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Editorial
Changing practice in the intensive care unit

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The topics in this issue are of direct relevance to clinical intensivists. As the evidence base for intensive care increases, so it becomes more important to incorporate those actions and treatments that have been shown to improve patient outcome into our practice.

The 4th Asia-Pacific Consensus Conference on Critical Care Medicine addressed infection control in critically ill patients. Sepsis remains the leading cause of death in intensive care units. Many patients require intensive care during treatment of community or hospital acquired infections, but others acquire nosocomial infection in the intensive care unit. The risk is increased by the impaired immune defences associated with critical illness, severe trauma or major surgery. However, the procedures carried out during intensive care such as central venous catheterisation and endotracheal intubation place further breaches in host defences. The Consensus report reviews the evidence for infection control measures. Adherence to the principles outlined will reduce nosocomial infection in the ICU and the policies advocated for antibiotic use should help slow the increasing problem of antibiotic resistance.

The Academy for Infection Management, supported by an educational grant from AstraZeneca, is taking many of these messages to multidisciplinary groups of healthcare professionals. Again, the process being used, as described in this issue by Park, has the aim of changing practice.

Cadman & House provide a guide to the compatibility of drugs commonly given by continuous intravenous infusion during intensive care – information that can be difficult to access and, I suspect, often overlooked.

Insights into the practice of intensive care outside North America and Europe are provided by Eguma, with a review of 12 years’ experience in a Nigerian ICU, and by Swaiss with a study of discomfort and awareness during intensive care in Jordan. These reflect a willingness by intensivists everywhere to examine their practice and share the lessons with others. Those in less economically challenged countries will reflect on the resource constraints in Nigeria and the effect this must have on practice.

A new opportunity for further globalisation of standards of intensive care practice has been provided by the Surviving Sepsis Campaign. Its direction from North America and Europe and commercial sponsorship provoked, it must be said, a degree of scepticism about the motivation and intended outcomes of the campaign. Information is available at http://www.survivingsepsis.com and it is clear that a useful outcome has been the development of key recommendations for the early and later management of severe sepsis.

While not all the recommendations are applicable to all practice settings because of their cost or need for sophisticated technology, they do provide a summary to guide locally applicable evidence-based practice. A survey and audit tool have also been developed, and the involvement of the Institute for Healthcare Improvement, a Harvard Institute of recognised integrity is welcomed. They have a record of improving health outcomes through changes to medical practice. The WFSICCM is now a sponsor of the campaign.

With this issue of the Journal I am delighted to welcome Prof Sats Bhagwanjee as Deputy Editor. It will be my intention to step down as Editor in August 2005 after 18 years as Editor of a World Federation Publication – first Intensive Care World and later this Journal. This should ensure a smooth transition.
World Federation news

World Federation Council Meeting

The Council of the World Federation met in Durban, South Africa on 5-6 August 2004. The Federation is grateful to the South African Society of Critical Care and Prof Sats Bhagwanjee for their hospitality in hosting this meeting. The issues discussed included:

- The World Federation of Societies of Intensive and Critical Care Medicine Calendar for 2004-2005. This is supported by a grant from BOC Medical.
- Development of the Journal.
- The World Federation Congress for 2009, to be held in Florence, Italy with proposed dates of 29 August – 3 September 2009.
- The World Federation website, now attracting a steady and increasing number of visitors. The abstracts from presentations at the 2001 Congress were to be made available on the website in response to enquiries.
- Establishment of a permanent Secretariat: the concept was approved and a discussion paper on this and potential appointment of an Executive Director will be presented to future meetings, including the General Assembly in Argentina.
- The World Federation Constitution: this is being reviewed with the aim of making it an easier and more workable document that reflected changes that have occurred since the Federation was founded. Amendments to the Constitution will be reviewed at the next meeting of Council, with the object of circulating them to member Societies and adoption of the changes at the General Assembly in Argentina.
- Incorporation of the World Federation as a charitable organisation: Council approved incorporation of the World Federation in the United Kingdom.
- New membership applications: these will need to be ratified by the General Assembly according to the current Constitution.
- Conference endorsement by the World Federation.
- Links with regional associations of intensive and critical care medicine.
- Relationships with the World Federation of Critical Care Nurses: Societies representing nurses are eligible for membership of the WFSICCM but with the founding of the WFCCN in a spirit of constructive collaboration it will be important to establish the role and inter-relationship of the two bodies.
- A detailed presentation was given on the planning for the World Federation Congress in Buenos Aires, Argentina 27-31 August 2005. An excellent scientific programme has been organised, with over 100 confirmed Faculty members present at the meeting from all over the world. The programme is now well developed and it is envisaged that there will be six or seven simultaneous presentations taking place. An unforgettable social programme is also in prospect, together with good deals on pre- and post-Congress tours for those able to stay a little longer and enjoy the many and varied delights that South America has to offer.

The next meeting of the Council will be in Trieste, Italy. The Council is again indebted to Prof Antonino Gullo and APICE for making this meeting possible.

The Mediterranean School of Critical Care Medicine

The President of the WFSICCM, Prof Lumb, had the opportunity to attend the second organisational meeting of the Mediterranean School of Critical Care Medicine in Caltanissetta, Sicily. Professor Gullo has initiated this endeavour. The website provides a preview of the organisation's potential and value: http://anestit.unipa.it/med

It is currently housed at CEFPAS – www.cefpas.it – a government sponsored organisation formed to provide distance learning and educational credits to Italian physicians and allied health providers. The campus was opened by Pope Jean-Paul II and provides residential space for up to 200 course participants. A conference room for up to 500 people is also available as are numerous small conference facilities with excellent electronic support and internet access.

Representatives from Italy, Israel, Slovenia, Croatia, Albania, Egypt, and Libya attended; unable to attend were founding members from Tunisia, France and Spain. Ultimately, the Mediterranean School will encourage participation from Bosnia-Herzegovina, Serbia-Montenegro, Greece, Syria, Lebanon, Malta, Algeria and Morocco. The Mediterranean School has been sponsored by the WFSICCM from inception and a health future seems assured.

Dr Iqbal Mustafa

It was sad news when Dr Iqbal Mustafa, a leader in intensive care medicine in the Asian Pacific region, died suddenly and unexpectedly on July 19, 2004. Iqbal was the Director of the intensive care unit at the Harapan Kita Hospital in Jakarta, Indonesia. He became known to intensivists throughout the
region and internationally through his endeavours to improve intensive care throughout Indonesia and Asia, with an emphasis on the less developed countries. His contribution to the development of intensive care teaching and training in Indonesia was immense.

Tireless in his determination to encourage research, scientific understanding and fellowship, he served as President of Indonesian Societies, President of the Western Pacific Association Critical Care Medicine, Editor-in-Chief of the Critical Care and Shock Journal, and played a dominant role in organising the annual Critical Care and Shock Meeting, usually held in Bali, Indonesia each August. This had evolved to become one of the largest regional meetings, always enhanced by an international Faculty and idyllic setting that was an ideal breeding ground for truly global collaboration in critical care medicine. He recently completed his PhD. His dream was to build solid foundations on which intensive care medicine could develop and flourish in the Asia-Pacific region.

He was an acknowledged leader, innovator and organiser. All who knew him will remember him for his ability and warm smile. In his death, Iqbal has left a void which will be hard to fill for both family and colleagues. He was a fine gentleman in the truest sense.

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**Letter to the Editor**

**Over humidification: an under recognised problem?**

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**Dear Editor,**

In the February issue of the Journal, Thiyagarajan et al. described the effects of over humidification problems on intubated patients. We agree with the normal physiology described by the authors, but not with their recommendation of optimal humidity for patients with artificial airways. There is a big difference between normal airway and intubated artificial airway regarding humidity problems, which is not well appreciated.

When you inspire gas of 25-30mgH\(_2\)O/L absolute humidity, which seems to be recommended in the article, your normal airways can tolerate this well and give the inspired gas an additional 19-14mgH\(_2\)O/L of water vapour. If you are intubated, inspired gas is deficient of 19-14mgH\(_2\)O/L of water vapour for the secretions in the tracheal tube or in the trachea just below the tip of an endotracheal tube. As a result, inspissation of secretion may lead endotracheal obstruction and impairment of epithelial function.

A normal airway has a compensatory mechanism against the dry environment, as humidity can be supplied from tissues below, but the endotracheal tube does not. We have been arguing that the primary objective of airway humidification in critical care is to prevent obstruction of artificial airways. Certainly, mucociliary function is important; life cannot be sustained without a patent endotracheal tube.

The authors only mentioned about the pitfall of over humidification such as water load, mucociliary dysfunction, hypothermia and thermal injury, without any references. Williams et al. showed the 100% relative humidity and core temperature to be the optimal humidity using the analysis of 17 references. We totally agree with their views.

A patent artificial airway is of paramount importance in critical care. We may safely say that, *Under humidification is an under recognised problem*.

**References**

4th Asia Pacific Consensus in Critical Care Medicine: Infection control in critically ill patients

Held in conjunction with the 8th Indonesian Symposium on Shock and Critical Care

Bali, Indonesia
Sponsored by the Indonesian Society of Critical Care Medicine
Co-sponsored by the Western Pacific Association of Critical Care Medicine

Scientific co-chairs
B Currie (USA) & J Carlet (France)

Organising co-chairs
V Kvetan (USA) & I Mustafa (Indonesia)

Alphabetic listing of participants (*moderator)
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Chapter 2
E Abraham (USA), E Benjamin (USA), GJ Dobb* (Australia), A Hanafie (Indonesia), J N’tonoyim (USA), KS Ng (Singapore), N McKenzie (Australia), J Reeves (Australia) & LG Thijs (Netherlands)

Chapter 3
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Chapter 4
D Cook (Canada), SO Koh (Korea), A McLean (Australia), P Papadakos (USA), PSK Tan* (Malaysia) & P Thorborg (USA)

Prologue
The organisers of the Asia Pacific Consensus Conference have developed an annual consensus process to function in parallel to similar processes on critical care science and practice in Europe and North America, the support of the Western Pacific Association of Critical Care Medicine, and of the member societies.

Infection control is a major challenge for every critically ill patient and health care giver attending to such patients. The economic burden of nosocomial infection, increased length of hospital admission and mortality, assumes great proportion in developing economies. Measures to promote infection control are necessary to reduce this burden and contribute substantially to growth and development of their populations.

This document is a summary of the proceedings of the 4th Asia Pacific Consensus Conference in Critical Care Medicine on Infection Control in the Critically Ill held in conjunction with the 8th Indonesian Symposium on Shock and Critical Care in Bali, Indonesia.

Chapter 1: What are the best methods to survey nosocomial infections in the ICU setting?

Introduction
Around 20-45% of all nosocomial infections in the hospital occur in the intensive care unit (ICU) setting, even though ICUs only represent 5-20% of total hospital beds. The vast majority of these infections are endemic and a minority are epidemic or outbreak-related. Further evidence characterising these infections indicates that they are largely device-associated or surgical procedure-related – intravascular catheter related bloodstream infections (CR-BSIs), ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (UTIs), and surgical wound infections associated with surgical procedures.

The epidemiology of ICU nosocomial infections described above was largely determined in United States1, European2 and Japanese ICUs3. Specific information regarding the epidemiology of ICU nosocomial infections in the Western Pacific region is limited. The prevalence of extended spectrum beta-lactamase-producing bacteria (ESBL) organisms in some Asian countries is summarised in Table 1.

The primary purpose of surveillance is to generate information that can be used to target interventions to reduce both endemic...
and epidemic nosocomial infections. The methodology chosen represents a balance between the sensitivity and specificity of identifying infections and the resources available for the task. The more sophisticated methods would generate risk adjusted incidence density measures that would allow internal and external benchmarking and risk factor investigation. Finally, it should be noted that the generation of surveillance data requires an infection control infrastructure to analyse and interpret the data and to implement interventions to reduce the incidence of infections.

Effective infection control interventions can be helpful for justifying increased resource allocations, provided their outcomes are appropriately documented. Initial investments associated with surveillance activities facilitate identifying appropriate targets for intervention as well as documenting their impact.

**What are the best methods to survey nosocomial infections in the ICU setting?**

The most sensitive and specific method to survey nosocomial infections involves continuous prospective surveillance of all patients in each ICU for endemic and epidemic nosocomial infections. While the method is labour intensive, the limited geography and number of patients in the ICU lends itself to continuous, prospective, unit-based surveillance to provide a sensitive capture of nosocomial infections, detect epidemic infections, generate incidence rates and allow risk factor investigation. ICU surveillance activities should be focused on CR-BSIs, VAP, catheter-associated UTIs and surgical wound infections because of their major impact on health outcomes and fiscal expenditure.

Surveillance should utilise established case-definitions and case-finding methodologies, for example with the National Nosocomial Infection Survey. The advantages are that internal and external benchmarking are possible, there is an increased specificity of cases, and the methodology is well established. Calculated incidence rates should be monthly device-specific incidence density rates, i.e. intravascular CR-BSIs/total patient intravascular catheter days.

This approach allows some degree of risk stratification of infections based on device utilisation, a known significant risk factor. Further attempts at risk stratification are not warranted until validated methodologies become available. Due to the relative lack of risk stratification, hospitals may consider monitoring the census of the ICU for changes in patient type. This may be particularly important in mixed medical/surgical ICUs.

**Can the incidence of nosocomial infections be used as a quality indicator?**

In general, unless surveillance efforts incorporate methodologies that can reliably permit valid external benchmarking for comparative purposes, they may not be viewed as reliable quality indicators.

**What methods should be used for surveillance of antibiotic resistance among nosocomial pathogens?**

Each hospital should produce an antibiogram of individual patient isolates at least on an annual basis. The antibiogram should distinguish resistance rates between community-acquired, hospital-acquired and ICU-acquired patient isolates. The hospital antibiogram should be widely distributed to physicians.

Ongoing microbiology laboratory surveillance for key antibiotic resistance combinations and timely notification of patient care providers is highly recommended. Consider meticillin-resistant S. aureus (MRSA), vancomycin-resistant enterococci (VRE), ESBL-positive Gram-negatives and any Gram-negative isolate sensitive to one or less antibiotics as targets. Early notification is intended to allow appropriate and early institution of isolation precautions.

The practice of obtaining routine individual patient clinical isolates for surveillance purposes is not recommended, although supported by some, to ensure systematic collection of data in the ICU. Periodic culture of patients for MRSA and VRE colonisation rates may prove to be useful in hospital settings where the prevalence of these pathogens has been low.

**Chapter 2: How can intravenous (IV) catheter related infections be prevented?**

The annual sales of multi-lumen IV catheters (MLCs) in Asia, excluding Japan, has, according to one manufacturer, increased 165% to 1.75 million between 1994 and 2000. Information on CR infection rates in Asia are not available, but the infection rates in the United States and Australia are estimated at around 4% of inserted catheters. The potential for CR infection with increased morbidity and healthcare costs emphasises that priority be accorded to the prevention of infection in the use of these devices. The Hospital Infection Control Practices Advisory Committee of the United States’ Centers for Disease Control and Prevention published guidelines for the prevention
of intravascular device related infections in 1995. The consensus group reviewed these guidelines together with other subsequent relevant studies and meta-analyses during their deliberations. Discussion and recommendations refer to short-term intravascular devices.

How can CR infections be defined? Can we make the diagnosis without removing the catheter?

Definitions

- **Local infection**: diagnosed when there is evidence of an insertion site infection such as a purulent discharge, erythema, excessive tenderness and/or swelling.
- **Catheter colonisation**: diagnosis is technique dependent. Although many different techniques are available, the semi-quantitative technique is the most commonly used by group members and in the Asia-Pacific region. Using this technique, greater than 15 colony forming units must be grown from a catheter segment, usually the central venous catheter (CVC) tip.
- **CR-BSI**: the isolation of the same organism causing catheter colonisation and bacteraemia. The blood culture is preferably drawn from a peripheral vein.

Mechanism of CR infection

The sources for contamination of intravascular catheters are the patient’s skin flora (which may contaminate the catheter tip during insertion), the flora on the hands of medical and nursing staff (which may contaminate the catheter hub during catheter disconnection and may also affect the patient’s skin flora), hematogenous spread of microorganisms from other sources and contaminated infusion fluids. Most CR infections appear to result from migration of skin microorganisms at the insertion site into the cutaneous catheter tract (along the outside of the catheter), with eventual colonisation of the catheter tip.

There is increasing evidence that contamination of the catheter hub may result in migration of microorganisms along the internal surface of the catheter, which importantly contributes to the intraluminal colonisation of catheters. Although there is still debate on the relative importance of these two mechanisms, evidence suggests that duration of catheterisation influences which mechanism predominates – in short-term catheterisation, skin related contamination is more important, whereas for long-term catheters, hub contamination seems the more likely mechanism.

Catheter tip colonisation by hematogenous spread and infusion of contaminated fluids are much less common causes of CR infections.

Techniques for diagnosis of CR-BSI

A clinical diagnosis of CR-BSI is made when a patient has symptoms and signs of bacteraemia, growth of the same organism from peripheral blood, and either a catheter segment or blood culture aspirated from the catheter, and no other apparent source of infection.

The methods available, number of studies, sensitivity and specificity for the diagnosis of CR-BSI are summarised in Table 2. All the catheter segment techniques require removal of the catheter to provide the specimen for culture.

Diagnosis of CVC-associated sepsis remains a problem because standard culture techniques rarely detect organisms embedded in biofilms. The semi-quantitative roll method only samples the external surface of the catheter. Methods that are better at sampling the internal lumens of the catheter, such as sonication and quantitative broth methods, are potentially more accurate for catheters that have been in place for extended periods. If a catheter is removed, semi quantitative catheter segment culture is recommended based on common practice and cost.

Diagnosis without catheter removal

Definite diagnosis of CR-BSI requires the removal of the implicated catheter. Under circumstances where the patient continues to require central venous access, a new catheter will have to be placed; this is preferably done at a new site. Reinsertion incurs risk of mechanical complications, patient discomfort and associated cost. A method of diagnosis that does not require catheter removal would be very useful.

Blot et al. prospectively evaluated the differential time to positivity (DTTP) of 93 paired blood cultures drawn simultaneously via the catheter hub and from a peripheral venous site. A cut-off DTTP of 120 minutes gave the greatest specificity (91%) and sensitivity (94%) for the diagnosis of CR-BSI without the need for removal of the catheter. However, in a prospective study of 100 patients with suspected CR-BSI, Rijnders et al. found no significant difference in the median DTTP between CR-BSI and non-catheter bacteraemia.

<table>
<thead>
<tr>
<th>Studies</th>
<th>( n )</th>
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<th>Specificity (%)</th>
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Table 2. Diagnosis of CR-BSIs.
Kite et al. assessed the Gram stain and acridine-orange leucocyte cytospin test (AOLC) in suspected cases of CR-BSI. They compared this technique with two methods that require catheter removal (tip roll and tip flush) and a third method, endothelial brush. A total of 128 cases in 124 adult surgical patients were assessed; 16 cases were excluded from analysis because CVC blood was not obtained. CR-BSI was diagnosed in 50 cases. The sensitivity of the Gram stain and AOLC test was 96%, specificity 92%, with a positive predictive value of 91% and a negative predictive value of 97%.

Another study evaluated 55 blood samples and their corresponding central catheter tips. These were examined using AOLC, semi-quantitative roll plate and broth immersion methods. Four catheters (7.3%) were found to be related to CR-BSI and 10 (18.2%) were colonised. The AOLC test detected only two (50%) of the cases of CR-BSI and two (20%) of the colonised catheters.

Infection in catheters used for total parenteral nutrition (TPN) may also be predicted from positive insertion site cultures, positive peripheral venous blood cultures and positive central venous blood cultures. Other techniques available for the diagnosis of CVC infection include ELISA for staphylococcal infections and endoluminal brush culture.

Availability of techniques for diagnosing CR infection without catheter removal is an exciting development. At this point in time, these techniques are new and there are only one or two limited studies that have demonstrated the usefulness of these techniques; further clinical studies are needed to confirm the usefulness of these techniques. For diagnosis without catheter removal, time-paired blood cultures are recommended [Appendix I – A] but this test is costly and requires specialised equipment.

**What measures can be used to prevent CR infections?**

**Aseptic technique**

Proper handwashing and aseptic technique provide adequate precaution against infection during insertion of short peripheral venous catheters. The risk of infection during insertion of CVCs depends more on the extent of aseptic precautions than on the sterility of the surrounding environment. Maximal barrier precautions are required during CVC insertion in any environment. The continued use of aseptic technique when handling CVCs minimises catheter contamination and CVC-related infections.

**Hair removal**

It is usual practice to remove body hair from the CVC insertion site. Observational studies and case reports show that hair carries pathogenic bacteria. It can also become entangled in sutures or incarcerated in the dermis of the skin, causing foreign body reactions and granulomas. The methods available for hair removal include shaving, application of depilatory cream and clipping.

No studies have addressed hair removal in the specific context of CVC insertion. However, multiple studies have shown surgical wound infection rates are significantly lower when hair is removed with clippers rather than razors. One study has shown lower wound infection rates using depilatory cream rather than a razor (0.6% vs 5.6%). Shaving is associated with high frequency of skin damage. Allergic reactions can occur from depilatory creams and they should not be used on skin near the genitalia as they can cause serious irritation. For these reasons, clippers are the recommended method for hair removal [Appendix I – E].

**Skin disinfection for CVC insertion**

Povidone iodine 10% is widely used to clean the skin before CVC insertion. More recently, solutions containing chlorhexidine have been introduced and compared to povidone iodine. The chlorhexidine solutions vary in concentration and both alcoholic and aqueous solutions have been used. A formal meta-analysis of these studies has not been published and would not be appropriate because of the variation in chlorhexidine solutions. Also, varying techniques have been used to detect catheter colonisation, and the definition of CR-BSI has been inconsistent.

Nevertheless, three of four available studies show a significant reduction in the relative risk of catheter colonisation with chlorhexidine solutions (range of RR 0.25–0.49, 95% CI range 0.26–0.31, 0.66–0.85). The lowest relative risk for catheter colonisation was in studies using 2% chlorhexidine aqueous solution. The only study in which chlorhexidine was not significantly better than povidone iodine used 0.5% chlorhexidine in alcohol. Chlorhexidine solutions are generally more expensive than povidone iodine.

Chlorhexidine solutions appear a simple method for reducing CVC colonisation, but much larger studies are needed to demonstrate an effect on CR-BSI. A formal cost benefit analysis is not available. Aqueous chlorhexidine 2% solution is recommended for skin preparation before CVC insertion [Appendix I – B].

Use of an iodophor-impregnated sterile film following skin cleansing with alcohol eliminates contamination during central venous catheterisation. Contamination rates are similar following skin cleansing with povidone-iodine, tincture of iodine, isopropyl alcohol and povidone-iodine with 70% ethyl alcohol.

**Insertion site**

Several non-randomised contemporaneous control studies suggest a significant relationship between insertion site and CVC colonisation. Gil et al. reviewed the rate of catheter colonisation among 220 central catheters inserted at various sites in 145 patients. The result was 9/87 (10%) for subclavian, 26/118 (22%) for internal jugular and 7/15 (49%) for femoral sites. These differences were statistically significant (p<0.01) by chi-square analysis.
In a multi-centre study involving eight French hospitals, 503 CVCs were examined. In comparison with the subclavian and arm sites, the jugular site was found to be significantly associated with positive catheter tip culture (OR 2.7, 95% CI, 1.0-7.5, p<0.05)\(^9\).

Whereas central venous catheterisation via the subclavian site is associated with a significantly lower rate of catheter colonisation [Appendix 1 – III, D], this has to be considered in the light of a greater frequency of mechanical complications than with the other sites. For medium term CVC access, the infraclavicular subclavian approach is recommended to minimise the risk of infection [Appendix 1 – C].

**Catheter material**

Studies in animals and in man\(^3\) have demonstrated significantly less tissue reaction and thrombosis in and around silicone rubber catheters. Mitchell et al. \(^10\) did a non-randomised study with historical controls to compare the rate of catheter sepsis among PVC, silicone rubber and polyethylene catheters. Seven of the 37 (18.9%) PVC catheters and one of 80 (1.25%) silicone catheters became infected (p<0.01). Blacket et al. \(^5\), reported the catheter sepsis rate for polyethylene catheters as 17/77 (9.5%). Mitchell’s results have to be interpreted in the light that all 80 silicone catheters were tunnelled, whereas only eight of the 37 PVC were tunnelled. There is a general perception that silicone catheters carry a lower rate of catheter sepsis compared to PVC and polyethylene catheters [Appendix 1 – IV, E].

**Single (SLC) versus multiple-lumen catheters (MLC)**

We reviewed three randomised controlled trials (RCTs) looking at CR-BSI rates in SLCs verses MLCs. Clark-Christoff et al. \(^3\) found that the incidence of CR-BSI to be 2/78 (2.6%) for SLC and 13/99 (13.1%) for MLC (p<0.01). In a smaller series involving 75 patients, McCarthy et al. \(^3\) reported a higher incidence of CR-BSI with TLC, 12.8% verses 0% (p=0.055). Both these studies specifically indicated that the catheters were used for parenteral nutrition. The third study by Farkas et al. \(^7\) looked at 129 catheters from 91 patients. There was no indication that these catheters were used for parenteral nutrition. The rate of CR-BSI was not significantly different between MLC and SLC (11.5% vs 8.9% by qualitative tip cultures and 11.5% vs 16.2% by quantitative tip cultures).

CVCs should be removed when the need for central venous access ceases. In cases where there is no necessity for multiple central venous access, SLC should be used instead of MLC [Appendix 1 – II, C].

**Tunnelling CVCs**

Tunnelling is not easy to implement because it requires more training than the usual non-tunnelled catheter insertion. A meta-analysis of studies evaluating the efficacy of tunnelling short-term CVCs to prevent CR infections identified seven RCTs that included 735 patients and 772 catheters\(^11\). Overall, tunnelling decreases catheter colonisation (RR 0.61, 95% CI: 0.39, 0.95) and CR-BSI (RR 0.56, 95% CI: 0.10, 0.89) but reduction in risk is not significant in the five subclavian catheter trials (RR 0.71, 95% CI: 0.36, 1.43). The majority of the benefit in decreasing catheter sepsis was in a trial using the internal jugular site.

The current evidence does not support routine use of tunnelling CVCs [Appendix 1 – E]. Tunnelling appears to be of benefit for medium-term internal jugular catheters [Appendix 1 – B].

**Antiseptic and antibiotic-impregnated catheters**

Antiseptic-impregnated and antibiotic-coated catheters have been developed to reduce the risk of CR infection. These catheters are significantly more expensive than non-impregnated catheters. Technical concerns of coating the catheter and concerns of antibiotic resistance may limit the use of the antibiotic-coated catheters. Antiseptic-impregnated catheters do not require coating before insertion and may be less susceptible to antibiotic resistance. A meta-analysis of 13 studies comparing CVCs coated with chlorhexidine/silver sulphadiazine (C/S) to non-impregnated catheters indicated a significantly reduced risk of catheter colonisation in the treated group and a significantly reduced risk of CR-BSI (Table 3)\(^11\).

A RCT in 281 hospitalised patients who required 298 CVCs compared the outcome in 147 catheters coated with minocycline/rifampin (M/R) to 151 uncoated polyurethane CVCs. Colonisation occurred in 11 (8%) coated catheters and 36 (26%) uncoated catheters (p<0.001). CR-BSI did not occur in patients with coated catheters but developed in seven patients (5%) with uncoated catheters\(^4\).

A randomised comparison of C/S coated catheters with M/R coated catheters included 865 catheters of which 738 produced evaluable culture results\(^4\). Colonisation occurred with 87 C/S catheters and 28 M/R catheters (23% vs 8%) and CR-BSI occurred with 13 C/S catheters and 1 M/R catheter (3.4% vs 0.3%). These differences were highly statistically significant.

The release of antibiotic and antiseptic from catheters occurs over 2 weeks following insertion. The effectiveness of antibacterial protection following that duration is not known. In view of their additional cost, it is recommended that use of the antiseptic coated catheters is restricted to high-risk patients and those likely to require a CVC for 3 days or more [Appendix 1 – I, A]. The cost-benefit of antiseptic coated catheters will depend on local infection rates and the cost of catheter replacement and antibiotic treatment for CR infections.

**Dressings**

Dressing material must be acceptable for use on CVCs, permit frequent inspection of the insertion site and suture points, tolerate exposure to high humidity therapy devices, be comfortable for the patient, and minimise nursing hours.
Adhesive tape placed close to CVC sites has been associated with local infection. In one study, 74% of tape specimens were colonised by pathogenic bacteria. However, when specimens were taken from an inner layer after discarding the outside layer from each roll, only 5% of specimens had a growth of pathogenic bacteria.

A meta-analysis of studies comparing transparent polyurethane film to a gauze and tape dressing identified seven studies of CVC dressings. The analysis was somewhat confounded by the use of topical antibiotic agents in five of the CVC studies. Catheter tip infection was evaluated for 1200 catheters and over 650 catheters for associated bacteraemia. The RR for colonisation using polyurethane dressings was 1.78 (95% CI: 1.38, 2.30) and for bacteraemia the RR was 1.63 (95% CI: 0.76, 3.47). The studies of newer, semi-permeable transparent dressings to other impermeable alternatives are small, show variable effects on infection rates and no meta-analysis is available. Transparent occlusive dressings are not recommended.

The use of trained infusion therapy teams implementing specific protocols for the insertion and care of catheters reduces CR sepsis.

**Thrombosis**

CR venous thrombosis is relatively common. A survey in which veins were examined by duplex ultrasound scanning within 24 hours of catheter removal found CR venous thrombosis occurred in 33% of cases – limited in 8%, large in 22%, and occlusive in 3%. The risk of CR sepsis was 262% greater when thrombosis occurred.

A meta-analysis of 12 RCTs evaluating prophylactic heparin in patients with CVCs shows patients receiving heparin had a decreased risk of CR venous thrombosis (RR 0.43, 95% CI: 0.23-0.78), bacterial colonisation (RR 0.18, 95% CI: 0.06-0.60) and a trend to decreased CR-BSI (RR 0.26, 95% CI: 0.07-1.03). In the absence of absolute contraindications to anticoagulation, prophylactic heparin is recommended for patients with CVCs.

<table>
<thead>
<tr>
<th>Antiseptic-impregnated catheters in preventing CR-BSI and catheter colonisation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chlorhexidine/Non-impregnated</strong></td>
</tr>
<tr>
<td>CR-BSI</td>
</tr>
<tr>
<td>Colonisation</td>
</tr>
</tbody>
</table>

NNT = number needed to treat to prevent one event

**CVC changes**

**Administration set changes**

Bacterial colonisation or infusion related septicemia in IV administration sets arises principally through non-aseptic handling and frequent replacement, causing hub contamination. Implementation of appropriate and standard procedures in handling IV administration sets reduces infection risk. The incidences of thrombophlebitis and bacterial colonisation of catheters increase dramatically when catheters are left in place more than 72 hours. In patients at low risk for infection from infusion or CR infection and who are not receiving TPN, blood transfusions, or interleukin-2, delaying the replacement of IV administration sets up to 7 days may be safe and cost-effective.

In neutropenic oncology patients, a randomised comparison of 48 vs 24 hourly routine changing of IV changing of IV administration sets found no difference in the incidence of colonisation or infusion related septicemia. Based on three well controlled studies, it is recommended that administration sets are changed 72 hourly but more frequent changes are needed for administration sets associated with TPN (24 hourly), propofol infusion (24 hourly), and blood products (24 hourly or less).

**Routine changing of CVCs**

CVCs are routinely changed in some ICUs. The practice arose from several observational studies indicating a positive correlation between rate of catheter infection and duration in situ. The two methods used are either a guide wire exchange over an existing CVC or insertion at a new site. Routine replacement of central vascular catheters every 3 or 7 days has not been shown to alter the infectious risks of CVCs in randomised studies or a meta-analysis. Up to two thirds of CVC may be sterile and unnecessarily removed. Exchanging catheters with the use of a guide wire increases the risk of BSI and insertion of catheters at new sites increases the risk of mechanical complications. CR bacteraemia may be managed by adequate antimicrobial therapy without CVC removal or with guidewire CVC exchange under adequate antimicrobial therapy. Routine CVC replacement is not recommended.

Chapter 3: What is the role of IV and topical prophylactic antibiotics in the ICU?

**Introduction**

IV antibiotics pose a serious economic burden for hospitals across the world and resistance to these drugs is increasing everywhere. The judicious use of these agents for prophylaxis of infection is therefore warranted.
Can antibiotics prevent nosocomial infections, in particular, pneumonia?

ICU acquired pulmonary infections, often called VAP, are a frequent event in critically ill patients and represent the most important reason for antibiotic therapy in this setting. The majority of VAP are thought to develop from the aspiration of oropharyngeal secretions containing potentially pathogenic organisms. Aspiration of gastric secretions may also contribute, to a lesser extent. Tracheal intubation interrupts the body’s anatomic and physiologic defences against aspiration, making invasive ventilation a major risk factor for VAP. Endotracheal intubation, rather than the ventilator itself, is known to be associated with a high incidence of nosocomial pneumonia.

VAP is categorised as either early-onset VAP (occurring in the first 3-4 days of mechanical ventilation) or late-onset VAP. This distinction is important for pathophysiological and microbiological reasons. Aspiration before or at the time of intubation plays a likely role in early onset pneumonia. Some of those events are thus poorly related to quality of care and IV antibiotics are needed to prevent it. Early-onset VAP is commonly caused by antibiotic susceptible community-acquired organisms e.g., *S. pneumoniae*, *Haemophilus influenzae* and *S. aureus*. Late-onset VAP is commonly caused by more resistant nosocomial organisms e.g., *P. aeruginosa*, MRSA, Acinetobacter species, and Enterobacter species.

The prevention of nosocomial pneumonia in ventilated patients is best achieved by decreasing the volume and incidence of aspiration of oropharyngeal and nasal flora by means of a semi-recumbent position, tracheal aspiration and subglottic aspiration.

The only randomised, placebo-controlled study looking at IV antibiotic alone showed a significant decrease in the rate of nosocomial pneumonia and in mortality in patients with coma treated with 2 days of cefuroxime prophylactically, as compared to placebo. Prophylaxis of nosocomial infections with IV antibiotics, although widely used every day all around the world, have not been studied extensively, other than as part of selective digestive tract decontamination (SDD).

SDD is defined as the use of topical antibiotics in the oropharynx, gastrointestinal tract or the nose to prevent infection. In some instances (quinolones) antibiotics are also absorbed systemically. SDD is time-consuming and not all pharmacists are able to provide the paste for oropharyngeal decontamination. Some authors propose a combination of SDD and IV antibiotics while still utilising the term SDD, which is confusing. Oral disinfection and SDD reduce the severity and IV antibiotics prevent nosocomial pneumonia and treat bacteraemia, UTIs and CR infections.

The results of the meta-analysis on SDD are consistent with a reduction of nosocomial pneumonia rates from a combination of topical and systemic antibiotics. However, the changes in mortality only occurred in patients who received the combination of topical and IV antibiotics. In studies which compare topical plus IV antibiotics with IV alone, no difference is noted either for infection rates or mortality. The positive effect of SDD is only demonstrated for surgical and trauma patients.

Some studies show an increase in resistance to topical antibiotics and some do not, and thus, since the issue is crucial, additional data are warranted in this field. Finally, recent data from Nieuwenhoven shows an inverse relationship between the effect of SDD upon nosocomial infection rates and the quality of the study, confirming that meta-analyses should be considered with caution.

What non-antibiotic measures prevent ICU-acquired nosocomial infections?

Standard preventive measures are fundamental for VAP prevention, including hand hygiene, careful mouth, oropharynx and nose disinfection, ideally with antiseptics (chlorhexidine in particular), tooth brushing, aspiration of oropharynx and nose secretions, sterile aspiration of tracheal and bronchial secretions [Appendix I – C]. Ventilator tubing should not be changed more frequently than once a week if it is not grossly contaminated with tracheal secretions [Appendix I – A]. Some authors propose not changing it at all during a given patient’s stay.

The comparison between heat and moisture exchangers and humidifiers (heated or not) is still controversial, although HME clearly bring a huge benefit for nursing care.

Non-invasive ventilation has been studied in several excellent randomised or case-controlled studies. All show a dramatic decrease in the incidence of nosocomial pneumonia as compared to invasive ventilation.

The semi-recumbent position has been studied in three studies from the same team. Two of them used nuclear medicine technique, the outcome being incidence of aspiration. A RCT of 86 ventilated patients showed a significant decrease in the incidence of nosocomial pneumonia without any effect upon mortality.

The continuous aspiration of subglottic secretions has been studied in three randomised trials (Table 4). The technique needs a specially designed endotracheal tube. All three studies show the same trend toward a reduction of the incidence of VAP, but in only one of them was the difference statistically significant. No effect upon mortality was noted.

H2-antagonists, which must be used only for a targeted population at high risk for stress ulcer, when compared to sucralfate, have a clinically marginal trend to increase the incidence of VAP [Appendix I – D].
How should prophylactic antibiotics be chosen and when should they be commenced?

- Currently available data on local resistance patterns should be reviewed [Appendix 1 – C].

- Current data on local or national antibiotic policies should be reviewed [Appendix 1 – C].

- Only one study has recommended 1 or 2 days’ therapy using antibiotics active against pneumococcus, *H. influenzae* and methicillin-sensitive *S. aureus* (MSSA) for hospital admissions with very high risk for aspiration and infection such as head trauma, polytrauma and chest trauma. Additional studies are needed to determine if this would increase the risk of late-onset pneumonia and antimicrobial resistance. Whether prophylaxis would do better than very early therapy remains to be studied [Appendix 1 – C].

- Empirical treatment of severe necrotising pancreatitis with antibiotics has been suggested. Additional data are warranted before routine clinical use [Appendix 1 – C].

- Antifungal agents should be considered in immuno-compromised patients or patients with intra-abdominal surgery for severe peritonitis or pancreatitis [Appendix 1 – C].

- Topical SDD alone has no significant effect on mortality and should be avoided in ICU patients [Appendix 1 – C].

- SDD with a short course of IV antibiotics should be considered for patients undergoing esophageal, gastric surgery and liver transplantation (and then SDD should be commenced preoperatively) [Appendix 1 – C].

- The use of a combination of topical and IV antibiotics is not recommended for routine medical ICU patients. Additional data are needed to know if this technique is more cost-effective than 24-48 hours of IV antibiotics in trauma and surgical patients at high risk of VAP [Appendix 1 – B].

- The use of IV prophylactic antibiotics, in patients without any evidence of infection or who do not fit the criteria mentioned above, is strongly discouraged.

Chapter 4: Antibiotic resistance

What are the trends in antibiotic resistance worldwide?

Microorganism resistance to the broad use of antibiotics in the community and hospital wards, including the ICU, is being disseminated rapidly throughout the world, including Asia-Pacific countries. The mechanisms of acquired antibiotic resistance include enzymatic inhibition of drugs, alteration of proteins targeted by drugs, changes in metabolic pathways and membrane permeability, antibiotic efflux and alterations in porin channels. This has generated a crisis in the management of critically ill patients and set a strategic priority for hospitals worldwide.

Several factors contribute to this trend. These include inappropriate prescription of antibiotics in areas of uncertain efficacy, inattention to infection control measures ( principally lack of handwashing among healthcare workers) lack of infrastructure to monitor, track and feedback antimicrobial resistance, and lack of appropriate enforcement when infrastructure is available. In addition, marketing strategies by the international pharmaceutical industry, unrestricted antibiotic purchasing by the public (especially in developing countries), and indiscriminate antibiotic administration in livestock industries have created environmental pressures to promote the rapid emergence of resistant microorganisms.

The emergence of penicillin-resistant *S. pneumoniae* strains, while not a recent phenomenon in industrialised countries, has a serious economic impact on developing countries because more expensive antibiotics are needed. VAP due to multi-resistant *P. aeruginosa, K. pneumonia, A. baumannii, E. coli, ESBL* as well as MSSA, MRSA, and enterococcus, account for the largest proportion of positive isolates from ICU patients. MRSA, vancomycin-insensitive *S. aureus* (VISA) and VRE are about to be exceeded in terms of the potential for catastrophe by the emergence of antibiotic dependent organisms such as vancomycin-dependent enterococci.

Table 4. Continuous aspiration of subglottic secretions: three randomised trials.

<table>
<thead>
<tr>
<th>Study description</th>
<th>Relative risk of pneumonia (95% CI)</th>
<th>Relative risk of mortality (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koffel[34] 343 patients undergoing cardiac surgery and requiring mechanical ventilation</td>
<td>0.61 (0.27-1.40)</td>
<td>0.86 (0.30-2.42)</td>
</tr>
<tr>
<td>Valles[35] 153 patients requiring prolonged mechanical ventilation</td>
<td>0.47 (0.21-1.06)</td>
<td>1.09 (0.72-1.63)</td>
</tr>
<tr>
<td>Mahul[36] 145 patients requiring mechanical ventilation for more than 3 days</td>
<td>0.46 (0.23-0.93)</td>
<td>1.14 (0.62-2.07)</td>
</tr>
</tbody>
</table>
What are the best measures to prevent antibiotic resistance from being established?

The ICU is a prime setting of concern with antibiotic resistance. Patients with multi-resistant organisms are frequently admitted to ICU. Patients are also infected with multi-resistant organisms while in ICU. It is an ideal location to monitor the inappropriate prescribing and duration of antibiotic therapy\(^9\) and the close collaboration between ICU physicians and coworkers in nursing, pathology, infectious disease, infection control and pharmacy services fosters the process of close surveillance, control of nosocomial infections and prudent antimicrobial therapy.

Implementation strategies

The modification of human behaviour patterns among healthcare workers to achieve infection control objectives can be attained by implementing a variety of strategies over a period of time. The availability of incentives and removal of disincentives to optimise behaviour, and presence of academic detailing, computer-decision support systems, opinion leaders and institution-based protocol and guideline generation are other components in implementation but require validation [Appendix 1 – V].

Interventions

Effective interventions have focused on increasing compliance with infection control practices and reducing the unnecessary use of antibiotics. A well established relationship exists between improved hand hygiene and reduced infection rates\(^5\). Handwashing defines actions to decrease hand colonisation with transient microbiological flora through washing hands in detergent and rinsing in water; hand disinfection refers to the application of antiseptic solution; and hygienic hand rub consists of rubbing hands with a small quantity of rapidly acting, highly effective, usually alcohol-based, antiseptic\(^7\).

Most healthcare workers understand the importance of handwashing in reducing infections but routinely overestimate their compliance with this procedure\(^9\). All types of healthcare workers have a documented low compliance with handwashing practices\(^9\,10\). Risk factors for non-compliance include professional category, hospital ward, time of day and intensity of activity.

Effective handwashing requires 15-30 seconds\(^12\) and, cumulatively, is a significant time commitment which potentially restricts other patient care activities. Individuals with the highest workload levels are the least likely to wash their hands and lack of time is the most commonly cited reason for failure to wash hands\(^10\), emphasising that improving compliance with handwashing is a more pressing concern than the choice of different disinfectants or the method of drying.

Rewards or punishments are unlikely to improve compliance but measures to enhance the practicality of handwashing, such as increasing access to sinks, accompanied by verbal reminders of handwashing non-compliance would increase handwashing frequency. If measures to instill handwashing practices still result in failure, alternative strategies, for example, wearing gloves for all patient-handling procedures, may have to be applied\(^10\,11\) [Appendix 1 – III]. Colonising staphylococci are transferred from skin to equipment such as stethoscopes and ultrasound probes and such equipment should be disinfected after each examination\(^12\). The financial and human resource expenditure for interventions to improve handwashing is significant and their costs have to be balanced against the potential gain from reduced nosocomial infection.

Numerous guidelines for community acquired pneumonia have been developed and contain common principles covering prevention by immunisation, diagnosis, types of pathogens to be targeted in empiric therapy, antibiotic selection, drug resistance patterns, evaluation of the response and switching or cessation of therapy\(^12\).

To reduce over prescribing with antibiotics, the pharmacist has a role to provide academic detailing and daily reminders for physicians to review and discontinue antibiotic therapy and in maintaining compliance with institution-based policies on antibiotic prescribing. These executive functions should be empowered by committee\(^10\) [Appendix 1 – III]. Consultation with the infectious disease physician in the ICU is another simple method to achieve a reduction in antibiotic consumption\(^10\).

Cultures should be taken before commencing empiric antibiotics. Antibiotic effectiveness should be monitored by reference to culture results. Changes to or discontinuation of antibiotics should be implemented if indicated, taking into account cost, effectiveness and ecological impact. Antibiograms supply important information and should be part of a formal QA audit process. However, positive cultures must always be interpreted in the context of the general condition and other parameters of the patient in deciding whether or not to commence/alter antibiotics. The use of routine empirical antimicrobial coverage against MRSA pneumonia until MRSA infection is excluded is not recommended\(^10\).

The organisational characteristics of ‘closed’ medical ICUs (MICUs) improve resource utilisation and outcomes and can achieve greater compliance with guidelines for antibiotic selection and management of nosocomial infections than can ‘open’ MICUs\(^10\,111–113\). The early identification of multi-resistant organisms in patients should trigger the implementation of contact isolation strategies to decrease the risk of cross contamination\(^11\).

A decline in resistance rates can follow adherence to enlightened policies on antibiotic consumption. The resistance rates of Group A streptococcal isolates declined from 19-8.6% in Finland and from 61-3% in Japan in the years following reduction in the national consumption of erythromycin and are
examples of effective public health measures\textsuperscript{115, 116}. The quarterly rotation of empiric antibiotics in an institution can significantly reduce the incidence of antibiotic-resistant Gram-positive coecal infections, antibiotic-resistant Gram-negative bacillary infections, and mortality associated with infection\textsuperscript{117, 118}. The introduction of a short course empiric antibiotic therapy, based on a Clinical Pulmonary Infection Score (CPIS) as an operational criteria to stop antibiotics, reduces costs, antimicrobial resistance, superinfections and mortality\textsuperscript{119}. Further research is required in the following areas of infection control:

- Basic sciences (e.g. mechanisms of resistance).
- Epidemiology (e.g. the study of specific vectors of airborne transmission, of equipment transmission, the wearing of gowns in ICU).
- Clinical interventions (e.g. short- versus long-term antibiotic treatment for different conditions, crop rotation of antibiotics, long-term studies on antibiotic-impregnated CVC and cement).
- Health services (e.g. testing different implementation strategies to minimise antibiotic resistance).

Collaboration between infectious disease societies, pharmacy societies, critical care medicine societies and critical care nursing associations should be fostered, with the aim of directing national and international policies towards preventing antibiotic resistance from increasing its global impact on healthcare.

References


Grading of responses to questions

A. Supported by at least two Level I investigations
B. Supported by only one Level I investigation
C. Supported by Level II investigations only
D. Supported by at least one Level III investigation
E. Supported by level IV or Level V evidence


The ICU in a Nigerian teaching hospital: a 12 year review

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Abstract
The pattern of admissions, management, outcome of patients and problems in the intensive care unit (ICU) of the Ahmadu Bello University Teaching Hospital (ABUTH), Zaria in the 12 years from 1989-2000 were reviewed.

During this period, the ICU admitted 599 patients. More males and children under 10 years were admitted. A total of 345 patients (57.8%) survived and were discharged, while 254 (42.4%) died. The major cause of death was respiratory failure.

A total of 55% of patients came into the ICU as unplanned admissions following surgery. Trauma accounted for 29.4% of the admissions. The care of patients involved airway management, oxygen therapy and circulatory support. Nutrition was provided through nasogastric tubes or gastrostomy. Problems encountered included lack of adequate, well-trained staff, absence of functional monitoring equipment, inability of patients to pay for prescribed tests and drugs, poor infection control and inappropriate patient selection.

This review has provided an insight into the standard of anaesthetic practice and critical care delivery as well as the population that most requires this care. Its major findings are that, in developing societies like ours, children under the age of 10 years rather than the elderly are the ones that most frequently require intensive care. Secondly, the quality of care is below conventional standards. The mortality rate is higher than that in developed societies.

For there to be meaningful improvement in the quality of care, there has to be marked improvement in the number of trained staff at all levels as well as an adequate and steady supply of necessary equipment, drugs and laboratory support services. A health insurance scheme should be introduced so patients do not have to pay directly for health services. There also has to be a concerted effort to optimise the use of ICU resources through careful patient selection.

Introduction
Intensive care medicine is concerned primarily with management of patients with acute, life-threatening conditions within the specialised environment of an ICU. Starting about 40 years ago, intensive care medicine has progressed rapidly, and now includes resuscitation and transportation of acutely ill or injured patients. It is, everywhere, expensive and consumes a significant portion of hospital budgets. Inadequate resources facing most hospitals in the developing world tend to limit the capacity for coping with demands. Constraints are experienced from the lack of well-trained staff at all levels and the inadequate supply of necessary equipment and drugs.

The ICU of ABUTH, Zaria is a four-bed facility that serves a 1220-bed tertiary health care institution. It caters for surgical, medical and cardiac patients of all age groups. It has facilities for mechanical ventilation, blood-gas estimation, pulse oximetry, airway toilet and oxygen therapy. Specialised procedures such as pulmonary artery catheterisation, invasive blood pressure monitoring, renal dialysis and intravenous alimentation are not done. Patients pay for bed space, drugs, investigations and consumable items. In ABUTH, as in the developed world, a multi-disciplinary approach is adopted for optimal patient care. One consultant anaesthetist and two senior registrars in anaesthesia oversee the ICU. There are six trained nurses and nurse-aides.

In 1998, the hospital, with the assistance of the Petroleum Special Trust Fund (PTF), embarked on an expansion and renovation programme for the ICU. This work has not been completed until recently because of the abolition of the PTF by the Nigerian government.

This study reviews the major causes of admissions into the ICU of ABUTH, Zaria, examines the outcome of such admissions, identifies problems for the ICU, and proffers solutions necessary to improve the outcome of patients admitted into the ICU.

Materials and methods
The case histories of patients admitted into the ICU between 1989-2000 were reviewed. Data describing patients' age, sex, source of admission into the ICU, diagnosis on admission, duration of stay and outcome and location to which patients were discharged, were obtained from patients’ case files and the ICU registers. ICU nurses and physician anaesthetists were asked their opinion concerning the problems encountered in working in the ICU. The information obtained was analysed using tables and charts.
Results

A total of 599 patients were admitted into the ICU during the 12 year period. Of these, 394 (65.7%) were males and 205 (34.3%) were females. Their ages ranged between 3 hours of life and 95 years, with a median age of 15 years. A total of 28.3% of patients admitted were children under the age of 10 years. Figure 1 shows the age distribution.

As can be seen in Table 1, there were three main sources of admission. These were the operating theatre (post-operative patients), casualty department and the wards. Post-operative patients accounted for 55.1% of admissions. Referrals from the wards accounted for 27%. Casualty patients constituted 13.85%, while 4.02% of the patients were referred from outside hospitals.

Major causes of admission

Admissions based on diagnosis and specialty are shown in Table 2. Post-operative patients were admitted into the ICU following adverse events in the operating room. Such adverse events included failed intubation, cardiac arrest, cardiovascular collapse, failure to regain consciousness after anaesthesia and ‘neurological deficit’. Of the non-surgical causes of ICU admissions, 28.6% were due to tetanus.

Neonatal admissions were mainly due to respiratory insufficiency or gross congenital malformations at birth. In the paediatric age group, diagnosis at admission included perforated typhoid, foreign body in the respiratory tract, burns, laryngotracheobronchitis and omphalocele.

Table 1. Admissions, by referral source.

<table>
<thead>
<tr>
<th>Source</th>
<th>Number of patients</th>
<th>Distribution (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating theatre</td>
<td>330</td>
<td>55.09</td>
</tr>
<tr>
<td>Wards</td>
<td>162</td>
<td>27.04</td>
</tr>
<tr>
<td>Casualty</td>
<td>83</td>
<td>13.85</td>
</tr>
<tr>
<td>Others</td>
<td>24</td>
<td>4.02</td>
</tr>
</tbody>
</table>

Table 2. Admissions by diagnosis.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head injury</td>
<td>60</td>
<td>17</td>
<td>77</td>
</tr>
<tr>
<td>Perforated viscus</td>
<td>28</td>
<td>10</td>
<td>38</td>
</tr>
<tr>
<td>Foreign body</td>
<td>19</td>
<td>4</td>
<td>23</td>
</tr>
<tr>
<td>Blunt abdominal trauma</td>
<td>13</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Burns</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Fractures</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Cut throat</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Trauma (sub-total)</td>
<td></td>
<td></td>
<td>176</td>
</tr>
<tr>
<td>Other surgical conditions</td>
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<tr>
<td>Abdominal conditions</td>
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<tr>
<td>Cardiothoracic</td>
<td>22</td>
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<td>30</td>
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<tr>
<td>Others e.g. tumours</td>
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<td>9</td>
<td>25</td>
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<tr>
<td>Obstetric &amp; gynaecology</td>
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<td></td>
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<tr>
<td>Ruptured uterus</td>
<td>–</td>
<td>9</td>
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<tr>
<td>Abnormal deliveries</td>
<td>–</td>
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<td>Uterine fibroids</td>
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<tr>
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<tr>
<td>Eclampsia</td>
<td>–</td>
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<td>5</td>
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<tr>
<td>Ante-partum haemorrhage</td>
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<td>4</td>
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</tr>
<tr>
<td>Malignancies</td>
<td>–</td>
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<tr>
<td>O &amp; G (sub-total)</td>
<td>–</td>
<td>2</td>
<td>40</td>
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<tr>
<td>Medical</td>
<td></td>
<td></td>
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<tr>
<td>Tetanus</td>
<td>23</td>
<td>7</td>
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</tr>
<tr>
<td>Respiratory distress</td>
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<td>16</td>
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<td>Meningitis</td>
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<td>12</td>
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<td>Cerebrovascular accidents</td>
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<td>10</td>
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<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Snake bite</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Others*</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Medical (sub-total)</td>
<td></td>
<td></td>
<td>105</td>
</tr>
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</table>

* Guillain, Barre, congestive heart failure, chronic renal failure, etc.
Patient management and outcome
The major reason for admission to ICU was to provide ventilatory support. Procedures carried out in the ICU included mechanical ventilation of patients, suctioning the airway, oxygen therapy, blood-gas estimation and general nursing care of the unconscious patient. Patients were fed either through a nasogastric tube or via a gastrostomy tube. A 24 hour flow sheet was used to record physiological variables. On admission and discharge, the nurses wrote reports on each patient.

The immediate outcome of ICU patients shows that five patients were referred to other centres for more specialised management such as renal dialysis which was not available in the hospital, while relatives discharged nine patients against medical advice. There was no follow up monitoring of these patients after discharge from the ICU. A total of 331 patients (55.3%) were discharged to the wards, their condition having improved, while 254 (42.4%) died in the ICU. A total of 51% of post-operative admissions into ICU did not survive. The mortality rate on a yearly basis is shown in Figure 2. The overall mortality rate was 42.4%.

Problems identified
Information obtained from the ICU register and interviews with the nurses and physician anaesthetists revealed the following as reasons for poor patient outcome:

- Lack of drugs for patients.
- Late admission of patients into ICU.
- Poor patient monitoring and supervision of nurses.
- Admission of moribund patients.
- Absence of experienced physician anaesthetists to take charge of ICU.
- Frequent power failure resulting in equipment breakdown.
- Inadequate and obsolete monitoring equipment.
- Inability of patients to pay for specialised investigations.
- Poor infection control.

Discussion
It has been recommended that ICU beds should be at least 2% of total hospital beds\(^1\). The ICU component of number of beds in ABUTH is a mere 0.32%, grossly inadequate for this size of hospital. It was perhaps in recognition of this fact that the hospital embarked on expansion of its ICU in 1998. Unfortunately, the project has not been completed due to financial constraints.

Patients of all ages were admitted into the ICU during the period under study. It is interesting to note that patients under the age of 10 years were more frequently admitted into the ICU than patients in other age groups. This is different from the findings of Kilpatrick et al.\(^2\) in which over half the patients admitted in ICU were adults over the age of 55 years. It does, however, correspond with the findings by Kushimo et al.\(^3\) in Lagos University Teaching Hospital, Lagos, Nigeria, where they found that 28% of their ICU admissions were children less than 12 years of age. This reflects the difference in the demography of populations requiring critical care between the developed and under-developed societies.

More male patients were admitted than females. The study reveals a male : female ratio of 1.9 : 1. This is in agreement with findings in other studies of ICU admissions that reported a preponderance of males over females\(^4\).
More than 55% of the patients admitted during the period under study were post-operative patients. This is far more than found in a British study over a 10 year period by Cullen et al. 1 and the 40% seen by Keith et al. 1. It was not possible to ascertain from the records how many of these post-operative admissions were planned and how many were unplanned.

A study of the notes of post-operative patients admitted into the ICU showed that most post-operative admissions followed adverse events in the operating room. It has been suggested that unplanned post-operative admissions are a reflection of the quality of anaesthetic care 1. One is inclined to agree with this view judging from the fact that ABUTH has for years been plagued by a paucity of experienced physician anaesthetists. An unplanned post-operative admission is a major adverse outcome and impacts negatively on ICU resource utilisation 4, 5.

Trauma was one of the leading causes of admission in young adults, accounting for 29.3% of admissions. In this review, head injury following trauma accounted for 12.9% of ICU admissions and 61% of this group of patients died in ICU. Jeevaratnam et al. 6, in their survey of ICU management of severely head-injured patients in the UK, noted that severity of secondary brain damage, disability or even death was dependent on the quality of intensive care. The findings here tend to agree with those of Jeevaratnam as some of the reasons given for death of patients included lack of drugs for patients, late admission, poor patient monitoring and supervision and admission of moribund patients with terminal illness.

For many years, there had been no consultant anaesthetist with intensive care experience in charge of the ICU. As a result, many specialised, life-saving procedures commonly carried out in ICUs, were not done. It is instructive to observe the drop in mortality from about 1997 when two senior registrar physician anaesthetists became available in the department of anaesthesia. It seems more than coincidental that the mortality rate analysed in Figure 2 was so high before then.

Furthermore, it is the author’s opinion that the general downward trend in the economy has taken its toll on the outcome of patients admitted into ICU. There are frequent power failures, resulting in the breakdown of already obsolete equipment like the Cape Waine and East Radcliffe ventilators and blood-gas machine. Power failures also prevent the use of equipment like the Cape Waine and East Radcliffe ventilators. Power failures, resulting in the breakdown of already obsolete equipment like the Cape Waine and East Radcliffe ventilators and blood-gas machine. Power failures also prevent the use of equipment like the Cape Waine and East Radcliffe ventilators.

Running an ICU is expensive 4, 5. Outcome may be measured as the quality and duration of survival. It is not possible to effectively determine outcome in this review since there was no follow-up of patients after discharge from the ICU. That should form the subject of another study in which patients will be monitored after discharge. The balance between resources committed and outcome can judge whether the resources spent on ICU have been effectively utilised over the years.

This review has provided an insight into the standard of anaesthetic practice and critical care delivery in the ICU. It has also highlighted the problems inherent in the running of a third world intensive care facility. For there to be meaningful improvement in the quality of care, there has to be marked improvement in the calibre and number of trained staff at all levels, and an adequate and steady supply of necessary monitoring equipment, drugs and laboratory back-up services. Patients need to have health insurance that will ensure that they receive healthcare services when needed. The use of ICU resources also needs to be optimised by careful selection of patients.

Acknowledgement

I am grateful to Dr Mamuda and Dr Nwasor for help in the collection of data.

References

Discomfort, awareness and recall of patients during intensive care – still a problem?

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Abstract
During intensive care, undersedation or analgesia can cause significant psychological distress; however, this is rarely documented, and has never been done in our unit. We audited this problem in our general ICU, aiming to have a proper assessment in order to avoid it in the future.

A total of 70 patients (aged 20-60 years) were interviewed 1 day after discharge from the ICU about their memory of events during their stay. Questions related to patients’ memory of events and any distressing experiences and the same questions were repeated 5 days later. Patients with intracranial pathology or disorientation were excluded; the remaining 55 patients were oriented to place and time. Sedation was achieved using midazolam and morphine infusions titrated to achieve an appropriate Ramsay sedation score.

The most distressing experiences recalled were:

- Anxiety (68%).
- Discomfort from endotracheal tubes (60%).
- Fear (54%).
- Pain (52%).
- Discomfort from nasogastric tubes (48%).
- Difficulty in communicating (33%).
- Dreams and hallucinations (31%).
- Discomfort from physiotherapy (24%).
- Noise (15%).
- Insomnia (13%).
- Thirst (10%).
- Muscle paralysis (100%).

Five days later, there were no significant changes in responses. The sedation and analgesia we gave to our patients was not enough to prevent unpleasant experiences, mainly those related to patient awareness.

Introduction
During surgery, anaesthetists take care to prevent patient awareness under general anesthesia by using either inhalational or intravenous medications. However, patients in the ICU, particularly those intubated and on ventilatory support, may have a lot of psychological stress and frustration; these are often not documented.

Critical illness is one of the most significant stressful events that humans can endure. As with acute injury, total awareness of the potential and actual threat to survival can reduce the likelihood of survival. Pain and suffering contribute to initiating and maintaining the stress response; this is pathological and can increase mortality from prolonged illness. Modification of the stress response and human compassion are therefore reasons to use analgesics and sedatives in critically ill patients.

Methods used to achieve analgesia and sedation are often determined by tradition and convenience rather than by patient needs. Patients recovering from an episode of critical illness have reported factors they found distressing during their ICU stay. The most consistent unpleasant memories are of anxiety, pain, fatigue, weakness, thirst, the presence of various catheters, and minor procedures such as physiotherapy, nursing procedures such as turning and changing of dressings. Still one of the most frightening situations a patient can find himself in is to be therapeutically paralysed, yet totally aware.

The purpose of this study in our general ICU was to have a proper assessment of the awareness problem in our patients in order to avoid it in future and to get a proper consensus regarding its existence and possible solutions.

Patients and methods
The study was carried out after approval from the hospital Ethics Committee and written consent by the patients. Seventy patients aged 20-60 years were interviewed 1 day after discharge from the ICU about their memory of events during their stay in the ICU. Patients with head injury, central nervous system infection and those who were disoriented at the time of interview were excluded from the study, the remaining 55 patients were oriented to place and time.

The usual analgesia and sedation method used in our unit is continuous intravenous infusion of a mixture of 50mg morphine and 30mg midazolam mixed with 0.9% saline to complete a 60ml syringe. This is given by an infusion pump at rates of 1-15ml/hour, the actual rate being titrated by the
attending doctors and nurses to maintain a Ramsay sedation score of 4-5 at night and 2-3 during the day (Table 1). Long acting neuromuscular blocking drugs were only given as intermittent bolus doses when indicated, and were in addition to the above sedation method.

The questions asked of patients were about their memory of events and distressing experiences regarding pain, anxiety, dreams, fear, noises, thirst, lack of rest and other causes of discomfort during their ICU stay, such as the nasogastric tube, face mask, physiotherapy and insomnia. The same questions were repeated 5 days later during their stay in the hospital wards after having been discharged from the ICU.

Results
The sample of patients were representative of our regular ICU admissions in their age group, APACHE II score and duration of stay. After exclusion of head injury, central nervous system infection, and disoriented patients at the time of interview, the remaining patients totalled 55 (Table 2).

The most common experiences and the most distressing ones recalled are displayed in Table 3. Some of these distressing experiences, including anxiety, fear, dreams, hallucinations and insomnia, had continued since discharge in 6% of patients. None of the studied experiences correlated with age, sex or APACHE II score. On interviewing patients 5 days later, there were no significant changes in their response.

Discussion
The aim of intensive care sedation is to ensure that the patient is comfortable, rousable and tolerates uncomfortable procedures. The preferred level of sedation for critically ill patients has changed considerably in recent years. In 1981 Merriman questioned sedation practice in the ICUs and found that 67% of ICUs preferred their patients to be deeply sedated and unaware of their surroundings; 91% frequently used neuromuscular blocking agents. A similar survey in 1987 found that 69% of responding units preferred patients to be asleep but easily rousable and only 16% frequently used muscle relaxants. Sedation level is therefore tailored more towards the patients’ individual requirements.

The preferred level of sedation will also vary between ICUs. In well staffed ICUs, nurses spend more time talking to patients and medical staff may be available to carry out techniques which improve comfort without increasing sedation, like regional analgesia. Sedative drugs should be considered in all therapeutically paralysed patients, but their use does not guarantee absence of awareness in those patients. Sedative agents should be given with analgesics to all patients receiving neuromuscular blocking agents, if there is any chance of awareness.

Few studies have attempted to identify the need for sedation in the ICU patients. In general, attitudes towards sedation are influenced by informed anecdote, subjective impressions and

<table>
<thead>
<tr>
<th>Experience</th>
<th>% who found experience distressing</th>
<th>% who recalled experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>68</td>
<td>45</td>
</tr>
<tr>
<td>Discomfort from endo tube (38 patients)</td>
<td>60</td>
<td>35</td>
</tr>
<tr>
<td>Fear</td>
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<td>30</td>
</tr>
<tr>
<td>Pain</td>
<td>52</td>
<td>25</td>
</tr>
<tr>
<td>Discomfort from nasogastric tube</td>
<td>48</td>
<td>62</td>
</tr>
<tr>
<td>Difficulty in communicating</td>
<td>33</td>
<td>64</td>
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<tr>
<td>Dreams and hallucinations</td>
<td>31</td>
<td>8</td>
</tr>
<tr>
<td>Discomfort from physiotherapy</td>
<td>24</td>
<td>68</td>
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<tr>
<td>Noise</td>
<td>15</td>
<td>42</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13</td>
<td>33</td>
</tr>
<tr>
<td>Thirst</td>
<td>10</td>
<td>62</td>
</tr>
<tr>
<td>Paralysis (8 patients)</td>
<td>100</td>
<td>14</td>
</tr>
</tbody>
</table>
In patients with a high APACHE II score, deeper levels of sedation are achieved at lower plasma morphine concentrations than in patients who have less physiological disturbance.

Techniques for the assessment of sedation are difficult to categorise. The most common classifications are subjective and objective. Bergin and colleagues studied the problem of awareness in ICU patients and discovered that, regardless of what they thought was enough sedation and analgesia given to their patients, greater efforts should be made to ensure adequate sedation in the ICU.

A large number of sedation scoring systems have been described. In our ICU we use the Ramsay sedation scale, aiming at a target score of 2-3 during the day and 4-5 at night. Our drug of choice is a mixture of midazolam and morphine given by a continuous intravenous infusion, after a loading dose. We use neuromuscular blocking agents in a few selected cases, only when indicated.

As seen from the results, we didn’t achieve the ideal state of sedation to prevent awareness and recall in our patients. Since this study was completed, we have added propotol continuous infusion, 0.3-4mg/kg/hr, to our list of sedatives in the ICU, hoping to achieve a better outcome, and value for the cost. We had great benefit in pinpointing the problem of awareness in our ICU and trying to prevent it in future, by changing the medications used and improving our sedation scoring systems. Most recently we are aiming to apply some sedation measuring systems and policies when indicated, like cerebral function monitoring, electroencephalography and cerebral function analysing monitor.

### Conclusion

Our sedation and analgesia in the ICU is not enough to prevent unpleasant experiences, mainly those related to patient awareness. More work is still needed to improve our sedation and analgesia in the ICU.

### References

Case-based learning as a practical educational tool in infection management

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Cambridge, UK

Introduction
The importance of selecting the right initial antibiotic regimen for serious hospital-acquired infections should not be underestimated. Inappropriate use of antibiotics results in poor patient outcomes and serious sequelae, in addition to increasing the health economic burden of these infections. Indeed, inappropriate initial empiric therapy has been shown to be a key determinant of patient mortality within the critical care setting.

By definition, inappropriate antimicrobial treatment involves the use of agents that have little or no in vitro activity against microorganisms identified as causative at the site of infection. Antibiotic resistance among nosocomial pathogens – in particular Gram-negative bacilli and Gram-positive bacteria – is a major, but by no means unique, reason for patients to receive inappropriate empiric therapy. Conversely, appropriate therapy is an important contributing factor to clinical success in infections involving antibiotic-resistant bacteria.

There is good evidence to show that early use of appropriate empiric antibiotics improves clinical outcomes and reduces the length of hospital stay. The results of a large prospective cohort study of patients in medical and surgical intensive care units showed that patients who received inappropriate antibiotic therapy had a significantly higher mortality rate (42%) than those who were given appropriate therapy (18%) (p<0.001). Further studies in patients with various hospital-acquired infections, including nosocomial and ventilator-associated pneumonia, bacteremia and sepsis, support the beneficial effects of appropriate and early empiric therapy on mortality and length of hospital stay. For the initial antimicrobial agent to be effective, it is crucial that the choice, dose, timing and duration of therapy are adequate. Following initial appropriate antibiotic treatment, therapy can be tailored on the basis of local antimicrobial susceptibility data.

Worsening problems associated with the use of inappropriate antibiotics are expected over the forthcoming years owing to the lack of development of new agents active against Gram-negative pathogens, increases in the number of elderly and immunocompromised patients, and the rising global prevalence of biotic-resistant microorganisms. The rise in antibiotic resistance among nosocomial pathogens may result in an increase in clinical failures, and use of inappropriate antibiotics is only likely to make this problem worse. Clearly, action is needed to combat this trend.

The Academy for Infection Management – improving outcomes through education
The Academy for Infection Management (AIM) was formed in 2002 in response to the need for improved education in the management of nosocomial infections. The priority for AIM is to increase acceptance for the optimal prevention and management of infections so as to improve patient outcomes (mortality, morbidity and length of hospital stay). The Academy believes that this objective can be realised through practical and interactive education of healthcare professionals on key issues in infection management.

AIM is led by an international multidisciplinary group of experts, including intensive care and infectious disease specialists, surgeons, respiratory physicians, paediatricians, microbiologists and pharmacists, and is supported by an educational grant from AstraZeneca.

Education programmes that provide clinically relevant information and promote discussion among clinicians are likely to assist learning. A systematic review of the effect on clinician performance of formal continuing medical education interventions showed that interactive sessions that enhance participant activity and provide the opportunity to practise skills can actually change clinical practice and, sometimes, influence healthcare outcomes. In a study of continuing medical education for general practitioners, increased involvement of participants in programme development and improved interaction between learners and teachers was shown to result in greater satisfaction with the educational programme compared with a traditional lecture-based approach.

AIM’s educational materials have been developed by the expert group and are primarily based around interactive, real-life, patient case studies in various specialties (surgery, pneumonia, intensive care, paediatrics). These case studies are presented as decision support and traditional slide sets. The workmats are paper-based exercises that present the case study and pose multiple questions regarding decisions that clinicians would have made during various stages of that patient’s management (Figure 1). The workmats were specifically designed to promote discussion, understanding and learning among small groups of clinicians. Workmats similar to these have been used to great effect in continuing medical education, allowing sharing of best clinical practice.

Informative supporting materials are also available in a variety of formats on the following topics:
• The early use of appropriate empiric antimicrobial therapy.
• Mechanisms of antibiotic resistance.
• The impact of pharmacokinetic and pharmacodynamic antimicrobial profiles on treatment outcomes.
• The costs associated with therapeutic failure.

All the educational materials are available to download at no cost from the dedicated AIM website www.infectionacademy.org. The materials are designed for both teaching and self-guided learning, and can be adapted for local use.

The AIM programme was successfully introduced at three large global meetings with an audience of more than 650 people in total, and subsequently in numerous other country-specific and regional meetings. These meetings included educational lecture sessions and practical case-based and antibiotic-policy workshops.

The AIM experience in India

The success of the AIM initiative is typified by experience from four educational meetings held in various centres in India. The 1 day meetings, which all had the same format, comprised a combination of plenary presentations in the morning and afternoon workshop sessions in which small groups of clinicians discussed case studies presented as workmats. Around 120 clinicians attended these meetings.

At the beginning and end of each Indian AIM meeting, delegates were asked to complete a multiple-choice questionnaire (relating primarily to infection control and treatment issues) in order to assess the impact of the course (Table 1). Delegates were also asked to evaluate their perceived learning. Interestingly, learning improved by an average of more than 15% over the course of each meeting (Figure 2).

Figure 2. Learning improved as a result of using case study workmats during AIM meetings in India.

Treating infection right ... First time

Introduction

The core principles of the Academy — which set out the overall goals of the programme — include patient outcomes, evidence-based guidelines, and infection control.

Objectives

The objectives set out for the teaching by the Infectious Diseases Association are:

1. To provide a global education resource for physicians involved in the treatment of nosocomial infections (infectious disease physicians, surgeons, chest physicians, microbiologists).
2. To provide a platform for discussion within the context of the healthcare environment.
3. To share the latest clinical guidelines.
4. To share the latest clinical guidelines online on infectious diseases management with regard to improving patient outcomes.

Core principles

The core principles of the Academy — which set out the overall goals of the programme — include evidence-based guidelines, surveillance, and infection control.

Patient outcomes

1. Select the most appropriate antibiotic depending on the patient, risk factors, suspected infection and resistance.
2. Administer antibiotics, if appropriate, as outlined in the guidelines and for the recommended duration.
3. Assess the impact of therapeutic failure.
4. If appropriate, change antibiotic dosage or therapy based on results of antibiogram and pharmacokinetic and pharmacodynamic studies.

The vision for the Academy for Infection Management is to gain wider acceptance of the successful initiatives and to improve outcomes by reducing mortality and morbidity, and length of stay in hospital.

Core principles

● Share best clinical practice
● Share evidence of guidelines
● Share best outcomes

Objectives

1. Achieve a reduction in mortality and morbidity.
2. Improve patient outcomes.
3. Improve costs associated with therapeutic failure.
4. Reduce the impact of pharmacokinetic and pharmacodynamic studies.
5. Improve early use of appropriate empiric antimicrobial therapy.
6. Know the unit’s resistance profile and choose antibiotics accordingly.
7. Use antibiogram for the presence of resistant pathogens.
8. Remove indwelling devices as soon as they are no longer indicated.

Infection control

The core principles of the Academy — which set out the overall goals of the programme — include evidence-based guidelines, surveillance, and infection control.

<table>
<thead>
<tr>
<th>Question</th>
<th>Reason</th>
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</thead>
<tbody>
<tr>
<td>How could the educational value of this case be improved?</td>
<td>Please choose two of the following options:</td>
</tr>
<tr>
<td>Which are the key learning points from this case?</td>
<td>Please choose two of the following options:</td>
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</table>

Patient with simple abdominal pain complicated by nosocomial infection

A 49-year-old woman had been admitted to hospital for the past 24 hours. The patient was feeling nauseous and had been sick twice before admission. The patient has a history of paroxysmal atrial fibrillation.

History and examination

1. The patient has abdominal pain which is poorly localised.
2. An abdominal X-ray was normal.
3. The patient has a history of atrial fibrillation.

Results and clinical course on Day 7

1. A CT scan of the abdomen shows a perforated appendix (Figure 1). A pregnancy test is performed and is negative.
2. The patient has leukocytosis 17.0 x 10⁹/L (17 000/mm³).
3. A leukocyte count is performed and is normal.
4. The patient is given remifentanil for sedation and analgesia.
5. An examination of the patient shows:
   - pulse oximeter SpO₂ 85% on air
   - temperature 38.5°C
   - tachypnoea 30 breaths/min
   - tachycardia 125 beats/min
   - hypotension 105/50 mmHg
   - presence of bowel sounds
   - end-expiratory pressure (PEEP) 10 cm H₂O
   - maximum inspiratory pressure 40 cm H₂O
   - lung sounds decreased.
6. The patient has a weight loss of 0.5 kg.
7. The patient has a history of diabetes mellitus.
8. The patient has a history of smoking.

Further tests

1. A transabdominal ultrasound scan is performed.
2. A chest X-ray is taken.
3. A transoesophageal echocardiogram is performed.
4. A bronchoalveolar lavage is performed.
5. A Nondirected bronchoalveolar lavage is performed.
6. A blood culture is performed.
7. A sputum culture is performed.
8. A CT scan of the chest is performed.
9. A chest CT scan is performed.
10. A CT scan of the abdomen is performed.

Further treatment

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5. A bronchoalveolar lavage is performed.
6. A blood culture is performed.
7. A sputum culture is performed.
8. A CT scan of the chest is performed.
9. A chest CT scan is performed.
10. A CT scan of the abdomen is performed.

Further investigation

1. A transabdominal ultrasound scan is performed.
2. A chest X-ray is taken.
3. A transoesophageal echocardiogram is performed.
4. A bronchoalveolar lavage is performed.
5. A blood culture is performed.
6. A sputum culture is performed.
7. A CT scan of the chest is performed.
8. A chest CT scan is performed.
9. A CT scan of the abdomen is performed.

Further treatment

1. Nondirected bronchoalveolar lavage is performed.
2. A CT scan of the abdomen is performed.
3. A chest X-ray is taken.
4. A transoesophageal echocardiogram is performed.
5. A bronchoalveolar lavage is performed.
6. A blood culture is performed.
7. A sputum culture is performed.
8. A CT scan of the chest is performed.
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10. A CT scan of the abdomen is performed.
These findings mirrored those of the global meetings. In the third global meeting, 82% of the 364 attendees believed the AIM educational programme was very relevant to their clinical practice.

Conclusions

The use of appropriate antibiotic therapy early in nosocomial infections benefits patients and healthcare providers. AIM has been established to uphold this concept through an innovative and interactive educational programme. The success of the evolving AIM programme and its impact on clinical practice clearly highlight both a need for continued education about the optimal management of nosocomial infections and the desire of clinicians to learn.

References

Compatibility study on drugs used by continuous intravenous infusion in the critically ill

Brit Cadman & Tim House
Pharmacy Department
Addenbrooke’s Hospital, Cambridge, UK

Background
Safe and effective drug therapy is an essential part of the care of all patients. Critically ill patients present clinical practitioners with complex therapeutic and technical challenges; patients often require multiple therapeutic interventions and consequently need to receive several drugs. These drugs are generally administered by the intravenous route, often by continuous infusion.

Access is adequate in many patients and, in such cases, the infusions can be given separately. However, the need to infuse more than one drug down a catheter lumen is a common problem, despite most patients having multiple lumen catheters. Compatibility between different drugs becomes a problem when patients require more than three drug infusions (the number of lumens usually available for infusion), possibly in addition to total parenteral nutrition (TPN), insulin and electrolyte infusions.

Drug stability and compatibility are critical to the accurate and appropriate delivery of drug therapy to patients. The ICU pharmacist has a responsibility to ensure drugs are prepared and given safely to this vulnerable patient population; this includes compatibility of drugs infused down the same catheter. Drugs that are incompatible with each other must be infused using separate lines. The consequences of incompatibility include loss of drug potency, production of toxic products, blockage of cannulae and/or embolism. Any of these may compromise patient safety (Figure 1).

Drug incompatibility in this context refers to physicochemical phenomena (Table 1), such as concentration-dependent precipitation or acid-base reactions, which often result in a precipitate rather than chemical instability (Table 2). In addition, precipitation can be seen and detected visually (Figure 1), whilst chemical instability requires chemical analysis by a method such as high pressure liquid chromatography (HPLC).

In many ICUs, continuous intravenous infusions are given by syringe pumps; drugs are often diluted to 50 ml (Table 3) and infused at a rate determined either by the patient’s response or according to a standard dosing regimen. Drugs mix at the first common connection; the amount of time they spend in combination will depend on the flow rate of the drugs being infused, and the amount of drug available for interaction will depend on the volume of the catheter lumen.

Information on drug compatibility at the concentrations used on the ICU is limited \(^1,2\). Previous work at Addenbrooke’s Hospital has confirmed that it is not safe to assume that a more concentrated solution of a drug will also be compatible\(^3\). Our medicines information department receives many queries on drug compatibility issues that are not found in the literature.

Table 1. Types of common physical incompatibilities.

<table>
<thead>
<tr>
<th>Types of physical incompatibilities</th>
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</thead>
<tbody>
<tr>
<td>Concentration exceeds saturation solubility</td>
</tr>
<tr>
<td>Co-solvent diluted so drug precipitates</td>
</tr>
<tr>
<td>pH changes</td>
</tr>
<tr>
<td>Insoluble salt formation</td>
</tr>
<tr>
<td>Organic cations and anions</td>
</tr>
<tr>
<td>Salting out</td>
</tr>
<tr>
<td>Complex formation</td>
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<tr>
<td>Gas evolution</td>
</tr>
</tbody>
</table>

Figure 1. Drug precipitate in an intravenous catheter line.

Table 2. Chemical degradation.

Types of chemical degradation

<table>
<thead>
<tr>
<th>Types of chemical degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrolysis</td>
</tr>
<tr>
<td>Oxidation/reduction</td>
</tr>
<tr>
<td>Photodegradation</td>
</tr>
<tr>
<td>Racemisation/epimerisation</td>
</tr>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Acetylcysteine</td>
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<tr>
<td>Adrenaline</td>
</tr>
<tr>
<td>Adrenaline</td>
</tr>
<tr>
<td>Adrenaline</td>
</tr>
<tr>
<td>Alfentanil</td>
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<tr>
<td>Aminophylline</td>
</tr>
<tr>
<td>Amiodarone</td>
</tr>
<tr>
<td>Aprotinin</td>
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<tr>
<td>Atracurium</td>
</tr>
<tr>
<td>Clonidine</td>
</tr>
<tr>
<td>Ciclosporin</td>
</tr>
<tr>
<td>Dobutamine</td>
</tr>
<tr>
<td>Dopamine</td>
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<tr>
<td>Dopexamine</td>
</tr>
<tr>
<td>Dopexamine</td>
</tr>
<tr>
<td>Esmolol</td>
</tr>
<tr>
<td>Fentanyl</td>
</tr>
<tr>
<td>Frusemide</td>
</tr>
<tr>
<td>Heparin</td>
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<tr>
<td>Insulin</td>
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<tr>
<td>Isoprenaline</td>
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<tr>
<td>ISDN</td>
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<tr>
<td>Labetalol</td>
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<tr>
<td>Midazolam</td>
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<tr>
<td>Morphine</td>
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<td>Noradrenaline</td>
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<tr>
<td>Noradrenaline</td>
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<tr>
<td>Noradrenaline</td>
</tr>
<tr>
<td>Octreotide</td>
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<tr>
<td>Omeprazole</td>
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<tr>
<td>Phentolamine</td>
</tr>
<tr>
<td>Phenytoin</td>
</tr>
<tr>
<td>Remifentanil</td>
</tr>
<tr>
<td>Rocuronium</td>
</tr>
<tr>
<td>Sodium nitroprusside</td>
</tr>
<tr>
<td>Tacrolimus</td>
</tr>
<tr>
<td>Vecuronium</td>
</tr>
<tr>
<td>Verapamil</td>
</tr>
</tbody>
</table>

G: Glucose; N/S Normal Saline
Table 4. John Farman ICU compatibility chart.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration/Volume</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcysteine</td>
<td>(undiluted)</td>
<td></td>
</tr>
<tr>
<td>Adrenaline 5mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Adrenaline 10mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Adrenaline 20mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Alfentanil (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminophylline 500mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Amiodarone 900mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Aprotinin (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonidine (750mcg in 50ml G)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclosporin (75mg in 50ml N/S)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dobutamine 250mg</td>
<td>(in 50ml G)</td>
<td></td>
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<tr>
<td>Dopamine 200mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Dopexamine 50mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Dopexamine 200mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Esmolol (10mg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frusemide 50mg</td>
<td>(in 50ml N/S)</td>
<td></td>
</tr>
<tr>
<td>GTN (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin 25,000 units</td>
<td>(in 50ml N/S)</td>
<td></td>
</tr>
<tr>
<td>Insulin (I unit per ml N/S)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoprenaline 2mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>ISDN (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labetalol (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midazolam 50mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Morphine (1mg/ml in 50ml N/S)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noradrenaline 4mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Noradrenaline 8mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Noradrenaline 16mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Octreotide 500mcg</td>
<td>(in 50ml N/S)</td>
<td></td>
</tr>
<tr>
<td>Omeprazole 200mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Phentolamine 20mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Phenylephrine 20mg</td>
<td>(in 50ml G)</td>
<td></td>
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<tr>
<td>Remifentanil 5mg</td>
<td>(in 50ml N/S)</td>
<td></td>
</tr>
<tr>
<td>Rocuronium (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium Nitroprusside</td>
<td>50mg (in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus 1mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
<tr>
<td>Vecuronium (undiluted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil 20mg</td>
<td>(in 50ml G)</td>
<td></td>
</tr>
</tbody>
</table>

KEY:
- Incompatible Immediately
- Incompatible after 24 hours
- Compatible

G = glucose 5%
N/S = sodium chloride 0.9%
This lack of information on drug compatibility results in some nursing staff infusing drugs through the same lumen when there is no alternative. More information on drug compatibility would improve patient care and reduce costs by eliminating the need for additional venous access with its inherent risks, such as infection. We therefore decided to study this problem further.

Methods

Solutions of the drugs to be tested were aseptically prepared and diluted based on our standard concentrations used on the ICU (Table 3). These are based, where possible, on the manufacturers’ recommendations for each product. It was important to specify the brand tested since there may be variations between different brands because of the potential for different solvents, buffering systems and/or preservatives used in the formulation of a drug made by different manufacturers.

For each drug, 1ml of each of the drug solutions to be tested were mixed together in a glass test-tube at room temperature. The resulting solution was then examined visually immediately after mixing, against a white and black background, to check for precipitation. This examination was repeated at 24 hours after mixing. This method was repeated a second time to validate the results for each drug combination.

Physical compatibility was defined as no visibly detected indication of particulate formation, haze, precipitation, colour change or gas production. Methods for detecting non-visible particles, such as observation under high intensity monodirectional light, examination by turbidimeter and particle size counter were not employed.

Results

The results are summarised in Table 4. A total of 39 infusions were prepared and 1,444 different drug combinations were tested – 101 were found to be incompatible. A total of 62 of the combinations precipitated immediately and the remaining 39 combinations took up to 24 hours to develop. Ideally the admixtures would have been examined after 1 hour to establish if the interaction was significantly time-dependent; in such cases co-infusion of the two drugs may be possible due to the short contact time associated the method of administration used to infuse the drugs. Examination of the admixtures at 1 hour post mixing was difficult to achieve in practice (with the resources available) and as preparation and mixing of the solutions took considerable longer than 1 hour.

Although some reactions took 24 hours to develop, we considered these to be ‘incompatible’ to reduce the risk of precipitation and/or chemical interaction, and potential for patient harm. In the absence of confirmation of chemical stability, we decided this cautious approach was preferable. Delayed reactions were mainly associated with omeprazole and aminophylline.

Some of the incompatibilities seen were possibly pH-dependent reactions (e.g. with aminophylline or frusemide); whereas, in the case of omeprazole or GTN, incompatibilities may arise due to lack of solubility in aqueous solutions. Establishing the mechanism of incompatibility is beyond the scope of this study and further investigation is required.

Discussion and conclusions

This study has only looked at physicochemical compatibility and not chemical stability; the justification for this is that chemical degradation of drugs is very much time dependent, although we appreciate the absence of visual incompatibility does not rule out chemical deterioration.

Y site compatibility information is designed with the assumption that the ratio is 1:1 of the subject drug and the infusion or admixture, and that the contact time for drugs is short, often in the range of 15 minutes and hardly ever more than 60 minutes. Relatively few drug combinations are so unstable that Y site administration of the combination is precluded.

Non-visible particulate contamination may be present in both small and large volume parenteral infusions and ICU patients often receive more than 107 particles >2µm every 24 hours. In the absence of firm evidence for the harmful systemic effects of such drug particles, the clinical significance of non-visible particles was considered to be negligible and therefore further methods for detection of particulates were not performed.

A few manufacturers of pharmaceuticals were contacted to establish if visual inspection was a method used when describing a drug to be compatible with another in their Summary of Product Characteristics (SPC); this was confirmed by the manufacturers contacted. In addition, it is routine clinical practice for large volume infusions and drugs to be reconstituted with dilutents for intravenous bolus administration, with visual inspection as the only routine safeguard against particulates.

The results have been made available on the ICU, to be used by all staff to ensure compatibility of the drugs given by continuous infusions. Further investigation of the combinations found to be compatible in this study, in terms of chemical stability, is desirable to confirm drug potency in combination and that no harmful degradation products are produced by a chemical reaction.

References

6. Poik A. In-house compatibility study, Addenbrooke’s Hospital, Cambridge, UK.
Instructions for authors

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