Meeting report

22nd International Symposium on Intensive Care and Emergency Medicine, Brussels, Belgium, 19–22 March 2002

Jonathan Ball[1], Richard Venn[2], Gareth Williams[3] and Lui Forni[4]

[1]Lecturer in Intensive Care Medicine, Department of Anaesthesia & Intensive Care, St George's Hospital Medical School, University of London, UK
[2]Consultant in Anaesthesia and Intensive Care, Worthing Hospital, UK
[3]Clinical Research Fellow, Intensive Therapy Unit, St George's Hospital, London, UK
[4]Consultant in Renal Medicine and Intensive Care, Worthing Hospital, UK

Correspondence: Jonathan Ball, jball@sghms.ac.uk

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The International Symposium on Intensive Care and Emergency Medicine continues to grow every year, with in excess of 4000 attendees. With six parallel sessions for four frenetic days, it covers all aspects of critical care from a variety of perspectives. This year, as in previous years, the symposium was marred only by the perennial problems of overcrowding and audiovisual glitches. The organisers, to their credit, had attempted to counter the problems with use of lecture rooms beyond the congress centre. Sadly, however, many sessions remained oversubscribed. Web casting of lectures to second venues has successfully been employed elsewhere and would greatly enhance this, already pre-eminent, international critical care symposium.

Opening session

As is traditional, the exuberant and charismatic Jean Louis Vincent (Brussels, Belgium) opened this year's meeting, espousing 'The great step forward'. His personal tour through the events of the past 12 months focused on the first Hippocratic tenet: 'first, do no harm'. Iatrogenic injury was his major theme, be it by the use of excessive tidal volume [1], excessive sedation [2,3], delayed resuscitation [4], poor glycaemic control [5], inadequate renal replacement [6], or failure to cool the brain post anoxic injury [7,8]. He went on, however, to caution against the vagaries of fashion. Despite negative studies, he argued, there is still a place for the pulmonary artery catheter [9], for albumin [10,11] and for dopamine [12], but their use must be intelligently tempered.

Two items of breaking news were also raised. First, the recent sepsis consensus conference may shortly result in the abandonment of the Systemic Inflammatory Response Syndrome (SIRS) criteria in favour of PIRO [13] (see also [14]). Second, participation in the up and coming Sepsis Occurrence in the Acutely Ill Patient (SOAP) study (1–15 May 2002) was promoted to all participants.

Jean Carlet (Paris, France) and Derek Angus (Pittsburgh, PA, USA) then presented a report from the presymposium round-table conference, 'Surviving intensive care'. To date, the vast majority of intensive care unit (ICU) interventional studies have used short-term morbidity and mortality as outcome measures. However, there is an increasing desire and necessity to establish the long-term outcomes. What little evidence does exist suggests that survivors of critical illness have diminished life expectancy, functional limitations, neuropsychological morbidity and, unsurprisingly, a reduced quality of life [15–20]. The round-table group reached the following conclusions:

- Established and evolving best practice has identified, and will continue to identify pre, intra and post ICU causes and modifiers of a poor long-term outcome. In particular, preventing neuro-musculo-skeletal sequelae by ensuring early and successful feeding, coupled with a proactive approach to physiotherapy and rehabilitation, is essential.
- Historical precedents should remind us that good short-term outcomes can result in poor long-term outcomes (e.g. milrinone in the treatment of chronic congestive cardiac failure). Long-term follow up as routine practice in all interventional trials is thus to be encouraged and should have a place in everyday practice. However, this is almost certainly beyond the scope of intensivists, hence creative partnerships between ICUs, referring and primary care clinicians need to be forged.

ALI/ARDS = acute lung injury/acute respiratory distress syndrome; CV = conventional ventilation; HFV = high-frequency ventilation; ICU = intensive care unit; NIV = noninvasive ventilation; PEEP = positive end-expiratory pressure; RBC = red blood cell; RRT = renal replacement therapy.

Jean Mira (Paris, France) gave a whirlwind tour through the topic of genetic predisposition as it genuinely begins to impact at the bedside. Polymorphisms in both the promoters and the coding regions of specific genes, affecting the quantity and quality, respectively, of the gene product, have now been identified that confer a quantifiable risk of disease severity and fatal outcome in critical illness [21–27]. With the rapid and dramatic advances in nanochip and microarray technology, bedside genotyping is set to become a reality over the next few years [28]. This raises the possibility of designing specific therapeutic cocktails to counter the susceptibilities identified by genotyping. However, enthusiasm for this science fiction approach must be tempered by the enormous gulf between identifying genotypic risk and successful development of therapeutic interventions. The even thornier issues of the socioeconomic ramifications of genotype profiling need legislative consideration now if the worst elements of eugenic prejudice are to be avoided.

Steven Opal (Pawtucket, RI, USA) gave an overview of the complex integration between dysregulation of the innate immune and coagulation systems [29]. Although a number of recent discoveries have illuminated this field, it appears to have been around for at least 800 million years [30]! The relevance of this subject relates to the success of recombinant human activated protein C in severe sepsis [31] in contrast to the failure of antithrombin III [32].

Greet Van den Berghe (Leuven, Belgium) presented results from the landmark intensive insulin study [5]. She reminded the audience that although the renal glucose threshold is in the order of 12 mmol/l, other tissues (in particular, the lung) might exhibit thresholds as low as 8 mmol/l. The intensive group in this study demonstrated not only a much lower incidence of multiorgan failure and nosocomial infection, but demonstrated decreased polyneuropathy and mortality. Whether this is the effect of higher doses of insulin or lower levels of blood glucose remains speculative. What is clear is that high insulin requirements are associated with a worse prognosis. This study also serves to demonstrate the vital importance of attending to routine care, as this can achieve benefits equal to or greater than novel therapies, and at a fraction of the cost.

Peter Andrews (Edinburgh, UK) presented the evidence for, and mechanisms by which, isolated brain cooling can be achieved [33]. This work may help explain the contradictory results from trials of systemic cooling following neurological injury [7,8,34,35].

The final two lectures in this session covered the issues of terrorist attacks and mass casualty response. The lessons learned from recent and ongoing world events are that education, preparedness and practice [36] are the vital elements in meeting the harrowing challenges presented by such events.

Early haemodynamic stabilisation

In this enthusiastically attended session, chaired by Christopher Doig (Calgary, Canada) and Daniel De Backer (Brussels, Belgium), some of the more practical issues concerning the care of the haemodynamically unstable patient were discussed.

Jesse Hall (Chicago, IL, USA) opened the session stressing that by the bedside, as yet, we are only able to assess global oxygen delivery and consumption and to monitor surrogates of tissue hypoxia. We presently have no direct means of assessing tissue perfusion, let alone specific vascular beds. However, Jesse Hall questioned the practice of oxygen delivery/consumption goal-directed therapy in the critically ill patient, citing a number of papers demonstrating disappointing or adverse outcomes [37–39].

In firm and eloquent rebuttal to this, Robert Grounds (London, UK) presented the evidence for goal-directed therapy, particularly with respect to the high-risk surgical patient. He suggested that there is now an increasingly convincing body of evidence to support the practice of preoperative 'optimisation' in the form of fluid and inotropic manipulation of the circulation to improve cardiac output and, hence, tissue oxygen delivery. A number of studies over the past decade have shown impressive reductions in postoperative mortality by employing this technique [40–43].

It was a treat to hear a landmark paper presented by its first, now famous author, Emmanuel Rivers (Detroit, MI, USA) [4]. In studying a group ($n = 263$) of patients admitted to the emergency room with severe sepsis and septic shock, subjects were randomised to either early goal-directed therapy (treatment group) or standard therapy (control). They used traditional resuscitation end points, blood pressure, central venous pressure and urine output, as well as central venous saturation, to target therapy. Results were striking, to say the least, with 60-day mortality of 44.3% and 56.9% in the treatment and control groups, respectively. Food for thought that 6 hours of simple resuscitation, if prompt, can have such an impact on the mortality rate in severe sepsis without recourse to novel and massively expensive pharmacological strategies.

Finally in this session, Konrad Reinhart (Jena, Germany) reminded us of the potential use of central venous saturations as a guide to therapy, thereby possibly avoiding the need for pulmonary artery catheterisation [44].

Noninvasive mechanical ventilation

The session on noninvasive ventilation (NIV) proved popular. It summarised the research in this field, discussed various practical problems and suggested remedies. Umberto Meduri (Memphis, TN, USA) divided the evidence for NIV in acute respiratory failure on the basis of timing into *early* (to prevent intubation), *established* (as an alternative to intubation),

resolving (to wean from mechanical ventilation), and *postextubation* (to prevent reintubation). Overall, the eight randomised studies for patients with chronic obstructive pulmonary disease showed significant reductions in intubation requirements and mortality, when used early. The evidence for early intervention in patients without chronic obstructive pulmonary disease and in the remaining time frames suggested favourable outcomes, but more studies are required.

An analysis of the need for intubation following NIV showed that mask intolerance resulted in 11% of cases [45]. Paolo Navalesi (Pavia, Italy) reiterated that faces are all different and there was therefore a need for a wide variety of facemasks for the individual to try, if NIV was to be successful.

The problem of gas leaks was discussed by Robert Kacmarek (Boston, MA, USA), and the mannequin model of Schettino and colleagues [46] highlighted the fact that inappropriately high pressure support can greatly exacerbate leaks. To prevent rebreathing, Robert Kacmarek stressed the need for adequate positive end-expiratory pressure and that the exhalation port should be ideally placed in the facemask [47]. Laurent Brochard (Creteil, France) continued on the subject of leaks and suggested the use of ventilators, which are capable of monitoring inspiratory and expiratory tidal volumes early in acute respiratory failure, to identify insufficient ventilation as a consequence of leaks. Asynchrony as a result of leaks may be aided by the use of time-cycled ventilation, although this will obviously not resolve any leaks. Finally, the addition of helium to NIV may reduce the work of breathing, although limited space may prevent placement of the large tanks of helium required, and only certain ventilators are able to work with helium.

Massimo Antonelli (Rome, Italy) reviewed the trials for the use of NIV in acute lung injury/acute respiratory distress syndrome (ALI/ARDS). He concluded that the present favourable evidence should not be interpreted to support the extensive use of NIV in ALI/ARDS, but rather it should be used to design a randomised, controlled trial for NIV early in ALI/ARDS.

Finally, Phillipe Jolliet (Geneva, Switzerland) concluded that there was no solid evidence to support the use of NIV in community acquired pneumonia except in the subgroups of patients with chronic obstructive pulmonary disease and in the immunosuppressed. In all groups, however, NIV improves blood gases in community acquired pneumonia, NIV does not increase nursing workload in experienced units, no adverse effects have been demonstrated and, importantly, intubation is not delayed since it occurs early in community acquired pneumonia if required.

PEEP recruitment: do we understand it?

An afternoon was devoted to answering this question and, consequently, there was a good deal of overlap between speakers. All agreed that recruitment was necessary to establish alveolar patency in all recruitable lung zones and to therefore avoid repeated opening/closing of lung units with consequent inflammation and lung injury.

Jordi Mancebo (Barcelona, Spain) highlighted that recruitment is a time-dependent process, and that approximately 40 s is required during a sustained high-pressure ($P_{max} = 40$ cmH_2O) recruitment manoeuvre. Other recruitment manoeuvres include sighs, progressive PEEP (with fixed peak pressure and tidal volume), and repositioning (e.g. prone position, lateral position), although how PEEP is best selected following recruitment is not known. Biological variable ventilation (i.e. varying tidal volume as would happen physiologically) is an interesting new concept. It has been shown to improve recruitment and to reduce interleukin-6 levels, and therefore may reduce lung injury. Prof. Kacmarek (Boston, MA, USA) summarised that pressure/volume curve analysis is no longer considered clinically useful in determining best PEEP since methodology has not been standardised for curve derivation, and the upper inflection point and point of maximum curvature may be affected by different methodologies.

Fernando Suarez (Madrid, Spain) gave a very clear presentation of his work investigating oxygenation (PaO_2/FiO_2 ratios) versus lung mechanics (static compliance) in identifying best PEEP. Using a decremental PEEP trial (i.e. following recruitment), oxygenation and compliance were improved in comparison with an incremental PEEP trial (i.e. prior to recruitment), although optimal positions for oxygenation and compliance were at different positions on this curve. We are consequently none the wiser at predicting the point to set PEEP where lung overdistension and lung collapse are at a minimum. The moderators (Michael Pinsky, Pittsburgh, PA, USA, and Antonio Pesenti, Monza, Italy) commented that PaO_2/FiO_2 ratios may not be the best measure of shunt since PEEP can cause ventricular dysfunction, which affects shunt. Finally, Laurent Brochard (Creteil, France) discussed the influence of tidal volume on alveolar recruitment [48], and suggested that PEEP may need to be increased if using protective low tidal volume ventilation.

Although this session left the audience none the wiser in clinically determining best PEEP, the evidence to date suggests that the lung should be kept open to prevent ventilator-induced lung injury, although to achieve this we may be simultaneously subjecting the lung to overdistension and ventilator-induced lung injury. Finally, it was commented that the NIH PEEP trial had recently been abandoned since initial analysis had shown no effect, and because subsequent power analysis had revealed that the numbers of patients therefore required to show an effect would be massive. Perhaps the high PEEP was not applied appropriately since the method of recruitment in the decremental PEEP trial was not used in this study.

High-frequency ventilation: pro/con debate

A very amusing debate followed, with Arthur Slutsky (Toronto, Canada) directing his attack at ridiculing Robert Kacmarek (Boston, MA, USA) with the use of surreptitiously obtained holiday photographs of the latter, to remove his credibility as a speaker! This left Arthur Slutsky with very little time to discuss the evidence that high-frequency ventilation (HFV) is beneficial.

Robert Kacmarek led a strong defence and showed that animal studies comparing HFV with conventional ventilation (CV) had utilised a nonprotective lung strategy in the CV arm, and so comparison was not valid. Similarly, human data from the second multicentre oscillatory ARDS trial (MOAT II) showed a trend towards a reduction in mortality at 90 days, although the study was not powered to investigate this. However, the CV group in this trial received mean tidal volumes of 10.2 ml/kg, which more recent evidence [1] suggests is too large and hence detrimental.

Following the debate, both speakers agreed that HFV and CV are equally efficacious, although HFV should theoretically be superior. The benefits seen in the neonatal ICU (although the incidence of intraventricular haemorrhage was higher in this particular HFV population when compared with CV) may be the result of being able to use higher frequencies compared with adults. In the adult ICU, HFV frequencies are halved to enable adequate carbon dioxide clearance.

Renal failure

A broad range of subjects relating to renal failure were touched on, and the usual questions when considering renal failure in the critically ill (namely choice of renal replacement therapy [RRT] modality, type of membrane and adequacy) were raised.

Daniel Traber (Galveston, TX, USA) entertained us with an overview of the kidney's response to sepsis, which led us into the debate regarding modality. The overall consensus seemed to be in favour of continuous treatments, although no major antagonists were present: perhaps the battle has been won. As John Kellum (Pittsburgh, PA, USA) pointed out: are continuous therapies better? Probably!

There were the usual statistics with regard to mortality of acute renal failure. It is important to remember, however, that single-organ acute renal failure carries a mortality $<8\%$. The $\geq 50\%$ mortality reflects the overall picture of multiorgan failure of which acute renal failure is a part.

Kurt Lenz (Linz, Austria) discussed the hepatorenal syndrome and cemented the view that this remains a diagnosis of exclusion. Finally, Claudio Ronco (Vicenza, Italy) outlined the concept, beloved to nephrologists, of adequacy. It was one of the few times I have heard K_t/V (the RRT clearance of urea, in other words a measure of the adequacy of RRT [49]) discussed outside a renal ward, and it perhaps may have helped clear up some misconceptions with regard to RRT. Ronco also gave an excellent plenary lecture on extracorporeal support in sepsis, although unfortunately the jury remains out on this treatment. As he said: until the randomised, controlled trial is carried out, we will not know.

Acid–base

David Bennett's (London, UK) honesty must be commended in suggesting that strong ion difference and strong ion gap are difficult to comprehend. In fact, his explanation of the subject was extremely clear. Recent work at his hospital had unfortunately not found strong ion difference a useful prognostic marker for patients admitted to the ICU.

John Kellum (Pittsburgh, PA, USA) showed that acidosis worsens shock in an animal model, and that acidosis is proinflammatory in cultured lung macrophages. The implication is therefore that, under most conditions, acidosis should be avoided in the critically ill. This does not necessarily, however, imply that mild acidosis requires correction with sodium bicarbonate, not least as the controversies surrounding this intervention remain [50].

Head trauma

Andrew Maas (Rotterdam, The Netherlands) discussed the pros and cons of using cerebral perfusion pressure, blood flow or oxygen to target therapy in the management of head trauma. Oxygen-targeted therapy using jugular venous oxygen saturation monitoring was appealing, although this has not yet been validated. Other treatment modalities presented by other speakers (e.g. raising cerebral perfusion pressure, hypothermia) have unfortunately continued to show disappointing results in the management of head trauma. Andrew Maas ended the session, however, by explaining that these treatments may in fact be beneficial but the outcome assessments were invalid. In many of these trials, the Glasgow Outcome Scale was used and outcome was dichotomised into good/poor, when in fact this is a four-point scale. If reanalysed using a sliding-dichotomised method, as previously used in many of the stroke trials, then many of the head trauma studies were grossly under-powered.

Transfusion

This excellent session covered all aspects of the increasingly muddy waters surrounding the issues of red cell transfusion in resuscitation and critical illness. With the landmark Canadian study of restricted transfusions in critically patients [51], the possibility of disease transmission (in particular, new-variant Creutzfeldt-Jacob Disease) and the simple economics of demand outstripping supply, the questions regarding what you should transfuse and when it should be transfused have escalated.

The effects of storage on red blood cell (RBC) deformability and oxygen dissociation are well established [52–55]. What

happens to such cells once in the circulation remains more contentious. Timothy Walsh (Edinburgh, UK) presented the preliminary results of a study in which the haemoglobin concentration of critically ill patients was closely monitored peritransfusion. His group found that the haemoglobin concentration returned to baseline (transfusion threshold) within 48 hours. Further investigations suggest that, despite this and the gross morphological abnormalities of the stored RBCs, these cells persist in the circulation well beyond this 48-hour period. He stressed that the haemoglobin concentration and RBC mass do not have a linear relationship, especially in critically ill patients who tend to exhibit low mean corpuscular haemoglobin concentration. Timothy Walsh concluded by reminding the audience that the risk–benefit profile of top-up transfusion has yet to established.

The immunosuppressive effects of allogenic RBC transfusion are well established [56,57]. One of the major contributors is thought to be the presence of allogenic leukocytes. Indeed, the positive findings of the Canadian restricted transfusion study [51] have been attributed, at least in part, to the reduced dose of allogenic leukocytes in the restricted group. Hence the widespread interest in investigating the effects of universal leukocyte depletion. Such a strategy appears to have benefits, although these may depend on whether the removal is performed prestorage or pretransfusion [58]. Jean-François Baron (Paris, France) presented the results of the recently published French study, which investigated the incidence of postoperative infections in patients undergoing abdominal aortic aneurysm repair who received leukodepleted or nonleukodepleted blood transfusions [59]. Although no statistically significant different was found between the two groups, the study was grossly underpowered. The results of a larger Canadian study are keenly awaited.

Alternative strategies to packed RBC transfusion were also discussed. Howard Corwin (Lebanon, USA) presented the case for routine use of recombinant erythropoietin [60,61]. In essence, the evidence to date demonstrates that erythropoietin significantly reduces transfusion requirements but has failed to show a morbidity or mortality benefit. Intriguingly, erythropoietin appears to have extensive neuroprotective properties, and human trials in a variety of acute neurological insults are eagerly awaited [62].

Marcos Intraglietta (La Jolla, CA, USA) presented an emerging alternative hypothesis to the dogma of maintaining oxygen delivery by maintaining oxygen carrying capacity (i.e. RBC transfusion). He presented the evidence that maintenance of blood viscosity and hence functional capillary density is the critical factor [63]. He went on to present his and others work on PEGylated haemoglobin solution, which not only increases blood viscosity, but also is the first free haemoglobin solution to exhibit near identical oxygen dissociation characteristics to RBCs. PEGylated haemoglobin solution consequently does not induce the limiting hypertension and microvascular pathophysiology associated with other free haemoglobin solutions [64–66].

In the context of acute, severe/unstoppable haemorrhage, Mauricio Lynn (Miami, FL, USA) presented data that recombinant activated factor VII offers a new life-saving intervention [67–69]. Indeed, it seems probable that this drug will be the subject not only of clinical studies into the treatment of haemorrhage, but may also have a role in immune modification as it avidly binds tissue factor. Recombinant activated factor VII is thus being investigated as a carrier molecule to neutralise this major proinflammatory mediator.

Conclusion

As the preceding sections hopefully demonstrate, the breath and depth of this year's symposium, as in previous years, left attendees spoilt for choice and, potentially at least, exhausted. Undoubtedly, the International Symposium on Intensive Care and Emergency Medicine will continue to expand both as an educational forum and as a research forum, creating ever greater challenges to the programme designers.

Competing interests

None declared.

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