

## Commentary

# Recently published papers: pulmonary care, pandemics, and eugenics in surviving sepsis?

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## Abstract

Respiratory failure is one of the leading admission diagnoses on the critical care unit, and the journals have reflected this over the past few months. An understanding of the aetiology of pulmonary sepsis is important but your choice of ventilator gas humidification system is not. There are prophecies of more pandemics, but panic is futile because survival is all down to your genes.

Health-care-associated pneumonia (HCAP) refers to a pulmonary infection that develops in individuals recently hospitalised, or undergoing renal replacement therapy or other long-term out-patient care. Over the past few years it has been postulated that this reflects a distinct group of pathogens with consequent implications for therapy and also on outcome. However, no study had looked at the pathogens of both HCAP and community-acquired pneumonia (CAP) and compared them with those of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP).

Kollef *et al.* [1] have attempted to do this by retrospective analysis of a large USA database of culture-positive pneumonia, in 59 US centres over a 1-year period. The study defined 4,543 positive pneumonias, of which 2,221 were CAP, 988 HCAP, 853 HAP and 499 VAP. The results showed that patients with HCAP were slightly older than those with CAP but were broadly similar to those with HAP. Half of the patients with HCAP came from nursing homes. Illness severity was almost identical in both HCAP and VAP, but was higher than in HAP and CAP. Bacterial pathogen identification showed a high rate of *Staphylococcus aureus* infection in all types of pneumonia but this may be an artefact; however, also of interest was the low rate of pneumococcal infection in CAP. Overall, bacterial species in HCAP were broadly similar to those in HAP and VAP; *Pseudomonas* accounted for just over 25% and methicillin-resistant *S. aureus* 56%, with the rest made up of the usual Gram-

negative types. It was also noted that patient mortality for HCAP was similar to that for HAP but higher than that for CAP and lower than that for VAP.

The authors suggest that HCAP is a distinct entity from CAP and should be treated as a hospital-acquired type of infection from first presentation; the paper certainly supports the recently published guidelines from the American Thoracic Society [2].

Staying with the pulmonary sepsis theme, Lacherade *et al.* [3] shed further light on the debate over which factors may influence the development of VAP, in particular the use of differing humidification devices. This five-centre prospective trial randomised 369 unselected patients who had required ventilation for more than 48 hours, to receive treatment with either a heated humidifier or a heat and moisture exchanger during their stay. They showed no difference between the treatments in incidence of VAP. Given previous data on this subject it increasingly appears that the mode of respiratory gas humidification is not critical.

The optimal specimen collection technique for the diagnosis of VAP continues to be strongly debated. The paper by Brun-Buisson *et al.* [4] looked at 68 patients with clinically apparent VAP and prospectively performed blinded endotracheal aspiration, blinded protected telescoping aspiration (PTC) and bronchoscopic aspiration. Their results confirmed that bronchoscopic aspiration provides the best cultures with fewer false positives, with PTC being close behind. However, endotracheal aspiration produced more false positives. This means that the use of PTC can be used to obtain specimens for the diagnosis of VAP and to guide therapy, and avoids the need for a more invasive procedure and expensive equipment.

Finally on the respiratory theme, the role of non-invasive ventilation (NIV) makes another appearance [5]. This paper

compared the role of NIV with mechanical ventilation for patients with acute respiratory failure from all causes who fulfilled defined criteria for conventional mechanical ventilation (CMV). A total of 64 patients were randomised, 31 to NIV and 33 to CMV, with 18 in the NIV group converting to CMV. The mortality rate in the NIV group was 23%, compared with 39% in the CMV group; complication rates and durations of ventilation were similar. They also showed that patients who did not respond to NIV did no worse overall than those who received CMV from the start, and of interest is the finding that all patients with pneumonia who underwent NIV required CMV, a finding consistent with other studies. As identified in the accompanying editorial [6], the study numbers are small, particularly given the all-cause inclusion criteria and as such interpretation of results should be cautious.

The world recently seems to be an ever more dangerous place, with increasing reason to be troubled by apocalyptic nightmares. There is a superbug near you – be quite sure of it – and it will probably try to kill you given half a chance. Methicillin/vancomycin-resistant *S. aureus*, severe acute respiratory syndrome, pandemic and avian influenza have dominated both the medical and lay press. The antecedents of these organisms are well known to us, but it seems they have started taking steroids and going to the gym a lot. There is now mounting evidence that *Clostridium difficile* has undergone a similar process. *C. difficile*, a spore-forming Gram-positive anaerobic bacillus, has been recognised as the causative agent of an antibiotic-associated colitis since the mid-1970s. Given appropriately altered colonic flora this bacterium will replicate and produce endotoxins (classically A and B) causing a spectrum of disease from troublesome watery diarrhoea to life-threatening pseudomembranous colitis, depending largely on host characteristics such as age and severity of underlying disease, therefore making its incidence on the intensive care unit particularly high. Furthermore, outbreaks were largely isolated to individual wards or institutions. However, in recent years much larger outbreaks in both North America and Europe have suggested increased prevalence, resistance and virulence of *C. difficile*. This raises the ugly spectre of an epidemic strain, and leads us to ask why this has occurred, whether it is spontaneous genetic mutation or a change in medical practice, and whether we can do anything about it. Two recently published papers with an accompanying editorial address some of these issues [7–9].

The work of McDonald *et al.* [7] consists of an impressively detailed microbiological survey of *C. difficile* outbreaks across six states in the United States. Genetic and toxicological profiles were compared with those from a historical database of *C. difficile* obtained before 2001. In the second paper a research group in Quebec [8] performed a prospective surveillance of 12 institutions to determine the incidence of hospital-acquired *C. difficile*-associated diarrhoea

and its associated risk factors. Isolates were also typed. The results from the two studies were largely corroborative:

1. A previously uncommon strain of *C. difficile* has markedly increased in incidence.
2. It is characterised by the production of a new toxin (binary toxin), a partial deletion of the *tcdC* gene, which normally downregulates toxin A and B production, and increased resistance to fluoroquinolones.
3. Morbidity and mortality, particularly among the elderly, are increasing compared with outbreaks in the 1980s and 1990s.
4. Risk factors include exposure to fluoroquinolones and cephalosprins.

A precise scientific link between the suggested virulence factors (binary toxin and *tcdC* partial deletion) and severity of disease is yet to be made. But the emergence of this relatively new strain of *C. difficile* concomitant with increased severity and prevalence of disease must be a cause for concern. In answer to the question ‘What can we do?’ the accompanying editorial [9] suggests that the following are essential:

1. Continued microbiological surveillance of disease outbreaks, along with early diagnosis and treatment.
2. Scrupulous infection control practice, above and beyond the normal, by all in contact with at risk patients.
3. The use of soap and water for hand washing given spore resistance to alcohol preparations.
4. Regular institutional review of antimicrobial stewardship, with early de-escalation of broad-spectrum antibiotics wherever possible.

Finally, presuming that you have kept up with *The Lancet* recently, you will be hoping that your mitochondrial DNA is of the haplogroup H variety. A group in Newcastle analysed mitochondrial DNA in 150 sequential adult admissions to the intensive care unit with a diagnosis of severe sepsis, the primary outcome measure being survival at 180 days [10]. Using logistical regression analysis they demonstrated that haplogroup H was an independent predictor of survival, patients with haplogroup H being 2.12 (95% confidence interval 1.02 to 4.43) times more likely to be alive at 180 days. The authors propose that this finding might be explained by the enhanced respiratory chain activity associated with this haplotype, citing cellular dysoxia secondary to mitochondrial dysfunction as a key factor in sepsis-induced organ dysfunction. Interestingly, haplogroup H patients generated significantly higher temperatures than patients with differing haplogroups. Fortunately, H is the commonest haplogroup, accounting for about 44% of patients in this study. The authors suggest that mitochondrial DNA haplotyping offers a new means of risk stratification in severe sepsis, although further work is clearly needed to identify possible therapeutic avenues.

## Competing interests

The author(s) declare that they have no competing interests.

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