

## Micro News

March 2007

### 1. Is PVL the major virulence determinant in CA-MRSA disease?

A seminal paper in *Science* published this month provides compelling evidence that the Panton-Valentine leukocidin (PVL) is the major virulence determinant in community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) disease, in variance with the conclusions of a recent publication (Voyich et al. 2006). Labandeira-Ray *et al.* (2007) used a mouse model of necrotising pneumonia to show that:

- a) PVL-positive strains cause necrotising pneumonia whilst PVL-negative strains do not. They use isogenic knockout bacteria to prove the point beyond doubt.
- b) The administration of native PVL resulted in concentration-dependent lesions in the lung.
- c) PVL is more than a virulence factor – it interferes with the global regulation of gene expression.
- d) The expression of PVL upregulates certain cell-wall anchored proteins, which are involved in the disease process, including spa.
- e) Further investigation into the role of spa suggested that PVL and Spa may act together to produce necrotizing pneumonia.
- f) The expression of other unknown genes thought to be involved in tissue adherence (the amusingly acronymed ‘microbial surface components recognising adhesive matrix molecules - MSCRAMMS’) are also upregulated by the expression of PVL.

This paper explains why PVL may be so important. Not only does it play a role directly as a virulence factor in necrotising pneumonia, but it also acts as a global regulator, altering the expression of many other genes.

### 2. USA300 CA-MRSA reaches Europe

CA-MRSA in Europe has most commonly been caused by the ST80, PVL-positive “European” clone, whilst USA300 has supplanted USA400 as the most common cause of CA-MRSA in the USA. A recent study reported the rather sinister emergence of USA300 CA-MRSA in Denmark, and what seems to be the beginning of an exponential increase with 2 cases in 2003, 11 in 2004 and 28 in 2005 (Larsen et al. 2007).

### 3. “Creeping” vancomycin resistance in MRSA

A case of decreasing vancomycin susceptibility was reported during the therapy of a patient in Canada over 6 months (Webster et al. 2007). The vancomycin minimum inhibitory concentration of the infecting strain (proven to be related by PFGE) increased from  $\leq 1$  to 4 mg/L over 6 months. The most resistant isolate had a thicker cell wall under transmission electron microscopy, validating the theory that cell wall thickening on exposure to vancomycin explains “creeping” vancomycin resistance in MRSA (Hiramatsu 2001).

### 4. MRSA environmental contamination: tourniquets and dentists’ chairs

A small prospective study in the UK identified MRSA on 10% of 50 tourniquets; worryingly, 66% of the tourniquet had never been washed or disinfected (Franklin et al. 2007)!

A prospective study of *S. aureus* environmental contamination in a 89 chair dental clinic identified MRSA contaminating surfaces in the emergency dental clinic and that clinical procedures increased the dispersal of *S. aureus* into the environment (Motta et al. 2007).

## 5. "TW" MRSA in London

An unusual strain of MRSA was reported as a cause of vascular-access device (VAD)-related bacteraemia in a London intensive care unit (ICU) (Edgeworth et al. 2007). Genetic analysis of the strain using a microarray provided evidence that the TW strain represents a "new improved" version of ST239 epidemic clones previously reported in the UK through acquisition of all detectable mobile genetic elements associated with virulence variably expressed by other epidemic ST239 clones.

## 6. Bleach cleaning reduces the incidence of CDAD

A 19-bed medical ICU (MICU) and 24-bed surgical ICU (SICU) at a 1400 bed university-affiliated tertiary care facility in St. Louis, Missouri, experienced acute outbreaks of *C. difficile*-associated disease (CDAD) in late 2002 (McMullen et al. 2007). Both units implemented bleach cleaning; the bleach was implemented unit-wide on the MICU and in rooms occupied by CDAD patients only on the SICU. Statistically significant reductions in the rate of CDAD sustained over two years on both wards were noted (16.6 to 3.7 cases per 1000 patient-days on the MICU and 10.4 to 3.9 cases per 1000 patient-days on the SICU by the end of the intervention period). The authors report several limitations: no environmental sampling was conducted, a hospital-wide hand hygiene initiative was implemented in the hospital (though this was after the intervention phase) and feedback of CDAD rates to the wards may have increased compliance with infection control measures. In addition, antimicrobial prescription and consumption were not reported. Despite these limitations, this study provides further data supporting the role of contaminated environmental surfaces in the transmission of *C. difficile*.

## 7. Updates on the epidemiology and virulence of *Acinetobacter baumannii*

There are signs that the prevalence of multidrug-resistance in *A. baumannii* is increasing worldwide; indeed, pan-drug resistant isolates (resistant to all available antimicrobials, including polymyxins such as colistin) have been reported (Falagas and Karveli 2007). *A. baumannii* infections are usually restricted to severely ill patients on ICUs. However, in this setting, crude mortality of patients affected with MDR-*A. baumannii* is high – 49% in a study reported this month from Taiwan (Kuo et al. 2007) – but the mortality attributable to *A. baumannii* acquisition remains controversial. An Australian study identified a polyclonal outbreak of carbapenem-resistant *A. baumannii* in one hospital (Valenzuela et al. 2007). The authors provide evidence of horizontal transfer of the carbapenem-resistance gene cassette raising the odd concept of an "outbreak" of an antibiotic resistance gene in several distinct clones as opposed to an outbreak of a single successful clone!

## 8. Plan to halve MRSA cases by 2008 probably not achievable

A news piece in the BMJ reports on a leaked memo from the UK Department of Health, which has conceded that its own target to reduce MRSA infection may not be achievable (Day 2007). In the memo, Liz Woodeson, the health department's director of health protection, states that the NHS "is not on course to hit that target and there is some doubt about whether it is in fact achievable" because "a certain level of MRSA is unavoidable and we don't know what that level is."

## 9. And finally...attention all ravers!

We already know that the risk factors for CA-MRSA are different to risk factors for HA-MRSA. However, a study published this month reported that more frequent visits to bars, raves, and/or clubs was a significant risk factor for CA-MRSA rather than CA- methicillin-susceptible *S. aureus* infection (Miller et al. 2007a)! Interestingly, a paper published by the same research group provided evidence that incision and drainage without antibiotics is safe and effective treatment for CA-MRSA skin and soft tissue infections, because the receipt of an inappropriate antibiotic did not adversely affect outcome (Miller et al. 2007b).

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