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VAP – quantum uncertainty in the ICU?

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“It’s the Heisenberg principle, me asking the question changes the answer”

Barack Obama, Vanity Fair, 2012

More has been written about ventilator-associated pneumonia (VAP) than any other nosocomial infection, with more PubMed records than the next two most prevalent nosocomial infections combined. However, despite this monumental research effort and plethora of devices, strategies and programs designed to prevent VAP, the condition itself remains elusive. We lack universally agreed diagnostic criteria 1, remain uncertain as to the optimal method of obtaining specimens for microbiological culture and indeed even whether microbiological testing is required 1. At the heart of the problem of VAP lies the huge diversity of pathologies which can cause radiographically detectable pulmonary infiltration 2 and the high frequency of bacterial colonisation of the proximal respiratory tract of ventilated patients 3. Distinguishing what is almost certainly benign pulmonary infiltrate with upper respiratory colonisation from genuine infection of the alveolar space remains a challenge we have yet to fully surmount.

A major impetus into VAP research and prevention efforts came when the 100,000 Lives Campaign declared VAP to be a preventable, adverse event 4. This was followed by many similar programs world-wide that established VAP rates as a metric of care quality. The discussion around the potential to stop reimbursement for episodes of hospital-acquired infections, including VAP, by some funders led to further scrutiny of VAP rates 5. However, to paraphrase Heisenberg, the simple act of turning attention to and measuring VAP is enough to alter its nature. A condition which is already challenging to diagnose with any confidence is, perhaps, more susceptible to apparent rather than real reductions through changes to diagnostic technique 6 or reclassification 1. The failure of antibiotic prescribing to fall as reported rates of VAP plummet 7 does suggest that whilst clinicians may no longer be diagnosing VAP, they have not stopped treating it. In a noble effort to consider wider causes of deterioration in ventilated patients, the CDC advanced the concept of ‘ventilator-

associated events' (VAE). With considerable discrepancy between VAE and VAP cases 8 and questions around how preventable VAE actually are 9, this may have simply replaced a well-defined, if hard to diagnose, distinct pathological entity with a rather nebulous syndrome comprising many disparate conditions.

In this edition of Critical Care Medicine Dananché and colleagues report data 10 from an eight year surveillance project of VAP in French intensive care units. Reporting data from 256 ICUs, and from 134,510 patients, this is one of the largest datasets yet described in VAP surveillance. In keeping with reports from national surveillance programs 11 and individual units 12, Dananché and colleagues show a progressive reduction in reported VAP over the period covered with reductions in MRSA infections, whilst enterobacteriaceae infections remained static and cephalosporin-resistant enterobacteriaceae infections increased. Where the authors add significant additional data to the field of VAP surveillance and prevention is their finding that amongst the very elderly (≥ 75 years) overall VAP rates were significantly lower than in the elderly (age 65-75) and young (18-65). However, there does not appear to have been as marked a reduction in VAP incidence in this group. Again, in keeping with trends in other developed nations, the proportions and total numbers of very elderly patients admitted to ICU has risen over the 8 years reported 13. It is reassuring that the findings of this current report are in accordance with those from Blot et al's 2014 cohort study 14, which also indicated lower overall rates of VAP amongst the very elderly, although by its nature Blot's study could not report on trends over time.

The questions begged by Dananché's study are why the elderly should be apparently protected against developing VAP, and why despite this protection they do not appear to benefit as much from the programs which have been associated with reductions in VAP in their younger co-patients? The authors took considerable care, within the limitations of the loss of granular detail inherent in nationwide surveillance programs, to account for potential confounding factors including availability bias (patients dying before they were 'available' to develop VAP), change in the composition of the contributing units and severity and nature of presenting illness. Although, as noted above, variable diagnostic approaches can lead to significant differences in reported VAP rates, the data presented do not indicate differences in diagnostic approach between very old and younger patients, and there is no obvious reason to specifically under-report VAP rates in the very elderly. Of course, the >75 year old population admitted to ICU are likely to be systematically different from their contemporaries who are not admitted, and the apparent protective effect may reflect unmeasured confounders created by differential admission approaches between older and younger patients. As to why incidence has not fallen as rapidly as it has in younger patients, we must again speculate rather than be certain. From a lower baseline, there is a smaller 'marginal gain' from each VAP-preventative measure and therefore this may account for the less impressive fall in VAP rates. It is also clear from Dananché's report that the microbial ecology of VAP in France is changing over time. It may be, as the authors imply, that organisms which have a predilection for the very elderly have become more prevalent over time. However, at the heart of these conundrums lies the issue alluded to at the start of this editorial "how do we know for certain that a patient has VAP?" In the context of such uncertainty, it is possible that even in large datasets such as those presented here, apparent trends and differences between groups are more due to noise in the system than real signal.

If we are to curb the prescribing of antibiotics, which should be the logical result of successfully reducing VAP rates, then we will have to develop more specific diagnostic criteria and techniques that can distinguish alveolar infection from its benign mimics. The reported rise in cephalosporin-resistant organisms gives further impetus to the need to control antibiotic prescribing. However, a beneficial side effect of reducing this diagnostic uncertainty may be to ensure that our reported VAP rates truly reflect changing patterns in this disease.

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