



## **Guidance for the Management of cases of *Bacillus cereus* in view of the current neonatal outbreak in England, June 2014**

### **Investigations in frontline laboratories**

*Bacillus cereus* typically appear as Gram positive spore, forming rods and produce flat, grey, irregular colonies with a ground glass appearance, often surrounded by a zone of beta haemolysis on blood agar; peacock blue colonies are produced on PEMBA medium.

It has been noted that API can mis-identify *B. cereus* (e.g. as *Cellulosimicrobium cellulans* etc). MALDI-TOF analysis is a reliable method of identifying members of the *B. cereus* group but will not distinguish between the individual species constituting the group. Please send all *Bacillus* isolates to the Foodborne Pathogen Reference Service at the Gastrointestinal Bacteria Reference Unit (GBRU), Colindale for speciation and subtyping. GBRU will forward all cultures to the Antimicrobial Resistance and Healthcare Associated Infections Reference Unit at Colindale for sensitivity testing.

### **Treatment:**

The Antimicrobial Resistance and Healthcare Associated Infections Reference Unit has determined antibiotic susceptibilities for 18 patient isolates of *B. cereus* from nine neonatal units involved in this outbreak. The isolates have all been sensitive to gentamicin (MICs 0.25- 2 mg/l, S ≤ 4 mg/l), teicoplanin (MICs 0.125–0.25mg/l, S ≤ 4mg/l), vancomycin (MICs 2-4 mg/l, S ≤ 4 mg/l), linezolid (MICs 2-4mg/l, S ≤ 4mg/l),



ciprofloxacin (MICs 0.064-0.125 mg/l, S  $\leq$ 1 mg/l) and moxifloxacin (MICs 0.064 – 0.125 mg/l, S  $\leq$ 1 mg/l) with antibiograms showing no significant difference between these isolates.

We are using generic break points, as there are no specific breakpoints for *B. cereus* in BSAC or EUCAST.

*B. cereus* naturally possesses a chromosomally located metallo beta-lactamase (MBL), known as BC-II. This MBL is not a transmissible element but should result in resistance to all beta-lactams regardless of any current inhibitor combination. In-vitro results indicating sensitivity to any beta-lactam, including carbapenems, should be treated with caution, as clinical efficacy could be impaired.

### **Frequently asked questions regarding the management of these cases:**

#### **1. What is the best treatment regimen for babies with *B. cereus* infection ?**

Based on the antimicrobial sensitivities of the outbreak strains, the best regimen would be to use vancomycin along with the usual first or second line treatment as per local antibiotic protocol. Other therapeutic alternatives to vancomycin include aminoglycosides, ciprofloxacin and linezolid (although the latter two are unlicensed, they can be used based on a risk benefit ratio assessment in neonates). Duration of treatment depends on type of invasive infection and response to treatment. It is vital



to remove the source of infection like central lines, umbilical catheters etc and the catheter tips sent for culture.

In consultation with neonatal colleagues and provided there is no clinical contra-indication, it is recommended that neonates with *B. cereus* septicaemia have a lumbar puncture to rule out meningo-encephalitis. If the CSF displays abnormal white cells, chemistry or microbiology results, the course of antibiotics should be extended to at least three weeks depending on the clinical response. If the CSF culture is negative, consider sending CSF (minimum 100-200ul) for 16S PCR (available at Molecular Identification Services Unit, Colindale). Antibiotics that penetrate into the CSF in neonates include quinolones, linezolid and to a lesser extent vancomycin. If lumbar puncture is not possible, it is advisable to continue antibiotics for minimum of 3 weeks to cover possibility of meningoencephalitis.

**2. What would you recommend in terms of duration of treatment for *B cereus* infection?**

This would be based on the same principles as for any other patient with sepsis or invasive infection and would depend on the clinical, biochemical and microbiological profiles.

**3. Is prophylaxis or pre-emptive treatment indicated for asymptomatic neonates /children who have received the contaminated TPN product?**

There is no evidence that this is beneficial.



However we recommend that neonates/children who have received the TPN product (see MHRA alert) should be treated with antibiotics till at least one surveillance blood culture (and preferably more than one) is negative as asymptomatic *B. cereus* bacteraemia has been noted in neonates. These babies should be closely monitored and treatment instituted if they come symptomatic.

As a risk mitigating measure we recommend that the long line/ long term intravascular catheter that has been used to administer the contaminated batch of TPN should be considered for removal even if the neonate is asymptomatic and surveillance blood cultures have been negative. Intravascular catheter tips should be sent for culture. At the time of line removal consider administering prophylactic antibiotics pre-procedure and for 48 hours thereafter.

Potential long term colonisation of the long term intravascular catheters with *B. cereus* is a risk if the contaminated batch of PN was administered via the device irrespective of the age of the patient or the type of catheter used ie Broviacs, Hickman lines or Portacaths. In asymptomatic patients with indwelling larger bore long term intravascular catheters (Hickmann, Broviac and Portacath) which have been used to administer the contaminated TPN, it is recommended that surveillance blood cultures taken via the catheter are done at weekly intervals for at least 3 consecutive weeks to rule out catheter colonisation or asymptomatic bacteraemia. Vigilance should be maintained for signs of sepsis if a clinical decision is made to retain the catheter.

In the event of a positive blood culture with *B cereus* from a intravascular catheter in a child who has had the implicated batch of TPN, it is recommended that the



catheter is removed and the catheter tip sent for culture. The risk of retention of a catheter following a positive blood culture with *B cereus* should be discussed with the treating clinician and microbiologist. Removal of catheter is based on the evidence that eradication of *Bacillus* in biofilms is extremely difficult and there is a heightened risk of endocarditis with this organism.

In asymptomatic patients with smaller bore intravascular catheters through which the contaminated TPN product has been administered and are left *insitu*, weekly surveillance peripheral blood culture are recommended for at least 3 weeks.

In an event that the baby is undergoing a course of suppressive antimicrobial therapy, the surveillance cultures should be taken soon after stoppage (24-48 hours) of antibiotics and at weekly intervals (for 3 weeks) thereafter if the child remains asymptomatic.

Since endocarditis has been reported after bacteraemia with *B. cereus*, it is recommended that an echocardiogram is included in the diagnostic profile for patients who have received the contaminated PN and who develop sepsis thereafter.

#### **4. What screening is required on high intensity units?**

Most high intensity units are currently undertaking weekly screening with umbilical, groin, axillary and rectal swabs for MRSA and /or Gram negative organisms. Please discuss with your local Microbiologist whether screening for *B. cereus* can be included in the protocol. Weekly screening on the neonatal unit for a period of 3 weeks after the last case or after the last suspect batch was infused is recommended (this can be extended if indicated).



*B. cereus* isolated from surveillance swabs of asymptomatic patients may represent colonisation. Screening of babies is being advised for the purposes of detecting onward transmission within the unit. Eradication for *B cereus* in asymptomatic babies is not advisable as it is an environmental contaminant. Treatment is recommended on development of clinical signs or symptoms.

#### **5. What sort of infection control precautions is needed?**

The risk of person-to-person transmission is low. Standard precautions with enhanced hand hygiene are recommended (as currently used in all neonatal units).

#### **6. What follow up is needed for these patients?**

The principles used for follow up for all babies with bacteraemia or invasive infections should also be applied to these babies.

#### **7. What are the guidelines for cleaning equipment on the affected unit?**

Standard cleaning procedures (chlorine based products where possible) are recommended. Please ensure manufacturers' instructions are followed diligently for cleaning equipment. Diapers should be immediately bagged and disposed of appropriately, with no surface contamination.

#### **Further reading:**

1. Brown CS, Chand MA, Hoffman P, Woodford N, Livermore DM, Brailsford S, Gharbia S, Small N, Billingham E, Zambon M, Grant K; United Kingdom incident



- response team. Possible contamination of organ preservation fluid with *Bacillus cereus*: the United Kingdom response. **Euro Surveill.** 2012;17 pii: 20165.
2. Gaur AH, Patrick CC, McCullers JA, Flynn PM, Pearson TA, Razzouk BI, Thompson SJ, Shenep JL. *Bacillus cereus* bacteremia and meningitis in immunocompromised children. **Clin Infect Dis.** 2001; 32:1456 -1462.
  3. Hilliard NJ, Schelonka RL, Waites KB. *Bacillus cereus* Bacteremia in a Preterm Neonate. **J Clin Microbiol.** 2003; 41: 3441– 3444.
  4. Ramarao N, Belotti L, Deboscker S, Ennahar-Vuillemin M, de Launay J, Lavigne T, Koebel C, Escande B, Guinebretière MH. Two unrelated episodes of *Bacillus cereus* bacteremia in a neonatal intensive care unit. **Am J Infect Control.** 2014; 42: 694 -695.
  5. Bottone EJ. *Bacillus cereus*, a volatile human pathogen. **Clin Microbiol Rev** 2010;23:382 - 398.
  6. Cotton DJ, Gill VJ, Marshall DJ, Gress J, Thaler M, Pizzo PA. Clinical features and therapeutic interventions in 17 cases of *Bacillus* bacteremia in an immunosuppressed patient population. **J Clin Microbiol**1987; 25:672–4.

#### Useful contact details

1. Clinical advice: contact a Medical Microbiologist via [ColindaleMedMicro@phe.gov.uk](mailto:ColindaleMedMicro@phe.gov.uk) or call 0208 327 6736.
2. Advice about environmental screening of high intensity units contact Dr Peter Hoffman, [peter.hoffman@phe.gov.uk](mailto:peter.hoffman@phe.gov.uk)



3. Referral of bacillus isolates to Food Pathogens Reference Service ;  
Gastrointestinal Bacteriology Reference Unit, Colindale ( referral form L4  
available on [www.hpa.org.uk](http://www.hpa.org.uk)) or contact [corinne.amar@phe.gov.uk](mailto:corinne.amar@phe.gov.uk)
4. Referral of CSF for 16S PCR for *B. cereus* contact Molecular Identification  
Service Unit, Colindale (referral form M1 available on [www.hpa.org.uk](http://www.hpa.org.uk)) or  
Great Ormond Street ( [kathyrn.harris@gosh.nhs.uk](mailto:kathyrn.harris@gosh.nhs.uk))
5. Referral of TPN / feed specimens for culture - contact Dr Nicola Elviss or  
Martin Lodge in the Food, Water and Environment Laboratory, Colindale at  
[nicola.elviss@phe.gov.uk](mailto:nicola.elviss@phe.gov.uk) / [martin.lodge@phe.gov.uk](mailto:martin.lodge@phe.gov.uk)

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