Ethics Committee application process, subsequent communication and liaison with pharmacy and sponsor representatives, and education of ICU doctors and nurses involved.

She has also been involved in the clinical performance of these studies at the bedside, including discussion with patients and their families regarding informed consent, randomisation of patients, application of the research protocol and completion of case report forms.

Julie has a keen interest in clinical trial design and management, which combined with her friendly personality and exceptional organisation skills, gives her a bright future in research at The Alfred.

Grants and Other Funding

Anderson M. The efficacy of enteral naloxone to treat opiate-induced constipation in critically ill patients. Alfred Research Trusts Small Project Grant. 2001: \$5,000.

Burdeu G, Ballan N, Torrance C. Nurses interaction with sedated ventilated patients in the ICU. Alfred Research Trusts Small Project Grant. 2001: \$5,000.

Cooper DJ. Current outcomes of patients with severe traumatic brain injury. Victorian Trauma Foundation. 2000-2002: \$132,525.

Cooper DJ, Myles P, McDermott F. Hypertonic saline in head injured patients: a prospective randomised pre-hospital clinical trial. NHMRC. 2000-2002: \$241,596.

Cooper DJ, Myles P, McDermott F. Hypertonic saline in head injured trauma patients: a prospective controlled clinical trial and two year cost benefit analysis. Victorian Trauma Foundation. 2000-2002: \$82,733.

Cooper DJ, Pellegrino V. Vasopressin in patients with septic shock. Alfred Research Trusts Project Grant. 2001: \$25,000.

Cooper DJ, Stockigt J. Anterior pituitary dysfunction in traumatic brain injury. Victorian Trauma Foundation. 2001-2003: \$88,500.

Millar I, Cooper DJ, Atkin C, Esser M. Hyperbaric oxygen therapy for patients with crush injuries: a randomised trial. Victorian Trauma Foundation. 2001-2002: \$320,000.

Norton R, Bellomo R, Cooper DJ, Finfer S, Boyce N, MacMahon S. Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients. NHMRC. 2001-2003: \$608,999 (administered by Sydney University).