Potential antibiotic resistant pathogens in community-acquired pneumonia: playing it safe is anything but

Grant W. Waterer[1,2,3]

Affiliations: [1]University of Western Australia, Perth, Australia. [2]Northwestern University, Chicago, IL, USA. [3]Royal Perth Hospital, Perth, Australia.

Correspondence: Grant W. Waterer, Level 4, MRF Building, Royal Perth Hospital, GPO Box X2213, Perth 6847, Australia. E-mail: grant.waterer@uwa.edu.au

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Since the introduction of the concept of healthcare-associated pneumonia (HCAP) in the 2005 update on the treatment of nosocomial pneumonias by the American Thoracic Society and the Infectious Diseases Society of America [1], there has been considerable controversy over whether this new category has been helpful or harmful. The core of the problem is the tension between clinicians perceiving that missing a methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa* may have dire consequences for their patient and the goals of antibiotic stewardship in reducing the use of too broad spectrum antibiotics driving patient-specific side effects like renal toxicity, *Clostridium difficile* or vancomycin-resistant enterocoli [2] infection, and the more generalised harm through the promotion of antibiotic-resistant bacteria within the hospital environment.

There has been a significant increase in the use of anti-pseudomonal and anti-MRSA antibiotics as empirical treatment in the setting of community-acquired pneumonia (CAP) since the classification of HCAP was introduced [3]. This increase in use is despite an abundance of epidemiological data that these pathogens are actually extremely uncommon in the setting of CAP, outside of a few centres in the USA [2, 4–6].

There is no doubt that patients with HCAP risk factors have worse outcomes than patients with CAP, but this is not unexpected given the much higher rate of comorbidities in the former [7]. The key question is whether treating with anti-MRSA or anti-pseudomonal antibiotics has improved outcomes. Although mostly observational data, the evidence from published studies is that the use of broader spectrum antibiotic coverage in patients with HCAP risk factors does not improve outcomes [8–11], although this has not been a uniform finding [12, 13].

While the community-level harm from excessive broader spectrum antibiotic use is well acknowledged, clinicians have a tendency to think mainly of their individual patients (hence the need for antibiotic stewardship programmes). Therefore, although the evidence for using broad-spectrum therapy is underwhelming, clinicians concerned about the patient in front of them may still opt for broader spectrum therapy "just in case" on the basis that this is a safer approach. In this issue of the *European Respiratory Journal*, Webb *et al.* [14] present data that should make clinicians rethink whether broader spectrum therapy is a safer option.

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In an observation cohort of nearly 2000 patients with pneumonia admitted to four hospitals in Utah, Webb *et al.* [14] compared the outcome of conventional therapy with broader spectrum therapy. Compared to previous retrospective studies, there was much better adjustment for severity at presentation, comorbidity and indication bias, aided by a comprehensive electronic medical record. Consistent with other studies already mentioned, they found that clinicians empirically treated nearly 40% of patients with anti-pseudomonal and/or anti-MRSA therapy yet only 3% of patients had these pathogens identified. Interestingly, only about one-third of those treated with broad-spectrum empiric therapy had identifiable HCAP risk factors. After adjusting for comorbidities and indication bias, broad-spectrum antibiotic therapy was associated with a 4.6-fold increased risk of mortality, longer hospital stay and increased *C. difficile* infection.

While the above data argues strongly against broad-spectrum coverage, clinicians will still legitimately ask "but what about the patients who were not given empirical therapy that covered the pathogen"? Interestingly this scenario only arose in 1.4% of those treated with broad-spectrum therapy and 0.6% of those treated with standard therapy. In a case chart review of the 40 fatal cases, inadequate antibiotic therapy was not identified as a causative factor in any case. In contrast, in 17.5% of fatal cases there was an antibiotic-associated adverse event, usually due to piperacillin/tazobactam or vancomycin or both, suggesting that antibiotics may have been contributing factors in some deaths. This finding is entirely consistent with the now well-recognised substantial increase in neophrotoxicity with the combination of vancomycin and piperacillin/tazobactam [15, 16].

The study by Webb *et al.* [14] is not a randomised, controlled trial, but it does put clinicians on notice that "playing it safe" by using broad-spectrum antibiotics may actually be "playing it risky". The only really robust predictor of MRSA or *P. aeruginosa* infection is prior culture [17–19], but there are individual centres where the prevalence is higher. It is extremely important that clinicians do not generalise findings from these high-prevalence centres to their own. There may be very specific circumstances where empirical therapy is warranted while samples are obtained and analysed (for example coverage of MRSA in a young adult with rapidly progressive pneumonia and severe sepsis in influenza season) but in general a treat "just in case" strategy is fundamentally flawed and almost certainly causing harm. There is no escaping the current reality that to practise good medicine clinicians must know the epidemiology of their local pneumonia pathogens and not use broad-spectrum antibiotics "just in case".

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