

Intensive care medicine

ALTHOUGH EVIDENCE-BASED intensive care medicine is gradually developing, progress in clinical trials has been hampered by the small number of patients, broad range of diagnostic categories, and lack of diagnostic criteria and illness severity measures.

Prevention. Preventing critical illness has become a focus of intensive care practice. As cardiac or respiratory arrest in hospital wards carries substantial mortality, it is essential that deterioration of a patient's condition be recognised as early as possible. In a detailed observational study conducted in three Australian acute-care hospitals,¹ at least 50% of patients who had an arrest were found to have had recognisable deterioration prior to the arrest. Ideally, it should be mandatory for nursing staff to call an emergency team if, during routine observations, they notice deterioration in a patient. Where such a system exists, the number of ward-based in-hospital cardiac arrests has fallen by 80%, with a 32% fall in all-cause mortality.

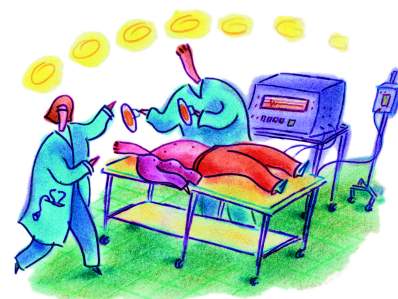
Diagnosis. Standardising and defining the illnesses encountered in the intensive care unit (ICU) has allowed the creation of "illness severity scores", which combine information on pre-existing illness, diagnosis and physiological derangement to predict outcome. Actual outcome is compared with predicted outcome to produce a "standardised mortality rate". Recently, widespread application of these methods has improved reliability and comparability of clinical studies.

Intervention. Systematic study of standard ICU therapies is relatively new. Debate over simple questions, such as what tidal volume should be used for ventilator settings, has raged for many years. The Australasian method uses a tidal volume of 7 mL/kg (to prevent barotrauma), while the US method uses a tidal volume of 10–15 mL/kg (to prevent atelectasis). In the Acute Respiratory Distress Syndrome (ARDS) study,² in which 861 ventilated patients with ARDS were randomly allocated to receive low-volume ventilation or standard-volume ventilation, mortality was lower in the low-volume group (31% v 39.8%; $P = 0.0007$).

A study by the Australian and New Zealand Intensive Care Society Clinical Trials Group (CTG) of the role of dopamine in preventing acute renal failure is another striking example of a known "proven" therapy finally meeting scientific rigour and failing.³

Red-cell transfusion has been a cornerstone of critical-care practice for many years. Routine transfusions were given to maintain the haemoglobin concentration at 100 g/L, with the aim of maximising flow and oxygen-carrying capacity. In 1999, the Canadian Critical Care Trials Group reported on the first randomised controlled trial of blood transfusion in ICU,⁴ which compared a conservative blood transfusion strategy (Hb 70–90 g/L) with a liberal transfusion strategy (Hb 90–110 g/L). Fewer patients in the conservative group died than in the liberal group (18.7% v 23.3%; $P = 0.11$). The rate of red blood cell transfusion was 2.6 units per patient in the conservative group versus 5.6 units per patient in the liberal group. The potential for saving a valuable resource, blood, without worsening out-

come is large. Reducing the amount of blood transfused would also lower the risk of transfusion-related infections.



Are the results of trials changing practice? To evaluate the Australian response to the transfusion study,⁴ the CTG surveyed transfusion practice in Australia in 2000. The national results of the survey are not yet available, but in our own unit there was compliance with the conservative transfusion protocol in all cases except one, in which transfusion was demanded by the surgical consultant preoperatively. After a Cochrane study showed that the use of intravenous albumin for resuscitation was associated with a higher death rate, the use of albumin in the United Kingdom and Europe fell by 20%. In Australia, the CTG has begun a trial to allocate 7000 patients randomly to treatment with either colloid (albumin) or crystalloid fluids for resuscitation. There is a need for definitive studies rather than meta-analysis, especially in the diverse ICU patient population.

The elucidation of the inflammatory cascade and pro-coagulant pathways in septic shock (a leading cause of death in ICU) has led to new therapies using naturally occurring anti-inflammatory and anticoagulant proteins synthesised *in vitro*. Although antiendotoxin antibody studies have been disappointing, activated protein C, which has anticoagulant and anti-inflammatory properties, appears promising. Protein C is activated by thrombin coupled to thrombomodulin. Thrombomodulin is down-regulated in sepsis by inflammatory cytokines. A low plasma level of activated protein C is a marker of sepsis and is associated with death from sepsis. In a study of 1690 patients performed in 164 centres in 11 countries, infused activated protein C was shown to decrease the mortality due to sepsis.⁵ Furthermore, activated protein C is showing promise for treatment of meningococcal septicaemia. Basic research into understanding the inflammatory system and its inter-relation with the coagulation pathway in sepsis may pay clinical dividends in treating septic shock.

The past decade has seen ICU evolve from an experience-based to an increasingly scientifically based practice. Continued advances should see further improvements in patient survival rates.

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