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- **Inspired oxygen and its effect on central venous oxygenation**
- **ECMO: a case series**
- **Fire in an ICU**
- **Antibiotic prescribing**
- **Isolation policies**
- **Trace elements**
- **Antidiarrhoeals**
- **Case Reports: Airway obstruction, ethylene glycol ingestion, bird's nest filter**
- **Audits: Consultant appointments, Antibiotic usage in Scotland**
- **CAT reviews: Inotropes, Albumin in head injury**
- **Regular features: Lemmingaid, Letters, meetings and reports**



The Intensive Care Society Annual Spring 2008 Meeting

Monday 19 - Wednesday 21 May 2008

The ICS Spring meeting will take place in the Manchester Conference Centre with a two and half-day programme that will commence at 14:00 on Monday 19th May. A faculty of international and UK experts will deliver a stimulating and interesting scientific programme. A full programme of parallel sessions will allow a broad range of topics to be addressed which will be of interest to a multi-professional audience. These will include:

- What's new and important in the literature?
- Recent developments in respiratory support
- What's new in the management of brain injury?
- Management of the difficult abdomen in ICU
- How to manage the long term ICU patient
- The role of handheld Ultrasound by Intensivists
- Update in renal replacement therapy
- Nosocomial Infections in ICU
- Nutrition in the Critically Ill
- New ways of staffing
- Safety in the ICU

In addition there will be the regular Trainees session and Members forum, the Gilston lecture, a range of Industry sponsored sessions and a full social programme including the annual Intensive Care Society Dinner & Dance. There will also be a Skills for Intensivists workshop (SKINT) on mechanical ventilation on Monday 19th May (limited availability).

Don't miss a great meeting. Book your leave now!

Further information and on line registration will be available at www.ics.ac.uk



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JICS Editorial Board

Jane Harper (Editor)
Kate Osborne (Editorial Assistant)
Bruce Taylor

Rupert Pearse
David Goldhill
Chris Cairns (CAT reviews)

Brian Cuthbertson
Carl Waldmann
Justin Kirk-Bayley

The Editor writes

Ruthin Castle is in North Wales, and was originally built by Edward I to quell the Welsh rebellions in the 13th century. In the first half of the twentieth century, it was converted into a 'state of the art' hospital designed on the Mayo Clinic model, with diagnostic and treatment facilities unavailable in other areas of Britain. All roads, it seems, led to Ruthin at that time. Its existence as a hospital came to an end in the 1950s because of reorganisation of services. Sound familiar? Visit the library (now the bar of a hotel) at the Castle, and bring down the volume there called 'The Hospitals Year Book 1950-51'. Open it to an article on 'The Hospital Service, Some Current Problems'. What are the issues? Herewith a brief list: Shortage of staff and beds, Saving beds by having more outpatients, Provision for the elderly sick, Hospital finance and Co-ordination of services.

Another article makes a plea for 'The Development of British Standards in the National Health Service' - to 'set a standard of quality... with fitness for purpose...'

Plus ça change... or perhaps, as one Chekov character says when told 'everything passes': 'nothing passes'. We have reorganisation of services, MTAS, lack of beds, same day admission for theatre, care in the community, finance targets, standards...

Peter Nightingale has written to remind us to mark the death of Dr Bjorn Ibsen, whose obituary appeared in the BMJ of 29th September 2007! Dr Ibsen is the 'grandfather' of our specialty.² He was an anaesthetist from Copenhagen who learned, while studying thoracic anaesthesia in Boston, that inadequate mechanical ventilation led to accumulation of carbon dioxide in patients, clinically recognised by signs of hypertension and sweating. At that time, blood tests could only analyse total carbon dioxide levels, i.e. all forms that carbon dioxide is carried in blood - dissolved carbonic acid, dissolved carbon dioxide and bicarbonate. When patients presented to his hospital with bulbo-spinal paralysis from polio, physicians interpreted the observed raised total carbon dioxide level as retention of bicarbonate from kidney failure secondary to overwhelming viral infection; they did not believe that it was due to raised carbon dioxide from respiratory failure because the patients were not cyanosed. Dr. Ibsen recognised the signs of respiratory failure that he had seen in patients at the Massachusetts General Hospital. He performed a tracheostomy on a 12 year old girl who was close to death, and ventilated her successfully with a circuit incorporating a carbon dioxide absorber. Thus the specialty of intensive care was born. With hand ventilation of patients via cuffed tracheostomies, mortality from polio dropped from 80% to 25%. In all, about 800 patients were treated for an estimated 165,000 hours with manual ventilation done by 1,500 medical students and other volunteers. The story of the polio epidemic and the birth of our specialty is truly remarkable.

Bruce Taylor steps down this month as editor of JICS and, with some trepidation, I step up to the plate. I hope that we can continue to develop the Journal as Carl Waldman and Bruce have so ably done. There is now an editorial board, and we aim to publish more original articles, case reports, CATs and audits, with the aim of ultimately applying for Medline listing. There will be changes in format and style over the coming issues. We encourage submissions from the whole of the critical care community in the UK. There are new instructions for authors which are on the website; all submissions will now be formally reviewed by at least two members of the editorial board.

I look forward to receiving your submissions.

SJ Harper

1. Richmond C. Obituaries: Bjorn Ibsen. *BMJ* 2007; **335**: 674.
2. Sykes K Bunker J. The anaesthetist and the fever hospital. Chapter 12 in: *Anaesthesia and the practice of medicine: Historical Perspective*. London. Royal Society of Medicine Press; 2007: 161-171.

Topical remarks by the immediate-past editor (TRIPE)

B Taylor

It is with a mixed sensation of sadness and relief that I have handed over editorial responsibility for JICS to Jane Harper. To claim that this feels a little like handing on an adopted child to a new foster parent would be a bit precious, but it is certainly similar to selling a car that I have become rather attached to and watching it being driven away. I have however complete faith in Jane's driving skills, and am confident that she will not only handle it carefully but also probably arrange for it to be more highly polished both inside and out! I will certainly not miss the tedious but essential tasks of re-writing stacks of references into the preferred format and spending hours trying to make sure that there are no typographical errors, knowing that I will still spot one when I open the next edition! I suspect that I may also be back-seat driving for a little while too.

The content of the current edition serves as a good reminder of the progress that JICS has made, and it is very encouraging that we are increasingly attracting original, high quality contributions from our membership. I am also grateful for the huge amount of support and assistance that I've had from the evolving Editorial Board and our reviewers, and in particular to Brian Cuthbertson (for suggesting) and Chris Cairns (for delivering) the concept of including the SICS CATmaker reviews in JICS. The next targets are to improve the online access to published articles and to aim for Medline accreditation, both of which will present significant challenges. Probably similar to Jane taking up rally driving!

In the parking space created by this handover, I've been rather enjoying hearing assorted comments from Berlin-blessed colleagues - most of which have confirmed my prejudiced preference that these huge meetings are really not for me. The last time I went to one I met one of our former trainees who is now working in Southern India, and in a brief conversation we agreed that we should meet for a meal later; great idea, except that the event was so overpopulated that I couldn't find him

again, and ended up having to call him on his mobile phone (via India) to trace him. For me, one of the main reasons for attending these meetings (apart from confirming that nothing much has changed) is the social benefit of being able to meet up with old friends and colleagues - something that doesn't work when they are so enormous. The other problem I have with them is that there is simply too much choice; for the same reason that I have never been able to handle shopping in London (too many places, options, and decisions) I tend to find myself stuck on which session to attend, and usually that the ones that I am interested in clash anyway. Clearly for some, big is better, but one size does not fit all.

And on that basis, I will finish with an unapologetic bit of marketing. The ICS has spent many hours considering the future of its meetings strategy, which has become hugely important in the wake of cut-backs in educational and study leave funding. After conducting a survey of our members, and much debate (not all entirely harmonious) we seem to be evolving to a consensus that the London-based State of the Art Meeting (SoTA) is regarded as being the most valued by both our clinical members and the vital Industry Membership (the financial support of whom is absolutely crucial). The future viability of the Spring Meetings remains uncertain, and difficult decisions may have to be made about these because of the fall in attendee numbers and the potential competition with other events. However, SoTA at least appears to be thriving, having apparently become something of an iconic event, and already the attendee numbers for the next one have exceeded those anticipated at this stage. So, if you like a good social event, and prefer the option of making relatively few decisions but still being able to attend high quality sessions, can I strongly recommend that you check out the programme for this year and consider registering for it. And for those who *do* like shopping in London, it is also a great opportunity to do so just before Christmas.

Delirious in the UK

V Page

Keywords: Delirium, change management

What is delirium and what can we do about it?

This article is about deranged brain function in critically ill patients. Delirium is defined as the acute onset of mental status changes accompanied by inattention and disorganised thinking or altered level of consciousness. During the last few years there has been an explosion of information and new work in the area of delirium - its incidence, monitoring, treatment and outcomes. The SCCM and the ICS recommend routine monitoring of delirium in critically ill patients. In Watford, we have implemented delirium assessment and treatment on our unit, and are now on the brink of spreading it nationally. I will describe:

- The inspiration,
- The implementation of the idea in Watford,
- Acquisition of funding for a national project
- The 'bleeding obvious'.

After all, patients like their brains to work after critical care.

The scene is set

In London, in November 2005 Professor Wes Ely gave a lecture at the Magill symposium called 'Brain Dysfunction in Critically Ill Patients.' He described the poor outcome associated with delirium.

Delirium is an independent predictor of mortality (34% six month mortality vs. 15% mortality without delirium), institutionalisation (increased hospital length of stay by an average of ten days) and increased associated cost.¹ There is an increasingly clear and consistent message across cohorts to date that duration of delirium is a predictor of long-term cognitive impairment following critical illness.²

We frequently discharge our patients with their hearts, lungs and kidneys optimised but not their brains. They can't function normally, nor remember people's names, nor where they have put things, and they don't go back to work. This is not a psychological but a pathological problem, and for some patients the legacy of delirium is long term dementia.

Delirium is usually 'quiet'. An apparently co-operative patient lays passively answering questions with a nod or shake of the head. You have to test the patient's thinking to assess delirium. The CAM-ICU test described by Professor Ely takes a minute and can be performed on any patient who can open their eyes on their name being called.³ Inattention is diagnosed by asking the patient to squeeze hands on pronouncing a particular letter in a sequence of 10. Disorganised thinking is diagnosed by asking a series of 4 questions (e.g. does a stone sink in water?), then the patient is asked to follow a simple command (show me how many fingers I have raised). Acute inattention plus disorganised thinking equals delirium. Delirium equals brain failure; it needs treating or, better, preventing. The CAMS-ICU³ is a score devised by Dr. Ely to detect delirium in 1988 and is the most widely used assessment tool (see www.icudelirium.org).

The impact of Professor Ely's lecture was enormous to me. I came away with the inescapable conclusion that here was something important and cost effective that we could (and should) do at Watford.

Frogs

Five frogs sit on a log and four decide to jump off. How many frogs are left on the log? The answer is: still five, unless they actually act on their decision.

Action speaks louder than words

How did we become a unit that routinely monitors all patients for delirium? Here's the Watford model in 10 steps.

1. We got medical colleagues and the senior nurses on board, went to their staff meetings and spread the word. "This will make a real difference to our patients' outcomes."
2. We waited for nurses to express interest; we pitched it right and they were keen to be involved.
3. We decided a date for implementation, and who would be responsible for delirium assessment (nursing staff in our case).
4. Dissemination: We made a poster. We had a photo of me at the top answering questions about delirium that were in thought bubbles above the photos of three nurses. We had Manga style, lots of '!!!' and jagged lines.
5. We drew up training manuals for the CAM ICU, treatment guidelines and other useful material from www.icudelirium.org.
6. We put together our own presentation and presented it to trainees, the post graduate medical centre, clinical governance group, other units, etc...
7. Attention Seeking: We got paper and marker and wrote "inattention" in bold letters and stuck it in a prominent place close to the ICU with our extension number in a corner, left it for a few days and replaced it with "disorganised thinking" then "if you don't look for it you won't see it".
8. We announced routine monitoring of delirium on the critical care was starting. By this time our colleagues and nurses knew what was expected.
9. On ward rounds we asked whether the CAM was negative, positive or not assessable. If it had not been done, I did it with the nurses and trainees to help them get over any self-consciousness or lack of confidence.
10. Progress and current issues were monitored and advertised in a single-sided A4 newsletter update.

'Going national'

By November 2006, we were flush with success but needed money; our aim was to ensure that all critically-ill patients in the UK were routinely monitored for delirium. From the beginning of the project I had considerable encouragement from Professor Ely, who was finding the UK a 'tough nut to crack.'

An Alzheimer's Society dissemination grant came to our aid. The head of research of the Society encouraged our application, and

150 lay people with experience of dementia assessed the form and gave the project their support. The committee of directors approved a grant of £18,000.

The project evolved into a series of meetings, visits and outreach work with a core of interested units over a year. Stage 1 has now been successfully completed. Wes Ely has lectured in a series of meetings in Watford, London, Oxford and Manchester, all with enthusiastic response from local clinicians. The multidisciplinary teams attending were all inspired to improve this aspect of patient care. Two of the executive directors from the Alzheimer's Society have attended and been impressed.

The Emperor has no clothes

Now I sit in meetings listening to conversations about MARS, extracorporeal carbon dioxide removal and ECMO. They all have their place but I think,

- Delirium monitoring does not involve machines,
- It costs no money,
- It could make a difference to over half of the patients who survive ICU.

Watch this space or, better still, get on and do something.

For illustration, a quote - "we followed up a nice little man on our unit who interpreted our requests that he try to eat more, as us trying to feed him up so we could eat him for Christmas - shared with us long after his discharge from the unit! And we had no idea because he was so quiet and co-operative."

Professor Ely will be lecturing on delirium at the ICS State of the Art meeting in December.

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The effect of inspired oxygen concentration on central venous oxygen saturation

R Jee and N White

Keywords: oxygen content

Summary

Recent research has generated widespread interest in the use of central venous oxygen saturation (ScvO₂) as a target for resuscitation in early sepsis. However, there are many factors which may affect the value of this variable and there is no published data examining the effect of varying the FiO₂ on ScvO₂. The purpose of this study was to investigate the influence of increasing FiO₂ on ScvO₂ in 20 stable critical care patients. Baseline arterial and central venous blood haemoglobin oxygen saturation measurements were obtained. FiO₂ was then increased to 1.0 for 30 minutes, after which arterial and central venous haemoglobin oxygen saturations were re-measured. Mean ScvO₂ increased significantly from 73.3% (SD 6.6) to 80.0% (SD 7.0); mean increase was 6.7% (95% CI 4.8 to 8.7; $p \leq 0.001$). Increasing FiO₂ was associated with a significant increase in ScvO₂ and may therefore complicate the interpretation of ScvO₂ data.

Introduction

There is widespread interest in the use of central venous oxygen saturation (ScvO₂) to guide fluid and inotrope administration. The adverse prognostic significance of values of ScvO₂ below 65% has been observed in a number of trials involving patients with myocardial infarction,¹ trauma,² severe sepsis,³ and cardiac failure.⁴ An interventional study by Rivers and colleagues involving septic patients⁵ demonstrated a reduction in morbidity and mortality in the early goal directed therapy (EGDT) group in which ScvO₂ was optimised to greater than 70%. This has fuelled interest in the use of ScvO₂ as a target for resuscitation in early sepsis. More recently, there has been also growing interest in the association of low values of ScvO₂ with morbidity in the perioperative and postoperative periods for patients undergoing major surgery.^{6,7}

In addition to cardiac output, ScvO₂ is also affected by a range of factors which affect blood oxygen content and tissue oxygen consumption. There are therefore many treatments which affect ScvO₂. FiO₂ was not controlled in the study by Rivers and colleagues and there has been no published data examining the effect of varying the FiO₂ on ScvO₂ in humans. The physiological importance of increasing FiO₂ on ScvO₂ is illustrated by the sigmoid shape of the oxy-haemoglobin dissociation curve. A small change in PO₂ would be predicted to have a much greater effect on oxygen saturation of haemoglobin on the steep part of the curve in the 50-75% saturation range (venous blood) than in the 90-100% range (arterial blood). The aim of this study was to look at whether increasing FiO₂ has an effect on ScvO₂.

Methods

Following Local Research Ethics Committee approval, written informed consent, where possible, was obtained from 20 stable critical care patients. In patients unable to consent, assent was

obtained from next of kin and retrospective consent was then sought. As there had been no previous published studies regarding our hypothesis we were unable to perform a calculation to determine the sample size and so the number was chosen arbitrarily. All patients had both radial arterial and central venous catheters (internal jugular or subclavian) in situ and none were due to undergo any events which would affect their oxygen consumption or delivery. Patients were not included if they were clinically unstable.

Baseline arterial and central venous blood samples were obtained and analysed by co-oximetry using a blood gas analyser (Radiometer Copenhagen ABL 700 Series) which was calibrated every 4 hours. FiO₂ was then increased to 1.0 in ventilated patients, and in the spontaneously breathing patients a Hudson RCI adult non-rebreathing mask was applied with oxygen flow at 15 l/min. After 30 minutes further arterial and central venous blood samples were taken and the patient's FiO₂ was returned to baseline. Haemoglobin concentration, SaO₂, PaO₂, ScvO₂ and the partial pressure of oxygen in the central venous blood (PcvO₂) were recorded at both baseline and high FiO₂.

The significance of any difference between SaO₂ pre and post high FiO₂ was assessed using the paired t-test. The same statistical analyses were employed with changes in ScvO₂. Mean differences are presented with 95% confidence intervals. A two-sided 5% significance level was used. Data were analysed using Microsoft Excel.

Oxygen content (ml/100 mls of blood) was calculated using the formula $(1.34 \times \text{Hb} \times \text{SpO}_2 \times 0.01) + (0.023 \times \text{PaO}_2)$ where Hb is presented in g/dl and PaO₂ in kPa. The significance of any difference between arterial blood oxygen content (CaO₂) before and after high FiO₂ was assessed using the paired t-test. The same statistical analyses were again employed with changes in central venous blood oxygen content (CcvO₂). Mean differences were presented with 95% confidence intervals. A two-sided 5% significance level was again used.

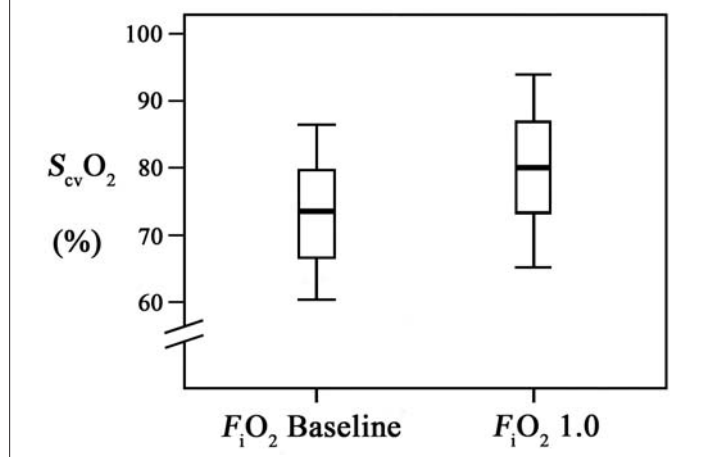
Results

We recruited 20 patients in our critical care unit, 18 of whom were spontaneously breathing via a facemask and two were intubated and ventilated. The patients had a variety of medical and surgical conditions (**table 1**, see page 9) and had been established on the critical care unit for more than 24 hours. All patients were haemodynamically stable and none were severely anaemic. Thirteen patients had internal jugular and seven patients had subclavian central venous catheters in situ.

SaO₂ and ScvO₂ before and after the increase in the FiO₂ for each of the twenty patients are presented in **table 2** (see page 10). CaO₂ and CcvO₂ before and after the increase in the FiO₂

are presented in **table 3** (see page 10). On analysis, both groups of data were normally distributed, with non-significant skewness tests. Mean baseline FiO_2 was 0.35. Mean SaO_2 increased from 97.5% (SD 1.6) to 99.5% (SD 0.6) following 30 minutes of high flow oxygen; mean increase 2% (95% CI 1.3 to 2.6; $p \leq 0.001$). Mean ScvO_2 increased significantly from 73.3% (SD 6.6) to 80.0% (SD 7.0); mean increase 6.7% (95% CI 4.8 to 8.7, $p \leq 0.001$) (**figure 1**). Mean CaO_2 increased from 13.82 (SD 1.6) to 14.9 (SD 2.2) ml/ 100 mls of blood following 30 minutes of high flow oxygen; mean increase 1.08 ml (95% CI 0.36 to 1.81; $p=0.005$). Mean CcvO_2 increased from 10.59 (SD 1.4) to 11.19 (SD 1.9) ml/ 100 mls of blood; mean increase 0.6 ml (95% CI 0.22 to 0.98; $p=0.004$).

Figure 1: Central venous oxygen saturation (ScvO_2) at baseline and after 30 minutes of FiO_2 1.0. Box plot (Mean; 1 SD; 2 SD).



Discussion

The principal finding of our study was that increasing FiO_2 resulted in a mean increase in ScvO_2 of 6.7%. This observation may have significant implications for the interpretation of ScvO_2 data in clinical practice. Although we were unable to find any human studies supporting our conclusion, Rheinart and colleagues⁸ examined the correlation between ScvO_2 and mixed venous saturations (SvO_2) in anaesthetised dogs under different conditions including normoxia and hyperoxia at 100% O_2 . Although no statistical test was employed, an increase in the mean saturation was observed but not specifically commented on in the article. The adverse prognostic significance of low values of ScvO_2 (less than 65%) has been demonstrated in patients with myocardial infarction,¹ trauma,² severe sepsis,³ and cardiac failure.⁴ Recently Pearse and colleagues observed that low ScvO_2 values during the first eight hours after major surgery was associated with increased risk of postoperative complications.⁵ A further study has confirmed the association between low ScvO_2 and postoperative complications.⁷ In the only interventional study to target ScvO_2 , Rivers and colleagues demonstrated a reduction in morbidity and mortality in the EGDT group of septic patients in which ScvO_2 was optimised to greater than 70%.⁵ These studies emphasise the importance of a clear understanding of ScvO_2 physiology.

Although the importance of the current findings seems most likely to relate to the interpretation of ScvO_2 data, it is also

possible that the increase in ScvO_2 may reflect a beneficial effect of oxygen therapy. Tissue hypoxia is a key feature of critical illness which arises in part due to an imbalance between oxygen delivery and demand and is a key development preceding multi-organ failure and death.⁹ High oxygen partial pressures may increase the distance of interstitial oxygen diffusion with a subsequent reduction in tissue hypoxia.¹⁰ In surgical patients, high tissue oxygen tension is associated with a reduced risk of wound infection,¹¹ which may be partly explained by the oxidative killing of bacteria by neutrophils.¹² Clinical trials suggest the use of a high FiO_2 in the perioperative period may also decrease the incidence of wound infection.^{13,14}

The principal arguments against the use of high FiO_2 in critical care patients are the risks of absorption atelectasis and pulmonary oxygen toxicity. Absorption atelectasis may be associated with the use of high concentrations of supplemental oxygen, although a number of studies have shown no significant increase in postoperative absorption atelectasis with high FiO_2 administration over periods up to eight hours.¹⁵⁻¹⁹ Pulmonary oxygen toxicity may only occur after prolonged exposure²⁰⁻²² and interestingly, in experimental models, sepsis may be associated with an increased resistance to hyperoxic lung injury.²³ The Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock recommend targeting a ScvO_2 of more than 70%.²⁴ Whilst our study suggests that this can be partly achieved by increasing FiO_2 , the only protocol which has been shown to improve outcome focussed on the use of fluid and inotropic therapies to achieve this.⁵ There is at present no evidence that other approaches to increasing ScvO_2 would result in similar improvements in outcome.

There are some weaknesses in the methodology of this study. As eighteen out of the twenty patients were breathing oxygen through a facemask, the values of initial FiO_2 and subsequent high FiO_2 could not be accurately assessed. However the study was designed to evaluate whether increasing FiO_2 had any effect on ScvO_2 rather than to quantify the magnitude of this effect. The position of the central venous catheter tip was not assessed prior to data collection. However, a retrospective review of chest radiographs confirmed that the tips of all twenty catheters were within the superior vena cava. The lack of cardiac output data may also limit interpretation of these findings. However, we selected haemodynamically stable patients to avoid the introduction of bias and we believe that cardiac output would have been unlikely to change significantly during the 30 minute study period.

In conclusion our study showed that FiO_2 has a significant effect on ScvO_2 and emphasises the importance of taking FiO_2 into consideration when evaluating ScvO_2 data, either in research or clinical practice. Further research might assess the degree of increase in ScvO_2 with high flow oxygen in acutely unwell patients with initially low ScvO_2 rather than our cohort of haemodynamically stable patients.

Acknowledgements

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Table 1: Characteristics of each of the twenty patients in the study.

No.	Diagnosis	Age	Hb* (g/dl)	FiO ₂ [†]	SV/ CPAP ASB [‡]
1	Community acquired pneumonia	78	11.1	0.35	CPAP ASB
2	Post op oesophagectomy	52	11.5	0.35	SV
3	Pneumonia	81	9.6	0.35	SV
4	Post op gastrectomy	41	8.0	0.4	SV
5	Post op axillo-bifem. graft	75	11.8	0.35	SV
6	Post VF arrest	71	10.8	0.4	SV
7	Post op emergency AAA	77	9.6	0.24	SV
8	Routine AAA	72	10.9	0.28	SV
9	Post op small bowel perforation	61	9.8	0.28	SV
10	Post op small bowel perforation	61	9.2	0.4	SV
11	Urinary tract sepsis	81	11.6	0.4	SV
12	Acute renal failure	62	9.7	0.21	SV
13	Small bowel perforation and sepsis	52	11.3	0.6	CPAP ASB
14	Variceal bleed	52	9.0	0.6	SV
15	Acute on chronic renal failure	74	10.3	0.24	SV
16	Laparotomy: small bowel obstruction	40	11.6	0.35	SV
17	Laparotomy: toxic megacolon	55	9.6	0.4	SV
18	Left ventricular failure	80	10.9	0.3	SV
19	Status epilepticus	83	12.5	0.3	SV
20	Post op debridement infected THR	78	10.1	0.24	SV

*Hb, haemoglobin concentration; [†]FiO₂, fraction of inspired concentration of oxygen; [‡]SV, spontaneous ventilation; CPAP ASB, continuous positive pressure ventilation with assisted spontaneous breaths.

Table 2: Arterial oxygen saturation pre and post increasing the FiO₂ from baseline to 1.0 (%). Central venous oxygen saturation pre and post increasing the FiO₂ from baseline to 1.0 (%). Data presented for each of the twenty patients in the study.

No.	SaO ₂ * Pre	SaO ₂ Post	ScvO ₂ † Pre	ScvO ₂ Post
1	94.2	99.3	86.4	97.5
2	98.4	99.7	70.4	70.4
3	98.7	100	61.2	70
4	98.9	99.9	84.3	81.8
5	96.8	99.3	73	77.7
6	98.2	100	65.2	70.9
7	98.4	99.7	74.5	83.4
8	99.4	100	70.8	75.1
9	99	98.9	77.6	82.9
10	94.8	99.3	72.1	81.8
11	97.8	99.5	77	79.3
12	98.1	99.3	76	83.1
13	98.3	99.7	80.4	85.7
14	97.5	98.7	74.5	78
15	98.2	99.7	68.2	81.5
16	94.7	99.6	78.1	89.1
17	95.2	97.7	70.5	79.2
18	98.2	99.9	62.8	68.6
19	97.9	100	75.7	84.8
20	98.2	99.7	66.6	80.1

*SaO₂, arterial oxygen saturation; †ScvO₂ central venous oxygen saturation.

Table 3: Oxygen content in arterial and central venous blood for each of the 20 patients pre and post increasing the FiO₂ from baseline to 1.0 (ml/100 mls blood).

No.	CaO ₂ * Pre	CaO ₂ Post	CcvO ₂ † Pre	CcvO ₂ Post
1	13.84	15.00	13.01	14.83
2	15.2	16.14	10.96	11.06
3	10.94	11.58	8.67	7.75
4	10.93	11.63	9.29	8.36
5	15.55	16.33	11.66	12.31
6	14.59	15.32	9.62	10.37
7	12.7	20.1	9.9	10.98
8	15.05	15.76	10.55	11.09
9	13.37	13.66	11.56	11.02
10	12.26	12.33	9.29	10.11
11	15.5	16.12	12.1	12.35
12	12.69	13.7	10.32	11.08
13	15.43	15.84	12.19	13.24
14	12.2	12.66	9.2	9.43
15	13.45	14.63	10.52	10.51
16	14.68	16.54	12.06	14.15
17	12.73	12.9	9.37	9.89
18	14.61	15.56	9.27	10.22
19	16.92	18.19	13	14.12
20	13.69	14.03	9.2	10.86

*CaO₂, oxygen content in arterial blood; †CcvO₂, oxygen content in central venous blood.

A case series of adults treated with ECMO

N Schofield and D Lowe

Keywords: extra corporeal membrane oxygenation, ECMO, case series

Introduction

ECMO (extra-corporeal membrane oxygenation) is a form of extracorporeal life support. An external artificial circulation or circuit carries venous blood from the patient to an oxygenator, where oxygen is added and carbon dioxide removed, then the blood is returned to the patient circulation. Flow through the circuit may be achieved either using a pump (centrifugal or roller) or pumpless circuit using the patient's own arterio-venous pressure gradient.

In 1975, Zapol and colleagues reported a prospective randomised trial of veno-arterial ECMO in adults with acute respiratory distress syndrome (ARDS). This nine centre study showed survival rates of 10% in both the control and ECMO treated group.¹ The high mortality rates and other problems associated with earlier techniques led to a decline in its use over the following decades.

Improvements in technology have meant significant advances in pumps, circuits and oxygenators, resulting in more efficient gas exchange with less resistance to flow, decreased haemolysis and plasma leak that were problems associated with earlier circuits.

A randomised control trial of its use in ARDS (CESAR) is anticipated. Encouraging results from a number of other groups worldwide, especially when used to treat children, have led to an increase in its use in many centres. A number of centres report survival rates of 50-70% in patients with ARDS treated with ECMO.²⁻⁷

Types of ECMO

ECMO can be either veno-venous (VV) or veno-arterial (VA).

With VV ECMO, blood is taken from a large central vein and returned to the venous system near the right atrium after it has passed through an external circuit and oxygenator. A variant of this (high flow VV ECMO) uses two access cannulae to remove venous blood from the patient before entering the oxygenator. High flow VV ECMO is used when circuit flow via a single access cannula is inadequate to maintain safe oxygenation and is used for more severe cases of respiratory failure or high cardiac output states. VV ECMO is used to treat isolated respiratory failure when adequate heart function is present.

Peripheral VA ECMO involves peripheral cannulation, eg femoral vein - femoral artery, allowing venous blood to be taken from large central veins and returned to the patient's arterial system after it has passed through an oxygenator. VA ECMO is used for the treatment of patients with cardio-respiratory or cardiac failure when the use of a ventricular assist device (VAD) is deemed inappropriate, or as a bridge to transplant or VAD insertion.

Central VA ECMO, in which the cannulae are attached directly to the major vessels (including the ascending aorta) during surgery, is required for cardiac support when there is poor lung function, because the use of peripheral VA ECMO in this case would lead to the delivery of hypoxic blood from the pulmonary circulation preferentially to the cerebral and coronary circulation. Peripheral VA ECMO is appropriate when there is reasonable lung function and cardiac surgery is not required.

Indications

ECMO is indicated for potentially reversible, life-threatening forms of respiratory and/or cardiac failure which are unresponsive to conventional therapy. Common uses of VA ECMO include: graft failure post heart/heart-lung transplant, cardiogenic shock, post cardiac surgery when weaning from cardiopulmonary bypass using conventional methods fails, sepsis with profound cardiac depression, and drug overdose with profound cardiac depression. There are a number of other, less common, indications such as myocarditis, chronic cardiomyopathy as a bridge to transplant / VAD insertion, pulmonary embolism, cardiac or major vessel trauma, massive haemoptysis, pulmonary trauma and acute anaphylaxis.

VV ECMO can be used in patients who are hypoxaemic because of severe pneumonia, ARDS, acute lung (graft) failure following transplant, pulmonary contusion, airway obstruction, status asthmaticus, pulmonary aspiration syndromes, alveolar proteinosis and smoke inhalation.

Case Series

Between March 2004 and April 2006, we treated 10 patients with VV or VA ECMO in St Vincent's Intensive Care Unit, Sydney, Australia. Of these, 5 had VV ECMO and 5, VA ECMO. Of this cohort, 7 patients survived to discharge from hospital (70% survival rate). The indication, type of ECMO and mortality for this cohort are shown in **table 1**.

Discussion

The survival rate in this series is in the order of that seen in other studies.²⁻⁷ ECMO is a form of extracorporeal life support which should be reserved for patients with reversible cardiac or respiratory failure which is not responding to maximal medical therapy, at the discretion of the treating physician.

Treatment with ECMO is not without associated risks, including bleeding, limb ischaemia, difficulty with fluid shifts and volume replacement, problems associated with anticoagulation, weaning and reinstating mechanical ventilation, and other problems associated with multiple organ support.

Bleeding and Anticoagulation

Bleeding, anticoagulation and heparin induced thrombocytopenia (HIT) are all problems which may occur whilst on ECMO life support. The use of heparin coated circuits is standard in our unit

Table 1: Summary of indication, type of ECMO and survival.

Patient	Type of ECMO	Indication	Survived
Case 1, 62y M	VV ECMO	Reperfusion lung injury post lung transplant	Yes
Case 2, 28y M	VA ECMO	Post heart transplant for dilated cardiomyopathy	Yes
Case 3, 34y M	VV ECMO	ARDS	Yes
Case 4, 62y M	VA ECMO	Post CABG surgery	No
Case 5, 30y M	VA ECMO	Post heart transplant for idiopathic dilated cardiomyopathy	Yes
Case 6, 68y F	VA ECMO	Post CABG	No
Case 7, 62y F	VV ECMO	ARDS	Yes
Case 8, 37y F	VV ECMO	ARDS post bilateral lung transplant	Yes
Case 9, 44y M	VA ECMO	Post heart transplant for dilated cardiomyopathy	Yes
Case 10, 22y M	VV ECMO	ARDS and recurrent pneumothoraces due to PCP	No

and an anticoagulation protocol is used. After successful guidewire insertion for ECMO cannulae, a 5,000-10,000U bolus of heparin is given to maintain an ACT of >200 seconds. The ACT level is used to titrate the heparin dose in the first 24 hours, and measured six hourly. Target ACT in the non-bleeding patient with a platelet count >80,000/mm³ is 140-180 seconds. After 24 hours, the APTT is used for monitoring, with a target range of 60-70 seconds. Plasma free haemoglobin is also measured, aiming for a safe level of <0.1 g/l. Protamine administration is contraindicated as it can cause circuit related thrombosis.

Bleeding is a life threatening complication of ECMO treatment. There is a balance between systemic anticoagulation and the risks of bleeding, and the risk of thrombosis. Careful monitoring, prompt treatment of bleeding and assessment of signs of thrombosis are essential.

HIT is also well described in the literature. Cessation of heparin and use of other anticoagulants such as bivalirudin (direct thrombin inhibitor)⁹ and lepirudin^{9,10} have been described to deal with this problem.

Ventilator Settings

VV ECMO is used to treat isolated respiratory failure when there is adequate heart function. Once commenced on ECMO, intermittent positive pressure ventilation can be reduced. It is current practice to wean mechanical ventilatory support to approximately 4 breaths per minute; PEEP is usually kept high, and pressure support reduced to prevent alveolar collapse and reduce volu/barotrauma. This rests the lungs until the pulmonary disease process is reversed.

PaCO₂ levels can be controlled by altering the flow rate of oxygen into the circuit.

Weaning

Weaning of ECMO should be undertaken when there is evidence of reversal of the pathological process leading to cardio-respiratory failure. It is a gradual process, and involves increasing mechanical ventilatory support whilst reducing support given by the ECMO circuit. Careful monitoring of vital signs and arterial blood gas analysis and the patient's overall condition must all be taken into account.

To wean VA ECMO, the circuit flows must be reduced so that native cardiac function can be assessed (transoesophageal echocardiography (TOE) is useful for this). Ventilatory support must be increased and oxygenator gas flow settings adjusted. Additional heparin may be required to prevent thrombosis at this time, because as ECMO flow rates are reduced there is an increased risk of thrombosis due to stasis. When flow rates are less than 1.5 l/m it is possible to assess the oxygenation achieved exclusively by ventilation by turning off the gas flow to the oxygenator. This creates an artificial right to left shunt, which if tolerated suggests that native respiratory function is adequate to achieve gas exchange off ECMO.

Weaning of VV ECMO is best achieved by turning off the gas flow to the oxygenator and increasing mechanical ventilation. Circuit flow should not be reduced until adequate function is assessed without ECMO support (TOE is not required, nor an increase in anticoagulation).

Other Problems

The risk of lower limb ischaemia associated with VA ECMO can be reduced by the insertion of a distal bypass to supply the distal limb of the leg with the arterial cannula. This involves inserting a side arm into the arterial line which can be placed to supply the distal limb with oxygenated blood.

Problems with hypovolaemia and 'sucking down' of the access cannula can be overcome by using two cannulae to supply the venous limb of the ECMO circuit. This also reduces the need for fluid volume loading and the associated risk of interstitial oedema.

Conclusion

Through lessons which have been learned from this series, and through national and international sharing of experience, associated morbidity should decrease.

The main determinant of mortality is, perhaps, the choice of appropriate patients. With experience, it is easier to identify patients and disease processes which respond to ECMO.

The Cesar trial may provide more answers about the appropriate use of ECMO in patients with ARDS. Recruitment has now finished and results are expected towards the end of 2007.

Other units in Australia, particularly The Alfred in Melbourne¹¹ have a wide experience of ECMO, as have other centres internationally. Learning from their experience should lead to increased survival rates.

ECMO is currently a rescue therapy that is available to the physician when maximal medical therapy fails. With the relevant expertise and resources, it is a treatment which could be used more frequently in intensive care units in the UK.

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Evacuation of an intensive care unit after a fire

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Keywords: disaster planning, fire

Introduction

On the 3rd September 2006 a dishwasher caught fire in the kitchen of the Intensive Care Unit (ICU) at Chesterfield Royal Hospital NHS Trust, resulting in the unit being evacuated.



Temporary level 3 location

Evacuation of an ICU may be necessary for either an internal event, such as a fire, or in response to an external disaster, when multiple level three beds are required.¹ Evacuation of ICU patients presents many challenges, and a large manpower force is usually required. Patients may be unstable and moving them is potentially dangerous.²

Thankfully, hospital fires are rare, and a fire necessitating evacuation of an ICU is rarer still. However, whenever such an event occurs, the information gained from examining the sequence of events is both invaluable and educational. It is applicable to medical, nursing, support staff and the fire services, to prevent repetition and enable reflection on evacuation plans and fire policy.



Moving the last level 3 patient to the temporary ICU

There have been fires reported recently at Wythenshawe and Warrington Hospitals. Following these reports Chesterfield Royal Hospital NHS Trust revisited their fire evacuation plan for intensive care.

Topography

The hospital has two distinct but linked theatre areas. Phase One was built in 1984 and has eight theatres. It is immediately adjacent to the ICU and separated by two sets of half-hour fire doors. Phase Two, built in 1986, has four theatres and is approximately 50 metres from the ICU. It is reached via Phase One. Each area has its own reception and Post Anaesthetic Care Unit (PACU) facilities. In 2004 the Phase Two reception area was upgraded as a temporary location for the adjacent special care baby unit (SCBU) during refurbishment. It has the infrastructure to manage level three patients in the event of an emergency.

The ICU (six beds), and High Dependency Unit (HDU) (eight beds) are immediately adjacent to the theatre complex. Both link, via half-hour fire doors, to the Phase One theatres. The HDU, commissioned in 1998, was designed to accommodate level three patients if required.

Fire and Evacuation Plan

The fire and evacuation plan had been revised following recent hospital fires and guidelines published.³ The fire plan designates Phase Two theatre reception and two adjacent bed spaces as the primary evacuation site for ICU. This assumes a fire occurring during a period of maximum theatre activity. In this instance the HDU, both PACUs and almost all theatres would be occupied by patients who could not be safely or easily moved to alternate locations. Patients awaiting surgery could be safely moved from the Phase Two reception area. The bed spaces adjacent to theatres are never occupied.

The Fire

At 07:21 on Sunday morning 3rd September 2006 a member of the nursing staff observed flames coming from one of the work surfaces in the kitchen on the corridor of the intensive care unit (ICU). The heat sensor in the kitchen had not detected the fire at this point. The nurse activated the fire alarm manually. Neither the resident SHO nor registrar in anaesthetics received the fire alarm bleep or heard the fire alarms from their respective locations, but they were contacted immediately by the ICU staff.

Smoke rapidly seeped round the kitchen fire door but initially no smoke was present in the ICU. The timing of the fire coincided with nursing handover and there were two nurses per bed for the six patients in the ICU. The sister in charge of the unit acted promptly according to the rehearsed drill. All patients were disconnected from wall oxygen to prevent fire tracking down pipelines and connected to portable backup cylinders. Mains cables were disconnected and battery backups to monitors/syringe drivers checked. No immediate decision to evacuate was taken and no advice to this effect received.

Six level three patients were in the unit. Two patients were unstable and on high dose inotropic support with high FiO₂ requirements due to severe sepsis. Both these patients were transferred onto portable ventilators immediately, as it was felt that their oxygen requirements would not be sustained by manual ventilation in the event of an evacuation. One patient was undergoing renal replacement therapy. This was immediately discontinued. All other patients stayed on their ventilators or oxygen therapy supplied by portable cylinders. After a short time all the ICU patients were ready for transfer. The senior staff on the unit decided that the most appropriate destination for the patients was the Phase One PACU. This was contrary to the Fire Plan but, as it was empty, close by and in a different fire zone, deemed to be the safest place. It also could accommodate all the level three patients in one area and had the required infrastructure (medical gasses and monitoring equipment, although not medical air).

At 07:24 the decision was made to evacuate the unit as dense heat-driven smoke overcame the normal positive pressure inside the ward and began percolating through the wall vent. The two most unstable (and sickest) patients went first, because they happened to be adjacent to the exit door, followed in sequence by the other patients. The patients without transport ventilators managed either with manual ventilation or with spontaneous ventilation via a Waters circuit. The two managed with spontaneous ventilation were already weaning from the ventilator.

The ventilators were moved immediately after the patients. All patients were reconnected to their ventilators and their original settings restored. Pipeline air was not available. Medical engineers had been alerted and air cylinders were obtained quickly.

From the decision to evacuate to the last patient arriving in PACU, 11 minutes had elapsed. Evacuation was completed with no morbidity, haemodynamic compromise or decline in oxygenation saturation.

Within minutes of the fire alarm sounding, all available staff converged on the unit to assist. They were coordinated initially by the sister-in-charge. In addition to the nursing and medical staff in the ICU, there were night matrons, theatre staff including nurses and operating department practitioners (ODPs) who played a valuable role in gathering and setting up transfer equipment, HCAs, porters, fire crew, switchboard staff and hospital fire staff.

The fire occurred at a fortunate time with nursing staff in handover, thus allowing two nurses per patient for the evacuation. Thus the evacuation was easier, close observation of the patient was possible and no nurse had to return to the ICU to help evacuate a second patient.

The evacuation of the unit complete before the fire service arrived. The fire itself was extinguished by a single hose unit fire team. It had originated from a faulty solenoid on the kitchen dishwasher,⁴ which was designed for domestic use.

On arrival of senior medical, management and nursing staff, decisions were made about the best areas for ongoing patient management. Stable patients from the HDU were moved to the wards. Less stable patients were moved to the Phase Two reception area for ongoing level two care. The level three patients were then moved from the Phase One PACU to the HDU. Relatives were informed promptly to prevent them hearing first on local media.



Temporary level 2 location

The intensive care unit was out of action for five days while it was cleaned and was without a kitchen for two weeks. No elective surgical cases were cancelled and theatre operated normally the following day.

The total cost of repair to the unit was £17,000, which, due to the terms of the insurance policy excess (£250,000) had to come from the ICU budget.

What went well

- The time from activation of the alarm to the last patient arriving in PACU was 14 minutes. This is a tribute to the efficiency of all of the staff.
- There was no morbidity, haemodynamic compromise or desaturation to any patient during the evacuation.
- There were no injuries to any staff member.
- The senior staff assessed the situation and appropriately deviated from the published plan in the light of the situation 'on the ground.' The fire plan was designed to deal with a fire in normal working hours, when the nearby Phase One PACU would be occupied. Due to the timing of the event, the nearby PACU was empty, safe and closer than the planned site. If necessary, the oxygen supply could have been turned off to ICU, but continued to PACU. Although nearby, the Phase One PACU was isolated from the fire by two, one-hour fire doors. The extra distance to travel to the Phase Two theatre reception was deemed unnecessary and potentially unsafe.
- In this case there was no clearly defined leader. Decisions were made rapidly by the staff at individual locations. When necessary, these were brought to the attention of senior nursing staff and ICU registrar. In this unusual situation of a

rapid evacuation, the staff at the bed spaces were best placed to make sensible decisions regarding their patients. The lack of a clear leader managing the entire situation did not lead to any notable problems. In fact the opposite was the case and a rapid and uncomplicated evacuation the result.

- Wisdom might suggest that the 'most well' patients (with the best survival chances) should be evacuated first. In this case the patients went by proximity to the exit door. This gave the remaining patients an unobstructed route out (i.e. no patients/beds in their way). Coincidentally the patients nearest the door were the sickest on the unit and were therefore evacuated first.



The damaged kitchen

Learning Points

- The fire bleep system did not work. This has been addressed. The senior trainee/cover consultant are now on the fire bleep.
- The fire plan needs to cover a variety of states the hospital may be working in. Working hours form only part of the total hours when a fire may occur.
- Using the Phase Two reception area as a level two facility demonstrated that it was only able to accommodate three adult patients, not four as in the fire plan. It is advisable to test areas in a controlled fashion if they might be needed urgently to accommodate level three patients.
- When moving patients quickly, obstructions in the path are a major problem.
- Is a domestic dishwasher appropriate to be used in an ICU kitchen?

Summary

We have described the events surrounding a kitchen fire on an Intensive care unit, which required the safe and quick evacuation of six patients. We have also described the fire evacuation plan, as it was designed, and the deviations that occurred from it, and the reasons why.

It is very difficult to practice evacuation of an ICU in any sort of real-time, unprepared way. However, clear instructions designating the fire evacuation plan, regular updates for the staff, 'group specific' fire lectures, and 'run-throughs' using a floor plan or empty beds may all help prevent errors occurring and improve outcome in the event of a fire and subsequent evacuation. Patient specific decisions need to be made at the time, by the relevant staff and the allocation of resources as necessary. We were fortunate that our patient group allowed two to be transferred by portable ventilator, two by manual ventilation and two ventilating spontaneously. This avoided particularly difficult decisions about resource allocation, or the delay of safe evacuation. The timing of the event was also fortuitous with plenty of nurses and other staff available to assist with the transfer. The timing also allowed a choice of evacuation destination.

Fortunately, this kind of event is rare, but this report shows how it can be done safely, quickly and efficiently.

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Antibiotic prescribing in critical care: general principles

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Keywords: Antibiotics, Infection

Introduction

The past decade has seen a global increase in microbial resistance to antibiotics, particularly among patients in intensive care units (ICUs).^{1,2,3} Extensive use and misuse of antibiotics, particularly cephalosporins and quinolones, have contributed to the development of resistance in enterococci, coagulase-negative staphylococci, pseudomonads and enterobacteriaceae. Antibiotic use may also encourage colonisation with methicillin-resistant *Staphylococcus aureus* (MRSA) and superinfection with *Clostridium difficile*. The EPIC (European Prevalence of Infection in Intensive Care) study of 1992 produced data on 10,038 patients in 1,417 intensive care units across Western Europe over a single 24-hour period.⁴ Infection was present in 44.8% of patients, and had been acquired within ICU in 20.6%. At that time, 60% of *S. aureus* isolates were methicillin-resistant and 65% of *Pseudomonas aeruginosa* isolates were resistant to one or more anti-pseudomonal antibiotics.

Selective pressure for antibiotic resistance is inevitable in ICUs, given the high prevalence of infections in this vulnerable group of patients requiring frequent and often prolonged courses of antibiotic therapy. However, there is evidence that antimicrobial resistance can be reduced by adopting rational policies for antimicrobial use and optimising the duration of empirical treatment.^{5,6}

Optimising antibiotic use in Critical Care

The best approach to the problem of antibiotic resistance is to use the correct antibiotics and restrict use to proven or probable infection, guided by strict protocol and by rapid and accurate microbiological diagnosis. It is important to recognise the high prevalence of microbial colonisation in the ICU, particularly involving the respiratory and urinary tracts, and to avoid unnecessary treatment. Non-infective causes of the Systemic Inflammatory Response Syndrome (SIRS) can also cause diagnostic confusion, which may lead to overuse of antibiotics. Rigorous diagnostic principles should be applied whenever infection is suspected, the need for antibiotics should be reviewed daily, and withdrawal of antibiotics should be considered in the absence of positive microbiology. Close liaison with the hospital microbiology department is essential when formulating antibiotic policy and in the treatment of individual patients. Involvement of a consultant microbiologist and infection control nurse in the daily ICU round is strongly recommended.

Antibiotic Guidelines

Written guidelines for antibiotic use have been shown to limit the emergence of resistant micro-organisms, reduce the incidence of secondary infections, shorten the duration of mechanical ventilation, reduce costs and improve mortality rates.^{6,7,8} Each ICU should have a written antibiotic policy which takes into account national guidelines and the results of local microbiological surveillance.⁹ Locally-developed guidelines can be refined to take

account of local patterns of infection and resistance, and are more likely to be accepted by health care providers. Policies should define standardised treatment regimes for specific situations, including doses and durations of treatment.

Antibiotic choice and method of administration

Factors determining antibiotic choice include clinical efficacy for a given indication, adverse drug effects, interactions with other drugs, pharmacokinetic and pharmacodynamic factors, available routes of administration and costs.¹⁰

For treatment to be effective, an adequate concentration of antibiotic must be maintained at the site of infection for a sufficiently long period to effect bacterial inhibition or killing. In most critically-ill patients with life-threatening infections, the intravenous route is indicated. Although adequate blood levels of agents such as fluconazole and the quinolones can be achieved by enteral administration, normal gastrointestinal function is necessary. In selected cases, oral or nasogastric administration may be substituted when gastrointestinal function is reliable and the patient's condition has stabilised. Allowance must be made for any change in bioavailability - for instance, the oral dose of ciprofloxacin should be 25% higher than the intravenous dose.¹¹

Adequacy of penetration to the site of infection must also be considered. Antibiotic concentrations in soft tissues reached via diffusion from the blood approximate those in plasma, though equilibration may be slow. Penetration to other sites, such as cerebrospinal fluid, ocular fluid and lung epithelial lining fluid, is limited by restrictive barriers. Concentrations at these sites cannot be predicted from serum pharmacokinetics, and there may be marked differences between different drugs from the same class. Among the fluoroquinolones, levofloxacin demonstrates markedly better penetration than ciprofloxacin into both lung epithelial lining fluid and alveolar macrophages.¹² Intracellular delivery of antibiotics, which is important for the treatment of infections due to *Chlamydia* and *Legionella* species, may show similar variability. Treatment of urinary tract infections requires hydrophilic and polar drugs which are excreted into the urine.

Pharmacodynamic factors are also important. Aminoglycosides demonstrate a linear relationship between concentration and bactericidal effect, combined with prolonged duration of action. Efficacy is determined by the ratio of peak concentration to Minimum Inhibitory Concentration (MIC), while toxicity is related to trough concentration.¹³ Single daily dosing with gentamicin is therefore logical and cost-effective, and has been widely adopted.¹⁴ Beta-lactams and glycopeptides, on the other hand, demonstrate concentration-independent bacterial killing. Efficacy of these antibiotics is related to the *time* for which the MIC is exceeded, and in the case of vancomycin, to the ratio of area under the concentration-time curve (AUC) to MIC.¹⁵ Administration of beta-lactam antibiotics by continuous infusion has been shown to

result in improved pharmacodynamics. A small number of trials have demonstrated clinical outcomes as good as intermittent dosing, with less antibiotic use and lower costs.^{16,17} Continuous infusion may improve outcomes from gram-negative infections in neutropaenic patients, but there is little evidence of clinical benefit in gram-positive infections.¹⁸ This is probably because beta-lactams have a prolonged post-antibiotic action against gram-positive cocci, but not against gram-negative rods.¹⁹ Continuous infusion of beta-lactam antibiotics cannot be recommended as standard practice but may be effective in the treatment of susceptible gram-negative infections not responding to conventional therapy. In the case of vancomycin, continuous infusion has been shown to achieve target concentrations more rapidly than intermittent administration, with fewer blood samples required and reduced costs but with no evidence of improved clinical outcomes.²⁰

Appropriate empirical therapy and de-escalation

If empirical treatment is started early and the initial choice of antibiotic is appropriate, clinical outcomes from serious infections are significantly improved.^{21,22} Knowledge of the pathogens commonly implicated in ICU-acquired infections, coupled with information on local resistance patterns, is of vital importance to the development of appropriate antibiotic strategies. The commonest organisms isolated in ventilator-associated pneumonia (VAP) are *P. aeruginosa*, *S. aureus* and Enterobacteriaceae.^{23,24} Some units also experience significant rates of infection with *Acinetobacter baumannii*.^{24,25} ICU-acquired bacteraemias may involve similar organisms, but are increasingly caused by *Enterococcus* species, coagulase-negative staphylococci and *Candida*.^{23,26} Increasing use of intravascular catheters is likely to be the cause of this change. Antibiotics used for the empirical treatment of ICU-acquired infections should therefore be active against multi-resistant Gram-negative organisms and staphylococci. Appropriate choices include carbapenems, broad spectrum penicillins such as piperacillin-tazobactam, and quinolones. In units with high rates of MRSA, it may be appropriate to add glycopeptides to empirical regimens.

Appropriate microbiological investigations should be undertaken when empirical antibiotic treatment is started, so that narrower-spectrum agents can be used when a causative pathogen has been identified (de-escalation). De-escalation reduces inappropriate antibiotic use, minimises superinfection with organisms such as *Clostridium difficile* and *Candida*, and reduces selection pressure for the development of antimicrobial resistance.^{22,27} In a recent study of ventilator-associated pneumonia, de-escalation was feasible in 42% of patients.²² If investigations fail to identify a pathogen, consideration should be given to discontinuing antimicrobial therapy.

Antibiotic rotation

Rotation or cycling of antibiotics has been advocated as a means of reducing selection pressure and, thus, antimicrobial resistance.²⁸ A single antibiotic or an entire class of drugs is removed from the formulary for a defined period, and is re-introduced at a later date. Continuous cycling of antibiotics denies micro-organisms opportunity to develop resistance to any particular agent or class of agents. Some studies, using cycling periods of one to three months, have demonstrated reduced

resistance rates for both gram-positive and gram-negative organisms, and reduction in the incidence of ventilator-associated pneumonia.^{29,30} However, the results of more recent trials have not only failed to confirm these findings, but suggest that antibiotic rotation may promote resistance among gram-negative organisms.^{31,32} There are several possible reasons for these conflicting results. For rotation to be effective, antibiotic-resistant micro-organisms must exhibit a growth disadvantage when selective antibiotic pressure is withdrawn, so that resistance developed during a period of exposure to a particular antibiotic is selected out during the following period of non-exposure. Resistant organisms developing during one antibiotic cycle must be eliminated by exposure to a different class of antibiotics in the following cycle, and antibiotics should be chosen which promote resistance by different mechanisms.³¹ In practice, microbial cross-resistance to multiple antibiotics is an increasing problem and is likely to decrease the potential benefits of antibiotic rotation. Rate of patient turnover is also important - patients staying in ICU for prolonged periods may maintain populations of resistant micro-organisms, even into subsequent cycles of the antibiotics which initially induced resistance. Finally, variation in compliance with infection control measures may have acted as a confounding variable in studies showing benefits from antibiotic cycling.

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Isolation and cohort care

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Definitions

Two types of patient isolation are defined: Protective isolation is intended to protect immunocompromised patients from exposure to pathogens carried by healthcare workers, other patients, relatives and the environment. The number of such patients admitted to a general adult ICU is likely to be small. Source isolation is intended to prevent transfer of communicable pathogens from infected or colonised patients to other patients and staff. Source isolation has become a central element of attempts to control the spread of endemic, antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE). The gold standard is considered to be isolation of the infected or colonised patient in a single room^{2,3}. The limited availability of such rooms, in the face of increasing numbers of critically-ill patients carrying resistant pathogens, may require alternative strategies such as patient 'cohorting'. Cohorted patients are managed in adjacent beds, in a dedicated area of the ICU (geographical cohorting). Staff members working in this area are not involved in patient care elsewhere in the unit (nurse cohorting). This approach has been successful in both endemic and outbreak settings^{4,5}.

Source isolation for multidrug-resistant organisms (MDROs)

MRSA accounts for up to 60% of *S. aureus* infections in European and American ICUs^{6,7}. Vancomycin resistance is present in 28.5% of enterococcal isolates in US intensive care units, and *P. aeruginosa* shows a similar level of resistance to quinolones and third generation cephalosporins⁷. Infection with MRSA has been associated with higher mortality, longer hospital stays and greater costs than infection with methicillin-susceptible *S. aureus*^{8,9}. Similar findings have been documented for VRE, *Acinetobacter*, multi-resistant *Pseudomonas* and ESBL-producing gram-negative organisms^{10,11,12}. There are, therefore, compelling clinical and economic reasons for controlling the spread of these organisms.

Selection pressure due to antibiotic use is responsible for the initial development of MDROs. Transmission from patient to patient then plays a significant part in the spread of these resistant clones. The success or failure of source isolation in controlling MDROs depends upon the relative contributions of these two mechanisms. Genetic analysis of MRSA strains shows that global spread is due to dissemination of relatively few clonal types, rather than from frequent *de novo* introduction of new clones¹³. Virtually all patients colonised or infected with MRSA acquire the organism from an external source, and prevention of transmission by means of isolation and barrier precautions is of paramount importance. There is also clear evidence that colonisation pressure (the proportion of patients colonised) is an important factor in the spread of VRE, supporting the use of isolation and contact precautions for this organism too¹⁴. Data are less complete for gram-negative organisms, with no accurate estimates available of the proportion of antibiotic resistance due to patient-to-patient transmission, for any organism in a non-outbreak setting¹⁵.

A number of studies have demonstrated that source isolation is associated with reduced cross-transmission of MRSA within ICUs^{5,16,17}. However, most have also employed additional measures including strict contact precautions and decolonisation, and it is often impossible to determine the contribution of any single intervention. A systematic review of MRSA isolation policies found that one-third of studies were affected by such confounding factors, while evidence from most of the remaining trials was considered weak because of poor study design or risk of systematic biases¹⁸. A more recent prospective two-centre trial of source isolation alone, using single rooms or cohorting, showed no effect on cross-infection rates for MRSA¹⁹. Evidence concerning source isolation for other MDROs is less extensive and also inconsistent. Increased use of single-patient rooms has been shown to reduce rates of infection due to *Acinetobacter baumannii* and other gram-negative MDROs^{20,21}. VRE transmission may also be reduced by control measures which include isolation, though most trials have also included other interventions⁴. Other studies have failed to demonstrate any improvement in infection and colonisation rates attributable to isolation, for a range of organisms²².

Despite conflicting evidence for the benefits of single-patient rooms or cohorting, most guidelines recommend source isolation as a central element of programmes to limit the spread of DROs^{3,13,23,24}. It is notable that success in controlling MRSA has been greatest in those countries with a rigorous national programme which includes cohort nursing and isolation of patients^{25,26}.

Strategies for source isolation

Source isolation alone is not enough to prevent transmission of infectious agents - it must be applied as part of a rigorous programme of infection control measures. This should include appropriate barrier precautions, controlled use of antibiotics, eradication of bacterial carriage when appropriate, environmental cleaning, disinfection of equipment and education. Active surveillance cultures are also important to allow early detection and isolation of colonised patients³. New, more rapid screening tests for MRSA may reduce the incidence of ICU-acquired infections²⁷. Strict barrier precautions are also essential for control of MDROs and should include Standard and Contact Precautions in all cases^{3,28}.

Every ICU should have single rooms available for protective and source isolation, the number required depending on local case mix. NHS hospitals have a statutory duty to provide adequate isolation facilities²⁴. The design of single rooms should follow the recommendations of 'NHS Estates: Facilities for critical care' (HBN 57)². Clear indications for isolation must be agreed with the hospital infection control team. Each unit should have a written policy for the management of isolated patients in single rooms or cohorts, with specific references to hand washing, barrier precautions, screening and surveillance. Nursing staff should receive training in isolation procedure and compliance with protocol should be ensured by means of continuing education and audit. Nursing numbers must be adequate to allow isolated

patients to be managed by dedicated nurses, who should not have responsibilities elsewhere in the unit. When deciding whether or not to use single rooms or cohorting, the benefits must be weighed against the risks of moving critically ill patients and the need for increased numbers of nursing staff.

Adverse effects of isolation

Isolation and barrier precautions have been shown to reduce contacts between healthcare providers and patients by 50% in both medical and surgical ICUs, despite the fact that isolated patients are more likely to require invasive interventions.^{29,30} The application of contact precautions has been associated with an increase in the frequency of preventable adverse events and a reduction in documentation.³¹ Additional risk is introduced by the need to move infected or colonised, critically-ill patients to single rooms or cohort areas. It is important, therefore, to ensure that patients in isolation receive adequate clinical and nursing care.³

Facilities for isolation

Standards for isolation facilities within intensive care units have been published by NHS Estates²

- When building or refurbishing an ICU, the infection control team should be represented on the project team from the outset.
- Ideally, every patient should be cared for in an individual room. Where this is impractical, the number of side rooms required should be based on case mix and advice from the infection control team. It is recommended that 50% of all beds are enclosed in single rooms.
- The size of each side room should not be less than 26m².
- Each room should be equipped with a clinical hand-wash basin with automatic taps or foot control.
- Each side room should have a lobby, to prevent unauthorised entry and act as an airlock. The lobby should contain a clinical hand-wash basin, plastic apron dispenser and disposal facility.
- The use of a mechanical ventilation system, equipped with filtration, should be considered. The system should be capable of providing source isolation (negative pressure) and protective isolation (positive pressure).
- Doors to single rooms and lobbies should be tight-fitting, with neoprene seals to maintain positive/negative airflow. Windows should not be openable.
- Single rooms should have glass partitions for observation purposes, with integral blinds for the sake of privacy.

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Table 1: Indications for Source Isolation

Organism	Recommendation
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	Contact Precautions for infected or colonised patients. Decisions concerning isolation should be based on local factors, including ward design and available facilities. Single rooms are preferred, but cohorting may be necessary where there are a number of affected cases. ^{13,23}
Vancomycin- intermediate/resistant <i>S. aureus</i> (VISA, VRSA)	Single rooms, with full Contact Precautions. ^{23, 24}
Vancomycin/ glycopeptide-resistant enterococci (VRE, GRE)	Ideally in single rooms. If larger patient numbers and insufficient isolation rooms, cohort in bays on the open ward. Patients with GRE and diarrhoea or incontinence are at a higher risk of spreading GRE and must be given priority for single rooms. ³²
<i>Acinetobacter baumannii</i>	Single cases require contact isolation in a side room. For outbreaks patients may be cohorting in distinct areas with separate ancillary facilities and nursing staff. ³³
Other Gram-negative bacteria - e.g. <i>Pseudomonas aeruginosa</i> , extended-spectrum, β -lactamase (ESBL) - producing <i>E. coli</i> and <i>Klebsiella species</i>	Little evidence to recommend routine isolation. ¹⁵ CDC recommends single-patient rooms for all cases of infection or colonisation with multi-drug resistant organisms, or cohorting when single rooms are not available. ³
<i>Clostridium difficile</i> diarrhoea	Contact Precautions plus measures to ensure safe handling and disposal of faecal material. Infected patients should not be managed in open wards except as part of a cohort. ^{24,34,35}
Pulmonary tuberculosis	Airborne Precautions (including nursing in single room) if sputum status is unknown, if sputum is smear-positive, if multi-drug resistant TB is suspected or if the ward contains immuno-compromised patients. ³⁶
Pandemic Influenza	Staff and patient cohorting, plus Droplet Precautions. ³⁷
Severe Acute Respiratory Syndrome (SARS)	Strict adherence to barrier nursing, using Airborne, Droplet and Contact Precautions. ^{38,39} Ideally, patients should be isolated in negative pressure rooms or single rooms with their own bathroom facilities. Cohorting of patients in an area with an independent air supply and exhaust system may be necessary in outbreak situations.

Trace element and vitamin supplementation in critical illness

B Marshall and R Thomas

Keywords: trace elements, vitamins, critical illness

Introduction

Increased oxidative stress is well recognised in critically ill patients with systemic inflammatory response syndrome (SIRS). The increase in the production of toxic reactive oxygen species (ROS), and the depletion of endogenous protective antioxidant micronutrients are implicated in the initiation and continuation of critical illness.

This article examines the rationale and evidence for antioxidant trace element and vitamin micronutrient supplementation to combat aspects of oxidative stress associated with critical illness.

Oxidative Stress In Critical Illness

Critically ill patients are characterised by the presence of a general inflammatory process associated with any severe insult to the body, the systemic inflammatory response syndrome (SIRS).¹ These patients are at risk of increased oxidative stress ie "a state in which the level of toxic reactive oxygen species (ROS) overcomes the endogenous antioxidant defences of the host."²

ROS, or free radicals, are produced via a number of different pathways in critical illness, but mainly by the activation of polymorphonuclear leucocytes and by the respiratory mitochondrial chain.³ ROS include superoxide (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radical (OH^\cdot), all of which may lead to cellular damage. These cause injury by direct oxidative damage to cellular proteins, nucleic acids and induce a process of lipid peroxidation (resulting in cell wall damage).

ROS may also have a more systemic effect. By playing a role in cell signalling, ROS are thought to activate cytokine release from inflammatory cells, in particular leading to the production of nuclear factor κ B (NF- κ B)^{2,3} which has been shown to mediate the activation of endotoxins and inflammatory cytokines.⁴

In the normal physiological state, the host is able to manage and prevent the unwanted effects caused by ROS. This endogenous defence mechanism consists of a number of antioxidant molecules that are capable of deactivating ROS and neutralising their potentially harmful effects. Antioxidant molecules can be divided into two distinct groups, enzymatic and non-enzymatic.

Of the enzymatic molecules, superoxidase dismutase (SOD), catalase and glutathione peroxidase appear to be most significant, playing an essential role in the conversion of O_2^- and H_2O_2 to H_2O . The activity of these enzymatic antioxidants requires a number of trace elements in order to work at their maximum efficiency. These nutritional cofactors include selenium, copper, zinc, manganese, and iron.

The presence of selenium is critical for the function of glutathione peroxidase, and also plays a role in controlling the production of tri-iodothyronine from thyroxine.⁵

Non-enzymatic antioxidants include endogenous and exogenous molecules. It is the exogenous antioxidant vitamins that are most commonly discussed in the literature. These include the lipid-soluble vitamins (E and β -carotene), and the water-soluble vitamins (C and glutathione). Active vitamin E, also known as α -tocopherol, is capable of disrupting lipid peroxidation of cell walls and essential cell signalling pathways initiated by ROS.^{2,6,7} It also plays a role in the direct neutralisation of ROS.²

Critically ill patients are characterised by early depression of serum levels of many antioxidants, with the endogenous defence mechanisms rapidly becoming overwhelmed by the excessive production of ROS. Investigators have shown low serum levels of α -tocopherol and vitamin C in critically ill patients with sepsis and acute respiratory distress syndrome (ARDS).⁸⁻¹⁴ In SIRS, there is a redistribution of vitamins and trace elements from the circulating volume to tissues involved in inflammatory processes.¹⁵ Some animal models have shown this to be the case, particularly in relation to selenium and zinc.^{16,17} Reduced levels of antioxidants may also be attributable to excess losses, with zinc, selenium, copper and thiamine all detectable in biological fluids lost during critical illness. These include inflammatory exudates from burns,¹⁸ drain outputs from trauma,¹⁹ and effluents from continuous veno-venous haemodiafiltration.²⁰

Finally, the dilutional effects associated with fluid resuscitation may have some impact on serum antioxidant levels.

Antioxidant Supplementation

Supplementation with exogenous antioxidants to restore the oxidant/ anti-oxidant balance in critically ill patients has been considered for a number of years. However, there are few large, randomised, interventional trials that have investigated the role of antioxidant supplementation in the critically ill.

Heyland *et al*²¹ performed a meta-analysis of articles published between 1980 and December 2003, searching four bibliographic databases (MEDLINE, EMBASE, CINAHL, and the Cochrane Database of Systematic reviews). Search terms included "trace elements", "vitamins", "critical illness" and "intensive care". Studies excluded were primarily those that did not report clinically important endpoints and those that examined multiple nutrients in addition to trace elements and vitamins. Eleven original papers (886 patients) were included. With the exception of one study which included 770 patients,²² others had small numbers of patients.

The five main antioxidants that were investigated were the trace elements selenium, zinc and copper, and the vitamins C (ascorbic acid) and E (α -tocopherol).

When the results of all 11 trials of 886 patients were aggregated, Heyland *et al* found that there was a statistically significant reduction in mortality associated with those patients who had received antioxidant supplementation (CI = 0.44 - 0.97). In their subgroup analysis of the results, they found a statistically significant reduction in mortality associated with trials that only used single antioxidants (CI = 0.27 - 0.98) when compared to those trials that used a combination of antioxidants. Furthermore, when the results of those trials, when using the parenteral route to supply antioxidants were aggregated, antioxidant use was also associated with a statistically significant reduction in mortality (CI = 0.34 - 0.92).

Selenium

Of the eleven studies examined by Heyland, seven included the supplementation of selenium as an interventional strategy either alone, or combined with other antioxidants.²³⁻²⁹ All seven of these studies (n = 186) demonstrated a trend towards a lower mortality, but this was not statistically significant. There was also a trend towards a lower mortality in those studies using higher than the median dose of selenium (500 -1,000 μ g/day) when compared to those studies using lower doses (< 500 μ g/day). Again these findings were not statistically significant.

Another systematic review performed by the Cochrane Collaboration concentrated on the effects of selenium supplementation in critical illness, and included ebselen supplementation (a selenium containing organic compound).⁵ Primary outcome measures were mortality and infection rates. Seven articles published between 1997 and 2001 (n = 813) were reviewed. Three were multicentre Japanese trials of ebselen,³⁰⁻³² with the remaining four all single centre trials in Germany and Switzerland examining selenium alone.²⁴⁻²⁸

A statistically significant difference in mortality in favour of selenium supplementation was lost once statistical heterogeneity of the data was taken into account. There was no significant difference in infection rates, days spent on a ventilator, or days spent in ICU.

A recent review article specifically looking at the benefits of selenium supplementation³ has examined conclusions drawn from these meta-analyses. Currently there is insufficient evidence to recommend supplementation in all patients, despite the recognition that selenium plays an important role in immune response and tissue defence, and is commonly depleted in the critically ill. However, non-statistically significant trends towards improved survival seen after selenium supplementation have brought forward calls for further well-designed, high-powered studies. This recommendation has been highlighted by one recent double-blinded, randomised controlled trial by Angstwurm *et al*,³³ that included 238 patients with SIRS, sepsis, and septic shock. Patients in the experimental group received an intravenous bolus of 1 mg sodium selenite, followed by an intravenous infusion over 14 days, with the primary outcome measure being 28-day mortality. Results from the intention-to-

treat-analysis did not show a statistically significant reduction in mortality. However, when a further 49 patients were excluded for either not fulfilling inclusion criteria or violating study protocol, 28-day mortality was significantly reduced. Conclusions drawn from these results were based on an underpowered analysis, and the authors did accept a larger trial would be needed to confirm their results.

Other Trace Elements

Of the eleven articles identified by Heyland *et al*, three trials included the use of the trace elements zinc and copper.

In two of these trials, both in burns patients, the interventional group received a combination of zinc, copper and selenium.²³⁻²⁹ One trial demonstrated a significant reduction in rate of bronchopneumonia (p = 0.013), with a trend towards shorter hospital stay.²⁹

One trial examined zinc supplementation in sixty-eight ventilated patients with severe closed head injuries.³⁴ Patients in the treatment group received 12 mg zinc for 15 days, and were found to have significantly improved recovery of GCS at 28 days when compared to those not receiving zinc (p = 0.03). There was a non-statistically significant trend towards improved mortality in the treatment group.³⁴ It is debatable whether the improvement in GCS is of clinical relevance.

Vitamins

There were three articles selected by Heyland *et al* that focused on using antioxidant vitamins as a therapeutic intervention in critically ill patients.

All of these trials used a combination of Vitamins C and E, with one trial also using Vitamin A. The most recent of these, performed by Nathens *et al*,²² was a large scale randomised controlled trial analysing the effects of Vitamin C (1000 mg IV 8hrly) and α -tocopherol (1000 IU 8hrly) in 301 general surgical and trauma patients. Primary outcome measures were rates of ARDS and/or pneumonia. Although there was no statistically significant difference in pulmonary morbidity between the two groups, there was a significant reduction in the risk of developing MOF in those patients receiving vitamins (p = 0.04). As with previous trials discussed, the results collected by Nathens *et al* also showed a trend towards lower mortality in the antioxidant treated group. However, it should be noted that of a cohort of 595 patients, there were only 11 deaths.

Another trial by Preiser *et al*³⁵ compared the effects of an enteral solution enriched with Vitamins A, C and E with a control solution in 37 critically ill patients for a period of 7 days. They demonstrated good absorption of α -tocopherol and β -carotene, along with increased resistance of low-density lipoproteins to experimental oxidative stress. However, there was no statistically significant difference in mortality or infectious complications between the two groups.

When Heyland's group aggregated the results of non-selenium antioxidants (including Vitamins A, C and E), they found there was no significant effect on mortality or infectious complications.

Discussion

In critical illness, oxidative stress occurs by a combination of increased ROS production, and depression of endogenous antioxidant levels. The significance of increased oxidative stress in the development of complications of critical illness such as ARDS and MOF has been suggested by many authors. This has led to the approach of antioxidant supplementation as a method to address the oxidant/ anti-oxidant imbalance that occurs during critical illness.

Heyland *et al's* meta-analysis based on eleven trials of 886 patients did find statistically significant reductions in mortality once results were aggregated. However on an individual basis, none of the trials included in their meta-analysis demonstrated a significant difference in mortality. These findings appear to be confusing, and may be explained by the general complexities of meta-analysis and the consequences of including one large trial amongst ten significantly smaller trials. There are also many difficulties inherent in studying a heterogeneous population, specifically in the ICU setting. Of importance, however, is that supplementation with trace elements and vitamins is not associated with an increase in deleterious side effects, and it is therefore tempting to regard the practice as safe.

If the general consensus is that antioxidant supplementation is safe, a logical intervention by virtue of its hypothesised antioxidant function(s), and effective to some extent, a number of further issues arise. Firstly, what is the optimal antioxidant supplementation regimen for critically ill patients?

On the basis of Heyland's meta-analysis, the evidence shows that antioxidants should be given parenterally, and as a single agent. There was also a non-significant trend suggesting that selenium is the most effective antioxidant. However, this was not confirmed by the recent Cochrane review looking specifically at selenium supplementation⁵ which concluded that use should be restricted to clinical trials only.

Secondly, further work is required to determine when is the best time to initiate treatment and for how long to continue it. Antioxidants do not have the ability to repair damage already done by oxidative stress and their use should be thought of as prophylactic and as a result it is logical to initiate supplementation early.

Thirdly, what doses should be used? Although it has been suggested that higher doses of antioxidants have attributed to greater treatment effects, *in vitro* trials have shown that high doses of selenium, vitamin C and E are pro-oxidant.¹⁵

Finally, the evidence is that the parenteral route should be used. However some anti-oxidant supplementation does not come in a suitable preparation (e.g. Vitamin E), and other potential anti-oxidants also have logistical challenges.²

In conclusion, the evidence reviewed does suggest a role for anti-oxidant therapy in the management of critically ill patients. However, more large controlled randomised trials are required to define optimal management strategies.

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Drugs causing diarrhoea and antidiarrhoeals in the intensive care unit (ICU)

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Keywords: diarrhoea, antidiarrhoeals, critical care

Diarrhoea is a common occurrence in ICU patients, affecting almost half the patient population.¹ The presence of sepsis, hypoalbuminaemia, enteral feeding, and antibiotic treatment² increase the likelihood of the patient developing diarrhoea.

The definition of diarrhoea is difficult, as the amount of stool passed per day is often difficult to measure. The consistency of faeces depends on the transit time in the colon; the shorter the transit time, the higher the fluid and electrolyte content. Stool charts, such as the Bristol Stool Chart³ may aid in documentation and facilitate communication.

Medication-induced diarrhoea

Most commonly, diarrhoea in ICU patients is iatrogenic. Many commonly used and essential ICU drugs cause diarrhoea.

Antibiotics are most frequently responsible,⁴ usually causing non-specific inflammatory diarrhoea associated with other symptoms such as vomiting, abdominal cramps and abdominal bloating. Diagnostic tests are usually negative and electrolyte losses are minimal. Withdrawal of the offending antibiotic usually resolves symptoms quickly.

Antibiotic-associated (pseudomembranous) colitis results from *Clostridium difficile* infection and is a less frequent but potentially serious complication.^{5,6} The symptoms range from trivial diarrhoea to life threatening pseudomembranous colitis (1-3% of all infections). Antibiotic-associated colitis may be caused by any antibiotic, including agents used for treatment of the condition. Infections may occur after a single dose of antibiotic or following a prolonged course; the elderly, immunocompromised patients, patients with underlying malignancy, patients with chronic obstructive airways disease and patients with renal failure are particularly at risk.⁵ Continued treatment of the original infection is essential and it may be possible to choose antibiotics, which are thought to cause less antibiotic associated colitis such as aminoglycosides, macrolides, sulfonamides, vancomycin, metronidazole or tetracycline.⁷

Agents that increase the *osmotic fluid load* of the gut frequently cause diarrhoea, for example magnesium containing antacids, lactulose, or rapid oral replenishment of magnesium and phosphate. Inert substances used in medication, such as starches, may cause osmotic induced diarrhoea. Other medications capable of causing non-specific diarrhoea are colchicine, quinidine, anti-inflammatory drugs, thyroxine, aspirin, diuretics and beta-blockers, as well as various chemotherapeutic agents.

Enteral nutrition has often implicated as a cause of diarrhoea.^{2,8} This is rarely the case, and the usual cause of diarrhoea is

concomitant antibiotic use.^{4,9} Occasionally, in susceptible patients, the lactose and fat content of enteral nutrition is responsible.¹⁰

Enteral feeding is preferred to parenteral nutrition or starvation.¹¹ Villous atrophy occurs in parenterally-fed and in starved patients and therefore rapid re-introduction of enteral nutrition can mimic syndromes characterised by villous atrophy (e.g. coeliac disease, bacterial overgrowth).

Diagnosis:

Before antidiarrhoeal medications are prescribed, a diagnosis should be sought. History from the patient may be limited, but documentation in a stool chart³ after hospital and ICU admission will help to find a cause for the diarrhoea.

The following clinical examinations and investigations should be considered before prescribing medications:

- Examination of the stool colour, consistency and volume.
- Rectal examination - to rule out overflow.
- Sigmoidoscopy - to view pseudomembrane characteristic in *Clostridium difficile* infection.
- Stool microbiological examination - microscopy, culture and sensitivity, to rule out infection.
- AXR - to rule out ischaemic or inflammatory causes.
- Abdominal/ pelvis US scan or CT abdomen/ pelvis, if abscess is suspected.

Treatment:

General measures:

Acute diarrhoea should be treated promptly, by observing hospital infection protocols, by removing any presumed causative agents, especially medication, and by replacing fluid and electrolyte losses. This theoretically simple approach is often difficult in practice, as ICU diarrhoea is usually multifactorial, and many of the medications implicated may have greater benefit to the patient's overall recovery if they are continued.

Fluid resuscitation and electrolyte replacement are particularly important in infants and frail or elderly patients. If possible, a rectal tube should be inserted for patient comfort, prevention of soiling and measurement of fluid losses.

There has been considerable debate, but very little evidence in ICU patients, about whether temporary cessation of enteral feeding or administration of lactose-free feeds are helpful in reducing diarrhoea, and about whether early feeding may lessen diarrhoea.¹⁰ The current consensus opinion is that enteral feeding is beneficial in critical illness and should be established wherever and as soon as possible.^{2,11} Continued tube feeding is thought to cause less diarrhoea than bolus feeding.

A surgical opinion should be sought for refractory septicaemia if infarcted or inflamed bowel or bowel abscess is suspected.

Antidiarrhoeals

Antimotility drugs are used in the management of uncomplicated acute diarrhoea in adults, but should be avoided in conditions where abdominal distension may develop, for example ulcerative colitis or antibiotic-associated colitis. Concomitant fluid and electrolyte replacement may be necessary. Antimotility drugs are not recommended in young children. Loperamide and codeine phosphate bind to gut wall opioid receptors, reducing propulsive peristalsis and increasing anal sphincter tone. Overtitration of dose and overuse of medication leads to constipation. The route of administration deserves special consideration in ICU patients and will influence the choice of medication on occasion.

Loperamide

Dose: 4 mg (tablets or capsules) initially followed by 2 mg after each loose stool for up to 5 days. Daily maximum dose is 16 mg. There is no liquid preparation commercially available.

Side effects: include abdominal cramps dizziness and drowsiness, skin reactions including urticaria and constipation. Administer cautiously in liver failure.

Diphenyloxylate with atropine (Lomotil)

Dose: 1 tablet or 5 mls liquid = 2.5 mg diphenyloxylate and 0.025 mg atropine, i.e. 1 part to 100 parts. Two tablets or 10 mls four times a day initially, then reduce and titrate to symptoms.

Side effects: nausea, vomiting, constipation, drowsiness, larger doses produce respiratory depression and hypotension. Use with caution in renal and hepatic failure.

Codeine phosphate

Dose: 30–60 mg (tablets) every 4 hours prn, Syrup 25 mg/5 ml, i.e. 5 to 10 mls every four hours, daily maximum dose 240 mg.

Side effects: nausea, vomiting, constipation, drowsiness, larger doses produce respiratory depression and hypotension. Use with caution in renal and hepatic failure.

Antispasmodics (antimuscarinics) are used for gastrointestinal smooth muscle spasm, which can be associated with diarrhoea, especially in irritable bowel syndrome and in diverticular disease.

Atropine sulphate and dicycloverine hydrochloride are tertiary amines and propantheline bromide and hyoscine butylbromide are quaternary ammonium compounds. The latter may be better suited for treatment of diarrhoea because they are less lipid-soluble than atropine and are therefore less likely to cross the blood brain barrier. They are also less well absorbed.

Side effects of antimuscarinics include constipation, transient bradycardia (followed by tachycardia, palpitation and

arrhythmias), reduced bronchial secretions, urinary urgency and retention, dilatation of the pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of the skin. Occasional side effects include confusion (particularly in the elderly), nausea, vomiting, and giddiness. Antimuscarinics are contraindicated in paralytic ileus, pyloric stenosis, prostatic enlargement and myasthenia gravis. Antimuscarinics should be used with caution in children and in the elderly, in gastro-oesophageal reflux disease, ulcerative colitis, acute myocardial infarction, hypertension, conditions characterised by tachycardia, pyrexia and in individuals susceptible to angle-closure glaucoma.

Atropine sulphate

Dose: 600 mcg to 1.2 mg tablet at night; there is no liquid preparation commercially available. Parenteral administration is not suitable for the control of diarrhoea.

Dicycloverine hydrochloride

Dose: 10 - 20 mg tablets, 10 mg/ 5 ml syrup, 5 - 10 mls, up to three times daily.

Propantheline bromide

Dose: 15 mg tablets three times a day at least 1 hour before meals and 30 mg at night. Daily maximum dose is 120 mg. There is no liquid preparation commercially available.

Hyoscine butylbromide

Dose: by mouth 20 mg tablets up to four times a day. By intravenous or intramuscular injection, 20 mg for acute smooth muscle spasm and smooth muscle spasm associated with procedures, repeated after 30 minutes if necessary. Daily maximum dose is 100 mg. Hyoscine is contraindicated in acute porphyrias.

Oral rehydration therapy

These compounds are indicated when there is fluid and electrolyte loss in diarrhoea. They are suitable for rapid oral rehydration. The World Health Organisation¹² promotes a single formula to be used flexibly, i.e. with additional water based drinks in between doses. In infants, breast milk or formula drinks should be offered in addition. The oral hydration solutions in the UK are lower in sodium than the WHO formulation, as patients in the UK are presumed to have less severe sodium losses.¹³

Oral rehydration salts (ORS) enhance the absorption of water and electrolytes, replace electrolyte deficit adequately and safely, contain alkalinising solutions to counter acidosis and are slightly hyperosmolar to prevent the possible induction of diarrhoea.

Rehydration should be rapid, except in cases where severe hypernatraemic dehydration is suspected or diagnosed. The recommended dose of ORS is 200 to 400 mls after each loose motion for adults and children, and 1 to 1.5 times feed volume for infants.

	Dioralyte®	Electrolade®	Rapolyte®	WHO formulation
	10 tablets reconstituted in 1 litre of water	5 sachets reconstituted in 1 litre of water	5 sachets reconstituted in 1 litre of water	Oral powder reconstituted in 1 litre of water
Sodium	60 mmol	50 mmol	60 mmol	75 mmol
Chloride	45 mmol	40 mmol	50 mmol	65 mmol
Potassium	25 mmol	20 mmol	20 mmol	20 mmol
Citrate	20 mmol	-	10 mmol	10 mmol
Bicarbonate	-	30 mmol	-	-
Glucose	90 mmol	111 mmol	110 mmol	75 mmol

Cholestyramine binds unabsorbed bile salts and provides symptomatic relief in diarrhoea caused by ileal disease, small bowel resection, following vagotomy, in diabetic vagal neuropathy and following radiation. It cannot be recommended for the treatment of acute diarrhoea.

Adsorbents such as *kaolin* are not recommended for acute diarrhoea. Bulk forming agents such as *ispaghula* and *methylcellulose* are used for the treatment of diarrhoea in diverticular disease.

Probiotics are microorganisms with beneficial properties to the host. Their mechanism of action is not fully understood, but includes suppression of growth, epithelial binding and invasion by pathogenic bacteria, improvement of the barrier function of the gut and modulation of the immune system. Theoretically, probiotics should improve enteral tube feeding-associated diarrhoea, but there is currently insufficient evidence to recommend their routine use.¹⁴ Live yoghurt is commonly recommended as a source of probiotics, but fermented dairy beverages contain a much higher proportion of live cultures than yoghurt. They are also more suitable for individuals who are lactose intolerant. Recent systematic reviews have concluded that probiotics achieve up to 52% reduction in antibiotic-associated diarrhoea;^{5,16} but no studies to date have demonstrated a benefit for treatment or prevention of *Clostridium difficile*-associated diarrhoea.¹⁷

Specific Antibiotics for *Clostridium difficile* infection

There are several indications for antibiotic therapy in antibiotic associated colitis:

- Evidence of colitis
- Persistent diarrhoea despite cessation of the offending antibiotic
- Continued need to treat original infection with antibiotics
- Prevention of spread to other patients

Antibiotic treatment is not needed for asymptomatic patients with a positive *Clostridium difficile* toxin assay.

Vancomycin is a bactericidal antibacterial with activity against aerobic and anaerobic gram-positive organisms. It is poorly absorbed orally, but is suitable for oral administration in antibiotic-

associated colitis. The recommended dose by mouth or nasogastric tube is 125 mg every 6 hours for 7 to 10 days. This dose can be increased to 500 mg in severe infection or if the patient fails to respond. However, a study comparing low and high oral doses of vancomycin did not show a more rapid recovery in the higher oral dose group.¹⁸

In parenterally-fed patients, with normal renal function, 1 gram intravenously every 12 hours or 500 mg intravenously every 6 hours is recommended for the treatment of antibiotic-associated colitis, with less frequent administration in renal failure. All patients require plasma vancomycin measurements after 3 to 4 doses if renal function is normal, or earlier if renal function is abnormal. The commonest side effects of parenteral administration are ototoxicity and renal impairment. Ototoxicity can be minimised by slow intravenous infusion.

Metronidazole is an antimicrobial drug with high activity against anaerobic bacteria and protozoa. It is a good alternative in the treatment of antibiotic-associated colitis orally or by rectal tube, when oral or nasogastric administration is not possible.

Metronidazole should be used with caution in liver failure. Side effects include disulfiram-like reactions with alcohol.

Dose: 500 mg every 8 hours or 250 mg every six hours orally, 500 mg to 1 gram every eight hours rectally, for 10 to 14 days.

In the past, metronidazole has been shown to be as effective as vancomycin in treating antibiotic-associated colitis, but much cheaper.²⁵ A small, randomised study compared metronidazole alone and metronidazole plus rifampicin for the treatment of antibiotic associated colitis, and did not show any benefit from combination therapy.²⁰

A recent meta-analysis showed that metronidazole, bacitracin and fusidic acid were as effective as vancomycin, but teicoplanin was slightly more effective in achieving a clinical and microbiological cure.²¹

Treatment failure:

There are increasing failure rates of conventional treatment for *Clostridium difficile*-associated diarrhoea. This is in part related to

a new strain of *Clostridium difficile*, the NAP-1 strain, which is associated with resistance to standard treatment and with more serious infection.⁶ Treatment failure can also be attributed to misdiagnosis of antibiotic-associated diarrhoea or to diarrhoea from another cause.

A number of new treatments have been described;²² but only two agents have undergone randomly controlled trials: *Nitazoxanide*, an antiprotozoal agent, is as effective as metronidazole in one trial,^{23,24} but clinical experience in the ICU setting is limited to date.

Tolevamer is a novel soluble, high molecular weight, non-antibiotic polymer that binds *Clostridium difficile* toxins and neutralises them. Theoretically, this allows treatment of *Clostridium difficile* infection without antibiotics, encouraging restoration of the normal gastrointestinal flora. One clinical trial compares tolevamer to vancomycin with promising results;²⁵ however, this compound is not commercially available to treat antibiotic-associated colitis at the time of writing.

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An unusual cause of breathlessness

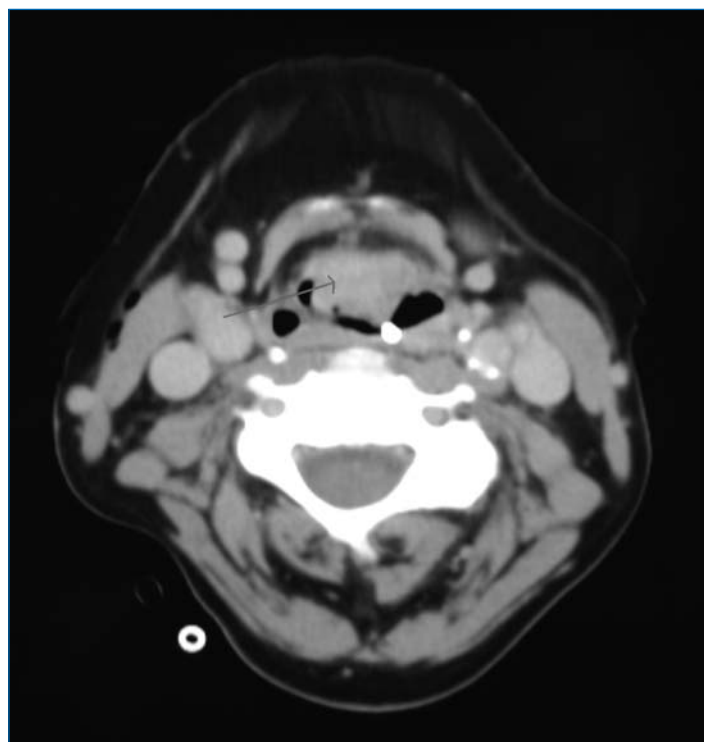
S Hutchings

Keywords: pulmonary oedema, laryngeal obstruction

The Case

A 68 year-old woman presented to the emergency department with severe breathlessness. She was a lifelong smoker who had chronic obstructive pulmonary disease managed with home nebulisers. She had never previously been admitted to hospital. During the week prior to admission she had become increasingly dyspnoeic and developed a non-productive cough. During transfer to hospital her dyspnoea worsened. She was treated for bronchospasm with intra-muscular adrenaline 0.5 mg and continuous nebulised bronchodilator therapy. On arrival in the emergency department she had ventricular tachycardia on ECG which was treated with amiodarone 300 mg and cardioverted to sinus rhythm. Arterial blood gases showed hypoxaemia and a mixed metabolic and respiratory acidosis. Chest radiography showed consolidation in the right lower and middle lobes. She had a leucocytosis (white cell count 15,000 /ml) and an elevated troponin I (0.15 µg/ml).

An initial diagnosis of type two respiratory failure due to an infective exacerbation of chronic obstructive pulmonary disease was made and the patient transferred to a respiratory high dependency unit for non-invasive ventilatory support. She improved rapidly after an hour of biphasic positive airway pressure ventilation (BiPAP). Her presumed pneumonia was treated with intravenous cefuroxime. A secondary diagnosis of acute coronary syndrome was made and she was started on aspirin, clopidogrel and low molecular weight heparin and the infusion of amiodarone continued.



Tumour obstructing the laryngeal aperture (arrow)

Over the next 48 hours she suffered three further episodes of acute respiratory distress requiring non-invasive ventilatory support. She was admitted to the intensive care unit after the second deterioration and again improved rapidly with a short period of non-invasive ventilation. During this admission it was felt that these episodes clinically resembled acute left ventricular failure. Trans-thoracic echocardiography was done and showed good left ventricular function with no valvular abnormalities. The patient was subsequently discharged from intensive care.

Eighteen hours later she re-presented with acute respiratory failure. When reviewed by the intensive care team she was *in extremis*, with a respiratory rate of 40. She was receiving non-invasive ventilatory support with BiPAP and was cardiovascularly compromised with atrial fibrillation at a rate of 140, and a systolic blood pressure of 80 mmHg. Her arterial blood gases showed that she was hypoxaemic with a mixed respiratory and metabolic acidosis.

She was transferred to the intensive care unit for intubation and ventilatory support. A rapid sequence induction was performed with midazolam 4 mg, propofol 50 mg and suxamethonium 100 mg. On direct laryngoscopy, a large stenosing supraglottic lesion was seen, almost completely obscuring the anterior glottic aperture. Fortunately the mass was mobile and pedunculated and could be moved to one side, allowing intubation.

Once intubated the patient's condition improved. On fiberoptic bronchoscopy there was minimal inflammatory debris in the right middle and lower lobe bronchi. A surgical tracheostomy was performed and a biopsy taken of the glottic lesion. Histological examination revealed this to be a poorly differentiated squamous cell carcinoma.

The patient underwent a total laryngectomy with an uneventful postoperative course. On subsequent follow-up she was found to have cervical lymph node metastases and she had a radical neck dissection, from which she made an uneventful recovery.

Discussion

The diagnosis of acute severe breathlessness can be difficult. The differential diagnosis includes asthma, other more chronic forms of airway limitation, left ventricular failure and pneumonia. Upper airway obstruction may not be considered in the absence of stridor. The association of an upper airway tumour with dyspnoea and stridor is recognised¹ and it has also been cited as a cause of failure of non-invasive ventilatory support.² It is, however, rare to find associated non-cardiogenic pulmonary oedema as the predominant clinical finding, as in this case.

Negative pressure pulmonary oedema secondary to upper airway obstruction has typically been associated with acute laryngospasm³ but a variety of other causes have been cited, implicating both airway device obstruction and upper airway

pathology.^{4,5} In the postoperative setting, the development of pulmonary oedema is seen more often in young fit male patients.⁶ The mechanism can be partially explained by Starling forces in the pulmonary vasculature. Normal capillary hydrostatic pressure is responsible for the efflux of fluid from the vascular space into the interstitial space. This is opposed by hydrostatic pressure in the lung interstitium. In the lung the alveoli, interstitial space and capillary endothelium form a closely associated unit, and forces are readily transmitted between them. Thus a large negative intrathoracic pressure applied to the alveoli and lung interstitium causes an increase in the transcapillary pressure gradient and a consequent increase in extravascular lung water.

A second, and probably more important mechanism for explaining the pulmonary oedema seen in this patient, relates to the changes in left ventricular preload and afterload associated with the exaggerated intra thoracic pressure changes which occur during spontaneous ventilation against an obstructed airway. The transmural pressure gradient between the left ventricle and the thoracic cavity is a key determinant of the left ventricular afterload, or the force needed to eject the stroke volume. During positive pressure ventilation this gradient, and hence the afterload, is reduced, explaining the beneficial effects of positive pressure ventilation in patients with poor ventricular function. Conversely, extremes of negative intra thoracic pressure cause a profound increase in the transmural pressure gradient and an increase in left ventricular afterload. The subsequent increase in left ventricular pressure may be great enough to cause frank pulmonary oedema as in this case. The negative intrathoracic pressure also increases venous return to the right heart and thus increased right and left ventricular preload. The effect of this change in preload will be dependent on the part of the Starling curve the ventricle is currently operating on, so may increase, decrease or have a minimal effect on cardiac output.

Unlike more chronic causes of left ventricular failure, the physical forces producing negative pressure pulmonary oedema tend to be transient and resolution of symptoms is common once the cause, such as airway obstruction, is removed. Application of positive pressure to the airway, such as occurs during treatment with CPAP, BiPAP or IPPV will increase the speed of resolution. The use of medical treatments such as nitrates and diuretics, although helpful in cases of pulmonary oedema caused by acute on chronic left ventricular dysfunction⁷ are unlikely to be of benefit, and treatment should be directed towards removing the primary cause.

In this case the clinical presentation of severe acute dyspnoea was suggestive of pulmonary oedema, but the cause was presumed to be cardiac because of the presence of ventricular tachycardia on presentation with an elevated troponin level. However the complete resolution of symptoms between episodes and good left ventricular function on seen echocardiogram made this diagnosis less likely. The absence of stridor in this case indicated that the airway was almost completely obstructed which explains the severity of the pulmonary oedema that followed.

This case suggests that a diagnosis of upper airway obstruction and consequent negative pressure pulmonary oedema should be

considered in patients presenting with severe dyspnoea. Some features useful in making this diagnosis are failure to respond to conventional medical therapy, a remitting and relapsing course with several episodes of sudden deterioration interspersed with periods of clinical normality and a dramatic response to the institution of ventilatory support.

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Ethylene glycol poisoning - a challenge for the intensivist

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Keywords: Ethylene glycol; ethics; organ donation

Ethylene glycol is a key constituent of antifreeze products, and is readily available to people of all ages in the home and workplace. In the United Kingdom the incidence of ethylene glycol poisoning is very low. There are case reports from the UK describing the use of ethanol and peritoneal dialysis or haemodiafiltration to treat severe ethylene glycol poisoning.^{1,2} On at least one occasion, brainstem death has been reported.²

We report a case of severe ethylene glycol poisoning culminating in brain stem death. The initial diagnosis and management is discussed, along with the toxicological and ethical issues of managing brain stem death and possible organ donation in this setting.

Case Report

A thirty-five year old man was admitted to the Accident and Emergency department with an alleged overdose of paracetamol. His GCS was 14. He denied taking any alcohol or other drugs. He had a previous admission to hospital with ethylene glycol poisoning, which he had survived.

Approximately three hours after admission, his GCS dropped to 7. He was found to have a severe metabolic acidosis (base deficit -23.9 mmol/l); urinary toxicology was negative for salicylates and paracetamol. Based on the history and presentation, we made a provisional diagnosis of ethylene glycol poisoning. He was sedated, intubated, established on mechanical ventilation and transferred to the intensive care unit. On advice from TOXBASE, he was treated with intravenous fluids and given a loading dose of intravenous 10% ethanol followed by a maintenance infusion to achieve a target blood ethanol level of 22 mmol/l. Subsequent blood results showed deteriorating renal function, raised serum osmolality and high anion gap acidemia. The clinical diagnosis of ethylene glycol poisoning was confirmed by the detection of one of the toxic metabolites of ethylene glycol, glycolic acid (430 mg/l), in the serum. He developed acute renal failure requiring continuous veno-venous haemofiltration (CVVH).

The following day he suffered a brief asystolic cardiac arrest requiring cardiopulmonary resuscitation for less than a minute. Post-arrest, he was haemodynamically stable and his pupils were reacting. Treatment continued with sedation, ethanol infusion and haemofiltration.

On day three, he developed acute hypertension followed by hypotension and seizures. His pupils were now fixed and dilated. He became apnoeic and lost cranial nerve reflexes (corneal, gag and cough reflexes). A CT scan of brain showed massive cerebral oedema with low attenuation in the basal ganglia, compatible with the clinical suspicion of brainstem herniation.

On discussion with his family it was agreed that, given the severity of his condition, should he suffer a further cardiac arrest, further

resuscitation would be inappropriate. His family expressed a wish that he be considered for organ donation and felt that this would be his wish also. To clarify the implications of ethylene glycol poisoning and its treatments for brain stem testing and organ donation, we contacted the National Poisons Information Service (NPIS) and the transplant coordinator. We were advised that in order to fulfil the criteria for brain stem testing, his serum glycolic acid level must be negligible. The transplant co-ordinator advised that he could be considered for internal organ donation.

The ethanol infusion was stopped on the fourth day after serum ethylene glycol levels diminished, and supportive intensive care was continued including CVVH. Throughout the course he remained unresponsive and apnoeic, with absent cranial nerve reflexes. He was started on an organ donor management regime. We continued to monitor serum glycolic acid levels. We also discussed possible withdrawal of treatment with the family in view of futility.

One week after admission, glycolic acid levels were sufficiently low to permit brain stem testing, and brain stem death was then confirmed. His death was reported to the coroner, who requested a post mortem; donation of internal organs was not permitted, although donation of skin and corneas was allowed.

Discussion

The first cases of ethylene glycol toxicity were reported in 1930 when two young men developed terminal respiratory failure and convulsions after ingesting 'Prestone' antifreeze (95% ethylene glycol).³ Human poisoning has occurred in isolated cases and in epidemics. Multiple cases of ethylene glycol poisoning occurred during the Second World War and also during the 1973 Arab-Israeli conflict. Eighteen soldiers who ingested ethylene glycol as a substitute for ethanol died during World War II.⁴ Currently, ethylene glycol poisoning causes hundreds of deaths annually worldwide, with quite variable global incidence.

Comprehensive data is lacking for the United Kingdom. It is estimated that many district hospitals will only see 1-2 cases every 2-3 years. In 2002, an annual report by American Association of Poison Control Centres (AAPCC) recorded 6,077 exposures to ethylene glycol in the United States, resulting in 40 deaths and 254 near-fatalities.⁵ The most common sources of ethylene glycol are automotive antifreeze (generally available in a 95% concentration), engine coolant, hydraulic brake fluid and paint. Patients may ingest ethylene glycol as an alternative to alcohol, to inflict self-harm or by accident. Multiple poisonings have been reported after environmental accidents due to contamination of water systems.⁶

Establishing the diagnosis of ethylene glycol poisoning can be challenging. The most conclusive diagnostic test is direct measurement of serum or urine ethylene glycol concentration. However, there is a poor correlation between the blood

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concentration of ethylene glycol and the severity of poisoning.⁷ Blood levels of metabolites of ethylene glycol, mainly glycolate, guide treatment with the antidote. Other features such as severe metabolic acidosis, raised serum osmolar gap, raised anion gap, hypocalcemia and presence of urine crystals support the diagnosis. In our patient, serum osmolality was 339 mosm/kg with an osmolar gap of 39 mmol/l (normal 10 mosm/l) and the anion gap was 33 mmol/l (normal 12 - 15 mmol/l). Laboratory results should be interpreted with caution, depending on the time of ingestion of ethylene glycol. In the early stages, acid metabolites may not yet have formed; late presentation may not reveal an increased osmolar gap because the ethylene glycol has already been converted to toxic, but osmotically inactive, products.

It has been reported that glycolate causes large artifactual elevations in plasma L-lactate measurements if tested with two analysers in common use, with the potential for misdiagnosis of lactic acidosis in ethylene glycol poisoning.⁸ In our patient initial lactate was measured as > 48 mmol/l.

As this patient was treated in a District General Hospital, samples for ethylene glycol and its metabolites were sent to another hospital laboratory. Not all laboratories can perform assays for ethylene glycol, creating potential delays in diagnosis and treatment. It is important not to delay initiating treatment in the absence of serum levels.

There are three primary goals in treating ethylene glycol poisoning:

- correction of the patient's metabolic acidaemia
- prevention of metabolism of the compound to its toxic metabolites
- removal of ethylene glycol and its toxic metabolites using haemodialysis if necessary.

The recommended antidote for ethylene glycol intoxication is ethanol.⁹ It binds to alcohol dehydrogenase preventing the metabolism of ethylene glycol into toxic products. Ease of availability, relatively low cost and clinical effectiveness have all promoted its use in this context despite availability of other alternatives (see below) and drawbacks with its use.¹⁰ The accepted target plasma ethanol concentration is 100 to 125 mg/dl (21.7 to 27.1 mmol/l).¹¹ Since patients treated with large doses of ethanol become intoxicated, they must be closely monitored. CNS depression, circulatory instability and respiratory depression from ethanol make management of the already poisoned patient more difficult. It is difficult to maintain effective concentrations of ethanol in the blood, especially during haemodialysis which removes ethanol. Because the kinetics of ethanol are unpredictable, blood concentrations must be measured frequently. For all these reasons ethanol is not an ideal antidote.¹²

In 1988 fomepizole (4-methylpyrazole)¹³ was introduced as an effective competitive inhibitor of alcohol dehydrogenase that appears to have none of the adverse effects of ethanol.¹¹ There are case reports suggesting fomepizole's efficacy. Phase 1 trials funded by US Food and Drug Administration (FDA)^{14,15} have been reported, proving its safety and providing pharmacokinetic data. There is at least one prospective study¹⁶ that confirms its safety

profile and its effectiveness in preventing renal injury by inhibiting formation of toxic metabolites. Given the practical problems related to ethanol administration and its side effects, fomepizole appears to be the preferred treatment. However, the cost of treatment with fomepizole (about \$4,000) per case still makes ethanol the preferred option if resources are limited.¹² Nevertheless, the use of fomepizole may be cost effective, in that there is no need to measure blood ethanol levels and that patients treated may need haemodialysis less often, and there may be reduced length of stay in intensive care unit.

In the UK the treatment for poisoning is assisted by guidelines from TOXBASE, an online database maintained by National Poisons Information Service (NPIS).¹⁷ Although NPIS guidelines¹⁸ recommend the use of fomepizole as an alternative to ethanol to treat ethylene glycol, there are practical barriers to its use. Fomepizole is not usually available from hospital pharmacies and has to be obtained from NPIS regional centres. This could result in an undesirable delay in treatment.

Because of the low incidence of poisoning, it is hard to obtain high quality evidence for best treatment. Although ethanol is the traditional antidote for ethylene glycol poisoning, it has not been studied prospectively nor approved by governing organisations such as the FDA.¹⁰ The FDA recently approved the use of fomepizole as an effective antidote for ethylene glycol intoxication. There are no clinical studies that directly compare the efficacy of fomepizole with that of ethanol.^{10,19}

Haemodialysis is effective to remove both ethylene glycol and its toxic metabolites from the circulation and to correct metabolic acidosis. It has been used in severe ethylene glycol poisoning for many years and prospectively studied to assess clearance rates and efficacy.²⁰ In a case series continuous veno-venous haemodiafiltration was used with significant clearance of ethylene glycol,² but there is insufficient data available regarding the use of haemodiafiltration or haemofiltration in this context.

Organ Donation

In a national survey conducted in UK it was shown that most transplantation physicians, surgeons and intensive care unit directors would consider those who die following acute drug intoxication and poisoning as potential organ donors.²¹ Although the number of reports is small, the literature shows in general that the transplanted organs from poisoned patients have good long-term survival. There are number of published cases of successful kidney, liver and heart transplantation, and one report of successful lung transplantation from methanol-poisoned patients. The largest series involved a total of 38 transplanted organs (29 kidneys, 4 hearts and 5 livers) from 16 donors who died from methanol poisoning.²² At 1 year follow up, the 3 heart and 3 liver recipients, and 92.6% of the kidney recipients had normal graft function. These figures are comparable to the short-term and long-term outcomes from non-poisoned donors in the same centres over this time.²² In another series, 13 kidneys, 3 livers, 1 heart and 1 bilateral lung were successfully transplanted from 7 methanol-poisoned donors.²³ There is no published data available relating to such transplants following ethylene glycol

poisoning. However, this evidence suggests that patients who have died of poisoning could be potential organ donors and who are at present probably not often referred for transplantation.

This case highlights an unusual clinical situation that presented difficult decisions at every stage. There were practical problems associated with diagnosis and treatment, dilemmas about the use of safe and effective antidotes and interventions, and difficult ethical issues surrounding organ donation. The major ethical dilemma was the appropriateness of continuing life support to ensure organ viability for donation when no longer beneficial to the patient's outcome. While this may be commonly done for short periods, in the poisoned patient it may take several days for toxic metabolites to reach acceptable levels before brain stem testing. Is such a delay acceptable? Is it ethical to prolong life artificially when there is no benefit to the patient? And if so, how long is acceptable? These questions do not have easy answers.

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Late, fatal complication of an inferior vena cava filter

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A 53 year-old woman presented to the Accident and Emergency department (A&E) with acute upper abdominal pain. She remained hypotensive (systolic blood pressure 70mmHg) and tachycardic (pulse rate 120 beats/min) despite 2,500ml of intravenous crystalloid. She was on warfarin for recurrent deep vein thromboses (DVTs) with pulmonary emboli, secondary to protein C deficiency. A bird's nest inferior vena cava (IVC) filter had been placed 10 years previously because of recurrent DVTs.

While in the A&E, she had a cardiac arrest. The ECG showed pulseless electrical activity and subsequent resuscitation was unsuccessful. Post-mortem examination revealed that the IVC filter had migrated into the right ventricle causing wall rupture with an haemorrhagic pericardial effusion. The cause of death was cardiac tamponade.

Post-placement complications of IVC filters occur in a minority of patients¹ and include recurrent pulmonary embolism, caval occlusion, erosion into contiguous structures (e.g. duodenum, aorta) and filter migration. Migration adjacent to the renal vein ostia can precipitate occlusion and renal failure. Migration to the heart is extremely rare and can cause acute myocardial infarction², arrhythmias³, tricuspid regurgitation, cardiac failure⁴ and cardiac tamponade.^{5,6} Entrapment of J-tipped guide wires and pulmonary artery catheters in IVC filters has been reported! Straight guide wires or fluoroscopy should be used for all central line insertions in intensive care patients with IVC filters.

To our knowledge there have been no previous reports of IVC filter migration to the right heart with subsequent tamponade occurring later than a few days post-placement. In our patient this was after 10 years, sadly proving fatal.

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Qualifications in intensive care medicine: An audit of consultant appointments in Wales

C Thorpe

Formal qualifications in intensive care medicine (ICM) have been available from the ICBTICM since 1999. Before that date, very few consultants had accredited intensive care training, and most consultants were appointed to joint anaesthesia and ICM posts with a CCST in anaesthesia. This audit was designed to find out to what extent formal recognised training in ICM had permeated through to consultant appointments in Wales. It also examined the sessional allocations for each appointment.

Methods

Nine intensive care units in Wales were audited to find out the qualifications of all new consultant appointments over the past 2 years. Each unit was also asked to predict the likely appointments over the coming 2 years. The second aspect of the audit was to ascertain the sessional commitment in intensive care for each of the new jobs.

Results

Results are shown in **Table 1**

There have been a total of 9 appointments over the past 2 years, all with a part time commitment to ICM. Of the consultants appointed, 2 had a joint CCT in ICM, 3 had advanced training and 1 had 'grandfather rights' - extensive ICM experience as a consultant in ICM previously. Two candidates had intermediate training and 1 had no formal qualifications in intensive care.

In the next 2 years there are predicted to be 15 potential consultant jobs with an interest in ICM. Four of these are planned as full time intensivist jobs and 11 are planned as part time posts.

Discussion

Formal qualifications in intensive care medicine play a crucial role in obtaining a consultant job with ICM sessions in Wales. This applies to both teaching Hospital and to District General Hospital (DGH) appointments. Five out of 8 consultants appointed to DGHs had advanced training, joint CCT or 'grandfather' rights. This proves that trainees who want a career in ICM should obtain formal training, and that they are unlikely to get a job in any hospital in Wales without this.

Planning for the future is difficult in Wales at present because of uncertainty surrounding service reconfiguration. This may affect the number of predicted appointments over the next few years.

Future appointments are likely to be more rather than less competitive. If there is a change to full time intensivist appointments, there will be a reduction in the number of jobs needed. Larger hospitals are able to appoint full time intensivists, but smaller hospitals need consultants with sessions in other specialties to sustain their on call rotas. Because of this, those who elect to obtain a single CCT in ICM will work mainly in larger units.

In Wales we are likely to have a mixture of intermediate and large size hospitals and I suspect that we will need to train a combination of joint and single specialty trainees in ICM to fill future need. The uncertainties will inevitably become clearer over time.

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Table 1: Appointments to Consultant Posts in ICM

Hospital	Last 2 years			Next 2 years	
	Number	Sessions	Qualifications	Number	Sessions
T1	0			3	10
T2	1	4	A	3	10 +3 +3
D1	0			2	10
D2	1	2	N	1	2
D3	0			2	3
D4	1	3	I	0	
D5	2	3	A; CCT	1	3
D6	2	2	I ; G	1or 2	2
D7	2	3	A; CCT	2	3

A =Advanced, I = Intermediate, G= Grandfather, N = None, T= Teaching Hospital, D = District General Hospital

Antibiotic use in Scottish intensive care units

A Timmins, J McCoubrey, F McKirdy, MG Booth and J Reilly

Keywords: antibiotics, audit

Summary

There has been considerable publicity recently about over-use of antibiotics, with intensive care units (ICUs) identified as one area of particularly high use. The aim of this study was to compare the usage levels of antibacterial and antifungal agents in 22 Scottish ICUs.

Antibiotic issue data for each of the participating ICUs was collected through the relevant pharmacy department and converted to Defined Daily Doses (DDDs). This was indexed against the number of patients treated and the number of bed days used in order to account for differing activity levels.

The usage of antibacterials ranged from 103 to 334 DDDs/ 100 bed days (mean 183). For antifungals the range was 8 to 286 DDDs/ 100 bed days (mean 36). There was a considerable variation in the relative use of specific agents.

Differences in case-mix and severity of illness have been suggested as possible reasons for the differences observed. Further studies are required; this preliminary study highlights issues which individual units can examine.

Introduction

In recent years there has been considerable publicity about the threat of bacterial resistance caused by overuse of antibiotics.^{1,2} Greater control of antibiotic use and minimisation of use are suggested as important measures in reducing this risk. One of the main aims of the 'Scottish Action Plan on Antimicrobial Resistance'³ is to promote prudent antimicrobial prescribing, alongside surveillance of resistance and control of healthcare associated infection.

The 'Recommendations for Good Antimicrobial Practice in Acute Hospitals' produced by the Scottish Medicines Consortium⁴ identified wide variations in antimicrobial prescribing policy and practice, and emphasised the need to standardise approaches to prescribing antimicrobials in acute hospitals.

Studies have shown that antibiotics make up a significant proportion of drug use in ICUs.⁵ Due to the condition of the patients and the interventions performed, 40-50% of patients on ICUs may have antibiotics prescribed at any one time,¹ whether for pre-existing infections or for infections acquired on the unit. Infections acquired on the ICU significantly increase the risk of death.⁶ Some ICU infections require treatment with atypical agents and so there can be a wide range of antibiotics used. This may contribute to increasing antimicrobial resistance in the ICU, in hospitals and potentially in the wider environment.⁷

As part of a larger pilot study about surveillance of ICU associated infections run by Health Protection Scotland and the

Scottish Intensive Care Society Audit Group,⁸ the Scottish Adult Critical Care Pharmacist Network was asked to collect data about antibiotic use in each of the ICUs in Scotland. The aim was to examine multiple aspects of surveillance of healthcare associated infection, microbial resistance and antibiotic use.

Method

Each of the ICUs included in the Scottish Intensive Care Society's audit programme were invited to contribute baseline data to the study. Of 25 eligible units, 22 contributed data. One unit was unwilling to provide information, one had technical problems in doing so, and one was unable to separate issues to ICU from those for another neighbouring ward area.

The pharmacists responsible for each of the ICUs taking part in the study were asked to provide usage data for antibacterial and antifungal drugs covering the period from April 2004 to March 2005.

The information was collated and converted to 'Defined Daily Doses' (DDD) using the World Health Organisation's Anatomical Therapeutic Chemical (ATC) system.⁹ The DDD for a drug is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. However it does not necessarily reflect the recommended or prescribed daily dose. This results in a method of quantifying drug usage that is not affected by varying costs or dosing schedules, so producing a standardised value.

To allow for different activity levels and sizes of unit, the total DDD figure for the year for each unit was divided by the number of bed days used over the period, to provide a figure referred to as the "Antibiotic Density"¹⁰ which can be used as a quantitative comparison of antibiotic use between units. Then the DDD per total number of patients treated over the period was calculated to see if this was different from Antibiotic Density. Values for individual agents, therapeutic classes (according to the British National Formulary) and total use were obtained, and the unit results compared.

Activity measures, measured as the number of occupied bed days used and the number of patients treated during the periods, were obtained from the electronic audit database system ("Wardwatcher", Critical Care Audit Ltd, England) which is used in each Scottish ICU unit as part of the data collection system for the Scottish Intensive Care Society Audit Group.

As part of the larger study, five of the units underwent an intensive data collection exercise looking at many aspects of infection surveillance during the summer of 2005. For these units, the antibiotic use data for the three month period of the full surveillance study was compared with that during the corresponding three months of the previous year in the baseline data collection period.

All of the information was collated and analysed using Microsoft Excel data analysis package.

Results

The overall antibiotic and antifungal use is shown in **Figure 1**. The median values were 176.01 DDD/100 bed days (interquartile range 144.62 - 203.41) for antibiotics, and 16.88 DDD/100 bed days (12.51 to 32.43) for antifungals. This means that for each occupied bed day, 1.76 'defined daily doses' of antibiotics were used. When calculated as DDD/patient the relevant figures were 9.95 (8.69 - 11.96) and 0.99 (0.62 - 2.02), or just below 10 full days dosage of antibiotics per patient, which could represent 10 days of one agent or 5 days of two agents etc. **Figure 2** shows the comparison of the two methods of expressing usage.

Figure 3 shows a comparison of the figures obtained from the study period in the five units taking part in the intensive surveillance study with the year-long baseline figures for the same units. These appear to be comparable.

The figures for particular drug groups are shown in **Figure 4**.

Discussion

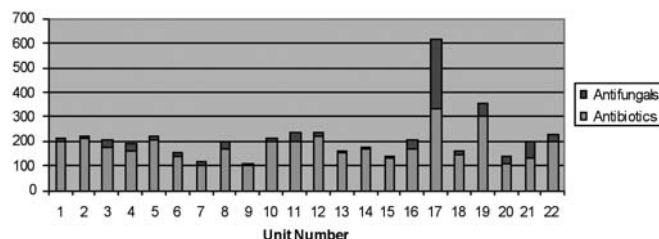
While similar programmes have been described in ICUs in Germany and USA^{11,12} this is the first study providing such information in the UK setting. This is important as there are significant differences in the way ICUs work in the three countries¹³, such as different proportions of lower dependency patients and different staffing levels.

A wide range of antibiotic densities was observed in the Scottish units. This suggests variation in practices between units; however the differences could also be due to other factors such as different case mix (with corresponding differences in the type of infection encountered). This might be affected by the ratio of surgical patients to medical patients (although analysis of the primary infection study appeared to show this was consistent amongst the five sites examined in detail in the infection surveillance study)⁸; by tertiary referrals or local specialisation. Further investigation would be needed to quantify these effects. One unit (17 on figure 3) is an outlier as it is the only one that uses selective decontamination of the digestive tract (SDD), a practice that involves the prophylactic use of significant quantities of certain antibacterial and antifungal agents specifically to prevent ventilator acquired pneumonia.

The choice of denominator used for the ratio has been debated, with some workers suggesting that the number of cases or patients treated is more relevant than the number of bed days used, particularly in situations where individual patients need prolonged rehabilitation rather than rapid treatment and turnover. The fact that the values for the DDD/patient showed a similar pattern to those of the DDD/100 bed days suggests that this did not make a significant difference to the quantification of antibiotic use in the units studied, and it is therefore appropriate to use the latter figure in order to be consistent with other areas of healthcare. It has been suggested however that both figures should be quoted to give an accurate description of use.¹⁴

The median value for DDD/100 bed days for antibacterials is 176.01, considerably higher than that reported in the Surveillance

Figure 1: Overall antibiotic and antifungal usage for each unit



System of Antibiotic Use and Bacterial Resistance in German

Figure 2: Correlation of DDD/100 patient days v. DDD/Patient

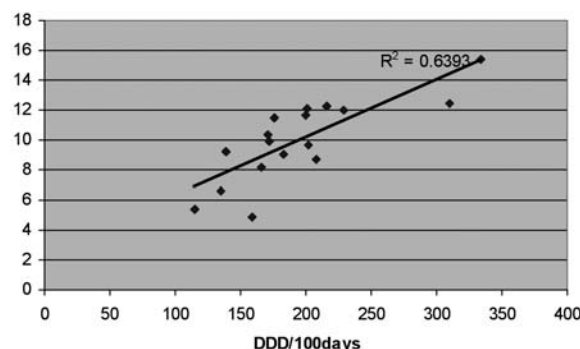
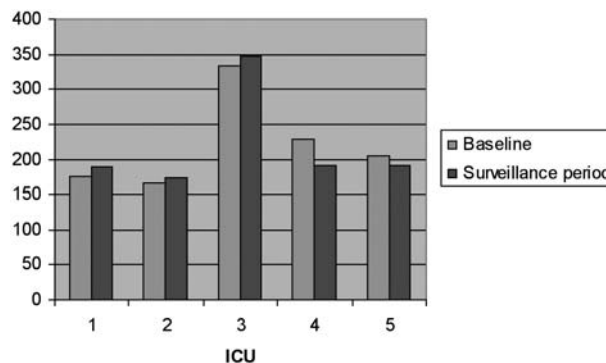
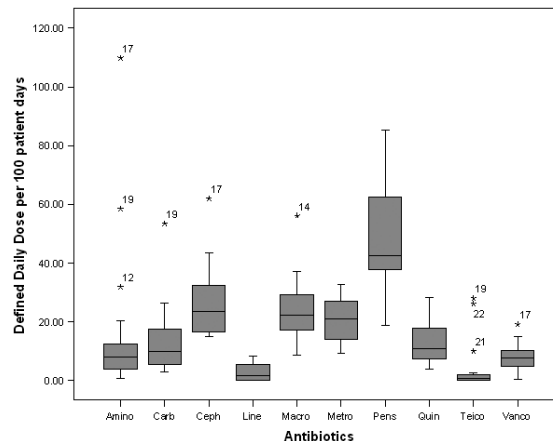


Figure 3: Comparison of Antibiotic Density for five units resurveyed



Intensive Care Units (known as the SARI programme) study

Figure 4: A box plot of the Daily Defined Doses per 100 patients for a range of antibiotic groups issued to 22 hospitals included in the study



Key:
 Amino = Aminoglycosides Carb = Carbapenems
 Ceph = Cephalosporins Line = Linezolid
 Macro = Macrolides Metro = Metronidazole
 Pens = Penicillins Quin = Quinolones
 Teico = Teicoplanin Vanco = Vancomycin
 * shows outliers with unit number. An outlier is a value of more than 1.5 Standard deviations above or below the median value

(133.2) which was itself higher than the figure observed in the USA.¹² This may reflect different ways of working in the three countries. This study classified the antibacterials according to the system used in the British National Formulary (BNF), which differs from the ATC system used by the German SARI programme, so comparison of drug groups is not possible. Future UK studies should probably use the ATC system to ensure direct comparisons.

While antibiotic issue data from pharmacy records may not be exactly equivalent to actual usage data, as not everything issued is actually administered to ICU patients, it is the most practical method available. The method used in this study is most likely to produce easily comparable information on the usage patterns of antibiotics in hospital settings at a national level and on an ongoing basis. Retrieving individual prescription records is impractical.

Differences in usage rates of specific drugs were observed, in particular for carbapenems, quinolones and drugs used against MRSA. This could be of particular significance for resistance patterns of bacteria and the incidence of infections caused by resistant organisms. There are different views on the optimal treatment strategies for infections in ICU patients.^{15,16,17}

The similarity between the baseline full year results and the three month intensive study period of the five units in the detailed infection surveillance study show reproducibility of the values obtained. This is reassuring for future studies. SARI reported the correlation of antibiotic density with infection rates, sites of infection and resistance patterns. This was not part of the current study, but will be examined in the full programme, intended to be put in place following the success of the pilot programmes.

This study has demonstrated a variable antibiotic density in Scottish ICUs. Further work should be carried out to investigate some of the possible reasons for this. The data obtained will provide a baseline for future work in this area, and the successful completion of the project has demonstrated that it will be feasible to carry out this type of data collection. The authors are aware that some units have already reviewed prescribing practices in the light of the information from this study.

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Epinephrine vs norepinephrine and dobutamine for the management of septic shock

D Annane

Bottom Line: There is no mortality benefit in use of epinephrine alone versus norepinephrine ± dobutamine in patients with septic shock.

Level of evidence: 1* (RCT with a low risk of bias)

Citation: Norepinephrine plus dobutamine versus epinephrine alone for the management of septic shock: a randomised trial. *Lancet* 2007; **370**: 676 - 84.

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Three-part Clinical Question:

Patients: Intensive care patients with septic shock.

Intervention: Epinephrine alone versus norepinephrine ± dobutamine.

Outcomes: Primary - mortality, secondary - safety

Search Terms: Septic shock, therapy, humans, RCT

The Study: Double-blinded, randomised controlled trial without intention-to-treat.

The Study Patients: Patients aged over 18 admitted to one of nineteen intensive care units in France between 12/10/1999 and 31/12/2004.

Inclusion criteria: presence for < 7 days of: 1) evidence of infection 2) at least 2 out of 4 criteria for systemic inflammatory response syndrome 3) At least 2 signs of tissue hypoperfusion or organ dysfunction. Three additional criteria: 1) SBP < 90 mmHg or MAP < 70 mmHg 2) administration of fluid bolus 3) need for > 15 µg per kilogram of bodyweight per minute of dobutamine or any dose of epinephrine or norepinephrine.

Exclusion criteria: pregnancy; evidence of obstructive cardiomyopathy, acute myocardial ischaemia or pulmonary embolus; advanced stage cancer, haematological malignancy or AIDS (with a decision to withhold or withdraw aggressive

therapies); persistent (longer than one week) neutrophil count of < 0.5 x 10⁹; inclusion in another trial.

1,591 patients were assessed for eligibility, 1,261 excluded, 330 randomised: 161 epinephrine, 169 norepinephrine. (8 did not receive either drug due to consent withdrawal, early death or problem in drug supply). In all patients, MAP was targeted using a treatment algorithm which included assessment and optimisation of both volume status and cardiac output.

Epinephrine group (N = 161; 161 analysed): Patients commenced on epinephrine 0.2 µg/kg per min ± placebo and titrated to algorithm to maintain MAP >70 mmHg.

Dobutamine & norepinephrine group (N = 169; 169 analysed): Patients commenced on norepinephrine 0.2 µg/kg per min ± dobutamine 5 µg/kg per min starting dose and titrated to algorithm to maintain MAP >70 mmHg.

The Evidence:

Outcome	Time to Outcome	Epi	Dop & NorEpi	RRR	ARR	NNT
Death	90 days	52.2%	50.3%	4%	1.9%	NS
	95% Confidence Intervals:	ns	ns	NS		
Death	28 day	39.8%	34.3%	14%	5.5%	NS
	95% Confidence Intervals:	ns	ns	NS		

There was also no difference with regard to: length of stay, number of days not on ICU until day 28, number of days not on intensive care until day 90, number of pressor-free days until day 28 or 90, time to haemodynamic success, time to vasopressor withdrawal, mean cost per patient.

With the epinephrine group arterial blood pH was significantly lower over the first four days. Arterial lactate levels were also significantly increased in this group on day 1 ($p = 0.0003$).

EBM Comments:

1. *Do the methods allow accurate testing of the hypothesis?* **Yes.** There was a sizable difference between the expected mortality (60%) in the epinephrine group used for the power calculation and actual (40%) mortality. However this is unlikely to bias the results. It is of some concern that 409 patients assessed for eligibility were excluded for "other reasons". The study took 5 years to recruit only 330 patients in 19 units suggesting either an abnormally low incidence of septic shock or a low recruitment rate. During this prolonged study duration other elements of patient management may have changed. Apart from these concerns, it was a well-conducted study.
2. *Do the statistical tests correctly test the results to allow differentiation of statistically significant results?* **Yes.** Statistical analysis by intention-to-treat. Chi-squared test used to compare the effects of treatment on frequency of fatal events.
3. *Are the conclusions valid in light of the results?* **Yes**
4. *Did any results get omitted and why?* **No**
5. *Did they suggest further areas of research?* **Yes.** 1) Clarification of optimum haemodynamic goals of vasopressor therapy in septic shock 2) Comparing efficacy and safety of epinephrine or norepinephrine with those of dobutamine.
6. *Did they make any recommendations based on the results and were they appropriate?* **Yes.** We can use either epinephrine or norepinephrine \pm dobutamine in patients with septic shock.
7. *Is the study relevant to my clinical practice?* **Yes.** Intensive care units in the UK routinely use the study vasopressors; this article tries to challenge aspects of our practice.
8. *What level of evidence does the study represent?* **1+**
9. *What grade of recommendation can I make on this result alone?* **B**
10. *What grade of recommendation can I make when this study is considered along with other available evidence?* **B**
11. *Should I change my practice because of these results?* **No.** This study demonstrated that there is no difference in outcome between the two treatment regimens if they are part of a management package that assesses volume status and cardiac index. If one does not routinely measure these variables one cannot apply these results to one's own patients. A different question, but one more relevant to most patients in intensive care, would be: Is there a difference in outcome between "blind" use of norepinephrine or epinephrine for hypotensive patients in intensive care. We are sure many clinicians have seen patients failing on norepinephrine despite an "adequate" blood pressure, due to hypo-volaemia, high afterload and a resultant low cardiac output state.
12. *Should I audit my current practice because of these results?* **Yes**

Appraised by: Dr Katrina Bramley (ST2) & Dr Chris Cairns - Consultant
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Kill or Update By: September 2012.

Reviewed & edited by Martyn Hawkins & Bruce Taylor

Is albumin SAFE in traumatic brain injury?

J Myburgh

Bottom Line: In critically ill patients with a severe traumatic brain injury, fluid resuscitation with normal saline rather than 4.5% albumin reduces mortality (NNT 8) and improves neurological outcome (NNT 8).

Level of Evidence: 1** (RCT with a very low risk of bias)

Citation: Saline or Albumin for fluid resuscitation in patients with traumatic brain injury. The SAFE study Investigators. *N Engl J Med* 2007; **357**: 874-84.

Lead author's name and email: Dr Myburgh, j.myburgh@unsw.edu.au

Three-part Clinical Question:

Patients: ICU patients with a traumatic brain injury (TBI) in need of fluid resuscitation.

Intervention: Fluid resuscitation with either normal saline or 4.5% albumin.

Outcomes: Functional neurological outcomes at 2 years.

Search Terms: Traumatic brain injury, intensive care, critically ill, resuscitation, saline, albumin.

The Study: Double-blinded, concealed randomised, controlled trial with intention-to-treat.

The Study Patients: Adult intensive care patients with a traumatic brain injury (TBI), in need of fluid resuscitation (post hoc analysis of SAFE study sub-group). TBI was defined as trauma plus a GCS of 13 or less at first hospital presentation and

an abnormality on CT of the head consistent with TBI. The intervention phase of the trial lasted until death, ICU discharge or 28 days after randomisation. Of the 515 patients enrolled in the study, 40 were lost to follow-up.

Control group (N = 255; 231 analysed): Fluid resuscitation with 4.5% albumin.

Experimental group (N = 260; 229 analysed): Fluid resuscitation with normal saline.

The Evidence (all patients):

Outcome	Time to Outcome	CER	EER	RRR	ARR	NNT
Death	28 days	26.4%	15.7%	41%	10.7%	9
	95% Confidence Intervals:	13-68%	3.3 to 18.1%	6-30		
Death	24 months	33.2%	20.4%	39%	12.8%	8
	95% Confidence Intervals:	13 to 64%	4.4 to 21.2%	5 to 23		
Favourable	24 months	47.3%	60.6%	-28%	-0.133	-8
GOSe	95% Confidence Intervals:			-49 to -8%	-23 to -3.6%	-28 to -4

The Evidence - severe TBI (GCS 3-8)

Outcome	Time to Outcome	CER	EER	RRR	ARR	NNT
Death	24 months	41.8%	22.2%	47%	19.6%	5
	95% Confidence Intervals:	22 to 72%	9.1 to 30.1%	3 to 11		
Favourable	24 months	36.7%	55%	-50%	-18.3%	-5
outcome	95% Confidence Intervals:			-81 to -19%	-29.8 to -6.8%	-15 to -3

There was no significant difference in outcome in patients with a GCS score of 9-12 (97 patients). Initial ICP tended to be higher in the albumin group.

EBM Comments:

1. *Do the methods allow accurate testing of the hypothesis?* **Yes.**
Although this was a post hoc analysis it was a large sub-group population.
2. *Do the statistical tests correctly test the results to allow differentiation of statistically significant results?* **Yes.**
3. *Are conclusions valid in light of the results?* **Yes.** "Saline is preferable to albumin during the acute resuscitation of patients with severe traumatic brain injury."
4. *Did results get omitted, and why?* **Yes.** 40 patients lost to follow up.
5. *Did they suggest areas of further research?* **No.**
6. *Did they make any recommendations based on the results and were they appropriate?* **No.**
7. *Is the study relevant to my clinical practice?* **Yes.** Although 4.5% albumin is not the most common colloid used for resuscitation in many centres. Individual clinicians will have to decide whether these results can be extrapolated to other colloid solutions.
8. **What level of evidence does this study represent?** 1**
9. *What grade of recommendation can I make on this result alone?* **A**
10. *What grade of recommendation can I make when this study is considered along with other available evidence?* **A**
11. *Should I change my practice because of these results?*
 - (i) Yes if you use 4.5% albumin routinely in these patients.
 - (ii) Perhaps, if you use other colloids and are willing to extrapolate these results.
12. *Should I audit my current practice because of these results?*
Yes.

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Kill or Update By: 2013.

Reviewed and edited by BC and SJH

Letter to the editor

S Bennett

Response to Dr Margaret Branthwaite

'An alternative approach to assisted dying in the terminally ill'

The guest editorial by Dr M Branthwaite in the Sept 07 JICS is clearly and precisely written. It should be compulsory reading for anyone in charge of an intensive care unit, in particular doctors who are gate-keepers out-of-hours, who feel obliged to admit patients whose prognosis is apparently hopeless. The current legal position is described succinctly.

All good intensive care doctors make end-of-life decisions a priority in their work and spend considerable time in the process involved. It is rarely something that can be left to juniors. It is not a series of random events but a sequence of well thought out steps, even though the patients involved are extremely heterogeneous. Most units have mortality rates between 20-40%, thus providing a good death is one of the most important parts of our work. In addition to the patient's end-of-life experience, it is a truly lasting experience for relatives and one which can create or extinguish complaints and litigation.

Often when faced with complex decisions and patients who request to die, especially earlier in my career, I have thought that the law should change to help protect the physician from accusations of unlawful killing. I considered this apparent lack of support the reason that so many physicians continue futile treatments. However even though I remain in favour of a good death and often stop futile treatment or prevent ICU admission, allowing patients to die, I now see that the current law provides a good position from which we may well be more exposed should we change.

Specifically, the 'alternative approach' proposed by Dr Branthwaite is essentially one that is removed from intensive care. One example that we would encounter is a patient with a high cervical spine injury; when presenting to intensive care, there is a clear treatment option which if not followed will result in death. The same patient when stable will not be in an intensive care unit. If this patient now requests 'voluntary active euthanasia' or 'physician-assisted suicide', the intensivist will not be the physician present. Instability caused by, say, a chest infection provides nature's opportunity to be allowed to die. The patient does not have to be brought to intensive care to die and the non-intensive care patient is capable of refusing treatment at times during their illness when death would follow.

The scenario of the 'non-voluntary assisted suicide' is one of great suffering and commonly occurs on intensive care in which the legal position is clear and correct. We would call it withdrawal of treatment, using drugs with 'double-effect' and non-initiation of futile treatments. This scenario is indeed awkward when the suffering occurs outside of the intensive care unit and when the patient cannot act to end their own life.

The point is that the scenario described is not an issue for intensive care. Already we intensivists feel that other physicians cannot see death nor face up to it. Often in intensive care we rescue patients from futile treatment. Should we now be expected to increase our role onto the wards and community simply because other health care workers cannot face these decisions?

It is disgraceful that people need to go to other countries to die. Let that issue be addressed, but it is not an intensive care issue. It may be that doctors from intensive care would be the ones who could provide the expertise used in Oregon, USA and the Netherlands, but that does not make it an intensive care problem. Any development or change in the law should not be mistaken for a shift in our moral and professional obligation on intensive care.

Multilateral decision making by those who understand the law and the disease processes we treat is the key to enabling humanitarian death. Improving this is more an issue of education and religious beliefs rather than a change of the law.

Sean Bennett - *Consultant in Intensive Care*

Castle Hill Hospital, Cottingham, East Yorkshire, HU16 5JQ

The author replies:

I welcome Dr Bennett's comments and wholeheartedly agree that the 'alternative approach is essentially one that is removed from intensive care'. But as Dr Bennett states, management of death and dying is an integral part of intensive care. The article was submitted to JICS because intensive care practitioners have had to learn over time - with the assistance of the law - how best to manage comparable difficult situations. They are therefore particularly well placed to help the profession as a whole to discuss assisted dying in a rational and objective manner. There was no intention to suggest that intensive care practitioners should play any special role in assisted dying, were it to be legalised.

Dr. M.A. Branthwaite

Letter to the membership of the Intensive Care Society

C Gillbe

Intensive Care Medicine has had a gradual but inexorable development in this country. The history of the specialty is well known to many of you - running from the establishment of the first intensive care unit at Oxford in the 1950s through to the foundation of the Intensive Care Society, the establishment of the Intercollegiate Board in the 90s, the first diploma examination in 1998 and then the approval of the joint CCT in Intensive Care Medicine in 2001.

Following the arrival of the joint CCT in ICM, and the increasing numbers of non-anaesthetists interested in the specialty, it has become apparent that the Intercollegiate Board needs to evolve to meet all the needs for regulation of training and professional activity required by an established specialty. There has been increasing discussion during the last couple of years as to how and when a Faculty of Intensive Care Medicine should be established. Informal soundings have suggested that this has widespread support within the intensive care community and within the Colleges that currently constitute the Intercollegiate Board. There is also widespread support amongst the Council of the Intensive Care Society.

There has been comprehensive discussion as to the relationship between the putative Faculty and the Intensive Care Society. The conclusion reached by both Council of the ICS and the Intercollegiate Board is that there is a continuing need for both organisations; there is a need to represent the profession as well as formalising the role of a faculty to oversee training and the public interest. If a faculty were to be formed by a merger of the ICS and the Intercollegiate Board it would then be very difficult, should the need arise, to re-establish the Intensive Care Society. In the event of the formation of a Faculty there would clearly be a significant overlap in the roles of the two bodies and it is anticipated that a Faculty of Intensive Care Medicine and the ICS would necessarily work closely together on matters such as education. This will simply be an extension of the collaboration that already occurs between the Board and the Society.

There is of course a downside to this development. At present the Intercollegiate Board is funded by the medical Royal Colleges and the College of Emergency Medicine which has recently joined the Board. This funding arrangement would no longer be available to a Faculty and consequently membership would require a subscription which it is anticipated would be of the order of £200 per annum.

I am sure this price is one that most members of the Intensive Care Society would consider well worth paying for a major step in the direction of recognition for the specialty.

Pete Nightingale is working on a proposal for a Faculty and the Board is keen to hear comments and suggestions, which should be mailed to Ernie Hayes (ehayes@rcoa.ac.uk) at the Intercollegiate Board. The time course for development should probably not exceed two years.

Kind regards

Yours sincerely

Charles Gillbe - *Chairman, IBTICM*



BUCKINGHAM PALACE

29 August 2007

Dear Dr Waldmann,

The Princess Royal has asked me to thank you for your letter regarding the extension of her Patronage of the Intensive Care Society. Her Royal Highness would be delighted to extend her Patronage for a further five years and sends everyone at the Intensive Care Society her best wishes.

Yours Sincerely,

A handwritten signature in cursive script that reads "Amy Briggs".

Miss Amy Briggs
Assistant Private Secretary
HRH The Princess Royal

President's Report

C Waldmann



President - Carl Waldmann

This is my second report; it seems like only yesterday that I wrote the first!

I would like to start by a comment about our Journal; Bruce Taylor has done a tremendous job in developing this, and I am confident that it will continue to advance under the editorial control of Jane Harper, who has taken to the role like a duck to water.

One of the aims of the journal is for it to become listed on Medline - which is not an easy process. The first step will be to obtain an ISSN number. An application must also be made to the Literature Selection Technical Review Committee which will look at the scope and coverage, quality of content, and the quality of the editorial work.

My second comment relates to the development of a Faculty for our speciality.

The Intercollegiate Board needs to evolve to cope with training needs and professional activity, and this would be best served by the development of a Faculty of Critical Care Medicine. Please read the letter to members in this edition by Charles Gillbe, whose excellent chairing of the Intercollegiate Board has ensured that the Board and the Intensive Care Society will work cohesively to navigate the successful development of the Faculty. Charles' term of office will come to an end soon, and the ICS would wish to commend him for his dedication and professionalism, particularly in coping with the complexities generated by PMETB and MTAS. Peter Nightingale, who not so long ago was our President, will be taking over as his replacement.

This takes me to my third comment. There are many organisations working to the benefit of critically ill patients, and it is imperative that the ICS works with them in order to maintain coordination of their activities and recommendations. Accordingly we have regular interaction with Jane Eddlestone and Keith Young representing the Department of Health, and with the help of such a strong link the NICE document 'Acutely Ill patients in Hospital' will have been released by the time you receive this edition of JICS. In addition NICE have now been persuaded to develop a guideline on 'Rehabilitation after a period of Critical Illness', which it is hoped will be released within the next 18 months.

I would like to remind members about the forthcoming Extraordinary General Meeting during the forthcoming State of the Art meeting where we will be asking the membership to vote on whether we can elect one of our 'non-doctor' members to Council.

Lastly, the recent House of Lords reception in July was an undoubted success, and by the time you receive this JICS Saxon Ridley and other representatives of the ICS will have attended a reception at Buckingham Palace on behalf of the Intensive Care Foundation, hosted by our Patron HRH Princess Anne. We are particularly delighted to be able to inform you that Princess Anne has agreed to continue in her role as our Patron for the foreseeable future.

News from IBTICM

C Gillbe

The Joint CCT Curriculum

Just when we thought we had the curriculum sorted out with PMETB approval, given in January this year, we found out from our masters that a joint CCT does not exist in PMETB speak; a dual CCT does, so what was in time honoured fashion the universal name for a CCT in ICM has to go. The next little problem was that a statement from PMETB earlier in the year only permitted dual CCTs to be appointed from the outset for both specialties. Eventually we established that the PMETB update in question did not convey policy, and that ICM could continue with its former method of appointment to the joint, sorry, dual, programmes on the former rules. Quite what status a statement in a PMETB update does have, if it does not contain policy, is not clear, but it may be best not to inquire. So now we have a 'dual' CCT in ICM and a specialty of primary appointment, not a 'joint' CCT. The distinction in practical terms continues to elude our masters in Hercules House, the home of PMETB, which it laughably shares with the Central Office of Information. PMETB has recommended to the GMC the inclusion of one applicant for Article 14 Equivalence on the basis that he met the criteria for ICM. He did not meet the criteria for the specialty of primary appointment, in this case GIM, and therefore does not meet the test of training or experience equivalent to that required by the joint curriculum. This is clearly an absurd position and the recommendation is being contested forcefully. The insistence on the use of 'dual' rather than 'joint', which does not make one iota of difference to the curriculum, has served only to waste many, many hours of time and to undermine still further our confidence in the competence of PMETB. Thanks are due to Judith Hulf for using her influence to disentangle a problem that threatened the continuation of the CCT programme.

One bit of good news is that PMETB has approved the ICM component of the assessment process for the joint, or should I say dual, CCT in ICM and another specialty. The application required a crash course in contemporary educational language; this caused me to think I was skating on thin ice for a while. The justification for the process is founded in 'Good Medical Practice', and this adds a great deal of meaning to what would otherwise look like a box-ticking exercise. The assessment process will be published on the ICM website around the end of October and will also appear on the PMETB website. Thanks are due to Pete Nightingale, Dilsh Arawwawala and Sarah Stirling and many others who have contributed.

Modernising Medical Careers (MMC)

This month's buzz word is 'uncoupling'. For those of you who have not heard the word since you were playing with train sets, it seems to be a euphemism for the reintroduction of the SHO grade. The general idea seems to be that Foundation trainees apply for a specialty programme or acute care common stem (ACCS), and after a period of two or three years apply, again competitively, for fewer numbers of posts in the same specialty to complete their training. There will therefore be an opportunity for

wastage of medical graduates at the end of the Foundation Programmes, at the point of uncoupling and at completion of training. Options available are on the MMC website (www.mmc.nhs.uk/). Undoubtedly, senior members of the medical profession will welcome this reversion to a former time. The idea that service delivery should be the privilege of the fully trained and that patients have a right to be treated by the fully trained has never been wholly accepted by the medical profession in this country. For many years the need for training has been used as a spurious reason to confine the activity of some senior doctors to the more congenial part of the day. Reintroduction of an SHO equivalent grade will perpetuate this.

ICACCST

Yet another bloody acronym, you must be thinking. Do we need it? More importantly, do I need to know about it? Well, that depends on how much involvement you have with the Acute Care Common Stem. The Intercollegiate Committee for Acute Care Common Stem Training (ICACCST) has been authorised by the Royal College of Anaesthetists, the Joint Royal Colleges of Physicians Training Board (JRCPTB) for Medicine, the College of Emergency Medicine and the IBTICM to manage the affairs of the ACCS that require central management. These include melding the curricula for the four specialties, detailing assessment processes in a mutually acceptable manner, advising on the management of the programmes and individual trainee problems that may arise and establishing a register of ACCS trainees along with their base specialties. The committee is chaired by Mike Clancy of Emergency Medicine. Until she left in September, superb administrative support was provided by Angela Burnett, and pending the probable move of the support into the College of Emergency Medicine, Claire Higgins (chiggins@rcoa.ac.uk) has kindly taken over this role in a temporary capacity. Informal approaches have been made to CoPMed to obtain the appointment of a lead Dean for ACCS to represent the interest of ACCS at CoPMed.

The proposed uncoupling currently promised by MMC is bound to have an influence on the continuing existence of ACCS training. The options are: to fold it, to leave it unchanged at two years or to extend it to three years. The first would be a failure of a great opportunity to train pluripotential doctors for acute specialties, the second would weaken the medical aspects of the training by competition with Core Medical Training (CMT), and the third would require a major re-planning process; none of these is appealing.

Specialty Status for ICM?

Current European legislation does not list ICM as a specialty. If sufficient representations have been made by the training authorities in each country, via their respective governments, to the appropriate European body by October this year there is a possibility that this position may change. The IBTICM has made overtures to the Department of Health requesting support for its cause, but in the rest of Europe various representatives of

specialties of primary appointment are resisting this move. These include anaesthesia and neurosciences; happily our own colleagues in the UK are supportive. In practical terms, specialty listing is important for the free movement of intensivists around Europe. It is a great pity that medical and surgical specialties continue to operate restrictive practices in the teeth of evidence that shows both patient outcome and healthcare economics are improved when critically ill patients are looked after by intensivists.

Nested acronyms and JACSTAG

One of my readers of the first column I wrote for JICS picked me up on the number of incomprehensible abbreviations that I used, particularly for those not well versed in the delicacies of MMC. Abbreviations are necessary in these times of continuous revolution because if we all used the full titles of organisations they may well have been supplanted by newer organisations by the time we had finished writing the whole title. JACSTAG is a case in point; he sounds like a fine fellow - the sort you'd be happy for your daughter to go out with so long as she was well equipped. In fact he is the first example I have come across of a first order nested acronym. Let me explain. He is the Joint Academy (AoMRC) Conference (COPMeD) Specialty Training Advisory Group, where AoMRC represents the Academy of Medical Royal Colleges and COPMeD the Conference of Postgraduate Medical Deans.

End of the Road

This is my last column for JICS as Chairman of IBTICM. It has been both a pleasure and privilege holding that office and I wish Pete Nightingale, my highly experienced successor, good fortune in bringing the Faculty and the freestanding CCT to a conclusion. Finally, I owe thanks to Ernie Hayes, IBTICM administrator, for his wisdom and advice, and my wife, Shirley, for her patience and support.

Charles Gillbe - *Chairman, IBTICM*
September 30th 2007

Lemmingaid: Lions led by donkeys

Wood and Trees

'Change has a considerable psychological impact on the human mind. To the fearful it is threatening because it means that things may get worse. To the hopeful it is encouraging because things may get better. To the confident it is inspiring because the challenge exists to make things better' King Whitney Jr.

Wood and Trees have been reflecting on work, education and the meaning of life. "Change is slow and challenging," proclaims Wood. "Fine" says Trees "but why do we need change?"

"The drivers to change are many: necessity, the adoption of previously proven successful strategies, or simply the desire to try something different. We buy a new sofa because our wives want something better, not because we need it. Usually, that choice is satisfactory or better - by thought and due consideration, in the knowledge that what we will get will supersede the current. Extrapolate then, these observations to changes that affect peoples' lives, and the complexities in measuring success." Wood, warming to his own rhetoric continues...

"Payment-by-results (PbR). The recognition of massive variation in 'quality of care' throughout the country, and increasing public demands (facilitated, some would say, by some DOH-favoured media campaigning) was one of the drivers. The targets set for achieving the financial indicators, superseded by doctors responding to the incentive (i.e. new contract negotiations), should be recognised as a gross mistake by Government. The targets were too low, or wrong, incentivised clinicians were switched on, or off, to the opportunities, or 'gaming' of the system was at play (i.e. manipulation - avoiding aspects of medical care that were less likely to achieve targets). The consequences, summed up as 'budget deficit' have led to a level of micromanagement never before seen in our workplace."

"Yes, but people want tight fiscal controls to sort out the NHS," Trees interjects, but Wood is already moving on: "But at what cost? Big Brother is here in a widening schism developing between those managing and running the service. The clinics, theatres and treatment areas of the health service are the factory shop floor - the bosses 'walk the patch', crunching the numbers, scrutinising service delivery and individual 'performance.' Dr Foster's numbers - 'Truth data' or 'blobbogram' is the *de rigueur* visual performance indicator to congratulate, blame or shame! No matter that it is derived from non-incentivised employees in small basement cubbyholes producing the ultimate 'rubbish in, rubbish out.'"

Results! Why, man, I have gotten a lot of results. I know several thousand things that won't work. Thomas A. Edison

Trees can identify with this. It is what he sees and hears in the corridors, every day, except nights and weekends when it all goes away.

Wood continues, "through PbR, hospitals will be paid a fixed price for every activity. If the treatment costs more, the hospital will have to find ways of bringing those costs down. It can either cut costs, or try to do 'more' to generate extra money."

Trees remembers a bumper sticker in New York:
*"National Health Insurance:
 The compassion of the IRS
 The efficiency of the Postal Service
 All at Pentagon prices!!!!"*

PbR is volume, not quality. Hospitals can make money if they bring costs down, or increase the amount of work they do. But cutting costs might be at the expense of better-quality equipment or staff numbers. (*Kings fund, May 05*). Staffing crises within London and elsewhere are already impacting on daily operational issues within ICU.

"And what about ICU? How is that to be costed? In financial terms - how much is it worth spending on the sickest patients, and for how long? Minimum data sets, delayed discharge, case complexity. A myriad of variables. The clinical activity data captured by the NHS data managers is close to useless. Augmented Care Period (ACP) and the ICNARC casemix programme dataset might help with correction or fudge factors like 'case mix'. It actually means heterogeneity that confounds clinical trials, epidemiology and inevitably any data sets. Will the weighting of such 'costs' be adequate to provide fair benchmarking for different ICUs? What of specialist units with inherently higher morbidity patients and higher mortality rates? Will their NHS foundation status be disingenuous to the idea of specialist ICU care due to higher daily costs, greater lengths of stay and a greater percentage of the Trust budget? Could the small ICU fair better financially due to higher turnover and lower acuity patients? Will the specialist units have access to supplementary funding as promised in the NHS plans or is that more Irish mist? Or will there be an inexorable momentum of unit mergers, hospital mergers, centralisation and downsizing of established hospital facilities?"

"The 'Superhospital' sounds wonderful. The super ICU sounds attractive. The Observer reader might well be excited by it but what of the man in trouble, needing an ICU bed somewhere close by? No local ICU to help out. An emergency bed service - read postcode lottery, an urban transport system that turns miles into hours, even with several 'cross rails' all leading to SuperICU, and an inevitable net bed loss (which merger has ever resulted in a net gain of beds?) Super units work best where the sheep count is higher than the head count and transport is easy. Best suited to sophisticated elective, not simple emergency (see USA and Australia). More thought required maybe, God forbid, a little bit of enquiry from elsewhere, and a solid debate - scepticism, bloody-mindedness and an accurate health-cost analysis of ICU care may be important tools to use in countering the political love affair with and implementation of the 'Darzi' vision." (surely hallucination - ed)

"The ostensible goal of PbR is improvement of quality of care, but 'efficiency' will be the focus. The process of this implementation will be deviled with error-poor clinical data collection and disincentivisation through erosion of the core medical principle of altruism."

The only thing that saves us from the bureaucracy is inefficiency. An efficient bureaucracy is the greatest threat to liberty.
Eugene McCarthy

"The shift from autonomy to accountability (rather than mutually exclusive ideals) and fee-for-service seems inevitable. A brave new world, 'volume' will be a byword for success, (coincidence then that obesity services are 'in' - no pun intended!) and abuse of 'quality' by those with clipboards may act as a convenient foil to streamline ICU activities."

Advice is judged by results, not by intentions. Cicero

You might be fooled into thinking that financial control is a villainous concept run by those against the ideals of a morally superior group of healthcare providers. "Not so," says Wood. "But the perception of 'extraneous control' within the NHS is one that sits uneasily with many - a cool breeze of reality is sweeping through the corridors of health and past us all - patients and their

illnesses are a commodity in the new NHS." Trees is struggling with such deep thought. "But with a price tag and a sell-by-date. I see - supermarkets were DGHs, but are now general traders and niche shops, whilst the bulk of disease management (at least chronic disease) will be transferred back to primary care, the corner shop." 'See, Sort, and Send out.'

'This isn't good or bad. It's just the way of things. Nothing stays the same.'

Wood looks perplexed. "There is a problem. What happens to acute services in this wave of momentous change - they don't really fit in." Rome wasn't built in a day, but the changes in the health system are beginning to feel like the long goodnight! Keep chummy with your neighbouring ICUs: they may be the financial competitor at present, but you might find yourself working in the same unit somewhere down the line!

However beautiful the strategy, you should occasionally look at the results.

Sir Winston Churchill

Trees has a headache - he has never liked profound thought - anyway, what is a 'financial result' in ICU - oops.

Further Reading:

Department of Health. FAQs on Payment by Results and the Critical Care Minimum Dataset. See DH website

Department of Health. Payment by Results: Technical Papers July 2003. See DH website.

King's Fund. Payment by results. 2005. www.kingsfund.org.uk/publications/briefings/payment_by.html

Department of Health - Payment by results : Policy and guidance. See DH website.

Klein R. Health Policy Report :The Troubled Transformation of Britain's National Health Service. *N Engl J Med* **355**: 409.

Fischer ES. Perspective Article: Paying for Performance - Risks and Recommendations. *N Engl J Med* **355**: 1845.

Academy of Experts meeting, 17 September 2007

J Harper

If the thought of testifying in court sets hairs on end or trickles of perspiration down your neck, a meeting at the Academy of Medical Experts will be an enlightening, if gut-clenching, experience. The Intensive Care Society and the Academy met at Gray's Inn in London on the 17th September for just this. Bob Winter bravely put his name 'in the frame' to both entertain and to educate us, by subjecting himself to a ruthless cross examination of a medical report which he had written about a fictional case of neurological damage following spinal surgery, allegedly brought to court 34 years after the event (ie the surgery was performed in 1973).



The Expert and his Nemesis

Bob's (fictional) thesis was that hypotension, hypovolemia and anaemia due to inadequate preoperative assessment of the patient's potential clotting disorder and inappropriate fluid resuscitation during surgery had contributed to an unspecified neurological injury. Mr. Bertie Lee, solicitor from Gray's Inn, dissected his testimony. Firstly, he elaborated Bob's qualification to testify about a case that had been done so long ago. He established Bob's experience of spinal surgery and then meticulously dismantled his interpretation of events in the context of what was acceptable practice at the time (Q. *When* did you qualify?). Using his knowledge of the medical textbook that Bob

referred to as a source (Q: 'who was it written by? A: a (male) anaesthetist Q: Does it make a difference that it was written by a woman, a professor in Missouri, writing in 1990?' 'Did you learn anything else from this book, Doctor?') he cited a familiar-looking copy of Gray, Nunn and Utting's 'Textbook of Anaesthesia' from 1980 to support what was current practice at that time and demonstrated that Bob's fictional character had committed the gravest of sins for an expert - namely straying outside his area of expertise.

Despite the obvious atmosphere of theatre, there was serious intent. The event highlighted some important issues about appearing in court. The dissection of evidence started with the written declaration of the doctor, and subsequently 'he lived with the environment he created', as one of the experts subsequently summed up. There were lessons for each of us in the audience - even if we are involved in less confrontational experiences, we must be very careful of our use of language, both written and oral, at all times. Bob never lost his temper although the lawyer was deliberately provocative. He did, however, stray outside his specialty and interpreted data which was outside his area of expertise (giving an opinion about the neurological causes of the injury) - and that was cruelly exposed.

There were 'tips' about how to deal with these very stressful experiences - don't look straight at the solicitor/ barrister, speak slowly, answer the question asked and never, never answer the question not asked, not even the ones you would like to answer instead. Place your feet to face the judge not the lawyer.

In the current social climate, it is likely that any doctor currently practicing will at some time during their career face the unpleasant prospect of appearance in court, whether as a witness, a defendant, in the coroner's court or worse, before the General Medical Council for disciplinary proceedings. Courses to help doctors and others to understand the professional duties of experts in the Courts and to help them perform well in these very difficult situations are available from the Academy of Experts, amongst others. Their website is <http://www.academy-experts.org/default.htm>.

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The Intensive Care Foundation at the House of Lords

S Ridley

The Society's Foundation was established to develop a network of critical care units and so facilitate multi-centre clinical trials in the UK. The main research centre of the Foundation's activities is organised by the ICS Trial Group at Oxford under the guidance of Dr Duncan Young.



Dr Harris receiving his fellowship

The Foundation also undertakes other activities designed to raise awareness of critical care research being undertaken in the UK and to encourage continued support. One such activity was to organise a lunchtime reception at the House of Lords on 24th July 2007.

The Society and the Foundation are very

fortunate to have the support of Baroness Pitkeathley, who was raised to the peerage as Baroness Pitkeathley of Caversham in the Royal County of Berkshire in 1997. Since 2002 she has been the Lord's Deputy Speaker and Deputy Chair of Committees. Most importantly, she has survived several admissions to intensive care and so has excellent insight into what we do.

The aims of the reception were to encourage support for the Society and Foundation from members of the Industry Membership Scheme, to introduce non-industry members to the Society and Foundation encouraging collaboration and finally to present the B Braun Intensive Care Foundation 2007 Fellowship.

Seventy-two people attended the reception, including two other peers and one MP. The Society's Executive officers, the Foundation Board and Ms Kemp and Ms Moore looked after the guests. After the 30 minutes for introductions on the Lords' Terrace, in surprising good weather, the main meeting was held in the Cholmondeley Room. A brief welcome by Baroness Pitkeathley was followed by lunch which was served over the next hour.

The formalities of the reception followed, and included a welcome and a description of the aims of the Foundation by Dr Ridley. The occasion was also used to present the B Braun Intensive Care Foundation 2007 Award to Dr Stephen Harris (UCL and Royal Free Hospitals) by Mr Marco Lorenz of B Braun. This is the second annual award made by the Foundation; it will allow Dr Harris to continue his MSc in Clinical Trials. Dr Mike Grocott, leader of the Caudwell Extreme Everest Expedition, described some of his experiences and outlined the relevance of the expedition's research activities about oxygen usage by patients in critical care. This theme was continued by Dr Rupert Pearse who outlined his study of improved peri-operative care. Fortunately the presentations were kept deliberately brief, lasting less than 30 minutes.

The cost of the event was covered by donations kindly made by the guests.

Dr Saxon Ridley -

Former President of the Intensive Care Society

Consultant in Intensive Care, Glan Clywdd Hospital, Wales

Royal Society of Medicine Critical Care Subsection

S Willatts

In May 2007 the Academic Board of the Royal Society of Medicine (RSM) approved the establishment of a Critical Care Subsection which had been proposed by the Anaesthetic Section of the Society. This is a very exciting development for the specialty of critical care medicine and should progress to development of a full Section of the Society by 2009 at the latest. It has the support of the Intensive Care Society.

The RSM originated over 100 years ago and is unique in that all specialties are represented. One of the main aims of the RSM is to produce high quality educational programmes for members and non-members and to encourage collaboration between sections.

The inaugural meeting of the subsection, entitled **Critical Care - The Way Forward**, will take place on February 15th 2008. The topics were selected to be of general interest to both

anaesthetists and those working exclusively in critical care and are aimed at those working in DGHs rather than those working in specialised units. Topics will include neuro-intensive care (managing raised intracranial pressure and systemic complications of head injury), paediatric intensive care (including retrieval), research (multicentre trials, epidemiology of intensive care, translational research), and career development.

Now is a key time to be involved in this development with multidisciplinary critical care services assuming far greater importance in patient management than ever before.

The secretary of the subsection is Professor Nigel Webster, Chair of the Academic Unit of Anaesthesia and Intensive Care, Aberdeen. The Vice-President is Dr Sheila Willatts, formerly consultant in charge of the adult intensive care unit at Bristol Royal Infirmary and a past president of the Intensive Care Society.

The Society Of Devon Intensive Therapists Annual Meeting Thurlestone Hotel, Thurlestone, South Devon, 17-18th October 2007

M Duffy and M Mercer

The SODIT (The Society Of Devon Intensive Therapists, also including Cornwall and Somerset) Annual Meeting took place on 17th-18th October 2007. The Society has always taken advantage of the beautiful scenery that the South-West has to offer and this year was no exception. The meeting took place at the hotel in Thurlestone (a small village nestled in the South Hams of Devon, with spectacular views over the protected South Devon Heritage Coastline). Over 50 delegates attended, including a number of members from the neighbouring SICOWE - Society of Intensive Care of the Western of England, and eminent visiting speakers.



View from The Thurlestone Hotel, with Thurlestone Rock clearly visible

The meeting opened with a welcome and introduction from the current SODIT president, Mike Swart. The first morning session had presentations from advanced trainees around the region that included updates on treatments for diabetes, 'off-label' use of recombinant factor VIIa and management of various aspects of liver failure. Following coffee, the second morning session was entitled 'Patient Centred Care'. Mick Mercer (Torbay) explained why DNR forms should now become obsolete and be replaced with 'Treatment Escalation Plans.' Marie Wright (Torbay) gave us her experiences of setting up and running critical care follow-up clinics, and Sharon Evans (Torbay) emphasised the value patients find in having diaries about their ICU stay. Jonathon Ingham (Torbay) updated us on the 'Safer Patient Initiative' and asked us to accept that some science is correct and to concentrate on implementing it reliably. After this session, Professor Kai Zacharowski from The Bristol Royal Infirmary gave a thought-provoking lecture titled 'The future of academic anaesthesia and critical care.' In the first part of his presentation he discussed the role of genetics, particularly of toll receptors, in the response to severe sepsis. He went on to speak about the challenges of encouraging academia in our discipline, and suggested that academic posts can attract the funding that will make them palatable to Trusts.

A working lunch followed, with a talk by the Travelling Fellow Lucy Obelensky about her experiences working in rural Kenya, and then a presentation by Peter Hilton from The Welsh Centre For Burns & Plastic Surgery in Swansea on the role of remifentanyl as part of a multimodal sedative regimen.

The early afternoon session consisted of various 'team-building' exercises, with teams made up from the various hospitals from around the region. The light-hearted activities seemed to be enjoyed by all and were thought to have succeeded in their stated aim! The rest of the afternoon was left free to enjoy a variety of activities such as golf, squash, and even surfing at the nearby Bantham beach. The famous SODIT run had an outstanding turnout - a third of all delegates! It was a beautiful coastal route, designed to be a test of navigational ability as well as running capability! It was won by Jim Webster (Charge Nurse on Torbay ICU) running only in his skimpy speedos, to the shock of passers-by on the coastal path. An equal number of delegates chose to support the runners by having a quiet drink on the hotel veranda and enjoying the sunset over South Devon. The evening Society Dinner was as delectable and enjoyable as always, and was rounded off by our President, Mike Swart, giving a toast to SODIT and presenting the inaugural SODIT cup for the performances in the team-building exercises and the run to the Torbay ICU Nurses - they had to win or The President would have been lynched! Delegates then adjourned to the bar for lively and interactive "networking"!



Teambuilding exercises (note the concentration!)



Sunset from hotel veranda on 17th October 2007

The first session the following morning was titled 'critical care'. This kicked off with Andrew Appelboam, A&E consultant from Exeter, on 'Emergency Room' management of sepsis in the United States. It seems that we in the UK could learn from their rapid and aggressive treatment early in the course of this condition - they have a 'code sepsis' urgent pager in addition to the more familiar 'cardiac arrest' and 'trauma' calls. Following this, Jerry Nolan from Bath gave an update on the current evidence on cooling post cardiac arrest, presenting data from some just published studies. Jonathon Paddle (Truro) then gave the results from a 4-year audit of renal replacement therapy across the Peninsula involving over 700 patients. Reassuringly, management of these patients was very similar across the region, and in the ensuing discussions Kathy Rowan promised us access to similar national data - very many thanks to her!

Following the coffee break there was the presentation of the inaugural SODIT medical student prize to Karen Prytherch for her essay on Sepsis. Well done! Jane Harper began the late morning session introducing us to use of the Liverpool Care of the Dying Pathway in critical care. Mary Armitage, the guideline development group chair for the recently published NICE guidelines on acutely ill patients in hospital, then gave a very informative and authoritative picture of how these guidelines were created - and in such a short time frame. There is a perception that most pieces of work from NICE are evidence-based, but because of the limited evidence available in this subject area, most of this current guideline is still very much opinion-based. The last presentation of this session was by Kathy Rowan, giving an update on the work done by ICNARC on outreach - masses of different outreach models have been adopted nationally, with some evidence of cost effectiveness.

The final "working lunch" session of the meeting was the annual pro-con debate, this year on Modernising Medical Careers. Colin Ferguson from Plymouth argued against, whilst Mary Armitage, the newly-appointed lead for MMC, argued for. On an initial show of hands before the debate started, it was clear that the majority had major concerns with MMC. However, after conceding some of the failings of the system and its implementation, Mary admirably swayed a sufficient number of delegates to win the final debate!

The SODIT committee would like to thank all the speakers for their excellent contributions to the academic programme.

Thanks also to the sponsors: Eli Lilly, Deltex Medical, Cook, Glaxo-Smith-Kline, Wyeth, and Sanofi Aventis. The event was agreed by all to be a resounding success and we look forward to the next SODIT meeting - we are going national for this and have the support of the Intensive Care Society. It will be at Exeter University, September 11th-12th 2008. All are welcome. To receive further details and an application form please contact: Karen Whittington, events coordinator at: karen.whittington@nhs.net.

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Interested in finding out the benefits of Industry Membership of the Intensive Care Society?

Contact **Pauline Kemp** on **020 7280 4350** or email pauline@ics.ac.uk

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First point of contact to Council is via Pauline Kemp, Head of Secretariat, by email pauline@ics.ac.uk

Forthcoming Intensive Care Society Events 2007 / 2008

17 - 18 December 2007

The State of the Art 2007 Meeting
Hilton London Metropole, London

16 January 2008

ICS Seminar - Update in Respiratory Medicine
Churchill House, London

8 February 2008

ICS Seminar - Dealing with Difficulty
Churchill House, London

11 March 2008

ICS Seminar - Update In Trauma Care
Churchill House, London

19 - 21 May 2008

Annual Spring Meeting
Manchester Central, Manchester

13 June 2008

ICS Annual Focus Meeting - Infection
Churchill House, London

December 2008

The State of the Art 2008 Meeting

STOP PRESS!

Date and Venue Change! Details to be announced in due course

For further information and registration forms please visit the
ICS website Meetings page at www.ics.ac.uk or contact

Tel: 020 7280 4350

Fax: 020 7280 4369

Email: events@ics.ac.uk

Churchill House, 35 Red Lion Square, London WC1R 4SG

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The State of the Art 2007 Meeting Monday 17th - Tuesday 18th December Hilton London Metropole

The 2007 Intensive Care Society State of the Art meeting will follow the successful format that has become established in recent years. Day one of the meeting will provide a choice of parallel sessions with the clinical practice forum and the research forum. Day two will be dedicated to a series of plenary sessions on state of the art topics of relevance to intensive care medicine.

A faculty of international and UK experts will present on a wide range of topics including:

- Advances in the management of major trauma
- Hypotensive resuscitation, non-surgical management of bleeding, choice of resuscitation fluid.
- Weaning from ventilation
- Protocols, the problem patient, automated weaning, weaning in spinal cord injury
- Cardiopulmonary resuscitation
- Current concepts, hypothermia in practice, UK outcomes, care of the acutely unwell patient
- Delirium in the critically ill
- Lessons from human physiology in extreme environments
- The Xtreme Everest Expedition
- Thrombolysis and thrombo-prophylaxis
- Acute coronary syndrome, thrombo-prophylaxis in ICU, thrombolysis in stroke, therapeutic anticoagulation
- Critical care into the next decade
- Predicting future demands, the DoH vision of emergency services, regionalisation of critical care, the changing role of critical care
- Hot topics including results from recent clinical trials

Submissions of abstracts of free papers will be accepted for presentation in the clinical practice and research sessions. Applications for the award of the ICS Research Gold Medal are also invited for presentation. Further details including the full meeting programme, registration details and guidelines for free paper and gold paper submissions may be obtained from the ICS website.

DON'T MISS A GREAT MEETING, BOOK YOUR STUDY LEAVE NOW!

Approved CPD Points: 14

For further details visit the ICS website: www.ics.ac.uk
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