

Acknowledgements

C.M.N.-C. is an investigator of the Brazilian Council for Science and Technology Development (CNPq).

Conflict of interest statement

None declared.

Funding sources

None.

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L.L.L. Moreira ^a

E.M. Netto ^b

C.M. Nascimento-Carvalho ^{a, c, *}

^aInfection Control Service of the Professor Hosannah de Oliveira Paediatric Centre, Salvador, Brazil

^bInfectious Diseases Unit, University Hospital, School of Medicine, Federal University of Bahia, Salvador, Brazil

^cDepartment of Paediatrics, School of Medicine, Federal University of Bahia, Salvador, Brazil
E-mail address: nascimentocarvalho@hotmail.com

Available online 13 December 2008

* Corresponding author. Address: Rua Prof. Aristides Novis, No. 105e 1201B, Salvador, Bahia, Brazil, CEP 40210-630. Tel.: p 55 71 32357869; fax: p 55 71 33320725.

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doi:10.1016/j.jhin.2008.11.001

Bacillus cereus heteroresistance to carbapenems in a cancer patient

Madam,

Bacillus cereus is a ubiquitous Gram-positive, motile, aerobic, non-encapsulated, endospore-forming rod. It is a cause of foodborne poisoning, wound infections, pneumonia, bacteraemia, meningitis, endophthalmitis, necrotising fasciitis, osteomyelitis and endocarditis. ¹ A *B. cereus* strain was isolated from a neoplastic ulcer on the arm of a 15-year-old female with rhabdomyosarcoma. It was cultured as a single organism, with high bacterial counts (200 cfu/plate) on sheep blood agar (bioMérieux, Marcy l'Etoile, France) after 24 h incubations in ambient air, and named BcA (*B. cereus* A). Typical *B. cereus* phenotypic features were observed; colonies were white, β-haemolytic, large, flat and irregular. Species confirmation was obtained by rRNA analysis. An agar disc test was performed on Müller Hinton agar (bioMérieux, Marcy l'Etoile, France) according to CLSI guidelines, and documented susceptibility of the isolate to imipenem, meropenem, vancomycin, erythromycin, gentamicin, levofloxacin, clindamycin, and tetracycline, and resistance to ampicillin, ampicillin/sulbactam, amoxicillin/clavulanate cefotaxime and cotrimoxazole. ² Discs were provided by Liofilchem s.r.l., Roseto degli Abruzzi, (Te), Italy. Two single colonies (named as strains BcB and BcC, standing for *B. cereus* B and C) were observed within the meropenem and imipenem inhibition zones, respectively. These were both subcultured on sheep blood agar, under aerobic conditions. Phenotypic features of colonies were the same as BcA; all of the three strains were genotypically related, but BcB and BcC were found to be fully resistant to imipenem and meropenem, so that resistance to carbapenems appeared to be heterogeneously expressed within the bacterial population studied.

Heteroresistance may be understood as mixed populations of drug-susceptible and drug-resistant organisms in a single clinical isolate and may remain undetected by standard agar or automatic sensitivity testing. This may lead to antimicrobial failure due to in-vivo selection and overgrowth of a mutant clone. Meticillin- and vancomycin-heteroresistance expressed by *S. aureus*, *S. haemolyticus*, *S. capitis*, *S. auricularis*, *S. warneri*, *S. epidermidis*, and *S. simulans* have been reported. In addition, metronidazole-heteroresistance by *Gardnerella vaginalis*, carbapenem-heteroresistance by *Acinetobacter baumannii* and fluconazole heterogeneous resistance by *Cryptococcus*

neoformans have been recovered. Furthermore, this phenomenon has so far been described in *Streptococcus pneumoniae*, *Enterococcus faecium*, *Mycobacterium tuberculosis*, but never in *B. cereus*. The frequency of heterogeneous resistance is known to be about one subclone in every 10^5 – 10^6 colonies, though this may vary among different species. Heteroresistance may be a tool for natural evolution to antimicrobial resistance, as it allows bacteria to grow in the presence of antibiotics before acquiring resistance by the major part of the microbial population.^{3e5} A possible explanation for this carbapenem-resistant mutant subclone may be metallo- β -lactamase (or MBL) gene derepression in BcB and BcC, due to contact with carbapenem on the agar surface, whereas resistance determinants were perhaps strongly repressed in BcA. Production of Gram-positive penicillinases often appears to be inducible, as the β -lactamase gene is commonly repressed. In this case enzyme expression is minimal, but may increase several hundredfold after adding a penicillin into the culture medium.⁶ This may partly explain the expression of phenotypical carbapenem-resistance only in a mutant subclone within the bacterial population studied.

B. cereus commonly produces Bush group 2a penicillinases I and III (typically affecting penicillins, and inhibited by clavulanic acid) and MBLs (which are able to hydrolyse all β -lactams, except for aztreonam).^{1,7} Resistance to carbapenems is emerging worldwide and is of serious clinical concern, as imipenem and meropenem have a broad spectrum of antimicrobial activity and are important therapeutic agents for treatment of infections caused by AmpC- β -lactamase-producing Gram-negative organisms, particularly MBLs were first described in *B. cereus*, *Stenotrophomonas maltophilia*, *Aeromonas* spp., *Bacteroides fragilis*, some flavobacteria, and later in *Acinetobacter* spp., *Pseudomonas aeruginosa* and members of the Enterobacteriaceae.⁷ Carbapenems play a crucial role in the treatment of severe hospital infections, so that the emergence of Gram-positive resistant organisms is of concern.⁷

To conclude, heteroresistance is increasingly recognised and its detection appears to be difficult. There are few laboratory or clinical data concerning this topic, so that we would suggest that laboratories pay attention in screening organisms for heterogeneous resistance to antibiotics; in routine clinical practice. The therapeutic implications of this phenomenon remain to be clarified; it has been known to cause in-vivo antimicrobial failure, but more experimental and clinical research data are needed.³ *B. cereus* is increasingly

becoming important as an agent of human enteric and non-enteric disease; hence, heteroresistance to carbapenems by this species represents a cause for concern in the field of hospital infection control management. In the case we cited, microbiological clearance of the ulcer was obtained by oral levofloxacin.

Conflict of interest statement
None declared.

Funding sources
None.

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V. Savini^{a,*}
M. Favaro^b
C. Fontana^b
C. Catavittello^a
A. Balbinot^a
M. Talia^a
F. Febbo^a
D. D'Antonio^a

^aClinical Microbiology and Virology Unit, Department of Transfusion Medicine, 'Spirito Santo' Hospital, Pescara, Italy

^bDepartment of Experimental Medicine and Biochemical Sciences, 'Tor Vergata' University of Rome, and Laboratory of Clinical Microbiology, Polyclinic of Tor Vergata, Rome, Italy

E-mail address: vincsavi@yahoo.it

Available online 18 December 2008

* Corresponding author. Address: Clinical Microbiology and Virology Unit, Department of Transfusion Medicine, 'Spirito

Santo' Hospital, via Fonte Romana 8, 65100, Pescara (Pe), Italy. Tel.: þ 39 3206265740; fax: þ 39 0854252607.

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doi:10.1016/j.jhin.2008.11.002

'Dog days' surgical site infections in a Finnish trauma hospital during 2002 e 2005

Madam,

In Finnish folklore, the hottest period of the year (23 July to 23 August) is called the 'dog days'. A literal translation of the Finnish term for dog days is 'rotten month', which derived from a Danish mis-translation during the middle ages: 'rode' (dog) and 'roden' (rot). According to tradition, the wounds acquired during this 'rotten month' do not heal per primum intendum and the healing process is complicated with infection. These beliefs are still common, both in patients and physicians (unpublished observations, July 2006).

Our aim was to investigate surgical site infection (SSI) rates in a trauma hospital during 2002 e 2005 and to compare the SSI rate following operations performed during the dog days with the rate among those performed at other times.

The study was conducted at the Helsinki University Hospital Trauma Centre (To'öölö Hospital) where there was hospital-wide nosocomial infection surveillance of all patients undergoing surgical procedures. Surveillance for SSIs includes both passive and active surveillance. The study population consisted of all patients who underwent surgical procedures in the years 2002 e 2005. The SSI rate in operations performed during the dog days was compared with the SSI rate during other times. Data were analysed with Epi Info statistical software (Centers for Disease Control and Prevention, Atlanta, GA, USA). Comparison of the groups was performed with the χ^2 -test and $P < 0.05$ was considered statistically significant.

During the study period 49 517 operations were performed, of which 3979 (8.0%) were performed during the dog days. The percentage of contaminated and dirty operations was higher during the dog days (16.0%) than during other times of the year (12.0%). The overall SSI rate during the study period was 1.36%.

There was a trend toward excessive infections in operations performed during the dog days. SSIs were identified in 58 clean and clean-contaminated procedures (1.72%) performed during the

dog days, whereas the corresponding numbers during the rest of the year were 565 (1.36%) of 41 698, a difference which nearly reached statistical significance (risk ratio: 1.27; 95% confidence interval: 0.97 e 1.66; $P < 0.049$).

Fifty-two (90.0%) of the 58 SSIs after clean or clean-contaminated procedures done during the dog days yielded one or more microbial species, 30 were monomicrobial and 22 polymicrobial. The number of infections with *Acinetobacter* spp. was 5 (0.15%) of the 3377 procedures during the dog days; the corresponding number during other times of the year was 48 (0.12%) of 41 698 procedures (not significant).

This study was conducted in order to challenge the myth that the rate of infections is higher during the dog days. To our surprise the myth was found to be true; the risk of deep incisional and organ/space infections was two-fold higher during the dog days than during other days of the year.

Trauma patients, as such, are at higher risk for SSIs and nosocomial infections than elective surgical patients.¹ Several factors place victims of multiple trauma at increased risk for infection: breakage in the skin barrier, haemorrhage and tissue hypoperfusion, complex bone- and soft-tissue defects; and length of the surgical intervention.^{2e 4} McDonald et al. have shown that the average rates of nosocomial acinetobacter infections are higher during July e October than during November e June, whereas no seasonal variation in nosocomial acinetobacter infections was observed in a study done by Seifert et al.^{5,6} In our study, acinetobacter was one of the major pathogens in SSIs during the dog days, but it was not isolated from SSIs after clean or clean-contaminated procedures more often than during the rest of the year.

Some skin infections (e.g. impetigo) have a seasonal variation, and the number of cases is higher during summer.⁷ Loffeld et al. speculated that looser clothing in the summer leading to more skin contacts and minor trauma causes the correlation between impetigo and climate. The same mechanism may lead to higher endogenous pathogen colonisation at, or contagious to, the operation site which is a risk factor for SSI.

The study was conducted in To'öölö hospital, a tertiary-care teaching hospital, with > 12 000 elective and emergency procedures done yearly. The study population is large enough so that it is very unlikely that clean or clean-contaminated procedures performed during the dog days would have differed substantially from procedures done during other times of the year. Most SSIs can be attributed to risk factors inherent to the patient, rather than to flawed surgical care.⁸ The results of this study