

Micro News

February 2007

1. Updates on *C. difficile*: severity of infection and an 18 base-pair red herring!

An 18 base-pair red herring?

The *C. difficile* NAP1/027 epidemic strain produces significantly more toxin than other genotypes of *C. difficile* (Warny et al. 2005). This was initially thought to be due to an 18 base-pair (bp) deletion in the *tcnC* gene, which is a putative negative regulator of toxin production. However, the 18-bp deletion is not unique to the outbreak strain, and has been identified in other *C. difficile* genotypes from the 1980s (McDonald et al. 2005). A study published this month has investigated the distribution of a 1-bp deletion in *tcnC*, first reported last year (MacCannell et al. 2006), which causes a frame shift mutation and truncation of the *tcnC* gene. Of the 199 isolates investigated, 31% were NAP1 and all 62 isolates were characterised by the 1-bp deletion in *tcnC* in addition to the 18-bp deletion whilst other current non-epidemic genotypes had other deletions, including 18-bp deletions, but not the 1-bp deletion. It would be truly remarkable if a single base-pair deletion was responsible for the global emergence of *C. difficile* NAP1/027.

Increasing severity of infections in the UK

A recent letter from Sunderland, UK, reported that the severity of *C. difficile* infection had not increased despite the emergence of *C. difficile* 027 (Hawkyard and Bignardi 2006). In contrast, a letter in the *Journal of Hospital Infection* this month from Birmingham, UK, reports seven cases of severe *C. difficile* disease in a 12 week period, six of which were ribotyped as 027 and half of which died within a month of severe disease, highlighting the potential severity of *C. difficile* 027 (Das and Jumaa 2007).

2. Prevalence of CA-MRSA in children: North America vs. UK

High and increasing prevalence of CA-MRSA in children in North America

Reports of CA-MRSA as a cause of skin and soft tissue infections (SSTI) amongst children and adolescents in North America continue to increase. For example, in the USA, the prevalence of CA-MRSA amongst SSTI at two geographically distinct paediatric emergency departments during 2003 was 22% or an alarming 53% of the abscesses cultured (Hasty et al. 2007). Similarly in Canada, the prevalence of CA-MRSA amongst children and adolescents has risen sharply in the Manitoba province in the last few years (Larcombe et al. 2007).

Low prevalence of CA-MRSA in children in the UK

In contrast to the high and increasing prevalence of CA-MRSA amongst children in certain parts of North America, relatively few CA-MRSA have been reported thus far in the UK. A paper published this month investigated the molecular epidemiology of 55 MRSA isolates from three Birmingham hospitals (Adedeji et al. 2007). The vast majority of the isolates were EMRSA-15/16 yet many were rather confusingly termed "community-acquired" using CDC criteria. The authors did not provide enough genetic information to relate the molecular characteristics of their isolates to

internationally recognised CA-MRSA; furthermore, none of the MRSA were PVL positive. A small number (6/55) were ciprofloxacin susceptible, a few of which may well have been PVL-negative "de novo CA-MRSA" (the authors' term for "true" CA-MRSA).

A number of outbreaks of PVL positive community-associated *S. aureus* in paediatric settings in the UK have attracted press attention (Dyer 2007). However, it seems that the prevalence of CA-MRSA remains low in the UK compared with North America.

3. Does rapid PCR screening for MRSA reduce transmission?

Rapid PCR-based testing for MRSA colonisation has proven to be sensitive and specific. However, few studies have investigated whether the implementation of rapid PCR testing reduces MRSA transmission. A study published this month compared the rate of MRSA acquisition on a critical care unit for five months of conventional culture compared with five months of rapid PCR testing (Cunningham et al. 2007). The rate of MRSA acquisition was significantly reduced during the PCR testing period (4.9 vs. 13.89 / 1000 patient days). This observational trial has several weaknesses, for example the short study period which would not account for seasonal variation. We eagerly await the results of a number of randomised controlled trials on this matter, which are currently in progress.

4. Sampling methods for the recovery of MRSA from environmental surfaces

The sampling of MRSA from environmental surfaces in hospitals requires a choice between swab-based or direct contact methods. A comprehensive study published this month has demonstrated that direct agar contact methods (using either contact plates or dip slides) are more efficient than the direct plating of moistened swabs for the recovery of MRSA from experimentally contaminated surfaces, although the study did not include swabs plus an enrichment step (Obee et al. 2007). The sampling methodology rather than the choice of medium proved to have the greatest impact on recovery. Direct contact methods cannot incorporate an enrichment step, are not appropriate for sampling many non-flat and porous hospital surfaces and can only sample a limited surface area. However, this study provides evidence that direct contact methods are the leading candidate for a standard method to assess the microbiological impact of hospital cleaning.

5. VRSA in a polymicrobial biofilm

The study of a polymicrobial biofilm on a nephrostomy tube in a patient in New York has demonstrated the transfer of *vanA* from VRE to MRSA to produce VRSA (with an MIC from 32 to >128 mg/L) (Weigel et al. 2007). The same study identified the transfer of other resistance genes, demonstrating the fluidity of inter-species genetic exchange and worrying therapeutic implications.

6. Widespread fungal contamination in a Greek hospital

A 12-month prospective study of filamentous fungal contamination of high-risk units in a Greek hospital, including haematology and the solid organ transplant unit, has reported widespread contamination of air and surfaces with potentially pathogenic fungi (Panagopoulou et al. 2007). The fungal load in air (FLA) ranged from 0.56 cfu/m³ and was elevated during building works and times of increased environmental temperature and humidity. 133 (62.7%) of 212 surfaces sampled were

contaminated, including surfaces that were disinfected daily such as nursing trolleys and night tables. Night-long daily UV light in the haematology unit proved inadequate for the eradication of fungi from air or surfaces. The majority of the fungi from air and surfaces were *Aspergillus* sp., including 64.2% of the FLA and 41% of the fungi from surfaces. Although these fungi are not harmful to healthy individuals, they can cause severe disease in immunocompromised patients.

7. Hospital-wide outbreak of metallo- β -lactamase producing Gram-negative pathogens

Metallo- β -lactamases (MBLs) are enzymes produced by bacteria that confer resistance to the β -lactam antibiotics, including carbapenem. They can be readily transferred on integrons between Gram-negative bacteria. An Australian hospital reported a hospital-wide, multi-genera outbreak of MBL bla_{IMR4} producing Gram-negative pathogens (Herbert et al. 2007). 62 patients were affected, 40 of which were thought to have acquired the organism on the intensive care unit. The presence of MBL-producing organisms may have contributed to the deaths of 65% of 23 infected patients. The majority of infections were caused by *Serratia marcescens*, but eight different genera were involved, suggesting horizontal transmission of bla_{IMR4} . Restriction of carbapenem use, glove and gown use and isolation of all patients with an MBL-producing organism brought the outbreak under control. The origin and route of transmission of the organisms remain unknown because staff and environmental screening were not conducted.

8. And finally..adopting MRSA?

Twenty-three children from six different countries adopted into Swedish family were screened for MRSA (Gustafsson et al. 2007). Remarkably, 13 (57%) of the children were carrying MRSA, all of which had prior healthcare contact in their native countries. Furthermore, 6 of 10 family members in 3 families became colonised. Importation of MRSA and intra-familial spread has been identified previously, particularly in low-prevalence countries (Huijsdens et al. 2006; Tietz et al. 2005).

References

- Adedeji,A., Weller,T.M. and Gray,J.W. (2007) MRSA in children presenting to hospitals in Birmingham, UK. *J Hosp Infect* **65**, 29-34.
- Cunningham,R., Jenks,P., Northwood,J., Wallis,M., Ferguson,S. and Hunt,S. (2007) Effect on MRSA transmission of rapid PCR testing of patients admitted to critical care. *Journal of Hospital Infection* **65**, 24-28.
- Das,I. and Jumaa,P. (2007) Has the severity of *Clostridium difficile* infections increased? *J Hosp Infect* **65**, 85-86.
- Dyer,O. (2007) New MRSA strain is not at epidemic level, expert says. *BMJ* **334**, 10-1b.
- Gustafsson,E., Ringberg,H. and Johansson,P. (2007) MRSA in children from foreign countries adopted to Swedish families. *Acta Paediatr.* **96**, 105-108.
- Hasty,M.B., Klasner,A., Kness,S., Denmark,T.K., Ellis,D., Herman,M.I. and Brown,L. (2007) Cutaneous community-associated methicillin-resistant staphylococcus aureus among all skin and soft-tissue infections in two geographically distant pediatric emergency departments. *Acad. Emerg. Med* **14**, 35-40.
- Hawkyard,C. and Bignardi,G.E. (2006) Has the severity of *Clostridium difficile* infections increased? *Journal of Hospital Infection* **63**, 111-112.
- Herbert,S., Halvorsen,D.S., Leong,T., Franklin,C., Harrington,G. and Spelman,D. (2007) Large Outbreak of Infection and Colonization with Gram-Negative Pathogens Carrying the Metallo- beta -Lactamase Gene blaIMP-4 at a 320-Bed Tertiary Hospital in Australia. *Infection Control and Hospital Epidemiology* **28**, 98-101.
- Huijsdens,X.W., van Santen-Verheuevel,M.G., Spalburg,E., Heck,M.E., Pluister,G.N., Eijkelkamp,B.A., de Neeling,A.J. and Wannet,W.J. (2006) Multiple cases of familial transmission of community-acquired methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol* **44**, 2994-2996.
- Larcombe,L., Waruk,J., Schellenberg,J. and Ormond,M. (2007) Rapid emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) among children and adolescents in northern Manitoba, 2003-2006. *Can. Commun. Dis Rep.* **33**, 9-14.
- MacCannell,D.R., Louie,T.J., Gregson,D.B., Laverdiere,M., Labbe,A.C., Laing,F. and Henwick,S. (2006) Molecular analysis of *Clostridium difficile* PCR ribotype 027 isolates from Eastern and Western Canada. *J Clin Microbiol* **44**, 2147-2152.
- McDonald,L.C., Killgore,G.E., Thompson,A., Owens,R.C., Jr., Kazakova,S.V., Sambol,S.P., Johnson,S. and Gerding,D.N. (2005) An epidemic, toxin gene-variant strain of *Clostridium difficile*. *N Engl J Med* **353**, 2433-2441.
- Obee,P., Griffith,C.J., Cooper,R.A. and Bennion,N.E. (2007) An evaluation of different methods for the recovery of methicillin-resistant *Staphylococcus aureus* from environmental surfaces. *J Hosp Infect* **65**, 35-41.

Panagopoulou,P., Filioti,J., Farmaki,E., Maloukou,A. and Roilides,E. (2007) Filamentous fungi in a tertiary care hospital: environmental surveillance and susceptibility to antifungal drugs. *Infect Control Hosp Epidemiol* **28**, 60-67.

Tietz,A., Frei,R. and Widmer,A.F. (2005) Transatlantic spread of the USA300 clone of MRSA. *The New England Journal of Medicine* **353**, 532-533.

Warny,M., Pepin,J., Fang,A., Killgore,G., Thompson,A., Brazier,J., Frost,E. and McDonald,L.C. (2005) Toxin production by an emerging strain of *Clostridium difficile* associated with outbreaks of severe disease in North America and Europe. *Lancet* **366**, 1079-1084.

Weigel,L.M., Donlan,R.M., Shin,D.H., Jensen,B., Clark,N.C., McDougal,L.K., Zhu,W., Musser,K.A., Thompson,J., Kohlerschmidt,D., Dumas,N., Limberger,R.J. and Patel,J.B. (2007) High-level vancomycin-resistant *Staphylococcus aureus* isolates associated with a polymicrobial biofilm. *Antimicrob. Agents Chemother.* **51**, 231-238.