Treatment success rates were significantly ($p \leq 0.01$) higher with combination therapy for infections that were associated with skin and soft tissues and for bacteremias of unknown origin. Overall treatment failures were greater for monotherapy. Overall mortality rates, deaths due to bacteremia, and treatment-related adverse events were similar between the two arms.

Tigecycline in combination with piperacillin/tazobactam, compared with the standard regimen of piperacillin/tazobactam, is more effective overall in bacteremias and clinically documented infections as well.

Interventions Aimed at Reducing MRSA BSIs Led to Decreased Rates of Nosocomial MSSA BSIs: Ten-Year Data from a UK Center

Written by Eric Butterman

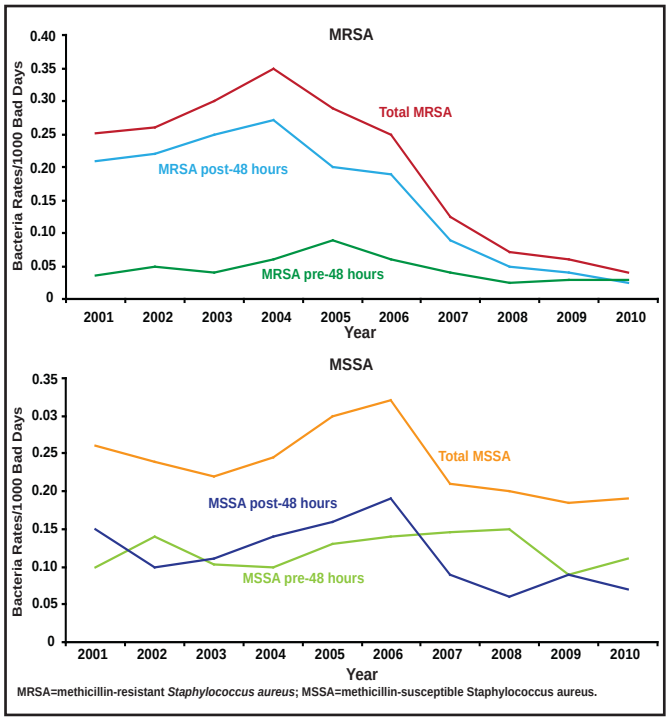
Addenbrooke's Hospital in Cambridge, United Kingdom, once known for having high rates of *Staphylococcus aureus* bloodstream infections (BSIs), has been able to significantly reduce rates of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) BSIs using a number of infection control interventions under the lead of Infection Control Doctor Nick Brown, MD. Staff physician Theodore Gouliouris, MD, presented data from a study that showed a decline in MRSA and MSSA BSI rates that was driven by reductions in nosocomial infections.

The purpose of the study was to analyze trends of MSSA and MRSA BSIs according to onset (community vs hospital) and assess the impact of infection control interventions. The interventions were initiated over several years and included: starting a hand hygiene campaign (November 2004), establishing a vascular access team (January 2006), improving line care bundles (June 2006), screening all emergency (April 2007) and elective (January 2009) admissions for MRSA carriage, and routinely decolonizing all MRSA-positive patients (entire study period). This was a retrospective study in a tertiary referral university hospital setting with 1200 beds and 70,000 in-patient admissions per year. All *S. aureus* bacteremia (SAB) episodes from January 2001 to December 2010 at Addenbrooke's Hospital were included. The number of episodes was converted to rates per 1000 bed days, which allowed comparison with other hospitals. Only the first episode of SAB per patient during the study period was analyzed. Patients were categorized according to onset: community onset (<48 hours from hospital admission) and nosocomial onset (≥48 hours from hospital admission).

There were 1607 SAB episodes following deduplication; 861 (53.6%) MSSA, of which 437 (50.8%) were community onset and 424 (49.2%) were nosocomial onset, and 746 (46.4%) MRSA, of which 163 (21.8%) were community onset and 583 (78.2%) were nosocomial onset.

MRSA rates started to decline in 2004, driven more by a reduction in nosocomial infections, with the largest decrease (53%) occurring during the 2006 to 2007 period. MSSA rates started to decline in 2006, driven again by reductions in nosocomial infections, with the largest decrease (59%) occurring during 2006–2007. Community-acquired infections remained stable over the same period (Figure 1). Hand washing affected MRSA transiently but not MSSA rates, while having a vascular access team and performing line care bundle had a large impact on decreases for both MRSA and MSSA. Extended MRSA screening may have contributed to the larger decline in MRSA infections. Potential confounders (hospital 1000 bed-day activity and number of blood cultures processed) did not influence results.

Figure 1. Community Acquired Infection Rates.



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The results of this study are limited by the fact that it was a retrospective, noncomparative study. There was also a lack of data regarding the MSSA molecular epidemiology in the hospital, the proportion of community-onset bacteremias that were health care-associated, and the proportion of nosocomial bacteremias that were line-related.

Dr. Gouliouris concluded from the study that local rates of nosocomial MSSA BSIs have declined since 2006, though not as markedly as those for MRSA. The establishment of a vascular access team and the implementation of line care bundles appear to have had the most impact toward reducing both nosocomial MRSA and MSSA BSIs. MRSA screening and decolonization likely accounted for the greater reductions that were achieved in MRSA BSIs compared with MSSA. Finally, MSSA-targeted interventions may be needed to achieve reductions that are comparable with those for MRSA BSIs.

Is the Effectiveness of Acellular Pertussis Vaccine in Pre-Adolescents Insufficient?

Written by Noelle Lake, MD

A retrospective, single-center chart review of the 2010 *Bordetella pertussis* outbreak in California found that a time interval greater than 3 year since vaccination with acellular pertussis (aP) correlated with increased risk for acquiring the disease. Research assistant Maxwell Witt, Kaiser Permanente Medical Center, San Rafael, California, USA, reported that children between 8 and 12 years had higher attack rates and reduced vaccine effectiveness compared with children aged 2 to 7 and 13 to 18 years, possibly a reflection of greater time since their last aP dose.

Since the replacement of whole-cell pertussis vaccine with the better-tolerated aP version in 2002, questions regarding its efficacy and durability have lingered [Zhang L et al. *Cochrane Database Syst Rev* 2011]. Researchers at San Rafael Kaiser Permanente (KP) Medical Center, led by David Witt, MD, saw the California outbreak as an opportunity to observe aP vaccine performance by age, time since last vaccine, and vaccine status.

Between March and October 2010, patients who presented to the San Rafael KP pediatrics department with a severe cough for greater than 1 week and a positive PCR for *B. pertussis* were considered infected and included in the review. Electronic medical records were examined for demographic information and vaccine status.

In all, 132 patients <18 years were included. Vaccination status among children aged ≤12 years at presentation revealed that 85% were fully vaccinated, 7% was under vaccinated, and 8% was unvaccinated (never vaccinated). *B. pertussis* attack rates were shown to be highest among 8- to 12-year olds, compared with 2- to 7- and 13- to 18-year olds (p=0.002, one sample t-test; Table 1). Among children <12 years, a trend toward lower attack rates among fully immunized children versus under- or never-immunized children was observed, but the difference was not statistically significant. In contrast, children aged 13 to 18 years who were not fully immunized had significantly higher attack rates compared with other age groups (p=0.009). No patients in the cohort were hospitalized or died from their illness.

Vaccine effectiveness, a metric of the field performance of the vaccine, was calculated by comparing attack rates between under- and never-immunized versus fully immunized patient groups (of note, *effectiveness* should not be confused with *efficacy,* which reflects performance in a prospective placebo-controlled trial). The effectiveness of aP varied by age group: 41% (95% CI, 21% to 54%) and 79% (95% CI, 73% to 84%) within the 2- to 7- and 13- to 18-year olds, respectively, possibly reflecting more recent immunization, but only 24% (95% CI, 0% to 40%) in the 8- to 12- year old age group.

Table 1. Peak Attack Rates Observed Among 8- to 12-Year Olds.

Age Group	Attack Rate in Vaccinated Persons*	Attack Rate in Under and Unvaccinated Persons*	p value
2-7	359	606	0.57
8-12	2453	3211	0.43
13-18	452	2189	0.009
2-18	1011	2073	0.01

The authors concluded that aP is highly effective within 3 years of administration after which its protection may diminish. Should larger studies confirm these findings, additional scheduled dosing or targeted vaccine programs during outbreaks may be proposed. One attendee, however, challenged the relevance of the findings including the use of the phrase "vaccine failure," arguing that strict case definitions had not been used. In Dr. Witt's opinion, *B. pertussis* carriage in the face of a viral illness had not been ruled out and therefore, these results cannot be used to question the efficacy of the vaccine.