Let’s be Serious About *B. Cereus*!

*Illinois Statewide Conference on HAIs*

November 20 - 21, 2013
Crown Plaza Springfield
3000 Dirksen Parkway
Springfield, IL

Susan A. Dolan, RN MS CIC
Hospital Epidemiologist
Department of Epidemiology
Children’s Hospital Colorado

(No Disclosures)
Objectives

• Review the key steps utilized in a *Bacillus cereus* investigation.
• Discuss laboratory techniques and results associated with product testing performed during the investigation.
• Explore issues related to the identified product and its use in healthcare.
Investigative Team

- **Children’s Hospital Colorado, Aurora, CO (CHCO)**
  - Susan A. Dolan, RN MS CIC
  - Elaine Dowell, MT, SM (ASCP)
  - Cynthia Littlehorn, MT, SM (ASCP)
  - Ann-Christine Nyquist, MD
  - James K. Todd, MD
  - Mary P. Glodé, MD

- **Colorado Department of Public Health and Environment (CDPHE)**
  - Wendy Bamberg, MD
  - Julie Duran, MPH
  - Mary Kate Cichon, BS
  - Karen Xavier, BS MT(ASCP)

1 University of Colorado, School of Medicine
Late Oct. - early Nov. 2010

- Two patients with severe invasive *B. cereus* infection prompted an outbreak investigation at Children’s Hospital Colorado (CHCO)

**Case #1 - Child**
- Newly diagnosed leukemic admitted to CHCO
- PIV and IV medications pre-operatively
- Clinical sepsis 24hrs post implanted Vascular Access Device (VAD)
- Transferred to PICU
Power-injected Contrast-Enhanced Computed Tomography (CECT scans)
Case #1 con’t.

– Extensive pain/cellulitis at insertion site
– Blood and tissue cultures – *B. cereus*
– Initial investigation found no breach in sterile surgical technique or infection control procedures related to the VAD
  » Unique lot # of VAD
  » Reported to FDA via MedWatch
– Extensive wound management – post discharge
Case #2 - Infant
- Congenital heart disease
- Admitted for respiratory distress
- Afebrile
- IJ line placed
- Confirmed respiratory virus by PCR
- Day 4 – developed fever and clinically septic
- Blood cultures
  » 2 on 11/12/10
  » 2 on 11/13/10
- All 4 blood cultures – *B. cereus*
ED case

- Also late October
  - Infant with URI symptoms in ED
  - Admitted
  - Peripheral blood cultures
    - 10/30/10 1 of 2 blood cultures positive *B. cereus*
    - 10/31/10 1 of 1 blood cultures no growth
  - Respiratory Virus identified
  - *B. cereus* - not treated – likely “contaminant”
Steps of an outbreak investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Define and identify cases
   a. case definition
   b. identify and count cases
5. Perform descriptive epidemiology
6. Develop hypotheses
7. Evaluate hypotheses

8. As necessary, reconsider/refine hypotheses and execute additional studies
   a. additional epidemiologic studies
   b. other studies - laboratory, environmental

9. Implement control and prevention measures

10. Communicate findings

http://www.cdc.gov/excite/classroom/outbreak/steps.htm
Objective

- Determine a possible source of the *B. cereus*
Methods

• 11/15 - 11/16/2010: Chart review of Fall 2010 *B. cereus* cases (positive blood cultures) conducted.
  – time, place, location, procedures, treatments, products.

• Products, procedures and surgical techniques were explored.

• *B. cereus* patient isolates compared – rep-PCR

• Three common products initially tested on 11-17-10
  – Terminally sterilized syringes pre-filled with sterile saline solution (#3)
• Solution from sterile applicators packaged with 2% chlorhexidine gluconate/70% alcohol solution for skin prep
  • #9 of 3 sizes
  • #3 of immersed smaller applicator
  “Applicator is sterile if package is intact”
• Alcohol Prep pads (APPs)
  • individually packaged (#4)
• 70% isopropyl alcohol (APPs)
• not labeled as either “sterile” or “non-sterile”
• “Antiseptic • For external use only”
• Use: “For preparation of skin prior to injection”
The following morning - (11/18/10)

- The gram stain of broth from 4/4 APPs:
  - Gram positive rods

- Colorado Dept. of Public Health notified
Same day 4-18-10

- Additional APPs
  - placed into a standard sterilization peel pack
  - subjected to low temperature hydrogen peroxide gas plasma sterilization
  - 1 steam sterilized
  - contents cultured
Results - (11-19-10)

• APPs
  • 4/4 APPs isolates ID’d as *B. cereus*
  • APP (s/p low temperature sterilization)
    – gram positive rods from inside the APP package but not the outside
  • Patient strains were each unique by rep-PCR analysis
    – Using 3 different kits

• Bacterial cultures all negative from:
  • 3 saline syringes
  • 9 liquid (+/- pad) cultures from chlorhexidine gluconate/alcohol applicators (3 sizes)
  • 3 cultures from immersed smaller applicators

And we said, “......”
YOU CAN'T B. CEREUS!
**Background – Literature Review**

- *B. cereus* is a gram positive spore-forming rod.

- Food “poisoning” intoxication due to toxin
  - Emetic form – short incubation (1-6 hrs):
    - N/V and cramps
    - Rice

  - Diarrheal form – long incubation (8-16 hrs):
    - Similar to Clostridium perfringens
    - Cramps and diarrhea
    - Meat or vegetables
**Bacillus cereus** infection

- Case reports
  - Immunocompromised patients
- “Bacteremia and Meningitis in Immunocompromised Children”  
  - 12 pts positive blood cultures 9/88 - 8/00
  - 3 w/ positive CSF
  - 1 possible CNS
- Outcomes
  - 2 deaths
  - 1 severe sequelae
  - 1 mild sequelae

*Gaur AH, et al. CID, 2001;32:1456-1462*
Healthcare-associated outbreaks

*Bacillus species*

- Exam gloves
- Hospital linens
- Construction dust
- Ventilation machinery
- Ambu bags
- Central venous catheters
- Calcium solution
- Alcohol swabs (cotton wool gauze pad)
- Plaster impregnated gauze – casting material
- Incontinence pads – made from virgin wood pulp
- Ethyl alcohol
- Blood culture bottles
- Air filtration system (?)
Healthcare-associated outbreaks

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- Plaster impregnated *gauze* – casting material
- Incontinence *pads* – made from virgin wood pulp
- Ethyl alcohol
- Blood culture bottles
- Air filtration system (?)
Dec. 1, 2010 - “Investigation of Increased Rates of Isolation of Bacillus Species”

• CDC investigation – Aug 2007 and 2008 queried sites to report any ↑ in Bacillus sp.
  – 2007 8 facilities
  – 2008 24 facilities

• Survey conducted – (2008 facilities)
  – Common products and procedures (none)
  – Rates of Bacillus-positive cultures over the preceding 24 months
    • 25 + B. cereus BC per 10,000 BC drawn (24 months)
    • 75 + B. cereus BC per 10,000 BC drawn (June – August 08)

• “The increase likely represented a pseudo-outbreak of *B. species* colonizing CVC lines or their accessories, such as needleless connectors.”

– Vigilant blood culturing practices recommended

*Meites E, et al  Infect Control Hosp Epidemiol 2010;31:1257-1263*
Additional information

- *B. cereus* and *Bacillus spp.* are resistant to killing by alcohol.

- Alcohol prep pads (APPs) are supplied both as sterile and non-sterile.

- The non-sterile products may not be clearly labeled.
  - may be mistakenly assumed to be sterile by users.
As I suspected, you’re full of bacteria. We’re going to have to throw you away.
Actions - (11-19-10)

- Internal recall of APPs initiated
  - APP product Distributor notified
  - Product sequestered

- Replacement product
  - “Sterile” APPs (exclusively)
  - Different manufacturer

- Internal staff and leadership communication

- Colorado Dept. of Public Health and Environment
  - Notified CDC and FDA on 11/23/10
• The internal contents and outside package of non-sterile APPs from 10 different lots manufactured by Triad Group®, Hartland, WI (and “sterile” APPs from a different manufacturer) were cultured on multiple occasions:
  – All procedures conducted in hood using gloves and sterile instruments.
  – Pads allowed to air dry and then cultured in Tryptic Soy Broth.
  – D/E Broth used for liquid samples (chlorhexidine/alcohol applicators).
  – Broth cultures incubated for 4 days; subcultured to Blood Agar plates.
  – Gram-positive rods recovered from APPs were identified as either *B. cereus* (*Beta*-hemolytic, *gram*-positive rods, *catalase*-positive, motile) or as *Bacillus* spp.
  – Rep-PCR technology was used by CHCO to compare patient and APP isolates.
Colorado Department of Public Health and Environment (CDPHE)

• Independent testing performed
  – 20 APPs from **10 different lots** from CHCO were cultured in the CDPHE laboratory.
  – Also, cultured 10 “sterile” APPs
    • replacement product
  – PFGE comparison
    • CHCO patient and APP isolates
    • State Dept. of Public Health Lab APP isolates
TCH Initial Results

• No breaches in infection prevention practices were identified.

• *Bacillus cereus* and other *Bacillus spp.* were cultured from the internal contents of 80% (63.3%) of the “non-sterile” APPs.
  – 8 of 10 lots cultured positive

• The outside of the "non-sterile" APPs grew *Bacillus spp.* (non-*cereus* > *cereus*) from 95% (100%) of the packages.

• *Bacillus spp.* was cultured from 10% (2/20) of the initial set of “sterile” APPs tested but all subsequent cultures with improved sterile technique have been negative. (3.3%)

( ) = Final results
B. cereus PFGE results – Colorado Department of Public Health and Environment

- 10/20 non-sterile APPs from 6/10 different lots grew Bacillus
- 0 of 10 sterile APPs no growth
- Most isolates differed

<table>
<thead>
<tr>
<th>P(#)</th>
<th>patient isolate</th>
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<tbody>
<tr>
<td>A(#)</td>
<td>alcohol pad isolate from CHCO</td>
</tr>
<tr>
<td>(#)</td>
<td>alcohol pad isolate from CDPHE</td>
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### Rep-PCR and PGFE Patterns

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<th>Strain Comparison</th>
<th>CHCO</th>
<th>CDPHE</th>
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<tr>
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**Key**

- **Rep-PCR** patterns are shown for each strain.
- **PGFE** patterns are indicated by different colors.
- **CHCO** and **CDPHE** are represented by red and yellow highlights.

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**Diversilab v3.4**

**Key:**

- 1-24: Study IDs
- 1-24: Strain patterns
- % Similarity: dendrogram with % similarity values.
Pad sections immersed for 15 min. in 2-mL of TSB followed by vigorous vortexing and Cx of the supernatant
Subsequent CHCO Laboratory Studies
9 rounds of testing

- No matches between patients.
- No patient/APP matches.
- Rare matches between APPs (usually different lots).

- The internal pads of APPs appear to be sparsely colonized with multiple Bacillus strains
  - Adherent to the internal pad.

- Lots from 2003 and 2005 consistently negative while 2008-2010 lots consistently positive ($p = 0.0004$)*.

* Fischer’s Exact Test
CHCO Blood and CSF cases 2003-2011

- True bacteremia
- Probable contaminant
- Indeterminate
- Total Blood and CSF

Number of Cases

Year

2003 2004 2005 2006 2007 2008 2009 2010 2011 (1st Qtr)

p = 0.007
Product Removed
TCH Patients with *B. cereus* blood cultures 2003-2010

CDC study – Hospital A
Contents:

1. Apparent Bacillus cereus Contamination of Alcohol Pads
2. Influenza Surveillance Update - Colorado and National
3. Denise Woods-Stout Retires

- CDPHE recommends that healthcare facilities ensure they are using sterile alcohol pads for tasks requiring disinfection, such as prepping blood culture bottles, medication vials and central line hubs before entry, disinfecting skin prior to obtaining blood samples, etc.
Recall notice
Jan. 5, 2011

Recall -- Firm Press Release

Triad Group Issues a Voluntary Nationwide Recall of All Lots of Alcohol Prep Pads, Alcohol Swabs, and Alcohol Swabsticks Due to Potential Microbial Contamination

Contact:
Eric Haertle, COO
262-538-2900

FOR IMMEDIATE RELEASE - January 5, 2011 - Hartland, Wisconsin, Triad Group, a manufacturer of over-the-counter products has initiated a voluntary product recall involving ALL LOTS of ALCOHOL PREP PADS, ALCOHOL SWABS, and ALCOHOL SWABSTICKS manufactured by Triad Group but which are private labeled for many accounts to the consumer level. This recall involves those products marked as STERILE as well as non-sterile products. This recall has been initiated due to concerns from a customer about potential contamination of the products with an objectionable organism, namely Bacillus cereus. We are, out of an abundance of caution, recalling these lots to ensure that we are not the source of these contamination issues.

Use of contaminated Alcohol Prep Pads, Alcohol Swabs or Alcohol Swabsticks could lead to life-threatening infections, especially in at risk populations, including immune suppressed and surgical patients. To date we have received one report of a non-life-threatening skin infection.

Alcohol Prep Pads, Alcohol Swabs and Alcohol Swabsticks are used to disinfect prior to an injection. They were distributed nationwide to retail pharmacies and are packaged in individual packets and sold in retail pharmacies in a box of 100 packets. The affected Alcohol Prep Pads, Alcohol Swabs and Alcohol Swabsticks can be identified by either “Triad Group,” listed as the manufacturer, or the products are manufactured for a third party and use the names listed below in their packaging:
• Check the labeling on APP pad to determine if sterile or non-sterile.

• Non-sterile pads are not intended to prep patients prior to procedures requiring strict sterility measures and should not be used on patients with a depressed immune system, to prep patients for catheter insertion, or to prep patients prior to surgery.

• Many patients in hospitals are particularly susceptible to infections, and the FDA recommends sterile antiseptics (including chlorhexidine gluconate, alcohol or iodine applicators, pads, and swabs) in that setting.

• If a pad does not state "sterile" on the label, HCPs should be aware that they are using a non-sterile pad.
Additional Triad recalls

H&P Industries, Inc.

“Initial recall” extended to Canada and Europe

2-16-2011
Sterile Lubricating Jelly

3-16-2011
Povidone iodine prep pads
• Elizabethkingia meningoseptica
Contamination of Alcohol Prep Pads with *Bacillus cereus* Group and *Bacillus* Species — Colorado, 2010

In October 2010, a child at The Children’s Hospital (TCH) in Aurora, Colorado, with newly diagnosed leukemia developed clinical sepsis 24 hours after insertion of an implanted vascular access device. The child also developed extensive cellulitis at the insertion site, requiring surgical debridement, intensive care, antibiotics, prolonged wound management, and outpatient treatment. Cultures of the child’s blood and tissue specimens grew *Bacillus cereus*. An investigation found neither breach of infection control procedures nor any violations of sterile surgical technique.

isolates, and no patient isolates matched APP isolates. Given this diversity and the time lapse between positive patient specimens and subsequent APP sampling, the lack of a match between the two groups was not considered to rule out APPs as the source of the *B. cereus* isolated from patients.

APPs are supplied both as sterile and nonsterile products. Sterile products are clearly labeled as such and should not be mistaken and/or interchanged for nonsterile products. *B. cereus* group and *Bacillus* species are resistant to killing by alcohol (1) and have caused health-care–associated outbreaks of invasive disease (2,3). Pseudoinfections caused by *B. cereus*–contaminated products also have been reported (4). Health-care facilities, health-care providers, and users of APPs should be aware that the APPs in clinical use are sterile products.

Reported by

SA Dolan, MS, E Dowell, C Littlehorn, MP Glode, MD, JK Todd, MD, The Children’s Hospital, Univ of Colorado School of Medicine, Aurora, Colorado; W Bamberg, MD, MK Cichon, Colorado Dept of Public Health and Environment.
April 6, 2011

The action follows the continued failure of H & P Industries to comply with the FDA's current good manufacturing practice (cGMP) regulations, which are intended to assure the safety, quality, and purity of manufactured drugs. Through this seizure, FDA seeks to prevent the company from distributing product that was manufactured in violation of federally mandated manufacturing requirements.

FDA completed its most recent inspection of H&P Industries on March 28, 2011. The inspection found multiple violations of cGMP requirements, including:

- continuing problems with the air handling system;
- failure to adequately investigate drug products that did not meet specifications affecting the majority of the products manufactured at the facility; and
- failure to take the proper measures to ensure the quality of incoming components.

U.S. Marshals, at the request of the U.S. Food and Drug Administration, have seized more than $6 million in products distributed by Triad Group Inc., at the company's facility in Hartland, Wis.
• Sen. Michael Bennet, D-Colo., and Sen. Lamar Alexander, R-Tenn request retrospective review of the FDA oversight

• 2 worrisome inspections & also a meeting in August 2010
  – Voluntary improvements in safety & sterilization
    • Versus a formal warning letter
      – an enforcement action that requires prompt and thorough response
Excerpts:

- Non-sterile APPS and swabsticks
  - No microbiological testing
    - Product testing is required to show it is free of objectionable microorganisms
- Sterile APPs
  - lots with sterility test failures not placed on hold; shipped to customers
  - Not all batches lab tested
  - Failure to thoroughly review unexplained discrepancies
- General - Staff education and training lacking
**6-10-11 Permanent Injunction**

- U.S. Department of Justice's Office of Consumer Protection Litigation and the U.S. District Court of the Eastern District of Wisconsin
- Must be signed by a Judge
- Then won't be able to "manufacture or distribute drugs or any medical devices until they have established acceptable quality assurance" in conformity with the cGMP
  - Independent expert in cGMPs
  - FDA decides compliance before resume activities
  - Develop a work plan
  - The expert monitors the firms for minimum of five years
Hartland wipes manufacturer Triad files for bankruptcy

By Rick Romell of the Journal Sentinel

Aug. 10, 2012

Shattered Trust

A pair of related Hartland medical products firms that were effectively shut down by federal regulators last year over contaminated alcohol wipes have filed for bankruptcy.

Triad Group Inc. and sister company H&P Industries Inc. are seeking protection from creditors under Chapter 11 - a provision that enables financially troubled firms to negotiate down their debts and continue in business.

Whether Triad and H&P can emerge as going concerns is open to question.
Alcohol Prep Pad - Regulation

• Monograph for topical antimicrobials
  – Monitored under FDA’s OTC Drug review
  – Tentative Final Monograph (TFM)
  • Federal Register - 59Fed. Reg. 31402
    (June 17, 1994)
  - 56Fed. Reg. 336444
    (July 22, 1991)
SUPPLEMENTARY INFORMATION: In the Federal Register of September 13, 1974 (39 FR 33103), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC topical antimicrobial drug products, together with the recommendations of the Advisory Review Panel on OTC Topical Antimicrobial I Drug Products (Antimicrobial I Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. Interested persons were invited to submit comments by November 12, 1974. Reply comments in response to comments filed in the initial comment period could be submitted by December 12, 1974. In response to numerous requests, the agency issued a notice in the Federal Register of October 17, 1974 (39 FR 37066) granting an extension of the deadline for comments until December 12, 1974, and for reply comments until January 13, 1975.

In the Federal Register of March 21, 1980 (45 FR 18398), the agency advised that it had reopened the administrative record for OTC topical antimicrobial drug products to allow for consideration of new data. The agency concluded that any new data and information filed prior to March 21, 1980, should be available to the agency in developing a proposed regulation.
– No specific requirement that APPs be sterile
  • Gamma irradiation
– Acknowledges “poor sporicidal activity”
– Indications for use: first aid, splinter removal, prep of the skin prior to an injection
– If sterile, must be per current Good Manufacturing Practices (cGMPs)
cGMP
Current Good Manufacturing Practices

• Regulations that describe methods, equipment, facilities and controls required for producing human products, medical devices...
• Safe, properly identified
• Correct strength, pure and of high quality
• Includes over-the-counter drugs...

Quality System Regulation - Section 520 of Food, Drug and Cosmetic Act.
• Microbial checks before the product is released for filling. (source of microbial contamination)
• Clean equipment, and documentation of it
• Cleaning SOP
• Lot # tracking
• Microbial checks on finished product before releasing for shipment
• Water system checks
More “notes from the field”...

- Materials Management: facility-wide APP recall
  - Replacement product
  - Command center usage
    - Identify returned product by location
  - Repeat/multiple communications
  - Prepackaged kits
  - Inspections for verification of removal
  - Who is the manufacturer – what other products might we have on site?
  - Storage for “quarantined product”
  - Save for FDA, etc.
    - Sorting by lot number and year – counts of each
• **Risk Management – Legal Council**
  – Notification process
  – Requests for information from regulatory agencies
  – Security issues (HIPAA, documentation – computer files, email, hard copies)
  – Information process set up
  – Legal/litigation requests

• **Media/Public Relations**
  – Talking points, designated spokesperson(s)
  – Public Relations collaboration
  – PR on all media calls with IP
Conclusions

- Severe cases of infection prompted a swift investigation at CHCO that discovered APPs contaminated with Bacillus.
  - Internal recall

- CDPHE laboratory validated initial results.
  - Colorado facilities promptly notified

- APPs from 2008-2010 were contaminated whereas APPs from 2003 and 2005 had negative cultures.
• Patient isolates did not match each other nor the multiple different strains from APPs.

• Labeling of APPs regarding non-sterility is not clear.

• Healthcare facilities, providers and users of APPs should use sterile APPs and avoid using those that are not.
Covidien has never recalled our alcohol preps, which we have always manufactured in the USA under strict quality standards. Though we’ve never had a problem, Covidien continues its commitment to patient safety. As a market leader, we’ve decided to only produce sterile alcohol preps. With Webcol™ and Curity™ alcohol preps, you never need to ask, “who makes my alcohol prep and is it safe?”

Know the manufacturer; trust the brand
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
[Docket No. FDA–2012–N–1040]

Antiseptic Patient Preoperative Skin Preparation Products; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing a public hearing to obtain input on how to address microbial contamination of patient preoperative skin preparation drug products. Currently, patient preoperative skin preparations are not required to be sterile. Bacteria can contaminate these products at the time of manufacture or during product use. Contaminated patient preoperative skin preparations have been associated with clinical infections and adverse outcomes. At this public hearing, FDA is interested in obtaining public comment about certain scientific and product use issues related to patient preoperative skin

please contact Lee Lemley (see Contact Person) at least 7 days in advance.

Requests for Oral Presentations: If you wish to make an oral presentation during the hearing, you must register by submitting a written or electronic request by close of business on November 27, 2012, to Lee Lemley (see Contact Person). Provide your name, title, business affiliation (if applicable), address, telephone and fax numbers, email address, and type of organization you represent (e.g., pharmaceutical company or consumer organization). You also should submit a brief summary of the presentation, including the discussion topic(s) that will be addressed and the approximate time requested for your presentation. We encourage individuals and organizations with common interests to consolidate or coordinate their presentations to allow adequate time for each request for presentation. Persons registered to make an oral presentation should check in before the hearing.

Participants should submit a copy of each presentation to Lee Lemley (see Contact Person) no later than December 7, 2012. We will file the hearing schedule, indicating the order of presentation and the time allotted to each person, with the Division of"
Microbial Stowaways in Topical Antiseptic Products
Christina Y. Chang, M.D., M.P.H., and Lesley-Anne Furlong, M.D.

In the 1970s, the Food and Drug Administration (FDA) developed regulatory pathways for a number of active drug ingredients that were on the market but had not been approved by the FDA. Antiseptic drug products fall into one class of drugs that was included in the regulations that resulted from the expert reviews of the 1970s. At the time, it was assumed that antiseptic drug products were free of microbial contamination because of their pharmacologic activity. The need for sterile manufacture for these products was therefore not considered. In recent years, however, there have been published reports linking outbreaks of infection to antiseptic products that
SPECIAL REPORT

Sterility of Antiseptic Products: FDA Investigates, Deliberates on Potential Recommendations

Editor’s note: The June and July 2013 print issues of Infection Control Today featured a two-part series exploring sterility of antiseptic prep products. This report draws upon those articles as background and adds new perspective from the FDA and other experts.

By Kelly M. Pyrek
Over-the-Counter Topical Antiseptic Products: Drug Safety Communication - FDA Requests Label Changes and Single-Use Packaging to Decrease Risk of Infection

[Posted 11/13/2013]

AUDIENCE: Healthcare Professionals, Risk Managers, Pharmacy

ISSUE: The U.S. Food and Drug Administration (FDA) is requesting label and packaging changes to enhance the safe use of certain over-the-counter (OTC) topical antiseptic products. This request is the result of our ongoing evaluation of infrequent but continuing reports of infections resulting from antiseptic products labeled for preoperative or preinjection skin preparation. When used properly, topical antiseptics are safe and effective products to reduce the number of bacteria on patients’ skin prior to surgery or injections. However, most often, contamination of topical antiseptics occurs when organisms are introduced into the product by users. Therefore, health care professionals and patients should follow all label directions to decrease the chances of infection.

Outbreaks associated with the use of contaminated topical antiseptics have been reported in the medical literature and to the Centers for Disease Control and Prevention (CDC). Clinical infections have also been reported to FDA, leading to some product recalls. The reported outcomes ranged from localized infections at injection sites to systemic infections that resulted in death. FDA has reviewed reports of four deaths, five cases of wound infection, seven cases of peritonitis, 10 cases of septic arthritis, 14 cases of indwelling catheters requiring replacement, 16 cases of injection site infection, and 32 cases of bacteremia. These infections have been confirmed to be caused by contaminated antiseptic products. Affected products included all commonly used antiseptic ingredients, including alcohol, iodophors, chlorhexidine gluconate, and quaternary ammonium products. Organisms implicated in the outbreaks included Bacillus cereus, Burkholderia cepacia, Pseudomonas aeruginosa, Achromobacter xylosoxidans, Ralstonia pickettii, Serratia marcescens, and Mycobacterium abscessus.

BACKGROUND: Over-the-counter (OTC) topical antiseptic drugs for use according to the label instructions to reduce the number of bacteria on the skin prior to surgery or injections. When used properly, over-the-counter (OTC) topical antiseptics are safe and effective products to reduce the number of bacteria on the skin prior to surgery or injections.
<table>
<thead>
<tr>
<th>Product and Mechanism of Contamination</th>
<th>Clinical Outcome</th>
<th>Responsible Organism*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodophor, including povidone-iodine and poloxamer-iodine</td>
<td>Peritonitis, replacement of dialysis catheter, pseudoperitonitis, pseudobacteremia, and infection at dialysis catheter insertion site</td>
<td>Burkholderia cepacia and Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Intrinsic contamination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic contamination</td>
<td>None reported</td>
<td></td>
</tr>
<tr>
<td>Alcohol product</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrinsic contamination</td>
<td>Pseudobacteremia</td>
<td>Bacillus cereus</td>
</tr>
<tr>
<td>Extrinsic contamination</td>
<td>Bacteremia</td>
<td>Burkholderia cepacia</td>
</tr>
<tr>
<td>Chlorhexidine gluconate alone or with cetrimide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrinsic contamination</td>
<td>None confirmed</td>
<td></td>
</tr>
<tr>
<td>Extrinsic contamination</td>
<td>Death, bacteremia, removal of indwelling central venous catheter in patients with cancer, replacement of dialysis catheter, pseudobacteremia, wound infection, and colonization</td>
<td>Burkholderia cepacia, Achromobacter xylosoxidans, Ralstonia pickettii, and Serratia marcescens</td>
</tr>
<tr>
<td>Quaternary ammonium compound, including benzalkonium chloride and benzethonium chloride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrinsic contamination</td>
<td>None confirmed</td>
<td></td>
</tr>
<tr>
<td>Extrinsic contamination</td>
<td>Death, bacteremia, septic arthritis requiring prolonged antibiotic therapy (occasionally necessitating surgery), and injection-site infection</td>
<td>Burkholderia cepacia and Mycobacterium abscessus</td>
</tr>
</tbody>
</table>

* Responsible organisms are listed only for cases in which genetic-fingerprinting methods have confirmed the source of contamination. Contamination of antiseptic drug products may occur either during manufacturing (intrinsic contamination) or during manipulations by the end user (extrinsic contamination).
References


CHCO Acknowledgements

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  - Elizabeth Whitehead
- Emergency Department
  - Beverly Lopez
Raising the Red Flag

The findings of an APIC member's outbreak investigation prompted an extensive international product recall, preventing patient harm across the globe.
Association of *Bacillus cereus* Infection with Contaminated Alcohol Prep Pads

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**BACKGROUND.** *Bacillus* species have caused healthcare-associated outbreaks of invasive disease as well as pseudo-outbreaks. We report an outbreak investigation of blood cultures positive for *Bacillus cereus* associated with alcohol prep pads (APPs) contaminated with *B. cereus* and *Bacillus* species resulting in a rapid internal product recall and subsequent international product recall.

**DESIGN.** Epidemiologic and microbiologic outbreak investigation.

**SETTING.** A 300-bed tertiary care children’s hospital in Aurora, Colorado.

**PATIENTS.** Patients with blood or cerebrospinal fluid cultures positive for *B. cereus*.

**METHODS.** Three patients with blood cultures positive for *B. cereus* were identified in late 2010. Breaches in procedural and surgical techniques, common interventions, and products were explored. The following 3 common products were cultured: sterile saline syringes, chlorhexidine/alcohol skin preparation solution, and APPs. Repetitive sequence-based polymerase chain reaction (Rep-PCR) was used to compare isolates obtained from patients and from APPs and was confirmed by independent pulsed-field gel electrophoresis.

**RESULTS.** There appeared to be a significant increase in blood cultures positive for *B. cereus* during 2009–2010. *B. cereus* and other *Bacillus* species were cultured from the internal contents of 63.3% of APPs not labeled as sterile, and 8 of the 10 positive lots were manufactured after 2007. None of the isolates obtained from the patients matched strains isolated from the APPs. However, some lots of APPs had strains that were indistinguishable from one another.

**CONCLUSIONS.** APPs that were not labeled as sterile were contaminated with *Bacillus* species. The product was immediately recalled internally and replaced with APPs from another manufacturer that were labeled as sterile. On January 3, 2011, the manufacturer voluntarily recalled its APPs. Healthcare facilities, healthcare providers, and users of APPs should avoid the use of APPs not specifically labeled as sterile.
Patients with Positive B. cereus blood cultures

<table>
<thead>
<tr>
<th>Year</th>
<th>Indeterminate</th>
<th>Probable contaminant</th>
<th>True bacteremia</th>
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<tr>
<td>2003</td>
<td></td>
<td>2</td>
<td></td>
</tr>
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</tr>
<tr>
<td>2007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td>4</td>
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</tr>
</tbody>
</table>
TCH Patients with *B. cereus* blood cultures
2003-2010
B. cereus Blood cultures – 2010
(TCH Preliminary data)

• 8 Patients:
  – 4 True bacteremia
  – 4 Probable contaminants

• 1 Brain tissue – autopsy
  – CSF + Gram positive rods at OSH prior to admission
    • infection
**Figure 1. Patients with Positive *B. cereus* blood cultures or invasive CNS cultures**

<table>
<thead>
<tr>
<th>Year</th>
<th>True bacteremia</th>
<th>Probable contaminant</th>
<th>Indeterminate</th>
<th>Clinical infection</th>
<th>Probable contaminant</th>
<th>Indeterminate</th>
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<td>2</td>
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<td>0</td>
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<td>3</td>
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